

PREPARATION AND PROPERTIES OF MOLECULES HAVING
HIGH STERIC CROWDING.

1, 8-DIPHENYLNAPHTHALENES

Thesis by
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to my high school and college classmate, present-day colleague,
lover, friend, and constant and patient companion, Dody

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I wish to express my appreciation to my research advisor, Dr. John D. Roberts, for his help and encouragement, and most of all for giving me the opportunity of generating and pursuing my own ideas. I also want to thank him for his continuous efforts, which included some hours of quiet exasperation, in assisting me with the writing of various scientific manuscripts, a skill at which I had been considered quite proficient during college - both by my English professors and by myself. In addition, I would like to express my delight with the environment at Caltech, which I consider remarkably well structured for providing intellectual stimulation and professional maturation for students. Finally, I wish to note appreciation for financial backing from the National Science Foundation, from the California Institute of Technology, and from the Department of Health, Education, and Welfare which provided me with a three-year NDEA Title IV Fellowship.

PREPARATION AND PROPERTIES OF MOLECULES HAVING
HIGH STERIC CROWDING. 1,8-DIPHENYLNAPHTHALENES

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ABSTRACT

The 1,8-diarylnaphthalenes have distinctive properties and geometric features which result from the forced proximity of the adjacent peri aryl rings. We have developed an efficient synthetic route to 1,8-diphenylnaphthalene derivatives which involves a direct coupling between the phenyl and naphthyl rings with an organonickel catalyst. The magnitude of the strain energy resulting from the overcrowding in 1,8-diphenylnaphthalene 1 is determined using combustion calorimetry. An X-ray analysis of peri-diphenyl-acenaphthene 2 is reported. The overcrowded phenyl rings of 2 are face to face and nearly perpendicular to the naphthalene ring plane. Large structural distortions are found, especially in the naphthalene framework. A comparison of the geometries of several 1,8-diphenylnaphthalenes having different types of steric interactions at the 4,5 positions is made, and an analysis of distortions in terms of induced stress vectors which act throughout the naphthalene framework is presented. Striking effects in both the proton and C-13 nmr spectra of derivatives of 1 are found which are correlated with a near-perpendicular solution conformation of the phenyl and naphthyl rings.

The phenyl rings in derivatives of 1 have surprisingly low barriers to a 180° rotation about the phenyl - naphthyl bond. Comparison of rotational barrier measurements for analogs and

derivatives of 1 including the highly strained 1,4,5,8-tetraphenyl-naphthalene, together with other observations, indicates that the transition - state to phenyl-ring rotation involves substantial concurrent warping of the naphthalene ring as a whole. Substitution in the phenyl-ring ortho position raises the rotational barrier considerably; cis and trans rotational isomers of 1,8-di-o-tolyl-naphthalene are isolated and studied.

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Preparation and Properties of Molecules Having High Steric Crowding.

1,8-Diphenylnaphthalenes

INTRODUCTION

There were a number of reasons for our interest in 1,8-di-arylnaphthalene derivatives. Nonbonding forces are rather poorly understood, and this system¹ is especially suited for a study of intramolecular crowding. We have determined the relative orientation of the peri aryl rings, measured the strain energy due to the crowding, and examined the consequences of extreme overcrowding in these compounds.

Synthesis of distorted molecules is itself a challenging problem. Development of a direct route to this system was especially interesting, since efficient techniques for generation of aryl-aryl bonds were lacking. We have established a route which proceeds by a catalyzed aryl-aryl coupling under very mild conditions, and which affords high yields of peri-diaryl derivatives despite the high steric requirements.

We were also interested in the question of how molecules adjust to accommodate an imposed stress. The precision of the X-ray technique has been improved in recent years; we have utilized this opportunity to examine a series of closely related molecules having a range of different distorting forces applied at one site, and have determined the size, nature, and distribution of the nuclear and electronic reorganizations which take place. Some data on the shapes of peri-disubstituted naphthalenes have been available for some time,² but no inclusive interpretation had been advanced for those distortions observed. Furthermore, no systematic study of molecular distortion has been carried out for any class of compounds. The work has allowed formulation of a model of molecular distortions in terms of a

simple picture of force vectors acting through the molecular bonds.

The peri aryl rings are compelled to assume a face-to-face conformation, and in this respect these compounds are similar to the paracyclophanes. However, in peri-diarylnaphthalenes, this face-to-face feature is attained without a simultaneous puckering of the phenyl rings. peri-Diphenylnaphthalene derivatives also possess the unusual feature of having adjoining aryl rings which are forced to assume a near-perpendicular conformation. UV spectroscopy is well known as an indicator of conjugation, and, as expected, the effects of perpendicularity in this system are seen using this tool. We have now discovered that proton nmr is indicative of the non-planarity of the adjacent phenyl rings in these molecules. Additionally, C-13 chemical shifts are found to be especially sensitive to the dihedral ring angle in this system; application of the C-13 findings to the long-standing question of the size of dihedral angles of other biphenyl-type compounds in solution is discussed. Other aspects of aryl-aryl perpendicularity are examined.

An additional problem with the peri-diarylnaphthalenes concerned the barrier to rotation about the phenyl-naphthyl bond. Earlier efforts at separating isomers of derivatives bearing one meta substituent in each phenyl ring had failed,³ and subsequent nmr measurements⁴ confirmed the surprisingly low barrier. We have further examined phenyl-ring rotation in this system by measurements on the barriers of other derivatives in an attempt to experimentally probe the transition-state of the conformational change, and have

drawn conclusions about distortions of the naphthalene ring during the rotation. Isolation of rotational isomers was realized with one derivative of this system.

One thing which emerges from this work is a picture of the naphthalene framework as substantially more pliable than had been expected. This observed ability of the molecular framework to sustain large distortions away from a classical structure (constructed from angles having an " sp^2 " value, bonds having an "aromatic bond" length, and "planar" aromatic rings) fits in with other recent work in structural chemistry. Organic chemists, having established rules for molecular shapes, have set about in recent years to search for compounds which would seem to defy those rules - and their efforts at constructing systems which tend ever farther from classical pictures continue to be met with remarkable success.

Each part of this thesis was intended for publication as an individual manuscript and consequently was written as to be able to stand alone.

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PART I

Coupling of Nonequivalent Aromatic Rings by Soluble Nickel Catalysts.

A General Route to the 1,8-Diarylnaphthalenes

Coupling of Nonequivalent Aromatic Rings by Soluble Nickel Catalysts.

A General Route to the 1, 8-Diarylnaphthalenes^{1a}

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A facile route to the 1, 8-diarylnaphthalene derivatives is described. The parent compound, 1, 8-diphenylnaphthalene, can be prepared in two steps with 35% overall yield from the commercial 1, 8-diaminonaphthalene. The key step in these preparations is the direct joining of two nonequivalent aromatic molecules by an organonickel-catalyzed Grignard-aryl halide coupling reaction at -15°. The coupling reaction is regio-specific with respect to the position of substitution of both aromatic halves. The yields of this coupling reaction are high, even though the 1, 8-diarylnaphthalenes are sterically crowded. The efficiency of the reaction under a variety of conditions is evaluated. The order of reactivity of aryl halides is found to be I > Br > Cl, and it is possible to effect coupling preferentially at an iodo group in the presence of a chloro group, the latter

being available for further synthetic functionalization.

Introduction

The 1, 8-diarylnaphthalenes are of interest because of their unusual geometry and their inherent strain due to steric overcrowding. The crowded peri-aryl rings are constrained to face each other.² Adjacent parallel π systems are also a feature of the extensively studied² paracyclophanes, though the phenyl rings of the latter are substantially warped from planarity,³ while the aryl rings of the diarylnaphthalenes, which are not bound together at both ends, retain their planarity.³ Many unusual properties have been observed with the paracyclophanes, and these have been related to the closely held parallel aromatic ring geometries.³

The 1, 8-diarylnaphthalenes have, at the same time, π systems which are nearly perpendicular, because the naphthyl and peri-aryl ring planes are restricted from approaching coplanarity. The barrier to a 180° rotation about a naphthyl-aryl bond has been measured⁴ as ~15 kcal which seems surprisingly low judging from examination of molecular models. The distance between atoms 1 and 8 in naphthalene is 2.44 Å, while the van der Waals separation between parallel π systems is 3.4 Å.⁵ Thus, substantial repulsive interactions must exist between the peri-aryl substituents.

We have undertaken a series of investigations of the conformational, thermodynamic, spectroscopic and chemical properties of 1, 8-diarylnaphthalene derivatives, which necessitated development of a con-

venient and efficient general synthesis for this class of compounds.⁶⁻⁹ The most straightforward approach envisioned was a direct joining of aryl and naphthyl groups, but preparative techniques for effecting carbon-carbon bond formation between two aromatic rings are notably lacking. Major classical methods for aromatic arylation are outlined below.

- I Ullman reaction¹⁰ $2 \text{ ArI} \xrightarrow{\text{Cu}} \text{ Ar-Ar}$
- II Scholl reaction¹¹ $2 \text{ ArH} \xrightarrow[\text{H}^{\oplus}]{\text{AlCl}_3} \text{ Ar-Ar}$
- III Radical-mediated coupling¹²
- $$\left. \begin{array}{l} [\text{Ar-N}_2]^{\oplus} \\ \text{Ar-N=N-Ar} \\ [\text{Ar-CO}_2]_2 \\ \text{Ar-I, } h\nu \\ \text{or other radical source} \end{array} \right\} + \text{Ar'H} \longrightarrow \text{Ar-Ar'}$$
- IV Benzyne-mediated coupling¹³
- $$\begin{array}{l} \text{Ar-X} + \text{Ar'-Li} \longrightarrow \text{benzyne} \\ \hspace{10em} \text{(from Ar-X)} \\ \hspace{10em} \downarrow \text{Ar'Li} \\ \hspace{10em} \text{Ar-Ar'} \end{array}$$
- V Grignard homo-coupling and
aryllithium homo-coupling¹⁴
- $$\begin{array}{l} 2 \text{ ArMgX} \xrightarrow{\text{catalyst}} \text{ Ar-Ar} \\ 2 \text{ ArLi} \xrightarrow{\text{catalyst}} \text{ Ar-Ar} \end{array}$$
- (catalysts include TlBr, CoBr₂, CrCl₃, CuCl₂).

These techniques suffer from various problems, including primary limitation to preparation of symmetric biphenyls (I, II and V), lack of regiospecificity with respect to both reactants resulting in mixtures of isomeric products (II, III and IV), rather severe reaction conditions, and often low yields.¹⁵ The investigation described here had two parallel goals, establishment of a convenient general synthesis for 1,8-diarylnaphthalenes and development of an efficient technique for the direct coupling of nonequivalent aromatic systems.

Results and Discussion

It has long been known that reaction of aryl halides with magnesium to form Grignard reagents is often accompanied by formation of a small amount of diaryl compound.¹⁶ The coupling of Grignards with activated alkyl halides is also well known.¹⁷ We have observed that under forcing conditions, some mixed aryl coupling may be effected, though this reaction probably has little preparative value. Thus, on refluxing phenylmagnesium bromide with 1-iodonaphthalene for 48 hrs in toluene, a yield of about 45% of 1-phenylnaphthalene was obtained. Naphthalene and biphenyl were also identified in the product mixture, along with unreacted 1-iodonaphthalene. An attempt to prepare the internally crowded 1,8-diphenylnaphthalene by this technique was completely unsuccessful.

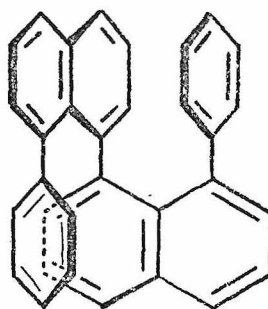
It has been reported that some transition-metal compounds, especially of copper, iron, nickel and silver, may catalyze the reaction between certain Grignard reagents and organohalides, though reports have concentrated almost exclusively on cross-couplings of the type

alkyl-alkyl, alkyl-vinyl, alkyl-aryl, and vinyl-aryl.¹⁸ We have employed catalytic amounts of soluble organonickel complexes to effect aryl Grignard - aryl halide coupling in high yield under very mild conditions, to provide a direct route to the 1, 8-diarylnaphthalenes. Experiments with two organonickel compounds, nickel(II) acetylacetonate $[\text{Ni}(\text{AcAc})_2]$ and dichloro-(1, 2-bis[diphenylphosphino]-ethane) nickel(II)¹⁹ indicated that both complexes were highly active in inducing hetero-aryl coupling, and that the relative effectiveness of the two was essentially the same. The former, a readily available commercial compound, was selected for use in further experiments. Reactions were found to proceed smoothly with a molar ratio of nickel catalyst : aryl halide of 1 : 100 (ratio of catalyst molecule : halide substituent 1 : 200).

1, 8-Dihalonaphthalenes were prepared for use in the coupling reaction from the commercial 1, 8-diaminonaphthalene using the Sandmeyer technique. The best success was obtained when the reactions were run at -30° . The yields were: 1, 8-diiodonaphthalene, 49%; 1, 8-dibromonaphthalene, 17%; 1, 8-dichloronaphthalene, 15%. A description of a preparation of 1, 8-diphenylnaphthalene is given below, followed by a discussion of results obtained under other conditions.

An eight-fold excess of phenylmagnesium iodide in ether was slowly added to a solution of 1, 8-diiodonaphthalene and a catalytic amount of nickel acetylacetonate in ether-benzene at -15° to -10° . The solution turned to a bright red which faded to brown during the course of the reaction. Pure 1, 8-diphenylnaphthalene was obtained in a yield

of 70% based on diiodonaphthalene; the reaction was repeated several times to give yields reproducible to within several percent. Biphenyl and 1-phenylnaphthalene were also isolated, and gas chromatography-mass spectral analysis provided evidence for the presence of small amounts of 1.



1

When the reaction was followed by gas chromatography, a transient peak was observed having a retention time between that of the starting diiodo compound and 1,8-diphenylnaphthalene, and for this, mass spectroscopy gave a molecular weight of 330, as expected for the monophenylmonoiodonaphthalene. The rates of coupling of the first and second phenyl groups were of similar magnitude, the first step being slightly more rapid. Interruption of the reaction and use of monoarylmonoiodonaphthalene as an intermediate in preparation of 1,8-diarylnaphthalenes having different aryl groups should be possible, though low yields would be anticipated. The reaction was seen to be essentially complete four hours after Grignard addition was begun, when the

reaction temperature was -15° to -10° . Use of a higher temperature gave enhanced reaction rate but decreased yields. The gradual color change during the course of the reaction suggested the possibility that the catalyst was slowly destroyed, and that the yield might be improved by periodic addition of catalyst. However, addition of catalyst at 45-minute intervals, beginning at the start of the Grignard addition, resulted in no change in yield.

The use of excess Grignard reagent is necessary to give good results. Use of 7:1 Grignard : diiodonaphthalene (3.5 moles Grignard/mole iodo substituent) was found to be an ample excess. Higher Grignard : halide ratios did not improve matters, while use of only 3:1 Grignard : diiodonaphthalene resulted in incomplete conversion of the diiodonaphthalene. The product was then largely the 1-phenyl-8-iodonaphthalene intermediate.

The $\text{Ni}(\text{AcAc})_2$ catalyst was found to cause some homo-Grignard coupling. When two portions of phenylmagnesium iodide, one of which contained added $\text{Ni}(\text{AcAc})_2$, were stirred overnight at 0° , the solution containing the catalyst was found to contain a significantly larger amount of biphenyl. Analysis of the freshly prepared Grignard solution showed that it contained some biphenyl but no iodobenzene.

Approximately 20% of the initial 1, 8-diiodonaphthalene was converted to 1-phenylnaphthalene under the conditions of the coupling reaction. It seemed possible that this unwanted side reaction might have proceeded by Grignard exchange between the phenylmagnesium iodide and the iodo compound. This would also cause some loss of phenylmagnesium iodide. For each molecule exchanged, two molecules of

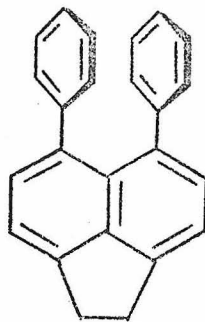
phenylmagnesium iodide would be converted to one molecule of biphenyl. That such an exchange is in fact facile was demonstrated when 1, 8-diiodonaphthalene was combined with excess phenylmagnesium iodide at 0° and kept overnight in the absence of catalyst. After hydrolysis, the reaction mixture was found to contain large quantities of 1-iodonaphthalene and iodobenzene in equimolar amounts, along with some remaining 1, 8-diiodonaphthalene. This exchange between an aryl Grignard reagent and an aryl halide is quite unusual. Earlier attempts at effecting such exchanges have been unsuccessful.²⁰ It seems likely that the driving force for the reaction in this system may stem from the high overcrowding of the peri-iodo substituents. Consistent with the observed Grignard-halide exchange, it was found that the yield of 1, 8-diphenylnaphthalene was critically dependent on the rate of Grignard addition. Thus, when the phenylmagnesium iodide was added all at once, a substantial increase in 1-phenylnaphthalene was found in the product mixture. Apparently the nickel catalyst becomes saturated, and Grignard exchange is enhanced more than coupling by the presence of a large amount of Grignard reagent.

The reactivities of aryl halides in this system toward $\text{Ni}(\text{AcAc})_2$ -catalyzed coupling with Grignard reagent was found to be $\text{I} > \text{Br} \gg \text{Cl}$. Thus, when a seven-molar excess of phenylmagnesium iodide was added all at once to $\text{Ni}(\text{AcAc})_2$ -containing solutions of 1, 8-diiodonaphthalene, 1,8-dibromonaphthalene and 1, 8-dichloronaphthalene at 0°, after 30 minutes the diiodo compound had completely reacted, while the dibromo compound reacted only to the extent of 50%. With 1, 8-dichloro-

naphthalene, the reaction was 30% complete after four hours. Dibromonaphthalene gave a yield of diphenylnaphthalene equivalent to that obtained with the diiodo compound. The yield was lower with dichloronaphthalene.

Interestingly, the Grignard reagents of iodobenzene and bromobenzene were found to give pronounced differences in the coupling reaction. Substitution of phenylmagnesium bromide decreased the yield of 1,8-diphenylnaphthalene by more than half. The major product of the reaction was 1-phenylnaphthalene. Apparently, the rate of coupling is relatively less rapid compared with Grignard exchange in the case of the bromo Grignard. It was expected that for reactions with non-crowded halides where Grignard exchange would not be a problem, good yields would be obtained with a bromo Grignard. Consistent with this, it was found that reaction of phenylmagnesium bromide with 1-iodonaphthalene gives 1-phenylnaphthalene in a yield of > 85%.

We have prepared peri-diphenylacenaphthene, 2, from peri-diiodoacenaphthene and phenylmagnesium iodide at -15° with $\text{Ni}(\text{AcAc})_2$ in 78 % yield using the procedure described for 1,8-diphenylnaphthalene.



The differences in reactivities of halides toward coupling with Grignard reagent suggested the possibility of coupling with an iodide in the presence of a chloro substituent. The substituent could serve as a site for further chemical functionalization of the aromatic product. This possibility has been realized. Thus, when a five-molar excess of m-chlorophenylmagnesium iodide was added to 1,8-diiodonaphthalene and $\text{Ni}(\text{AcAc})_2$ at -20° and the reaction mixture hydrolyzed immediately after it was judged to be complete by gas chromatography, 1,8-di-(3-chlorophenyl)naphthalene was obtained in 52% yield, based on diiodonaphthalene. Use of higher temperature or larger excess of Grignard gave lower yields. When the reaction was allowed to continue for a longer time, the yield of the product decreased, presumably because of a slow reaction of the chloro substituent.

Experimental

Proton nmr spectra were taken with a Varian Associates A-60 or T-60 spectrometer. All spectra were obtained using deuteriochloroform as a solvent, with TMS as an internal standard. Infrared absorption spectra were obtained on a Perkin-Elmer Model 257 Infrared Spectrometer. Mass spectra were run on an EAI Quad 300 Quadrupolar Mass Spectrometer under the control of an SCC 4700 computer. Elemental analyses were performed by Spang Microanalytical Laboratories, Ann Arbor, Mich. Glc separations were carried out on a Hewlett-Packard Model 5750 gas chromatograph with a flame ionization detection system, utilizing a 6' x 1/8" column packed with 3% SE-30 on 40-60 mesh chromasorb P. Injections were made at an oven temperature of 90° , and the instrument was programmed to raise the

column temperature to 300° at 20° per minute. The observed peaks were cataloged in accord with the oven temperature at which they began to appear.

1, 8-Diaminonaphthalene was purchased from Aldrich Chemical Company. Vacuum distillation [bp 137-142° (0.25 mm)] of the crude black material gave the white solid diamine, which was used without further purification.

1, 8-Diiodonaphthalene was prepared using low-temperature diazotization conditions similar to those described previously.²¹ Freshly distilled 1, 8-diaminonaphthalene (42.6 g, 0.27 mole) in 500 ml of 7 M H₂SO₄ was stirred mechanically at -15°. A solution of 54 g of NaNO₂ in 200 ml of water was added dropwise, while the temperature was maintained at -15° to -20°. A solution of 270 g KI in 225 ml of H₂O was then added dropwise while the reaction mixture was held at the same temperature. The cooling bath was removed and the flask was allowed to warm slowly to room temperature with continued stirring. The dark mixture was heated briefly to 80°, cooled and basified to litmus by addition of NaOH pellets. The black solid was collected by suction filtration and extracted five times with 500-ml portions of boiling ether. The combined fractions were extracted with 10% HCl, water, saturated Na₂S₂O₃, water, and 10% NaOH, and then dried over Na₂SO₄. The dark product obtained after evaporation of the solvent was submitted to column chromatography on silica gel with hexane as the eluent to give 50.2 g (49%) of buff-colored crystals, mp 108-110° (lit.²¹ mp 107-109°).

1, 8-Dibromonaphthalene. A solution of 44 g (0.28 mole) of freshly

distilled 1, 8-diaminonaphthalene in 500 ml of 7 M H_2SO_4 was stirred mechanically in a 4-l round-bottomed flask.²² The mixture was cooled to -20° and held at this temperature while 54 g of NaNO_2 in 200 ml of H_2O was added dropwise. The temperature was maintained at -20° , and 113 g of CuBr in 500 ml of 48% HBr was added slowly to give a black creamy mixture which frothed far up in the flask. The mixture was allowed to warm to room temperature as the stirring was continued, and was then heated to 80° , cooled to room temperature, basified to litmus by addition of NaOH pellets, and filtered. The black solid cake was extracted ten times by stirring with 400-ml portions of boiling ether. The combined extracts were washed successively with 10% HCl , water, saturated $\text{Na}_2\text{S}_2\text{O}_3$ (twice), water, 10% NaOH , and finally dried over Na_2SO_4 . The solvent was evaporated under reduced pressure to give 19 g of crude product which was subjected to chromatography on silica gel with hexane as the eluent to yield 14 g (18%) of 1, 8-dibromonaphthalene (mp $106-107^\circ$, lit.²³ mp $109-110^\circ$).

1, 8-Dichloronaphthalene. The diazonium salt was generated from 55 g (0.35 mole) of 1, 8-diaminonaphthalene in 560 ml of 7 M H_2SO_4 , and 70 g (1 mole) of NaNO_2 in 250 ml H_2O using the same conditions described for the 1, 8-dibromonaphthalene preparation. The resulting diazonium salt was stirred at -10 to -15° , while a solution of 140 g (1.4 mole) of CuCl in concentrated HCl was added dropwise. The cooling bath was removed and the mixture was stirred overnight. After being warmed to 80° , the flask was cooled to room temperature, basified to litmus with NaOH pellets, and filtered. The black cake was

extracted four times with 1-1 fractions of boiling ether, and the combined ether fractions washed successively with 10% HCl, water, saturated $\text{Na}_2\text{S}_2\text{O}_3$, water, saturated Na_2CO_3 , and water, and dried over Na_2SO_4 . Evaporation of the solvent afforded 19 g of crude product which was subjected to chromatography on a column of silica gel with petroleum ether (40 - 65°) as the eluent. The resulting white solid (15.6 g, 22%) melted at 80 - 90°. Recrystallization from petroleum ether gave pure 1, 8-dichloronaphthalene (mp 88 - 89.5°, lit.²⁴ mp 88 - 89.5°) as white needles.

Uncatalyzed Grignard-halide coupling. A solution of 0.01 mole of phenylmagnesium iodide from 2.04 g of iodobenzene and 0.24 g of magnesium in 20 ml of ether was added to 2.54 g (0.01 mole) of 1-iodonaphthalene in 15 ml of toluene. The excess ether was distilled and the mixture was allowed to reflux for 48 hours. After hydrolysis with 10% HCl, gas chromatographic analysis showed 45% conversion of iodonaphthalene to 1-phenylnaphthalene. Biphenyl and naphthalene were also present. The products were identified by retention times in the gas chromatograph. The 1-phenylnaphthalene was isolated by chromatography on silica gel with hexane eluent and its identity confirmed by comparison of the infrared spectrum with that of a commercial sample. When phenylmagnesium bromide was substituted for phenylmagnesium iodide in the above procedure, the gas chromatogram showed that, after 69 hrs at reflux, the conversion was only 25% complete. When 0.02 mole of phenylmagnesium iodide was heated to reflux with 0.01 mole of 1, 8-diiodonaphthalene for 96 hrs, no 1, 8-diphenylnaphthalene was formed.

1, 8-Diphenylnaphthalene. Magnesium turnings (0.59 g, 24 mmole) were placed in a three-necked round-bottomed flask equipped with a reflux condenser, and the system purged with nitrogen for 5 minutes while the flask and metal turnings were heated with a heat gun. To the cooled flask was added 3 ml of ether. Approximately 10% of a solution of iodobenzene (0.49 g, 24 mmole) in 20 ml of ether was drawn off from an addition funnel, and the mixture was heated to initiate the reaction. The remaining iodobenzene solution was added just rapidly enough to maintain a gentle reflux (about 45 minutes). The resulting Grignard reagent was pipetted through glass wool (to prevent contamination with small, unreacted slivers of magnesium) into an addition funnel and then added slowly (during 2 hours) to a solution of 1.14 g (3 mmole) of 1, 8-diiodonaphthalene and 0.005 g (0.027 mmole) of nickel(II) acetylacetonate²⁵ in 25 ml of a 1:1 mixture of ether and benzene, which was kept stirring in a Dry Ice acetone bath at -15 to -10°. The mixture was stirred an additional two hours at this temperature, at which time gas chromatographic analysis showed that all starting diiodo compound had reacted. The flask was left stirring overnight at room temperature, the mixture was hydrolyzed with concentrated NH_4Cl solution, the aqueous layer extracted once with ether, and the combined organic fractions dried over Na_2SO_4 . The 2.4 g of crude mixture remaining after evaporation of the solvent was subjected to chromatography on silica gel with hexane as eluent to yield 0.59 g (70% based on diiodonaphthalene) of pure 1, 8-diphenylnaphthalene (mp 147 - 148°, lit.⁷ mp 149 - 150°). The proton spectrum showed a

singlet at δ 6.9 (10 H) and a multiplet at δ 7.2 - 7.9 (6 H) at 60 MHz. The early chromatographic fractions contained 0.8 g of a white crystalline solid which was identified as biphenyl by its melting point (69°) and by comparison of its infrared spectrum with that of an authentic sample.²⁶ Several fractions collected between those containing biphenyl and those containing the diphenylnaphthalene were found to contain 0.14 g of a clear viscous liquid which was identified as 1-phenylnaphthalene by comparison of its infrared spectrum with that of an authentic sample.

A series of reactions analogous to the above was performed with one or more reaction conditions varied as described in the Discussion Part. Other parameters were held constant during these runs. Results were evaluated using gas chromatography retention times, and by isolation of products using column chromatography.

1, 8-Di(3-chlorophenyl)naphthalene. The best yield of 1, 8-di(3-chlorophenyl)naphthalene was obtained when a smaller excess ($\sim 5:1$) of Grignard reagent and somewhat lower temperature than that used for the 1, 8-diphenylnaphthalene synthesis was employed, with the reaction carefully monitored by gas chromatography and stopped immediately at completion. Thus, 15 mmole of m-chlorophenylmagnesium iodide, which formed readily on addition of 3.6 g (15 mmole) of m-chloriodobenzene²⁷ in 18 ml of ether to 0.36 g (15 mmole) of magnesium turnings, was added dropwise to a stirred solution of 1.14 g (3 mmole) of 1, 8-diiodonaphthalene and 0.02 g (0.1 mmole) of nickel acetylacetonate in 15 ml of benzene and 12 ml of ether.

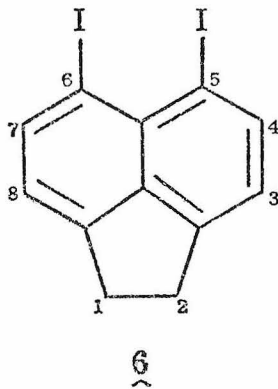
The reaction vessel was held in a -15° to -20° bath during the

2-hr Grignard addition. This temperature was maintained and the mixture stirred as the reaction was allowed to continue. During this time, the gas chromatograms of successive aliquots showed disappearance of the diiodo compound (210° peak) while a new peak (240°) grew and then disappeared at the expense of a higher peak (260°). At the end of four hours, the reaction was seen to be essentially complete. Hydrolysis with saturated ammonium chloride solution followed by column chromatography on silica gel with pentane as the eluent gave 0.53 g (52%) of 1,8-di(3-chlorophenyl)naphthalene (mp 95-97°, lit.²⁸ mp 97-98.5°). Mass spectrum: parent peaks m/e = 248, 250, 252, with expected ratio for two chlorine atoms.

Anal. Calcd. for $C_{22}H_{14}Cl_2$: C, 75.66; H, 4.04 Cl, 20.30. Found: C, 75.57; H, 4.14; Cl, 19.93.

When the reaction was run with a 10-molar excess of Grignard reagent at -10° to -5° for 6 hours, or at -4° for 12 hours, the gas chromatograms showed that the 1,8-di(3-chlorophenyl)naphthalene peak reached a maximum and then slowly decreased.

peri-Diiodoacenaphthene, 6, was prepared in four steps from acenaphthene by a sequence essentially in accord with that described previously.^{29, 30}



The reaction of 40 g (0.24 mole) of acenaphthene with 62 g of iodine and 90 g of mercuric iodide in refluxing ethanol gave 50.1 g (46%) of 5-iodo-acenaphthene, 3, which crystallized as white needles from methanol (mp 62 - 64°, lit.²⁹ mp 65°; picrate mp 97 - 99°, lit.²⁹ mp 100°). In the nitration of 3 (13.5 g, 0.48 mole) with 5 ml of fuming HNO₃ in 140 ml of glacial acid at room temperature, gas chromatography showed that the reaction was complete after four days. The 10 g of crude product which had precipitated was a mixture of isomers. Nine successive recrystallizations from glacial acetic acid gave 2.5 g (16%) of 5-iodo-6-nitroacenaphthene, 4, as yellow needles (mp 175 - 178°, lit.²⁹ mp 179 - 180°). Reduction of 10 g (31 mmole) of 4 by refluxing with 80 g of SnCl₂ in a solution containing 800 ml of concentrated HCl and 140 ml of ethanol gave 2.6 g (28%) of light yellow 5-iodo-6-aminoacenaphthene, 5 (mp 104 - 107°, lit.²⁹ mp 107 - 108°). Diazotization of 5 (2.6 g, 8.8 mmole) was accomplished by treatment with 0.75 g of NaNO₂ in 55 ml of 10% H₂SO₄ at -4° for 40 minutes. Addition of a solution of 2.5 g of KI in 10 ml of water precipitated the diazonium iodide, which was decomposed by refluxing in acetone for 1 hr. The black solid product was treated with Na₂S₂O₃ and subjected to chromatography on silica gel with ligroin as eluent to give 1.7 g (48%) of white crystalline 5,6-di-iodoacenaphthene (peri-diiodoacenaphthene), 6, (mp 156-158°, lit.²⁹ mp 159 - 160°); nmr (CDCl₃) δ 3.30 (s, 4 H), 7.59 (AB q, 4 H).

peri-Diphenylacenaphthene, 2, was prepared using the same conditions described earlier for preparation of 1,8-diphenylnaphthalene. Addition of 8 mmole of phenylmagnesium iodide to 0.41 g (1 mmole) of

6 at -14° to -10° during a 2-hr period, followed by a 2 1/2-hr period at -10° and 1 hr of slow warming to room temperature afforded, after column chromatography on silica gel with ligroin as eluent, 0.24 g (78% based on diiodoacenaphthene) of pure 2 (mp $156-157^{\circ}$); nmr δ 3.43 (s, 4H), 6.87 (s, 10H), 7.30 (s, 4H); mass spectrum 306.1410, 306.1408 calcd. for $C_{24}H_{18}$.

References and Notes

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PART II

Structural Analysis of Internally Crowded Naphthalene Derivatives.peri-Diphenylacenaphthene

Structural Analysis of Internally
Crowded Naphthalene Derivatives.
Peri-Diphenylacenaphthene.¹

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Summary
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The sterically crowded peri-diphenyl-  
acenaphthene<sup>1</sup> has been synthesized by  
an aryl-aryl coupling reaction, and its  
conformation in the crystal determined  
by X-ray diffraction. The strain induced  
by nonbonded interactions between the

phenyl groups greatly affects the geometry of the molecule as a whole. The phenyl rings are face to face, making an angle of  $57^\circ$  to the naphthalene plane and are splayed apart. The phenyl-to-naphthalene bonds are nearly identical in length with the interannular bonds of biphenyl and terphenyl, in which the aromatic rings are coplanar.

A comparison is made of the structures of 1,8-diphenyl-naphthalene <sup>2</sup>, peri-diphenylacenaphthene, and 1,4,5,8-tetraphenylnaphthalene <sup>3</sup>, which constitute a homologous series of peri-phenylnaphthalenes, differing only in the arrangement of groups at one end of the molecule. Substantial deformations of angles and bond lengths in the naphthalene framework of these compounds are analyzed in terms of force vectors acting throughout the bonding skeleton. This analysis correlates the structures of other peri substituted naphthalenes previously determined. The proton nmr spectrum indicates that the most favored conformation in solution of <sup>1</sup> is analogous to that found in the crystal.

### Introduction

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One of the most frequently considered factors in discussions of molecular conformation and of chemical reactivity is that of steric interactions. Most observations of steric effects have been made by measuring some resultant macroscopic property attributable to these interactions, such as relative rates of reaction and isomer ratios at equilibrium.

To allow for more direct observation of molecules in a state of high steric stress, we have undertaken an X-ray diffraction study of some substances with a high degree of internal crowding in the ground state. 1,8-Disubstituted naphthalene derivatives are especially suited for this purpose because the substituents are held in close proximity (2.4 Å is the distance between carbon atoms 1 and 8 in naphthalene) by what are expected to be parallel bonds to a relatively rigid framework³.

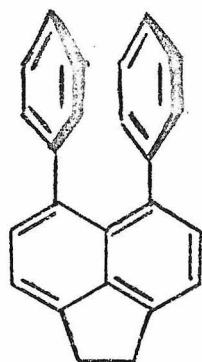
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Space-filling molecular models suggest that the steric interactions in 1,8-substituted naphthalenes should be quite large and especially so for 1,8-diphenyl substituted naphthalenes. Of considerable stereochemical interest is the fact that rotation about the bonds connecting the phenyls to the naphthalene nucleus seems from the models to be virtually impossible without breaking and reforming bonds. Despite the success of the use of molecular models in predicting high rotational barriers for 2,2'-substituted biphenyls, peri-substituted diphenylnaphthalenes act as though such models do not correctly interpret the interactions between the phenyl rings--there being rather strikingly low barriers (> 16 kcal) to the rotation about these bonds, and also for rotation about the bonds⁴ connecting tert-butyl groups to the 1,8-positions.⁵

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Many other interesting properties which arise in the peri-substituted naphthalenes have been investigated and have been recently reviewed in depth³; developing an understanding of the geometry of this class of compounds seemed especially important and timely.

The structure of peri-diphenylacenaphthene 1, which was synthesized in five steps from acenaphthene using an organonickel-catalyzed Grignard-halide coupling reaction⁶, may be contrasted with the structures of 1,8-diphenylnaphthalene⁷ 2 and 1,4,5,8-tetraphenyl-naphthalene⁸ 3.



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These three compounds constitute a homologous series of peri-diphenylnaphthalenes with different substituents at one end of the molecule which differ greatly in the type of strain interaction they provide.

The ethano bridge in C_{10}H_6 is about 1.54 Å in length as expected for a C-C single bond. Since this distance is 0.9 Å less than the distance between the peri carbon atoms in an unsubstituted naphthalene ring, the peri bonds to the ethano bridge can not be parallel, but have to be bent toward one another. Thus in C_{10}H_6 , the peri carbon atoms of the naphthalene framework at the end opposite the phenyl groups are being pulled together. 1,8-diphenylnaphthalene has no distorting force at the 4,5 peri positions; 1,4,5,8-tetraphenylnaphthalene has a pair of phenyl groups with strong repulsive nonbonded interactions at bond ends of the molecule.

Experimental Part
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Peri-Diiodoacenaphthene was prepared in four steps from acenaphthene essentially in accord with procedures described in the literature.<sup>9,10</sup>

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An overall yield of 1% was obtained as colorless needles of mp 157-159°, lit<sup>10</sup> 159-160°; nmr(CDCl<sub>3</sub>) δ3.30 (s,4H), 7.59 (ABq,4H).

Peri-diphenylacenaphthene 1. Phenylmagnesium iodide was generated from 0.49 g (20 mmol) of magnesium and 4.12 g (20 mmol) of iodobenzene in 20 ml of ether containing 5 ml of benzene. Half of the Grignard solution was added during a 2-hour period to a stirred mixture of 0.41 g (1 mmol) of 5,6-diiodoacenaphthene and 0.005 g (0.027 mmol) of nickel acetylacetonate dissolved in 16 ml of benzene and 8 ml ether held at -14° to -10°. The reaction was stirred an additional 2½ hours at this temperature, allowed to warm to room temperature overnight, and then hydrolyzed with saturated aqueous ammonium chloride solution. The crude mixture was chromatogrammed on 80 g of silica with hexane as the eluent and gave 0.24 g (78% based on diiodoacenaphthene) of 1. Recrystallization from hexane afforded clear prisms of mp 156-157°; nmr (CDCl<sub>3</sub>) δ3.43 (s,4H), 6.87 (s,10H), 7.30

63.43 (s,4H), 6.87 (s,10H), 7.30 (s,4H).

The crystals of  $\frac{1}{\infty}$  used for X-ray studies were obtained by slow evaporation of a hexane solution. They were pale yellow prisms elongated along b. Preliminary Weissenberg photographs indicated the triclinic space group P1. Lattice constants were derived from a least-squares fit to fifteen  $2\theta$  values ranging between  $105^\circ$  and  $120^\circ$ , measured on a quarter-circle diffractometer using Cu  $K\alpha$  radiation. The density was measured by flotation in aqueous solutions of  $ZnBr_2$ . The crystal data are given in Table I.

A crystal approximately  $0.43 \times 0.23 \times 0.10$  mm was mounted along the long dimension (b axis) and used for data collection. Intensities were measured using a Datex-automated General Electric three-circle diffractometer equipped with a copper-target X-ray tube, Ni filter, scintillation counter and pulse-height analyzer. Data were collected up to a  $2\theta$  value of  $150^\circ$  using a  $\theta$ - $2\theta$  scan mode at a scan rate of  $1^\circ$  per minute; the scan width varied from  $2.0^\circ$  at  $2\theta = 5^\circ$  to  $3.0^\circ$  at  $2\theta = 150^\circ$ . The takeoff angle was  $3.0^\circ$ . A thirty-second background count was recorded at each scan extremum. A check reflection (1,1,1) was recorded every 30 reflections and the other two check reflections (2,1,1), (3,1, $\bar{1}0$ ) were recorded every 60 reflections. These reflections all showed slow decay, up to 3% in F, at the end of the data collection. The recorded intensities were corrected for this decay, and for Lorentz and polarization effects; no absorption corrections were applied ( $\mu = 5.4 \text{ cm}^{-1}$ ). Observational variances

TABLE I

## Crystal Data

|                                         |                                                           |
|-----------------------------------------|-----------------------------------------------------------|
| 5,6-Diphenylacenaphthene                | $C_{24}H_{18}$                                            |
| Triclinic                               | F. W. 306.4                                               |
| Space Group $P\bar{1}$                  | $Z = 2$                                                   |
| $\underline{a} = 10.493(3) \text{ \AA}$ | $F(0,0,0) = 324$                                          |
| $\underline{b} = 7.861(3)$              | $\rho_{\text{meas}} = 1.22 \text{ g.cm.}^{-3}$            |
| $\underline{c} = 11.567(4)$             | $\rho_{\text{cal}} = 1.23 \text{ g.cm.}^{-3}$             |
| $\alpha = 71.25(1)$                     | $\mu = 5.4 \text{ cm.}^{-1}$ (for Cu $K\alpha$ radiation) |
| $\beta = 113.43(1)$                     | $\lambda \text{ (CuK}\alpha) = 1.5418 \text{ \AA}^0$      |
| $\gamma = 94.90(1)$                     | $\underline{R} = 0.040$ (3250 data points)                |
| $\underline{V} = 828.0 \text{ \AA}^3$   |                                                           |

$\sigma^2(\underline{I})$  were assigned on the basis of counting statistics plus an additional term  $(0.02S)^2$ , where  $\underline{S}$  is the scan count. Two equivalent data sets were collected; they showed excellent agreement, and the averaged set was used for final refinement. The total number of independent reflections was 3404, of which 154 had averaged intensities less than zero.

# Structure Determination and Refinement<sup>11</sup>

Approximate coordinates for the ten atoms of the

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(11) All calculations were carried out on an IBM-370/155 computer under the CRYM system of crystallographic programs.

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naphthalene ring were obtained from a three-dimensional Patterson map. Structure factors based on these ten atoms yielded an  $R$  index,  $\sum ||F_c| - |F_o|| / \sum |F_o|$ , of 0.63 and a subsequent Fourier map revealed the positions of the remaining carbon atoms. Initial coordinates for the 18 hydrogen atoms were calculated assuming C-H distances of 1.0 Å and idealized trigonal or tetrahedral bonding around the carbon atoms. Refinement involved least-squares minimization of the quantity  $\sum w(F_o^2 - F_c^2)^2$  with weights  $w$  equal to  $\sigma^{-2}(F_o^2)$ . In the final cycles, in which 380 parameters were adjusted, three matrices were collected: the coordinates of all 42 atoms were in one matrix; the scale factor, a secondary extinction coefficient<sup>12</sup>, and the anisotropic temperature parameters of the carbon atoms were in a second matrix; and the anisotropic temperature parameters of the hydrogen atoms were in a third. After four such cycles, no parameter shifted by more than 0.6%. The final goodness-

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of-fit  $[\sum w(F_o^2 - F_c^2)^2 / (N - P)]^{1/2}$  for  $N = 3404$  reflections and  $P = 380$  parameters was 2.56; the  $R$  index was 0.040 for the 3250 reflections with net intensities greater than zero. A final difference Fourier map showed no peak greater than  $0.18 \text{ e} \cdot \text{\AA}^{-3}$ . The coordinates given by the original authors for 1,8-diphenylnaphthalene<sup>7</sup> and 1,4,5,8-tetraphenylnaphthalene<sup>8</sup> were used to carry out supplementary calculations on the geometries of these molecules.

### Results and Discussion

The final coordinates and anisotropic temperature parameters are given in Table II.<sup>13</sup> Bond distances and bond

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(13) The carbon atoms are numbered according to the naphthalene and not the acenaphthene numbering system in order to facilitate comparison with other peri compounds; C1 and C8 carry the two phenyl groups and C4 and C5 are connected to the ethylene bridge. According to the standard numbering system for acenaphthene in which the atoms of the bridging ethylene group are numbered C(1) and C(2), compound 1 would be 5,6-diphenylacenaphthene.

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angles between the carbon atoms are shown in Fig. 1; the C-H distances and the C-C-H and H-C-H angles are listed in Table III. A stereoscopic view of the molecule is shown in Fig. 2 and a packing drawing of the structure is shown in Fig. 3.

The carbon-carbon bond distances in the half of the

TABLE IIFinal Coordinates and Anisotropic Temperature Parameters for peri-Diphenylacenaphthene

|     | <u>X</u> | <u>Y</u> | <u>Z</u> | <u>U11</u> | <u>U22</u> | <u>U33</u> | <u>U12</u> | <u>U13</u> | <u>U23</u> |
|-----|----------|----------|----------|------------|------------|------------|------------|------------|------------|
| C1  | 2740(1)  | -1228(1) | - 811(1) | 92(1)      | 180(2)     | 83(1)      | - 5(2)     | 60(2)      | - 64(2)    |
| C2  | 2866(1)  | -2653(2) | 311(1)   | 121(1)     | 192(2)     | 90(1)      | 17(3)      | 63(2)      | - 36(3)    |
| C3  | 2540(1)  | -2523(2) | 1350(1)  | 127(1)     | 259(3)     | 81(1)      | - 3(3)     | 73(2)      | - 16(3)    |
| C4  | 2078(1)  | - 901(2) | 1254(1)  | 101(1)     | 283(3)     | 79(1)      | - 31(3)    | 70(2)      | - 95(3)    |
| C5  | 1426(1)  | 2141(2)  | 178(1)   | 110(1)     | 265(3)     | 122(1)     | - 61(3)    | 110(2)     | -193(3)    |
| C6  | 1220(1)  | 3692(2)  | - 845(1) | 154(2)     | 214(3)     | 169(2)     | - 38(3)    | 166(3)     | -184(3)    |
| C7  | 1594(1)  | 3692(2)  | -1886(1) | 148(2)     | 171(2)     | 149(2)     | - 32(3)    | 154(3)     | - 99(3)    |
| C8  | 2132(1)  | 2203(1)  | -1953(1) | 102(1)     | 169(2)     | 106(1)     | - 39(2)    | 97(2)      | - 87(2)    |
| C9  | 2297(1)  | 516(1)   | - 920(1) | 86(1)      | 184(2)     | 84(1)      | - 31(2)    | 68(2)      | - 87(2)    |
| C10 | 1957(1)  | 584(1)   | 134(1)   | 89(1)      | 225(2)     | 91(1)      | - 44(3)    | 70(2)      | -117(2)    |
| C11 | 1627(1)  | - 305(2) | 2162(1)  | 131(2)     | 415(4)     | 94(1)      | - 18(4)    | 98(2)      | -147(4)    |
| C12 | 1158(1)  | 1694(2)  | 1432(1)  | 138(2)     | 361(4)     | 133(2)     | - 64(4)    | 130(3)     | -249(4)    |
| CA1 | 3009(1)  | -1660(1) | -1858(1) | 118(1)     | 155(2)     | 94(1)      | 6(2)       | 92(2)      | - 57(2)    |
| CA2 | 4278(1)  | -2477(2) | -1560(1) | 143(2)     | 250(3)     | 115(1)     | 93(3)      | 102(2)     | - 51(3)    |
| CA3 | 4510(2)  | -2946(2) | -2519(2) | 206(2)     | 297(3)     | 159(2)     | 156(4)     | 206(3)     | - 60(4)    |
| CA4 | 3492(2)  | -2621(2) | -3776(1) | 236(2)     | 263(3)     | 138(2)     | 32(4)      | 219(3)     | -114(4)    |
| CA5 | 2229(2)  | -1817(2) | -4082(1) | 184(2)     | 226(3)     | 103(1)     | - 62(4)    | 128(3)     | -108(3)    |
| CA6 | 1985(1)  | -1355(1) | -3128(1) | 125(1)     | 173(2)     | 96(1)      | - 27(3)    | 89(2)      | - 70(2)    |
| CB1 | 2538(1)  | 2492(1)  | -3097(1) | 110(1)     | 151(2)     | 97(1)      | - 36(2)    | 92(2)      | - 59(2)    |
| CB2 | 3887(1)  | 2118(2)  | -2907(1) | 104(1)     | 229(2)     | 97(1)      | - 37(3)    | 82(2)      | - 67(3)    |
| CB3 | 4251(1)  | 2453(2)  | -3983(1) | 122(2)     | 321(3)     | 117(1)     | - 23(3)    | 127(2)     | - 77(3)    |
| CB4 | 3285(2)  | 3173(2)  | -5259(1) | 167(2)     | 335(4)     | 104(1)     | 1(4)       | 136(3)     | - 56(3)    |

TABLE II (cont'd.)

|     | <u>X</u>        | <u>Y</u> | <u>Z</u> | <u>U11</u> | <u>U22</u> | <u>U33</u> | <u>U12</u> | <u>U13</u> | <u>U23</u> |
|-----|-----------------|----------|----------|------------|------------|------------|------------|------------|------------|
| CB5 | 1947(2)         | 3573(2)  | -5463(1) | 160(2)     | 286(3)     | 93(1)      | 34(4)      | 79(3)      | - 21(3)    |
| CB6 | 1576(1)         | 3241(2)  | -4391(1) | 119(1)     | 201(2)     | 114(1)     | 20(3)      | 83(2)      | - 46(3)    |
| HM1 | 242(1) - 49(2)  | 305(1)   | 14(2)    | 63(5)      | 10(2)      | 5(5)       | 3(3)       | -28(5)     |            |
| HM2 | 87(1) - 106(2)  | 234(1)   | 19(2)    | 33(4)      | 16(2)      | - 7(4)     | 19(3)      | -12(4)     |            |
| HM3 | 13(1) 196(2)    | 121(1)   | 13(2)    | 44(4)      | 21(2)      | 5(4)       | 22(3)      | -17(5)     |            |
| HM4 | 169(1) 251(2)   | 196(1)   | 25(3)    | 40(4)      | 16(2)      | -27(5)     | 19(4)      | -34(5)     |            |
| H2  | 318(1) - 386(1) | 38(1)    | 19(2)    | 18(3)      | 11(2)      | 6(4)       | 14(3)      | 0(3)       |            |
| H3  | 269(1) - 364(2) | 215(1)   | 21(2)    | 27(3)      | 10(2)      | 1(4)       | 13(3)      | 4(3)       |            |
| H6  | 82(1) 484(2)    | - 86(1)  | 24(2)    | 23(3)      | 26(2)      | - 6(4)     | 28(4)      | -30(4)     |            |
| H7  | 150(1) 487(2)   | -261(1)  | 26(2)    | 13(2)      | 19(2)      | 2(4)       | 28(4)      | - 3(4)     |            |
| HA2 | 502(1) - 273(2) | - 64(1)  | 16(2)    | 43(4)      | 11(2)      | 16(4)      | 7(3)       | -12(4)     |            |
| HA3 | 546(1) - 351(2) | -230(1)  | 22(3)    | 66(5)      | 13(2)      | 42(6)      | 13(4)      | -14(5)     |            |
| HA4 | 367(2) - 297(2) | -448(1)  | 35(3)    | 41(4)      | 16(2)      | 10(5)      | 34(4)      | -19(5)     |            |
| HA5 | 148(1) - 153(2) | -499(1)  | 20(2)    | 37(4)      | 8(1)       | - 5(4)     | 5(3)       | -13(4)     |            |
| HA6 | 106(1) - 79(2)  | -335(1)  | 11(2)    | 29(3)      | 11(1)      | - 2(3)     | 5(2)       | -18(3)     |            |
| HB2 | 459(1) 161(2)   | -198(1)  | 11(2)    | 32(3)      | 9(1)       | 3(4)       | 6(2)       | - 5(3)     |            |
| HB3 | 523(1) 212(2)   | -383(1)  | 13(2)    | 54(5)      | 11(2)      | 10(5)      | 12(3)      | - 8(4)     |            |
| HB4 | 356(1) 341(2)   | -606(1)  | 23(2)    | 72(6)      | 10(2)      | - 2(6)     | 22(3)      | -14(5)     |            |
| HB5 | 124(1) 415(2)   | -640(1)  | 19(2)    | 50(4)      | 8(2)       | 13(5)      | 5(3)       | 0(4)       |            |
| HB6 | 63(1) 355(2)    | -452(1)  | 13(2)    | 30(3)      | 14(2)      | 8(4)       | 12(3)      | - 6(4)     |            |

TABLE III  
Carbon-Hydrogen Bond Distances and Angles of  
Peri-Diphenylacenaphthene

| Acenaphthene Ring |      | Bond Angles, °     |       |
|-------------------|------|--------------------|-------|
| Bond Lengths, Å   |      | Bond Angles, °     |       |
| C(2)-H(2)         | 1.00 | C(1)-C(2)-H(2)     | 117.9 |
| C(3)-H(3)         | 1.01 | C(2)-C(3)-H(3)     | 118.6 |
| C(6)-H(6)         | 1.02 | C(5)-C(6)-H(6)     | 121.3 |
| C(7)-H(7)         | 1.01 | C(6)-C(7)-H(7)     | 117.9 |
| C(11)-H(11)       | 1.01 | C(4)-C(11)-H(11)   | 110.4 |
| C(11)-H(11')      | 1.00 | C(4)-C(11)-H(11')  | 110.2 |
| C(12)-H(12)       | 1.04 | C(5)-C(12)-H(12)   | 110.9 |
| C(12)-H(12')      | 1.01 | C(5)-C(12)-H(12')  | 109.5 |
|                   |      | C(3)-C(2)-H(2)     | 118.1 |
|                   |      | C(4)-C(3)-H(3)     | 123.0 |
|                   |      | C(7)-C(6)-H(6)     | 120.3 |
|                   |      | C(8)-C(7)-H(7)     | 118.0 |
|                   |      | C(12)-C(11)-H(11)  | 112.0 |
|                   |      | C(12)-C(11)-H(11') | 112.8 |
|                   |      | H(11)-C(11)-H(11') | 106.3 |
|                   |      | C(11)-C(12)-H(12)  | 113.4 |
|                   |      | H(12)-C(12)-H(12') | 104.8 |

| Phenyl Rings    |      | Bond Angles, ° |       |
|-----------------|------|----------------|-------|
| Bond Lengths, Å |      | Bond Angles, ° |       |
|                 |      | A              | B     |
| C(2)-H(2)       | 1.00 | 119.2          | 118.9 |
| C(3)-H(3)       | 1.02 | 119.6          | 119.2 |
| C(4)-H(4)       | 1.03 | 120.4          | 120.3 |
| C(5)-H(5)       | 1.00 | 121.7          | 120.0 |
| C(6)-H(6)       | 1.00 | 119.9          | 121.1 |
|                 |      | A              | B     |
|                 |      | 120.4          | 120.6 |
|                 |      | 119.8          | 119.9 |
|                 |      | 120.1          | 120.2 |
|                 |      | 118.0          | 120.1 |
|                 |      | 119.3          | 117.8 |

(a) E.s.d's for C-H bond distances are about 0.01-0.02 Å.

(b) E.s.d's for C-C-H bond angles are about 0.7° and e.s.d's for H-C-H angles are about 1.0°.

naphthalene nucleus connecting the phenyl groups appear to be longer while those in the other half are shorter when compared to the corresponding bond distances in naphthalene<sup>14</sup> and perdeuterionaphthalene<sup>15</sup>. The average difference between

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(14) D. W. J. Cruickshank, Acta. Cryst. 10, 504 (1957).

(15) G. S. Pauley and E. A. Yeats, Acta. Cryst. B25, 2009 (1969).

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these two groups of bond lengths is 0.026 Å (13σ). This is in agreement with the result of other peri compounds, e.g. the difference of 0.035 Å in 1,8-bis(dimethylamino)-naphthalene<sup>15</sup>, 0.025 Å in 1,8-di(bromomethyl)naphthalene,<sup>17</sup> and 0.023 Å in 1,8-diphenylnaphthalene.<sup>7</sup> The deviations

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(16) H. Einspahr, J. B. Robert, R. E. Marsh and J. D. Roberts, Acta. Cryst., B29, 1611 (1973).

(17) J. B. Robert, J. S. Sherfinski, R. E. Marsh and J. D. Roberts, J. Org. Chem., 39, 1152 (1974).

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of the carbon atoms from the best plane<sup>18</sup> calculated for C1-C10 are given in Fig. 4. The largest deviation within

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(18) The direction cosines for the least-squares plane of the naphthalene ring are: .7840, .3257, .2197.

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the naphthalene ring is 0.046 Å (C8). The crowding interaction causes no appreciable distortion of the phenyl rings;

the phenyl carbons within each ring were found to be coplanar to better than  $\pm 0.01$  Å.

The bridging ethano carbon atoms are quite close to the mean naphthalene plane ( $+0.034$  and  $-0.025$  Å) and the torsional angle for rotation about the C11-C12 bond is  $2.4^\circ$ . The eclipsed protons on these adjacent carbons show significant repulsion: the four angles of the type C11-C12-H12 (av.  $112.9^\circ$ ) are consistently larger than the four of the type C5-C12-H12 angles (av.  $110.3^\circ$ ). This increases the eclipsed hydrogen-hydrogen distances to  $2.32$  and  $2.33$  Å, slightly shorter than the normal  $H\cdots H$  van der Waals distance of  $2.4$  Å<sup>19</sup>. The angles C4-C11-C12 ( $105.2^\circ$ ) and C5-C12-C11

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(19) A. Bondi, J. Phys. Chem., 68, 441 (1964), and references therein.

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( $104.9^\circ$ ) are smaller than the C-C-C angles of linear alkanes, which average about  $112^\circ$ .<sup>20</sup> This angle reduction is not

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(20) R. A. Bonham and L. S. Bartell, J. Amer. Chem. Soc., 81, 3491 (1959); L. H. Jensen and A. J. Mabis, Acta Cryst., 21, 770 (1966).

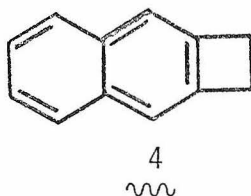
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accompanied by an appreciable opening of the H-C-H angles; the values of  $106.3^\circ$  and  $104.8^\circ$  are comparable with the average value of  $107^\circ$  for linear alkanes.<sup>21</sup>

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(21) T. F. Koetzle, M. N. Frey, M. S. Lehmann and W. C. Hamilton, Acta Cryst., B29, 2571 (1973).

The naphthocyclobutene 4 shows a similar behavior.<sup>22</sup>




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(22) J. L. Crawford and R. E. Marsh, Acta, Cryst., B29, 1238 (1973).

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The C-C-C angles of the four-membered ring of 4 are constrained to an even smaller value ( $87^\circ$ ), but the H-C-H angles remain at  $107^\circ$ . This lack of change seems surprising. By pulling the two pairs of C-C bonding electrons together, the repulsion of these pairs with the two C-H bonding pairs should be reduced, so that these C-H pairs can move farther apart. Further accurate data on H-C-H angles in small ring compounds is scarce; this point merits further experimental investigation.

The two phenyl rings in 1 are positioned face to face. The van der Waals separation for parallel aromatic systems was estimated by Pauling<sup>23</sup> to be 3.4 Å by consideration of the inter-layer distance in graphite and the packing distances in crystals of aromatic compounds.

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(23) L. Pauling, The Nature of the Chemical Bond, 3rd. Ed., Cornell Univ. Press, Ithaca, N.Y., 1960, p. 262.

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This estimated distance is about 1 Å greater than the distances between atoms 1 and 8 in an unsubstituted naphtha-

lene molecule.

To relieve the severe crowding caused by the peri-substituents, the phenyl groups are splayed making the C-9, C1, C1(A) angle  $124.8^\circ$ . The rings are rotated about  $33^\circ$  from the configuration which would have them perpendicular to the mean plane of the naphthalene carbons. The C1-C8 distance is 2.60 Å while the C1(A)-C1(B) distance is increased to 3.11 Å and the C4(A)-C4(B) to 4.31 Å as a result of splaying. The deviations of C4(A) and C4(B) from the mean naphthalene plane are -0.53 Å and +0.40 Å and this indicates that one of the two phenyl rings tilts up and the other tilts down about  $6^\circ$  from the naphthalene plane. This sideways distortion plus the rotation of the two phenyl rings result in a staggered configuration for the phenyl carbon atoms. The data in Table IV show that C1(B) is about equidistant from C1(A) and C6(A) while C1(A) is equidistant from C1(B) and C2(B). The staggered configuration is similar to that observed for 1,8-diphenylnaphthalene.<sup>7</sup> The residual strain from the interactions of the crowded phenyl groups in 1 is taken up by the naphthalene ring as will be described in detail later.

The fact that C-C single bonds which connect double bonds, triple bonds, or aromatic rings are substantially shorter in length than C-C single bonds between two aliphatic sites is well known. The phenyl and naphthyl rings are held nearly perpendicular in each of the peri-diphenylnaphthalene compounds 1, 2, and 3 (the dihedral



TABLE IV

Distances Between Carbons of the Adjacent Phenyl Rings, in Å

|   | Ring A |       |       |       |       |       |
|---|--------|-------|-------|-------|-------|-------|
|   | 1      | 2     | 3     | 4     | 5     | 6     |
| 1 | 3.108  | 3.991 | 4.645 | 4.596 | 3.857 | 3.039 |
| 2 | 3.041  | 3.430 | 3.941 | 4.107 | 3.787 | 3.257 |
| 3 | 3.862  | 3.981 | 4.021 | 3.950 | 3.823 | 3.787 |
| 4 | 4.593  | 4.914 | 4.880 | 4.311 | 3.936 | 4.100 |
| 5 | 4.650  | 5.328 | 5.381 | 4.783 | 4.010 | 3.939 |
| 6 | 3.990  | 4.929 | 5.320 | 4.911 | 3.970 | 3.427 |

angles are: 1,8-diphenylnaphthalene,  $67^{\circ}$ ; 1,8-diphenyl-acenaphthene,  $57^{\circ}$ ; 1,4,5,8-tetraphenylnaphthalene,  $58^{\circ}$ ). Interaction between the  $\pi$  systems across the inter-annular bond must therefore be minimal. In contrast, the phenyl rings of biphenyl and p-terphenyl are almost exactly coplanar in the crystal.<sup>24,25</sup> It is of considerable interest that the aryl-aryl bond lengths in all five compounds are not significantly different.

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(24) G. B. Robertson, Nature, 191, 593 (1961).

(25) H. M. Rietveld, E. N. Maslen, and C. J. B. Clews, Acta Crystallogr., 26, 693 (1970).

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This result accords with the view discussed at length by Dewar<sup>26</sup> that the relative shortening of bonds adjoining unsaturated sites is a direct consequence of hybridization changes in the bonding orbitals involved, and is not a result of resonance overlap between the two  $\pi$  systems.

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(26) M. J. S. Dewar, Hyperconjugation, The Ronald Press Company, N.Y., 1962.

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Bond lengths are given in Table V.

TABLE V

## Aryl-Aryl Bond Lengths

| <u>Compound</u>                     | <u>Dihedral<br/>Ring Angle</u> | <u>Aryl-Aryl Bond Length</u> |
|-------------------------------------|--------------------------------|------------------------------|
| 1,8-diphenylnaphthalene             | 67°                            | 1.487 (1.496)                |
| <u>peri</u> -diphenylacenaphthene   | 57°                            | 1.488 (1.491)                |
| 1,4,5,8-tetraphenyl-<br>naphthalene | 58°                            | 1.504                        |
| biphenyl                            | 0°                             | 1.496                        |
| <u>p</u> -terphenyl                 | 0°                             | 1.497                        |

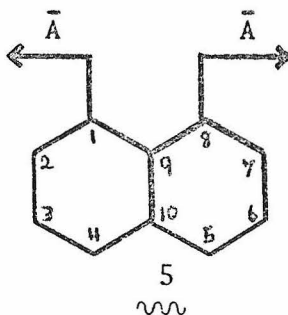
General Analysis of the Molecular Distortions of the  
 ~~~~~  
 Naphthalene Nucleus in peri-Substituted Derivatives.
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The perturbation introduced by steric overcrowding of the phenyl groups is spread throughout the naphthalene nucleus. The molecular framework adjusts to relieve the stress, and the resultant minimum energy conformation is presumably the best compromise of bond stretchings and compressions, angle deformations, and buckling of the ring, adjusted for interactions resulting from crystal packing. The overall changes in the naphthalene ring geometry may be understood in terms of the action of a series of force vectors induced into the molecule at the peri positions. The geometry of the unsubstituted naphthalene molecule itself may be taken as the minimum-energy structure. The bond framework has resistance to stretching or compressing and to in-plane or out-of-plane bending.

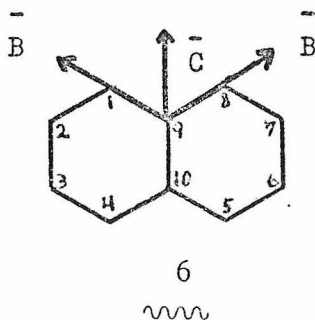
A perturbing force acting at a given site will be partly accommodated by a local deformation, but residual force will be passed along to adjacent sites. Angle bending usually has much smaller force constants for a given displacement than bond stretching or compression. The two types of peri strain, splaying and pinching, are considered. Both kinds of strain interaction are accommodated by in-plane distortions; splaying is also accommodated by out-of-plane distortion.

Repulsive forces between bulky peri substituents are

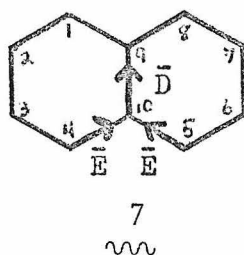
expected to produce vectorial forces  $\bar{A}$  of equal magnitude but opposite direction at atoms 1 and 8, see 5. These atoms are pushed apart and the C1-C9-C8 angle is forced open.



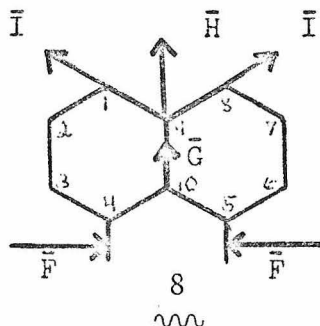
Vectors  $\bar{A}$  force C1 and C8 apart; the C1-C2-C3 and C6-C7-C8 angles are expected to be opened and C2 and C7 to be moved outward. As atoms 1 and 8 move outward, the C1-C9 and C8-C9 distances will be increased. However, because these bonds resist stretching and the C1-C2 and C7-C8 bonds resist compression, the bond lengths do not change sufficiently to take up the distortions produced by the increased C1-C9 and C8-C9 distances. We can hence envision two equal force vectors  $\bar{B}$  induced along the 1,9 and 8,9 bonds <sup>6</sup>. The resultant of these vectors is another vector  $\bar{C}$  at C9 which is perpendicular to  $\bar{A}$  and is collinear with the 9,10 bond.



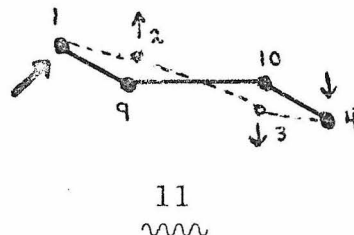
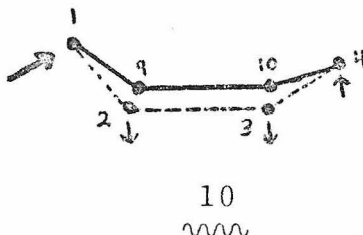
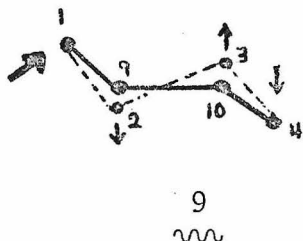
Carbon 9 is thus pulled toward the phenyl rings, the C9-C10 bond is stretched, and a residual vector  $\bar{D}$  having the same direction as  $\bar{C}$  but of reduced magnitude is induced at C10. As C10 is pulled toward C9, vectors  $\bar{E}$  are induced at C4 and C5 <sup>7</sup> pulling these atoms toward C10 and acting to force C4 and C5 together, closing the C4-C10-C5 bond angle.



The opposite type of induced peri strain, pulling together two peri carbon atoms, results in an analogous chain of distortions. Bringing together peri atoms C4 and C5 (vectors  $\bar{F}$ ) causes the C4-C10-C5 angle to be reduced <sup>8</sup> . The C4-C10 and C5-C10 distances are decreased, and resistance to bond compression induces a vector  $\bar{G}$  at C10 which forces it toward C9. The C9-C10 bond is compressed, and vector  $\bar{H}$ , which has the same direction but smaller magnitude compared to  $\bar{G}$ , is imposed on C9. As C9 moves away from C10, C1 and C8 are forced away from it. (vectors  $\bar{I}$ ). As a result, the C1-C8 distance and the C1-C9-C8 angle increase. C2 and C7 should experience outward pressure. As C4 and C5 are forced together, C3 and C6 can be expected to be pulled slightly towards one another.



Out-of-plane splay of overcrowded peri substituents induces force vectors of opposite direction at C1 and C8 which act to push these atoms to positions above and below the naphthalene ring plane. Though the C1 and C8 out-of-plane displacement should be larger than for any other atom in the naphthalene nucleus, this distortion is expected to be partly distributed among the other atoms. Thus, the folding of the peri atom into the ring plane should result in a buckling of the naphthalene nucleus. C-9 and C-10 are held relatively rigidly, and prevented from significant out-of-plane movement since they are contained in both of the six membered rings of the naphthalene, which are distorting in opposite senses. Taking the peri carbon to be the farthest out of plane, there are three basic warping patterns for the C-1, C-2, C-3, C-4 atoms relative to C-9 and C-10, which are shown below. (9, 10, 11). (The C-8, C-7, C-6, C-5 portion of the naphthalene nucleus simultaneously warps in the opposite sense.)



Of these  $\overset{9}{\sim}$  is expected to have the highest skeletal strain, since adjacent atoms are displaced in opposite senses. The peri-substituted naphthalenes exhibit either of the two conformations  $\overset{10}{\sim}$  and  $\overset{11}{\sim}$ ;  $\overset{11}{\sim}$ , which should have less skeletal strain, occurs most frequently.

The relative distribution of the strain between the in-plane and out-of-plane modes should depend on numerous factors determined by the nature of the substituents. There are two means of in-plane splay. The magnitude of the first of these, the increase of the C9, C1, peri-substituent angle, will be affected by the crowding interaction of the peri-substituent with the hydrogen (or other substituent) bonded to C-2, while the second type of in-plane splay, increase of the C1, C9, C-8 angle, will not be affected. Electronic interactions between the peri-substituent and the naphthalene ring could also inhibit the C-9, C-1, peri-substituent angle splay. The relative amount of in-plane and out-of-plane splay may be affected by the details of the geometrical fit between peri-substituents. If one mode of distortion is blocked for any reason in a given peri naphthalene, the strain energy is expected to be distributed into the other available modes.

#### Observed Distortions in the peri-Diphenylnaphthalenes

The effects discussed here can all be clearly seen by an examination of the geometries of the peri-phenyl-naphthalenes  $\overset{1}{\sim}$ ,  $\overset{2}{\sim}$  and  $\overset{3}{\sim}$ . The structures of naphthalene,<sup>1 5</sup> 1,8 diphenylnaphthalene,<sup>7</sup> 1,8-diphenylacenaphthene, and 1,4,5,8-tetraphenylnaphthalene<sup>8</sup> are shown together in Fig. 4,



with important bond lengths, angles, and displacements from the mean plane of the naphthalene ring indicated.

1,8-Diphenylnaphthalene <sup>2</sup> has force vectors induced at C1 and C8 which push these atoms apart to a distance of 2.563 Å; the C1-C9-C8 angle is splayed to 126.2°. The C1-C2-C3 and C6-C7-C8 angles are slightly opened (122.1°). The peri angle C4-C10-C5 opposite the phenyl rings is pinched to 119.3° compared to naphthalene when this angle is 121.6°. The force vector  $\bar{C}$  acting on C9 causes substantial stretching of the C9-C10 bond to 1.442 Å (the corresponding naphthalene bond has a length of 1.412 Å) and forces C9 and C10 to be moved toward the peri phenyl groups: C9 lies 0.10 Å to the peri-phenyl side of a line drawn between C2 and C7, while C10 is displaced 0.07 Å in the same direction relative to a line through C3 and C6.

The peri-diphenylacenaphthene molecule has splaying vectors imposed at one peri position, and squeezing vectors at the opposite one. These operate to produce reinforcing chains of stresses in the naphthalene ring (<sup>5-8</sup>). As expected, the distortions observed for 1,8-diphenylnaphthalene are found to be enhanced in this molecule. C4 and C5 are pulled together to a distance of 2.33 Å; the C4-C10-C5 angle is pinched severely to 111.5°. Angle C1-C9-C8 is splayed both because of the peri phenyl groups and because of the pinching at the opposite end by the ethano bridge. This angle is thus 3° larger than the corresponding angle in 1,8-diphenylnaphthalene. Also, C1 and C8 are 0.038 Å farther apart and the C1-C2-C3 and C6-C7-C8 angles are 2° larger.

For  $\text{1}$  there are strong forces acting on both ends of the C9-C10 bond in the same direction. The result is a larger displacement of C9 and C10 toward the phenyl groups than for 1,8-diphenylnaphthalene, but with less stretching of the C9-C10 bond. With  $\text{1}$ , C9 is 0.19 Å to the peri phenyl side of a line drawn through C2 and C7, while atom 10 is 0.18 Å to the same side of a line through C3 and C6. The C9-C10 bond has a length of 1.417 Å.

In both  $\text{1}$  and  $\text{2}$ , the naphthalene ring is elongated at the side bearing the phenyl substituents, as would be predicted by the stress vector analysis. This is most pronounced for  $\text{1}$  where the C2-C7 distance is 4.84 Å while the C3-C6 distance is 4.75 Å.

The tetraphenyl compound  $\text{3}$  has splaying vectors at both ends of the naphthalene system. This gives rise to two sets of force vectors within the naphthalene nucleus which tend to work against each other. It has been seen that splaying gives rise to a net pinching effect at the opposite end of the ring. Since there are two opposing interactions acting at each end of this molecule, the C1-C9-C8 angle is opened to only  $122.6^\circ$ --considerably smaller than for  $\text{1}$  and  $\text{2}$ , and only slightly larger than the corresponding angle in naphthalene itself. The peri carbons of  $\text{3}$  are separated by only 2.51 Å and the C1-C2-C3 and C6-C7-C8 angles are only  $121.0^\circ$ . Another difference between  $\text{1}$  and  $\text{2}$ , and  $\text{3}$  is that in  $\text{3}$ , C9 and C10 each experience a force vector along the 9,10 bond, but acting in opposite directions. The

9,10 bond is thus being pulled from both ends and, at 1.447 Å is the longest in any of these diarylnaphthalenes. Because splaying in the plane of the naphthalene ring by opening of the C1-C9-C8 angle, is largely blocked for  $\overset{3}{\sim}$ , the molecules of  $\overset{3}{\sim}$  must alleviate this strain in some manner. The strain is channeled into the out-of-plane mode; the phenyl rings in  $\overset{3}{\sim}$  are bent greatly to opposite sides of the naphthalene plane, much more so than for either  $\overset{1}{\sim}$  or  $\overset{2}{\sim}$ . An end view of  $\overset{3}{\sim}$  along the plane of the naphthalene ring is shown in Figure 4, with out-of-plane bending angles indicated. Angle  $\alpha$  is the out-of-plane twist of the peri carbon atoms;  $\beta$  is the out-of-plane angle between the phenyl to naphthalene bonds. Compounds  $\overset{2}{\sim}$  and  $\overset{3}{\sim}$  adopt the out-of-plane warping pattern  $\overset{10}{\sim}$ ;  $\overset{1}{\sim}$  adopts pattern  $\overset{11}{\sim}$ .

The crystal structure of acenaphthene itself<sup>27</sup> has been determined and the data is consistent with expectations for a naphthalene nucleus with pinching at the 4,5 peri positions. Thus, compared with naphthalene, the C1-C9-C8

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(27) H. W. W. Ehrlich, Acta Cryst., 10, 699 (1957).

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angle is larger and the C4-C10-C5 angle is smaller. As expected, neither angle distortion is as large as that observed for peri-diphenylacenaphthene, which has the two reinforcing peri strains. The C9-C10 bond of acenaphthene seems to be slightly shorter than for naphthalene, as

expected, but the error limits of this structure determination are large and these effects are of marginal significance.

The force vector analysis of distortions of the naphthalene nucleus is consistent with observations on other peri-substituted naphthalene compounds. The most pronounced geometrical changes discussed here, especially the splaying of the C1-C9-C8 angle, stretching of the C9-C10 bond, pinching of the C4-C10-C5 angle, and out-of-plane displacement of peri substituents accompanied by buckling of the naphthalene ring, can be discerned in several early X-ray structures which have substantially larger errors. <sup>28,29,30</sup>

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(28) M. B. Jameson and B. R. Penfold, J. Chem. Soc., 528 (1965).

(29) Z. A. Akopyan and Y. T. Struchkov, Zh. Strukt. Khim., 5, 496 (1964); Z. A. Akopyan, A. I. Kitaigorodski, and Y.T. Struchkov, ibid., 729 (1965).

(30) M. A. Davydova and Yu. T. Struhkov, Zh. Strukt. Khim., 2, 63 (1961). M. A. Davydova and Yu, T. Struchkov, ibid., 170 (1962).

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The geometries of 1,8-diiodonaphthalene,<sup>31</sup> 1,8-dibromomethylnaphthalene,<sup>17</sup> and 1,8-bis(dimethylamino)naphthalene,<sup>16</sup> and 1,8-bis(phenylethynyl)naphthalene<sup>32</sup> have been determined with accuracy comparable to the present study and are discussed here.

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(31) J. S. Sherfinski, J. B. Robert, R. E. Marsh, and J. D. Roberts, in preparation.

(32) A. E. Jungk and M. J. Schmidt, Chem. Ber., 104, 3272 (1971).  
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Overcrowding reaches an extreme in 1,8-diiodonaphthalene. The van der Waals separation expected for two iodo substituents is 3.92 Å according to Bondi¹⁹ and 4.30 according to Pauling.²³ The peri-iodo substituents splay, pulling C1 and C8 apart to a distance of 2.603 Å, and opening the C1-C9-C8 angle to 130.3°. The C9-C10 bond is stretched to 1.445 Å, and the C4-C10-C5 peri-angle is squeezed to 117.9°. The C1-C2-C3 angles are 122.1°. C-9 is displaced in the direction of the iodo substituents by 0.15 Å relative to a line passed through C-2 and C7; C-10 is moved in the same direction by 0.9 Å relative to a line through C-3 and C-6. The iodo substituents are displaced 0.38 Å to opposite sides of the mean naphthalene plane; the molecule adopts the warping pattern ¹¹~~~~.

1,8-Dibromomethylnaphthalene, 1,8-bis(dimethylamino)-naphthalene, and 1,8-bis(phenylethynyl)naphthalene show the same overall in- and out-of-plane distortions though mostly of smaller magnitude than for the diiodo compound. These are summarized in Table VI.

TABLE VI

Summary of Distortions for 1,8-Dibromomethylnaphthalene, 1,8-Bis-(dimethylamino)naphthalene, and 1,8-Bis(phenylethynyl)naphthalene.

| <u>In-Plane Distortion</u> | <u>1,8-Dibromomethyl-naphthalene</u> | <u>1,8-Bis(dimethylamino)-naphthalene</u> | <u>1,8-Bis(phenyl-ethynyl)naphthalene</u> |
|--------------------------------|--------------------------------------|---|---|
| C1, C9, C8 | 127° | 125.8° | 125.1° |
| C1-C8 | 2.57 A | 2.56 A | 2.54 A |
| C9-C10 | 1.44 A | 1.425 A | 1.43 A |
| C4, C10, C5 | 121° | 119.6° | 119.6° |
| C9-C1 <u>peri</u> -substituent | 125° | 120.5° | 123.7° |

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Out-of-Plane Distortion

| | | |
|----------------------|---------------|---------------|
| C1(C-8) displacement | -0.07(0.05) A | -0.15(0.15) A |
| Warping pattern | 11
~~~~ | 11
~~~~ |

As mentioned before, the relative amounts of in-plane and out-of-plane distortion for various peri naphthalenes must depend on the nature of the substituents.

The amount of in-plane splay of peri-substituents is expected to be somewhat hindered, because large in-plane splaying moves the substituents to slightly within the van der Waals distance of the 2,7 hydrogens. Thus, for example, for 1,8-diiodonaphthalene, the I(1)-H(2) distance found³¹ is 2.8 Å, while the H-I van der Waals distance may be estimated at 3.2 Å from the data of Bondi.¹⁹ The distance from the C-1 carbon of the phenyl ring to H-2 is found to be 2.55 and the phenyl C-2 to H-2 distance is 2.56 Å for peri-diphenyl acenaphthene, which may be compared with an estimated¹⁹ van der Waals separation of 2.9 Å between a hydrogen and an aromatic carbon. The C-1-amino bond of 1,8-bis(dimethylamino)naphthalene shows an especially small in-plane splay compared with other peri-substituted naphthalenes, while the peri carbon atoms and the amino groups have an exceptionally large out-of-plane displacement. The in-plane splay is hindered in this compound for two reasons: the naphthyl-amino bond has partial double-bond character, and the methyl groups are highly susceptible to becoming overcrowded with the C-2 hydrogen atom. The strain is thus channeled strongly into the alternative out-of-plane distorting mode.

The largest distortions in the naphthalene ring of the peri substituted naphthalenes, both in-plane and out-of-plane, occur at C-1 and C-8. Peri substituted naphthalenes have the bonds at C1 and C8 lengthened relative to those at the opposite end of the ring (C-4 and C-5 bonds) in the range of about 0.025 to 0.035 Å. It seems understandable that this bond lengthening may result from a decreased overlapping of the p orbitals of C1 and C8 with the p orbitals of adjacent carbon atoms due to the geometric distortion. The fact that the bonds involving C-4 and C-5 are somewhat shortened compared with the corresponding bonds in naphthalene suggests the interesting possibility that an electron redistribution has occurred; a decrease in bonding at the C1; C8 end of the ring may have made a higher electron density available for the π cloud at the C-4, C-5 end.

Proton NMR Studies of C_{10}H_6

The proton NMR spectrum (Figure 5a) of peri-diphenyl-acenaphthene C_{10}H_6 is striking in its simplicity. At 60 MHz, the spectrum consists of three sharp singlets (δ : 7.30, 6.87, 3.43; 4:10:4). The spectrum indicates that the conformation of C_{10}H_6 in solution is similar to that determined for the crystal. Replacement of a proton on an aromatic ring by a methyl or ethyl group gives rise to very small chemical-shift differences between remaining protons. Thus, the aryl portions of the spectra of toluene and ethylbenzene ³³ are in each case a single sharp peak at 60 MHz.

(33) Varian NMR Spectra Catalogue, Varian Associates, Palo Alto, California, 1962, No. 157,505.

However, replacement by a substituent having electronic properties quite different from a proton can result in a more complex aromatic signal. Diaryl systems in which the rings are relatively free to approach coplanarity³⁴ exhibit highly split multiplets for the aryl protons, as may be seen³⁵ in the spectra of biphenyl, m-terphenyl, p-terphenyl, and trans-stilbene.

(34) The dihedral angle of biphenyl in solution is presently under debate. Measurements of the depolarization of Rayleigh scattered light gave values of 24° and 31° . [I. A. Bogdanov and M. F. Vuks, Ser. Fiz. i. Khim., 3, 46 (1965) (Russ); A. Unanue and P. Bothorel, Bull. Soc. Chim. France, 5, 1640 (1966)]. U. V. measurements in solution give an angle of about 20° [H. Suzuki, Bull. Chem. Soc. Japan, 32, 1340 (1959)]. From molar Kerr constants [J.Y.H. Chan; C. G. Le Ferre and R. J. W. Le Ferre, J. Chem. Soc., 2666 (1959)] and magnetic anisotropy measurements [C. L. Cheng, D. S. N. Murthy and G. L. D. Ritchie, J. Chem. Soc., Faraday II, 1679 (1972)], an angle of 0° has been calculated. The energy barrier to rotation about the aryl-aryl bond is expected to be low, and essentially free rotation is assumed at room temperature.

(35) Varian NMR Spectra Catalogue, No. 289, 669, 671, 306.

However, for systems sterically constrained from assuming a nearly coplanar conformation, the aryl protons give a sharp single peak, as observed³⁶ with o-terphenyl and cis-stilbene. This phenomena likely arises from both a resonance interaction and a larger ring current shift for the more coplanar systems.^{37, 38}

(36) Varian NMR Spectra Catalogue, No. 670, 305.

(37) M. Katayama, S. Fujiwara, H. Suzuki, Y. Nagai, and O. Simamura, J. Molec. Spec., 5, 85 (1960).

(38) R. J. Kurland and W. B. Wise, J. Am. Chem. Soc., 86, (9), 1877 (1964).

Thus, the sharp singlet of the phenyl protons of $\overset{1}{\sim}$ at 6.87 δ is indicative of the perpendicularity of the system, and may be compared with biphenyl, Fig. 5b. The sharp singlet at 7.30 δ from the two naphthalene protons of $\overset{1}{\sim}$ may be contrasted with the protons of p,p'-bitolyl which give an A₂B₂ pattern having a chemical shift difference of 14 Hz at 60 MHz (Fig. 5c). The phenyl peak of 1,8-diphenyl-acenaphthene is shifted 0.5 ppm upfield from the phenyl signal of 1-phenylnaphthalene because of the ring current of the adjacent peri-phenyl ring, consistent with a parallel conformation of the two phenyl rings. The shift difference is nearly the same as for the phenyl-ring protons of 1-phenylnaphthalene and 1,8-diphenylnaphthalene,³⁹ and also of p-xylene⁴⁰ and [2.2.]-paracyclophane.⁴¹

(39) H. O. House, R. W. Magin, and H. W. Thompson,
J. Org. Chem., 28, 2403 (1963).

(40) Varian NMR Spectra Catalogue, No. 203.

(41) D. J. Cram, C. K. Dalton, and G. R. Knox, J. Am. Chem. Soc., 85, 1088 (1963).

The distortions induced in the naphthalene ring do not seem to have any appreciable affect on the chemical shifts of the naphthyl protons, which come into resonance very near to the β protons of naphthalene itself⁴² (7.30 δ vs. 7.38 δ).

(42) Sadtler Standard Spectra Catalogue, Sadtler Research Laboratories, Inc., 1966, No. 62.

FIGURE 1
peri-Diphenylacenaphthene

FIGURE 2

Stereoscopic view of peri-diphenylacenaphthene

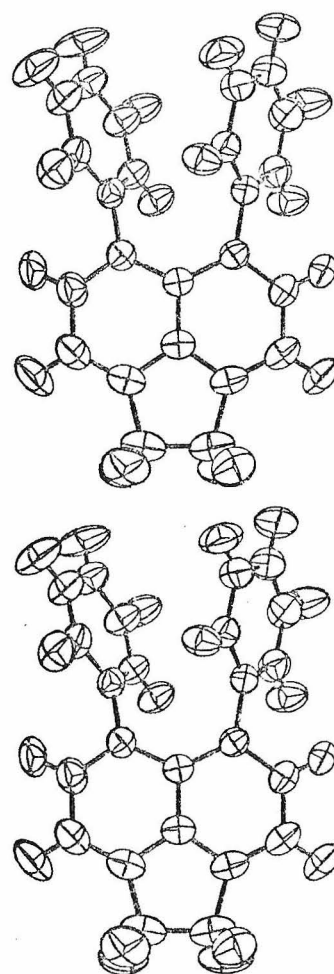


FIGURE 3

Packing diagram for peri-diphenylacenaphthene

FIGURE 4
Geometries of peri-diphenylnaphthalenes

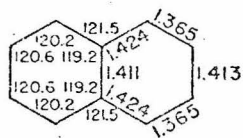
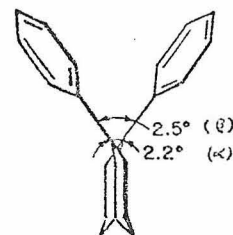
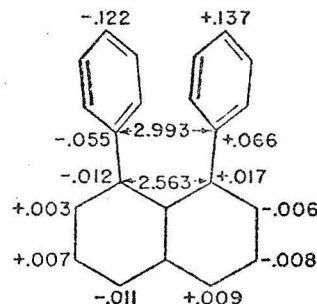
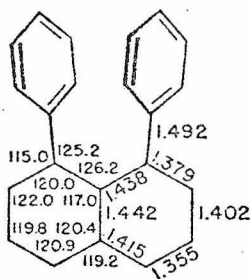
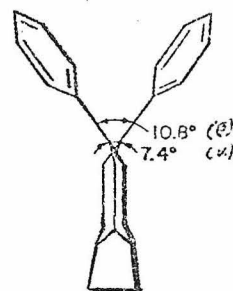
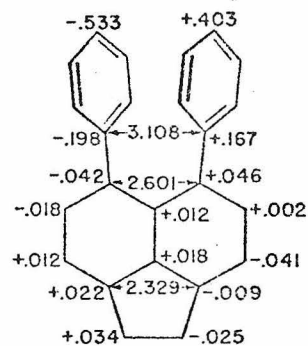
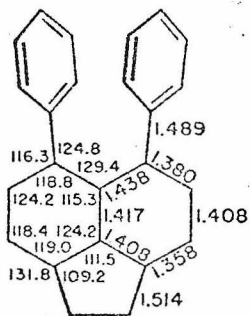
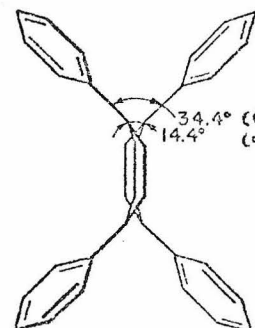
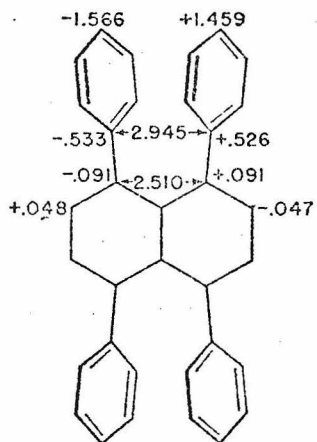
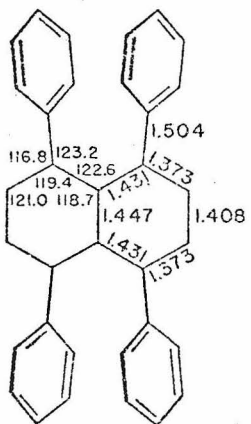
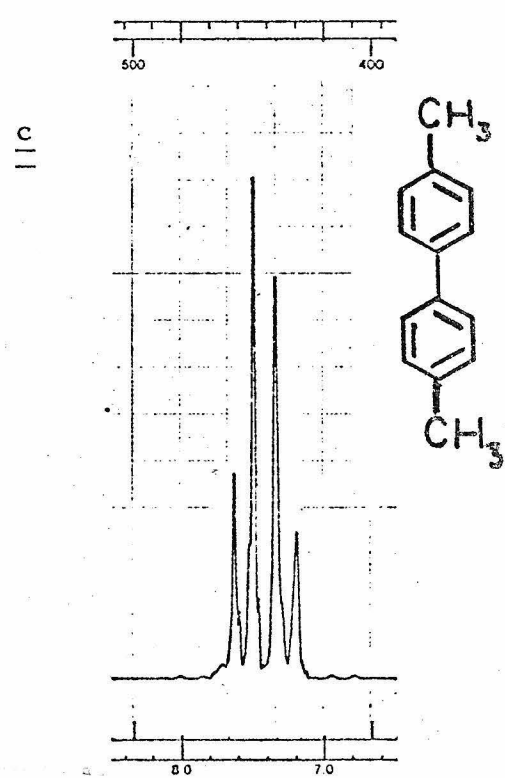
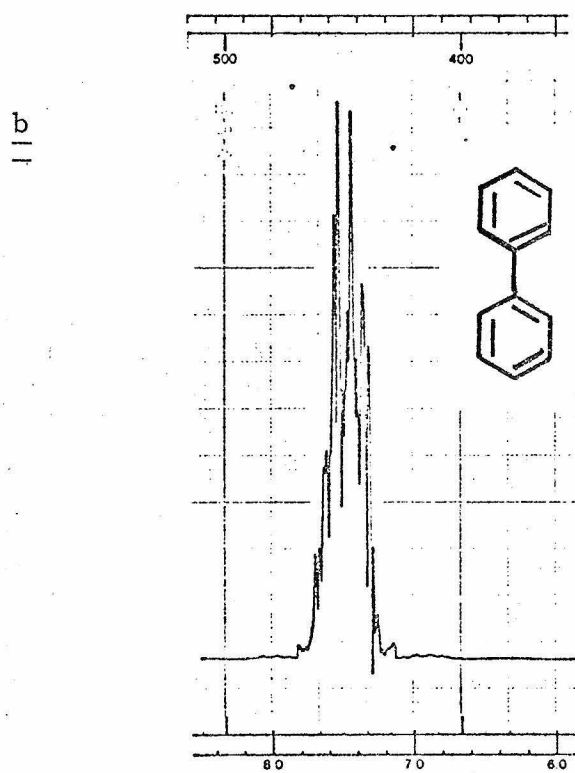
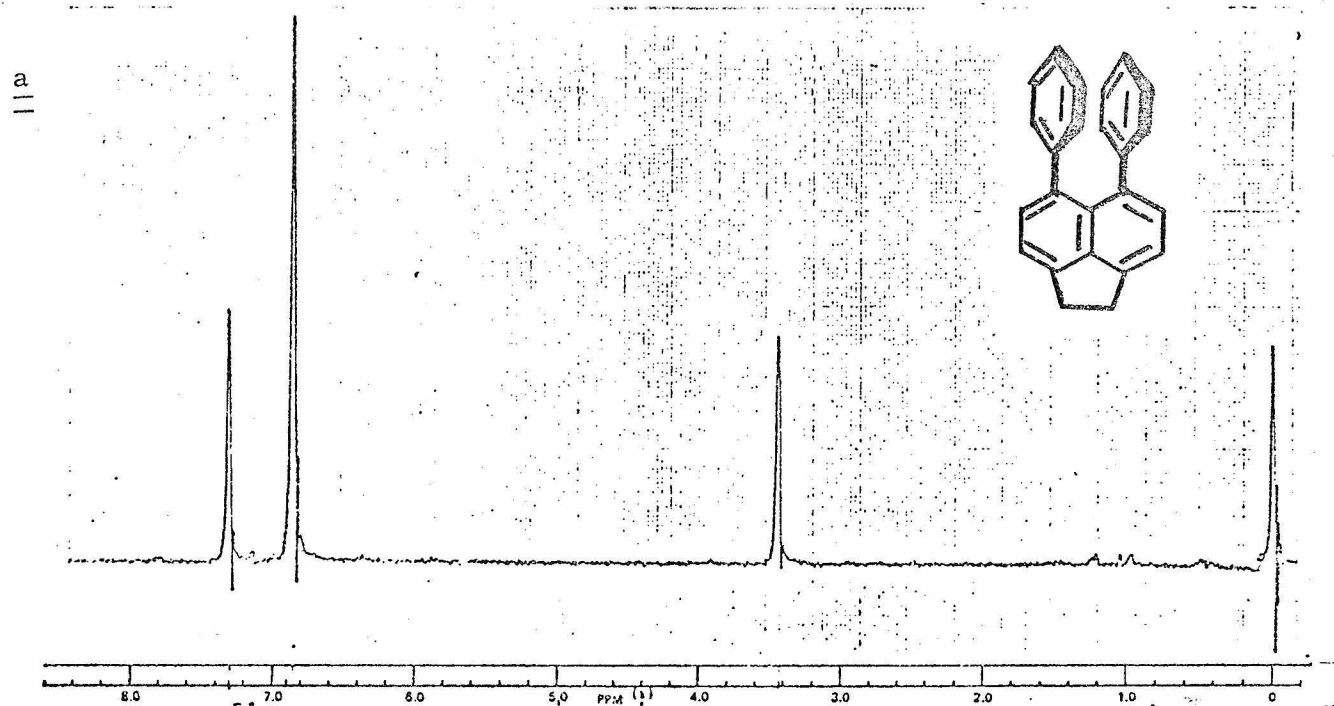
Naphthalene1,8-Diphenyl-naphthaleneperi-Diphenyl-acenaphthene1,4,5,8-Tetraphenyl naphthaleneAngles and
bond lengthsDistortions from the
mean naphthalene plane;
Intramolecular distancesOut-of-plane
angles

FIGURE 5

- a) Proton nmr spectrum of peri-diphenylacenaphthene
- b) Proton nmr spectrum of biphenyl
- c) Proton nmr spectrum of 4,4'-bitolyl

All spectra were obtained at 60 MHz



PART III

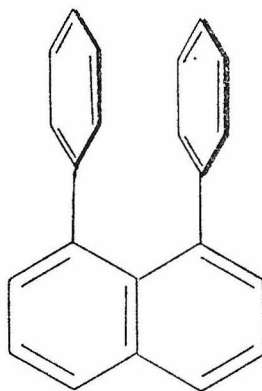
Internal Rotation in *peri*-Phenylnaphthalenes

Summary

A 180° rotation about a phenyl-naphthyl bond was expected to be effectively blocked for derivatives of the peri - diphenylnaphthalenes, in which steric requirements force the phenyl rings to assume a face-to-face conformation. However, surprisingly low barriers have been reported. The preparation and the measurement of the barrier to phenyl-ring rotation of a derivative of the highly crowded 1,4,5,8-tetraphenylnaphthalene system is described. The barrier is found to be 14.9 kcal/mol compared with the 16.4 kcal/mol determined for 1,8-diphenylnaphthalene; both of these barriers are much lower compared with the 33.5 kcal/mol reported for the stereotopically similar [3.4]paracyclophane. The differences are discussed in terms of a rotational transition-state having large deformations of the naphthalene ring, which is especially favored for the tetraphenyl derivative.

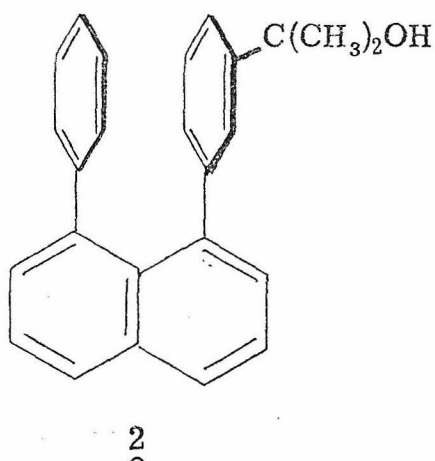
Introduction

Examination of molecular models leads to the conclusion that the only geometry possible for 1,8-diphenylnaphthalene must have the phenyl rings face to face, 1; even in this conformation severe crowding of the phenyl rings must remain. As a result of the imposed proximity, the aryl rings would be expected to exhibit a high barrier to a 180° rotation about the aryl-naphthyl bond. CPK space-filling models would seem to indicate that such a rotation is in fact impossible except by breaking a bond.

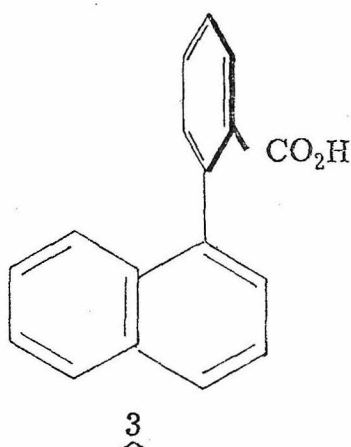
1

House and coworkers¹ have prepared several derivatives of 1,8-diphenylnaphthalene having a substituent at one meta position of each phenyl ring, with the expectation that they would be able to isolate cis and trans isomers. However, it was not found possible to obtain separate isomers, and instead a single crystalline compound was isolated in each case. Subsequent nmr measurements² on the alcohol

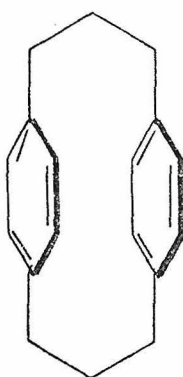
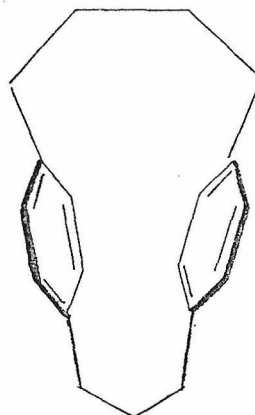
derivative, 2, showed that the barrier to rotation was only 16.4 kcal/mol, consistent with rapid rotation at room temperature.



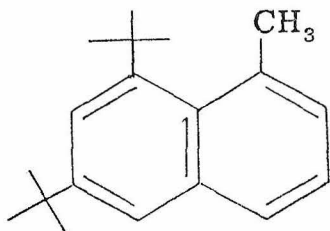
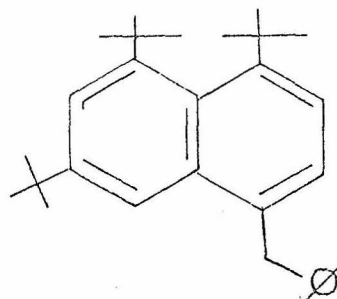
The 1,8-diarylnaphthalenes may be compared with the ortho-substituted biphenyls, for which many examples having rotational barriers high enough to allow separation of optical isomers are known.³ The naphthyl derivative, 3, has also been resolved,⁴ as has α,α' -binaphthyl⁵ for which a rotational barrier of 22.5 kcal/mol was obtained.



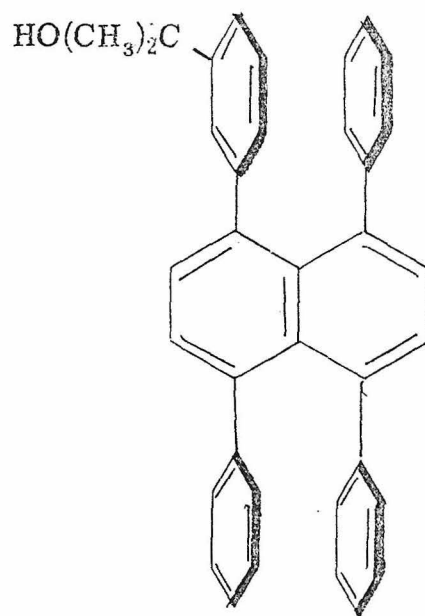
Cram has reported that a derivative of the [3.3]paracyclophane system, 4, showed no tendency racemize at temperatures up to 240° ,⁶ and that a derivative of the [3.4]paracyclophane system, 5, racemized only slowly at 160° .⁷ The barrier to phenyl-ring rotation in the latter was calculated to be 33.5 kcal/mol.⁷ These two compounds provide a striking contrast to the rotational barriers found for derivatives of 1 for which similar steric requirements would be indicated.

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Several naphthalene derivatives having other types of peri substituents have been recently studied, and were reported to have what seem surprisingly low barriers to rotation about the naphthyl-substituent bond.^{8,9} For example, the barrier to rotation of the tert-butyl group of 6 was <6 kcal/mol and that of 7 was estimated at about 6.5 kcal/mol.⁹

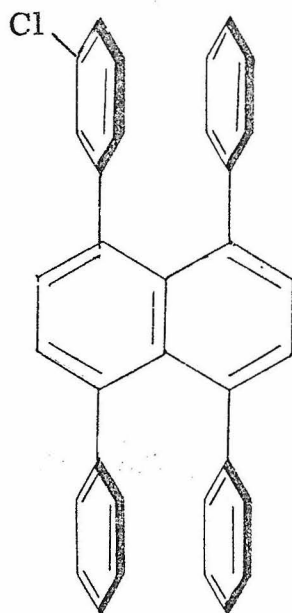
67

We report here the synthesis and measurement of the rotational barrier of the highly strained 8 which has two sets of crowded peri phenyl groups. The result is compared to that obtained for 2, and a discussion of the mechanism of ring rotation in the peri-phenylnaphthalenes is presented.



Synthesis of 8

The synthetic scheme for 8 had 9 as a key intermediate, with the meta-chloro group intended to serve as a marker which would be inert to conditions of the synthetic sequence, but which would permit functionalization of the aromatic ring after construction of the naphthalene framework. Clearly 9 could also serve as a precursor to other tetraphenylnaphthalenes.



9

Benzoisofuran derivatives readily undergo Diels-Alder addition, and have been successfully used as intermediates in the preparation of several polycyclic aromatic hydrocarbons, including 1,4-diphenylnaphthalene,¹⁰ 5,10-diphenylanthracene,¹¹ and 1,4,5,8-tetraphenylnaphthalene.¹² The preparation of 9 was patterned after these routes utilizing benzoisofuran, 10.

The complete reaction sequence is outlined in Figure 1. Reaction of triphenylcinnamylphosphonium chloride, 11, with 3-chlorobenzaldehyde gave 1-(3-chlorophenyl)-4-phenyl-1,3-butadiene, 12, in good yield. Diels-Alder addition of 12 and trans-dibenzoyl-ene proceeded on long reflux to give 13, which was aromatized to 14 by refluxing with bromine. Reaction with zinc and sodium hydroxide gave 10, which by Diels-Alder addition with acrolein yielded 15. Acid dehydration gave the aromatic aldehyde, 16. The attempted decarbonylation of 16 with tris(triphenylphosphine)rhodium (I) chloride, 17, in benzene resulted in the precipitation of the red dimer of the rhodium complex, a result which has been observed before for other aldehydes which are sterically crowded.¹³ Nitriles are reported to stabilize the monomeric rhodium species; when the aldehyde 16 was heated with an equivalent amount of 17 at 160-165°C in benzonitrile, the reaction was complete in eight minutes to give 9 in 80% yield.

The chloro group of 9 proved to be particularly inert. Stirring with a solution of n-butyllithium gave no exchange. No reaction could be induced between 9 and strips of lithium metal and no reaction was observed when 9 was added to a freshly prepared dispersion of sodium. We have developed a technique which effects rapid reaction of 9. The method was tested by reacting a model compound, 1-(3-chlorophenyl)-naphthalene, 18, to give 1-(3-hydroxyphenyl)naphthalene, 19, to ascertain appropriate reaction conditions. Thus when 9 was added to an excess of fine lithium dust (140 mesh) under argon with bromobenzene present to activate the metal and with ether as a solvent, the solution

turned to a deep purple on heating to reflux. Addition to acetone in ether gave 8 in 57% yield.

Internal Rotation in the 1,4,5,8-Tetraphenylnaphthalene System

In the absence of phenyl-ring rotation, derivatives of 1,4,5,8-tetraphenylnaphthalene having a substituent in the meta position of one phenyl ring must exist as enantiomers. Whether or not ring rotation is rapid in solution, the possibility exists that the enantiomers could crystallize separately, as has been observed for other large asymmetric aromatics including heptahelicene.¹⁴ Microscopic examination of crystals of 9 grown by slow evaporation of a hexane solution revealed that they are triclinic but have a center of symmetry and belong to the pinacoidal class, showing that 9 crystallizes as a racemic mixture.

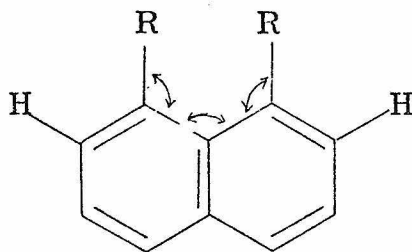
When ring rotation is slow on the nmr timescale, the two methyl groups of 8 become diastereotopic. The proton nmr spectrum of 8 showed that at 100°C the methyl protons gave a single sharp peak, while lowering the temperature caused this resonance to broaden and at 5°C to begin to split into two equal signals. Visual matching using computer-generated spectra allowed calculation of the energy barrier for rotation, ΔG^\ddagger of 14.9 kcal/mol.

The Rotational Mechanism of peri-Phenylnaphthalenes

Detailed calculations on the rotational barriers of certain 2,2'-substituted biphenyls were performed by Westheimer,¹⁵ who

showed that the rotational intermediates must have geometric deformations local to the interannular bond. Important distortions include a bending of the ortho substituents away from each other, interannular bond stretching, and C-H (ortho) bond compression.

There are two modes of distortion in the peri-substituted naphthalenes which would effectively increase the distance between the peri substituents. These two modes, which have no analogue in the bi-phenyls, are in-plane and out-of-plane splaying of the peri groups. In-plane splay can occur both by a bending of the exocyclic naphthyl-substituent bond which increases the C9-C1-substituent angle, and by an opening of the C1-C9-C8 angle of the naphthalene nucleus.



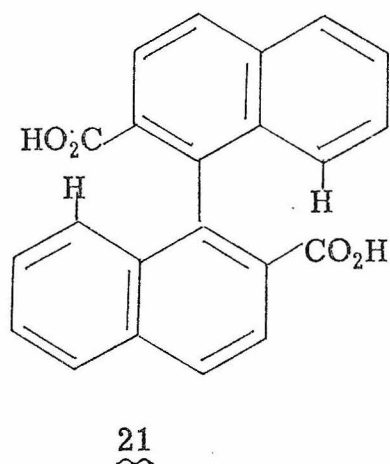
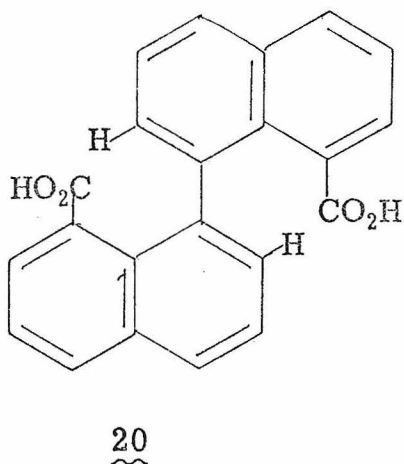
C1-C9-C8 angle opening should be especially effective, because the distance between the peri substituents is increased without a concomitant increase in crowding between the substituent and the adjacent naphthyl proton. Out-of-plane splay would involve displacement of the peri substituents (and to a lesser extent, the naphthalene atoms C1 and C8) to opposite sides of the naphthalene plane. Recent X-ray investigations¹⁶ demonstrate a surprising lack of rigidity of the naphthalene ring and show that non-bonded interactions between bulky peri sub-

stituents are considerably relieved by large in-plane and out-of-plane distortions of the type described above. The strain energy is effectively absorbed by the naphthalene nucleus; this is accomplished by a distribution of the strain throughout the framework which includes angle bending, bond stretching and compression, and in- and out-of-plane nuclear displacements. Distortions are substantial. In 1,8-diphenylnaphthalene,^{16,17} the C1-C9-C8 angle is forced open to over 126°, the C9-C1-phenyl angles open to more than 125°, and the naphthyl-phenyl out-of-plane angles are about 2°. The more crowded peri derivative, 1,8-diiodonaphthalene, shows these same distortions enhanced — for example, the C1-C9-C8 angle exceeds 130°. The X-ray structures of the peri-naphthalenes, which experience crowding in the ground state, provide a model for the geometry of the rotational transition-state of the 1,8-diarylnaphthalenes. However, in the more highly strained rotational intermediate, these distortions will be magnified because rotation must not occur with a ground-state geometry having only increased non-bonded interactions, but must instead occur by an intermediate possessing a combination of increased geometric deformations and increased residual repulsive interactions. The rotational barrier observed for a given compound will depend upon (a) the magnitude of the geometric change required between ground and transition state, and (b) the relative difficulty of the molecular distortion required to effect this change. In the light of the high ability of the naphthalene nucleus to sustain substantial distortion, the dramatic lowering of the rotational barriers of both 1,8-diphenylnaphthalene and 1,4,5,8-tetraphenylnaphthalene as compared with [3.3]paracyclophane and

[3.4] paracyclophane become understandable, because the cyclophanes have no possibility of phenyl-phenyl splaying.

The difference between the rotational barriers in the 1,8-diphenylnaphthalene and 1,4,5,8-tetraphenylnaphthalene derivatives is also a consequence of the involvement of the naphthalene-ring distortions in the phenyl-ring rotation. The tetraphenyl compound has crowding interactions at both pairs of peri positions, making this molecule more strained than the diphenylnaphthalene. The increased strain enhances the distortion of the naphthalene nucleus and consequently facilitates attainment of the rotational transition-state geometry. Evidence of this synergistic distortion is clearly seen by a comparison of the ground-state geometries of these two molecules, as determined by X-ray diffraction.¹⁸ The distribution of the distortions is somewhat different in these molecules as discussed elsewhere,¹⁹ but the total ground-state distortion is greatest for the tetraphenyl compound, resulting in a larger overall phenyl-phenyl splaying. Thus, the dihedral angle between the two phenyl rings in 1,8-diphenylnaphthalene is 20°, while that in 1,4,5,8-tetraphenylnaphthalene is about 36°.

A related example consistent with conjoint peri-distortion and ring rotation may be seen by comparison of the ease of racemization of the binaphthyl derivatives 8,8'-dicarboxy-1,1'-binaphthyl, 20, and 2,2'-dicarboxy-1,1'-binaphthyl, 21.



While numerous substituted binaphthyls have been studied,²⁰ the data for these two derivatives pose an anomaly. By comparison of their structures, 20 and 21 would be expected to have nearly comparable restrictions to a 180° rotation about the naphthyl-naphthyl bond. Resolved 20 has a half-life with respect to racemization of about 15 minutes at 50° , approximately the same as for binaphthyl itself, while 21 shows no change in optical activity after 8 hours at 175° .²⁰ The peri crowding in 20 is conducive to the naphthalene splaying interaction necessary for rotation, and in effect forces the ground-state geometry to be more like that of the transition-state.

Experimental.

Triphenylcinnamylphosphonium chloride, 11. Triphenylcinnamylphosphonium chloride was prepared by the method of Organic Syntheses.²¹ From 40 g (0.26 mole) of (3-chloropropenyl)benzene and 92 g (0.35 mole) of triphenylphosphine was obtained 101 g. (93%) of 11 (mp 224-226, lit.²² mp 224-226) which was used without further purification.

1-(3-Chlorophenyl)-4-phenyl-1,3-butadiene, 12. The procedure from Organic Syntheses²¹ for 1,4-diphenyl-1,3-butadiene was slightly modified for making the chlorinated derivative. Thus, 630 ml of 0.2 M lithium ethoxide (prepared from the dissolution of 2.1 g lithium wire in 1.5 l of absolute ethanol) was added with stirring to a solution of 50 g (0.121 mole) of 11 and 18.04 g (0.127 mole) of m-chlorobenzaldehyde in 150 ml of absolute ethanol. A deep red-orange color developed, which faded after the mixture had been stirred at room temperature for 45 minutes. Addition of 600 ml of H₂O precipitated the product, which was collected and washed with 150 ml of 60% aqueous ethanol. The crude diene was stirred with a solution of ethanol (20 ml) and refiltered to give 21 g (0.087 mole, 69%) of glossy, pale-yellow plates, which melted at 109-110° after recrystallization from ethanol-isopropyl alcohol and from cyclohexane: nmr δ (CDCl₃) 6.2-7.5(m); ir(nujol) 1009 cm⁻¹, 1092 cm⁻¹, 770 cm⁻¹; mass spec. 240.0706, 240.0706 calcd. for C₁₆H₁₃Cl.

1,2-Dibenzoyl-3-(3-chlorophenyl)-6-diphenylcyclohex-4-ene, 13.

When the Diels-Alder reaction of 12 with trans-dibenzoylethylene was carried out in gently refluxing isopropyl alcohol for 8 hours, a brown oil resulted ; however, the product was prepared in reasonable yield under more vigorous conditions. Thus, 18 g (0.075 mole) of 12 and 20 g (0.085 mole) trans -dibenzoylethylene were refluxed vigorously (no stirring; bath temperature = 136°) in 300 ml of isopropyl alcohol for 18 hours. The mixture was allowed to cool to 50° and the walls of the vessel scratched with a glass stirring rod to precipitate a white solid. The mixture was filtered at 50° , rinsed twice with 30 ml of warm isopropyl alcohol and refiltered. The solid was dissolved in acetone (1.5 ml / 1 g), filtered, and the filtrate evaporated slowly to dryness yielding 15.5 g (0.033 mole, 44%). The infrared spectrum showed the presence of two carbonyl peaks, a major peak at 1680 cm^{-1} and a minor one at 1697 cm^{-1} , both different from the starting material peak (1600 cm^{-1}). Repeated recrystallizations failed to yield a sharply melting material. When the reaction was carried out with 24 hours reflux, the product showed almost exclusively the 1680 cm^{-1} peak. Recrystallization from isopropyl alcohol-acetone gave a white, crystalline solid (mp= $136.5\text{-}139.5^{\circ}$); mass spec. 476.1542, 476.1543 calcd. for $\text{C}_{32}\text{H}_{25}\text{ClO}_2$. Aromatization of either the product with the two carbonyl peaks (presumably a mixture of isomers) or that with the single peak, by the method described below, gave similar good yields of compounds having identical spectra.

1,2-Dibenzoyl-3-(3-chlorophenyl)-6-phenylbenzene, 14. To a solution of 20.3 g (0.043 mole) of 13 in 130 ml of chloroform stirred at reflux was added dropwise (15 minutes) a solution of 90 ml of chloroform containing 4.3 ml of bromine. As the refluxing continued, large amounts of HBr were evolved. When the gas evolution had ceased (~ 30 minutes) the solvent was removed with a rotary evaporator to give a yellow-brown gummy substance which was crystallized by stirring overnight with absolute ethanol. Further purification was effected by stirring the finely powdered solid with 20 ml of methanol for 20 minutes, and washing with 5 ml of methanol to yield 18 g (0.038 mole, 89%) of a white, crystalline solid which was recrystallized from isopropyl alcohol-acetone to give opaque rods: mp 150-153°; ir (nujol) 1670 cm^{-1} ; mass spec. 472.1231, 472.1230 calcd. for $\text{C}_{32}\text{H}_{21}\text{ClO}_2$.

6-(3-Chlorophenyl)-2,3,6-triphenylisobenzofuran, 10. Zinc dust (7 g), activated by stirring with dilute NaOH solution, then washed with water and ethanol, was added with stirring to a refluxing solution of 7.5 g (15.9 mmole) of 14 and 7 g of NaOH in 165 ml of ethanol. Refluxing for short reaction times was found to give only partial conversion. During six hours reflux, the solution turned bright yellow-green, then faded. The reaction mixture was filtered into 150 ml of glacial acetic acid, and 20 ml of water was added to the filtrate. The solution was evaporated to about 25 ml, and the heterogeneous aqueous mixture was extracted twice with benzene. The combined organic portions were filtered through 15 g of anhydrous sodium sulfate, evaporated to a syrupy yellow liquid, and left standing overnight to yield 6.5 g

(14.2 mmole , 89%) of a brilliant-yellow solid having a powerful green fluorescence in benzene: mp 194.5-197°; ir (nujol) 1470 cm^{-1} , 1391 cm^{-1} , 855 cm^{-1} , no carbonyl; mass spec. 456.1282, 456.1281 calcd. for $\text{C}_{32}\text{H}_{21}\text{ClO}$.

Adduct of 10 with acrolein, 15. Freshly distilled acrolein (5 ml) was pipetted into a stirring, gently refluxing solution of 6.5 g (14.2 mmole) of 10 in 50 ml of benzene. After 30 minutes, an additional 2 ml of acrolein was added. Twenty minutes later, the bright yellow had faded to give a nearly colorless solution, and the reaction was stopped. The crude mixture was evaporated to dryness and crystallized from 10 ml of isopropyl alcohol to give a white product (6 g, 11.7 mmole, 83%); mp 148-151°; ir (nujol) 1725 cm^{-1} (carbonyl); nmr $\delta(\text{CDCl}_3)$ 9.3 (m, 1), 3.4 (m, 1), 2.5 (m, 2), 6.6-7.6 (m, 21); mass spec showed only peaks due to the retro-Diels-Alder product, 10.

Anal. Calcd. for $\text{C}_{35}\text{H}_{25}\text{O}_2\text{Cl}$: C 81.94, H 4.91, Cl 6.91.

Found: C 82.11, H 4.68, Cl 6.86.

5-(3-Chlorophenyl)-1,4,8-triphenyl-2-naphthaldehyde, 16. Anhydrous, gaseous HCl was bubbled for 25 minutes through a stirred solution of 7 g (13.7 mmole) of 15 in 50 ml of glacial acetic acid at 0°. The starting material largely dissolved, yielding a reddish solution. The reaction mixture was stirred for an additional hour without cooling after the addition of the HCl was stopped. The chilled mixture was filtered, and the filtrate rinsed with 8 ml of cold acetic acid. The crude yellow product (5 g, 10.1 mmole, 74%) was contaminated with 10, apparently due to a reversal of the Diels-Alder reaction of the previous step. Stirring with a small amount of isopropyl alcohol removed most of this

impurity. Recrystallization from isopropyl alcohol gave light-yellow crystals of 16: mp 208-210°; ir (nujol) 1683 cm^{-1} (aromatic aldehyde); mass spec. 494.1437, 494.1437 calcd. for $\text{C}_{35}\text{H}_{23}\text{ClO}$.

1-(3-Chlorophenyl)-4,5,8-triphenylnaphthalene, 9. When 0.2 g of 16 and 0.4 g of tris(triphenylphosphine)rhodium (I) chloride were heated to reflux in 4 ml of benzene, no reaction of the aldehyde was observed. Instead, the red rhodium dimer precipitated from solution. When 1 g of 16 was heated at 160-165° in 9 ml of benzaldehyde, the reaction was judged complete by tlc after 8 minutes. Chromatography of the crude mixture on silica gel with hexane as the eluent afforded 9 (0.80 g, 80%). Recrystallization from hexane gave clear prisms: mp 216-217°; nmr δ (CDCl_3) 7.5 (broad singlet, 4), 7.0 (broad singlet, 19); mass spec. 466.1490, 466.1488 calcd. for $\text{C}_{34}\text{H}_{23}\text{Cl}$.

Preparation of Carbinol, 8. All equipment was dried immediately before use in an oven at 150° overnight. The reagents were transferred to the reaction vessel in a dry box under argon. A positive pressure of argon was maintained in the reaction vessel throughout the course of the reaction. A solution of 0.23 g (0.5 mmole) of 9 in 5 ml of ether was combined with 0.04 g of lithium dust (Alfa chemical company, 140 mesh) and 2 drops of bromobenzene. The solution was refluxed with stirring for twenty minutes; a deep purple color was observed two minutes after the start of refluxing. The mixture was added to a solution of 1 ml of anhydrous acetone in 10 ml of ether and, after 5 minutes, hydrolyzed. Two successive preparative tlc runs using

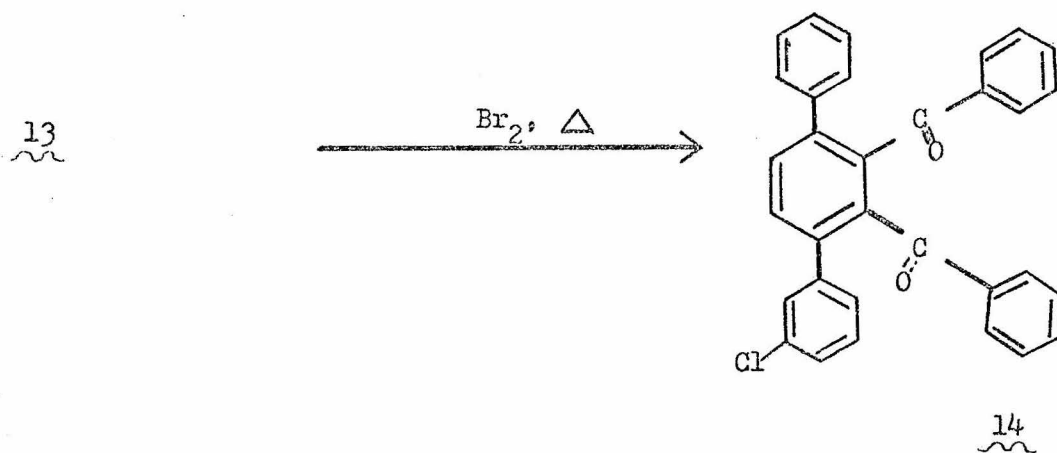
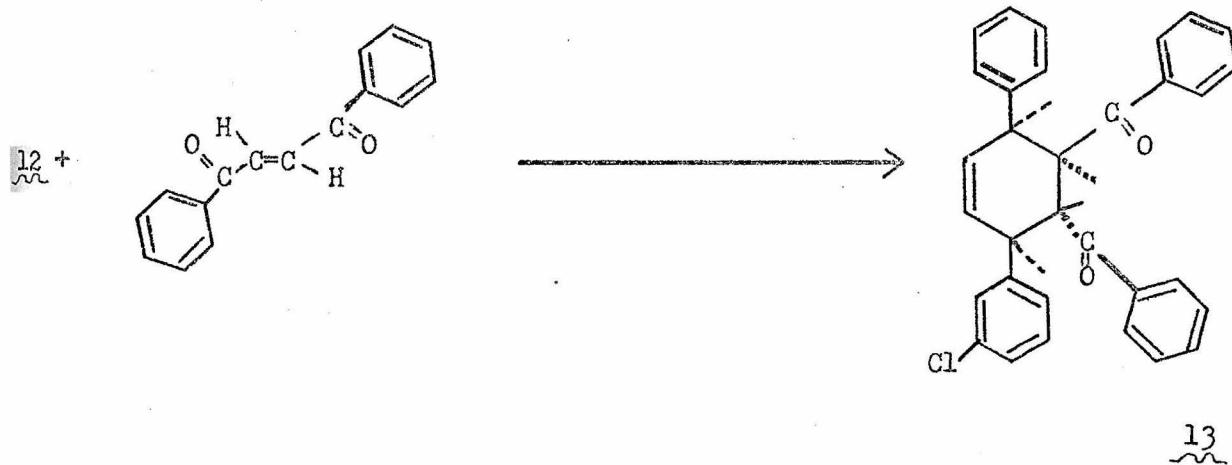
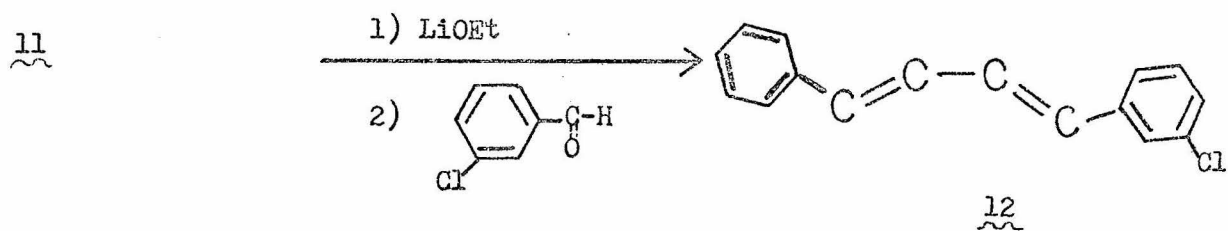
15% ether in benzene ($R_f = 0.45$) gave 0.14 g (57%) of 8 as clear oil: ir (nujol) 3590 cm^{-1} (O-H stretch); nmr δ (CDCl_3) 7.46 (s, 4), 6.85-7.15 (s, 19), 1.48 (s, 6), 1.90 (broad s, 1); C-13 nmr (in ppm relative to TMS, in CDCl_3) 31.4 (methyl), 81.0 (hydroxyl carbon); mass spec. 490.2293, 490.22965 calcd. for $\text{C}_{37}\text{H}_{30}\text{O}$.

Rotational Barrier Measurements.

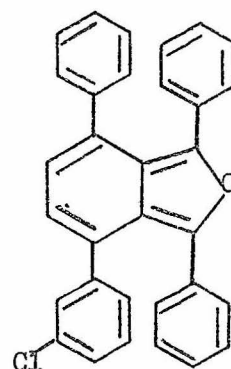
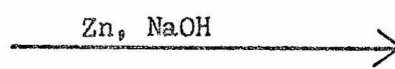
The spectra for the rotational-barrier measurement on 8 were obtained over a temperature range of 70° to -30° using a Varian Associates HR-220 nmr spectrometer. The temperature was determined for each measurement from the peak separations of standard samples of either methanol or ethylene glycol. The methyl signal from 8 broadened steadily from a sharp singlet at the high-temperature limit to the coalescence point at 5° . The peak separation reached a maximum of 3.6 Hz. at -10° . The natural linewidth of the methyl peak was taken to vary linearly from 1.1 to 1.5 Hz. over the temperature range examined. Computer simulated lineshapes were obtained with the program CLATUX,²³ and were visually matched to the experimental spectra. From the pre-exchange lifetimes, the free energy of rotation was calculated for each measurement using the equation $\Delta G^\ddagger = 4.575T(10.32 + \log T - \log K_r)$. Good agreement was obtained, particularly for measurements made in the coalescence region. From the values between -11° and $+38^\circ$, a ΔG^\ddagger of 14.9 ± 0.2 kcal/mole was obtained. Representative spectra are shown in Figure 2.

FIGURE 1

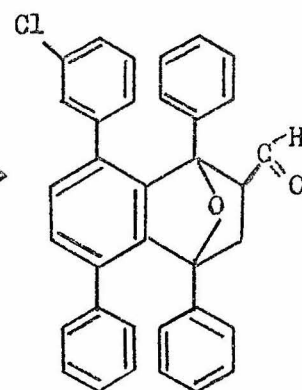
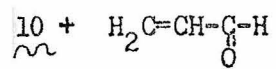
Reaction sequence for 1,4,5,8-tetraphenylnaphthalene derivatives



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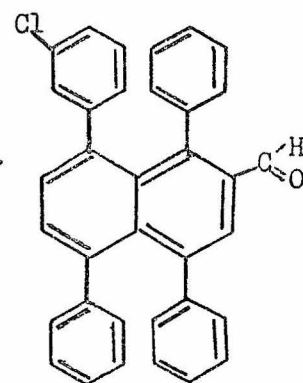
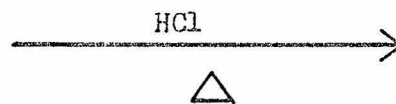


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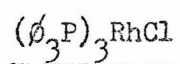


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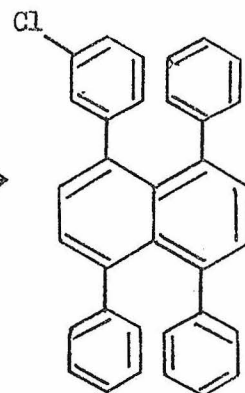
15
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16
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16
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benzonitrile, 160°

9
~9
~1) Li dust (140 mesh),
bromobenzene,

ether, reflux

2) acetone

3) water

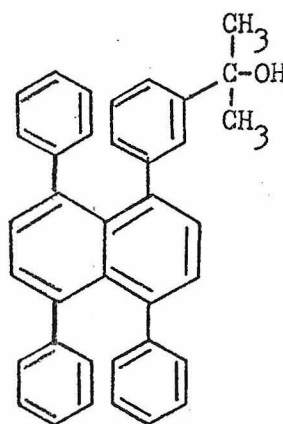
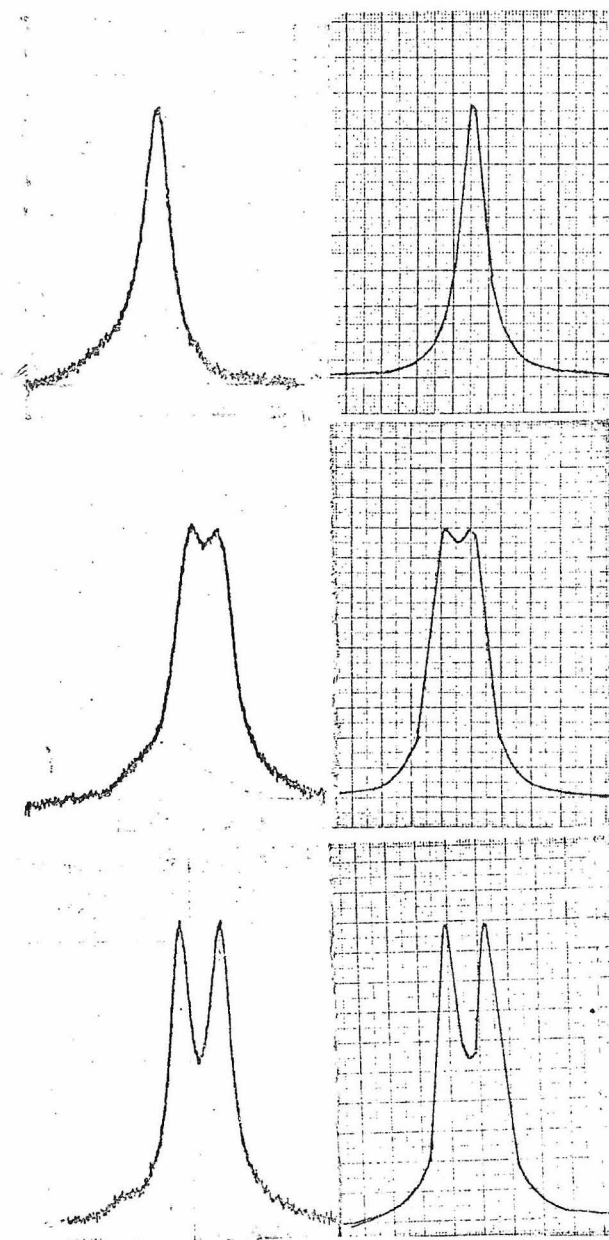
8
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FIGURE 2

Proton nmr spectra of the methyl signal of $\underline{8}$ in the coalescence region. The experimental spectra are shown at the left, with the matching computer-generated spectra given at the right.



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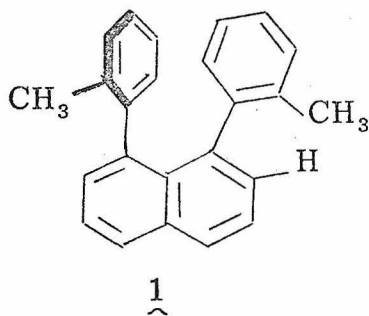
PART IV

Rotational Isomers of 1,8-Di-o-tolyl-naphthalene

Rotational Isomers of 1,8-Di-o-tolynaphthalene.

The 1,8-diphenylnaphthalenes have been shown by X-ray crystallography¹ to assume a conformation having the phenyl rings face-to-face, slightly splayed apart, and displaced to opposite sides of the naphthalene ring plane. The phenyl-naphthyl dihedral angles range from 60° to 70°. Due to steric restrictions, a high barrier to a 180° rotation about a phenyl-naphthyl bond was expected. Derivatives of 1,8-diphenylnaphthalene which bear a substituent at one meta position of each phenyl ring were expected to exist as cis and trans isomers. However, several such derivatives, including 1,8-di-(3-chlorophenyl)-naphthalene and 1,8-di-(3-methylcarboxyphenyl)naphthalene were isolated as single isomers.² Dynamic proton nmr studies of 1,8-diphenylnaphthalene derivatives have given values of 15-16.5 kcal/mole for a kinetic process in these molecules which was attributed to the rotational barrier about the phenyl-naphthyl bond, indicating that this process is rapid in solution at room temperature.³

The possibility of isolating cis and trans isomers in this system was intriguing. We prepared 1,8-di-o-tolynaphthalene, 1,



with the idea that the rotational barrier of this compound should be higher than that of other 1,8-diphenylnaphthalene derivatives because of unfavorable interaction of the methyl group with the adjacent naphthyl-ring proton in the rotational transition state. Such an interaction would tend to oppose in-plane splaying of the phenyl group during rotation.

We have succeeded in isolating cis and trans rotational isomers of this hydrocarbon. The difference in the thermodynamic stability of the two isomers has been determined, the barriers to their thermal interconversion have been measured, and an assignment of their stereochemistry has been made.

1,8-di-o-tolyl-naphthalene, 1, was prepared by a direct coupling of o-tolylmagnesium iodide with 1,8-diiodonaphthalene with a nickel acetylacetonate catalyst.⁴ The proton nmr spectrum of 1 showed two sharp singlets 1.85 ppm downfield from TMS, which were separated by 2 Hz. at 60 MHz. The chemical shift of the methyl groups for 1 is upfield from the methyl signal of toluene ($\delta = 2.32$) because of the ring current effects of the adjacent phenyl ring and the naphthyl ring. Two isomers, 1a, 1b, were separated from the reaction product by column chromatography on alumina. Each isomer gave a single methyl-group singlet in the proton nmr. The isomer 1a having the more downfield methyl signal was eluted last. The two isomers are stable in the crystalline state, but have a half life with respect to interconversion in solution of about one day at room temperature. Isomer 1a has the higher melting point (160°-162°), and the lower solubility in hexane; fractional crystallization from hexane gave enrichment in

1a, 1b melted over a large temperature range (120°-145°). When crystals of 1b were dropped on a hot plate at 135°, they melted immediately. Both isomers were identified by high resolution mass spectral analysis.

The kinetics for the interconversion of cis and trans rotamers were studied in CDCl₃ at 40° by proton nmr. A single isomer or mixture of isomers was allowed to equilibrate in the probe, and spectra were taken over a 24-hour period. First order kinetics were observed as expected. The equilibrium constant was found to be 3.21, giving a ground-state free-energy difference between the two rotamers of 0.73 kcal/mole. Isomer 1b was the more stable. The rate constants for rotation are given below.

$$k_{\underline{1b}-\underline{1a}} = 3.05 \times 10^{-5} \text{ sec.}^{-1}$$

$$k_{\underline{1a}-\underline{1b}} = 9.79 \times 10^{-5} \text{ sec.}^{-1}$$

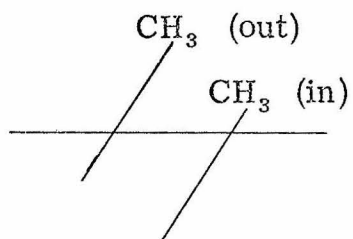
The rotational energy barriers, ΔG^\ddagger , were found to be about 8 kcal/mole greater than for 1,8-diphenylnaphthalene derivatives lacking ortho substitution. Values are given below.

$$\Delta G^\ddagger_{\underline{1b}-\underline{1a}} = 24.82 \text{ kcal/mole.}$$

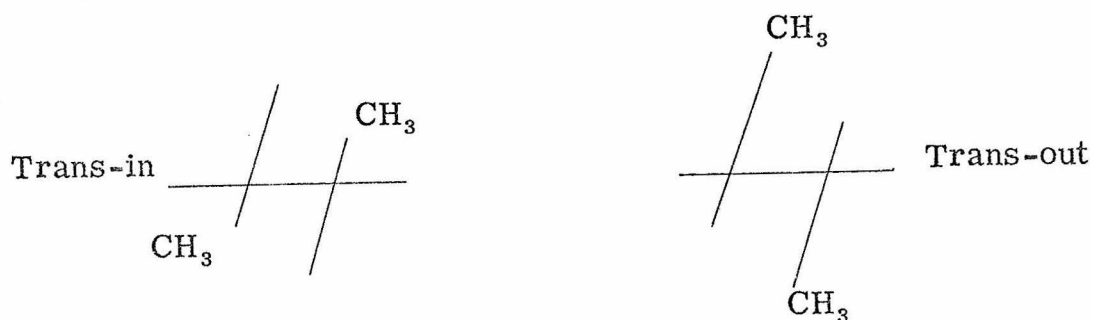
$$\Delta G^\ddagger_{\underline{1a}-\underline{1b}} = 24.09 \text{ kcal/mole.}$$

Assuming the solution geometry of this compound to be

qualitatively similar to that found for other peri-phenylnaphthalenes in the crystal, the two methyl groups of the cis isomer must occupy different positions, in and out. This is depicted below, where cis-1,8-di-o-tolyl naphthalene is viewed looking down along the plane of the phenyl rings toward the plane of the naphthalene ring.



If the two phenyl rings are flipping rapidly from one side of the naphthalene to the other, interconverting the two methyl groups, the resultant nmr signal would be a singlet with a shift corresponding to a 1:1 average of the two possible positions. The trans isomer should also have in and out methyl groups, but each trans molecule has both methyl groups simultaneously in or out.



Thus, there must be two isomers of the trans rotamer, an "in" isomer and an "out" isomer. Flipping of the rings interconverts the in and out isomers. Rapid interconversion will result in a single signal for the methyl groups of the trans isomer, but the average is not ex-

pected to be 1:1 since the in and out isomers of the trans rotamer should be of different energy. From steric considerations, the out isomer is expected to be favored and thus to contribute more heavily to the average signal. Unfortunately, it is not possible to determine which isomer is which based on the chemical shifts observed for their methyl groups, because of a superposition of two opposing shift effects for in and out methyl groups. The in methyl group is closer to the center of the adjacent phenyl ring, and experiences a larger diamagnetic shift due to this phenyl ring than that experienced by the out methyl group. However, the out methyl group has greater diamagnetic shielding from the nearby naphthyl ring. Consequently, the difference in the observed shift of the ortho methyl group in cis and trans rotamers is small.

If phenyl-ring rotation and phenyl-ring flipping were both stopped, 1,8-di-o-tolynaphthalene would exist as three distinct isomers: cis, trans-in and trans-out. Each of these three isomers would exist as a d,l-pair. The chemical-shift difference between an "in" methyl group and an "out" methyl group must be $>$ the observed shift difference between the methyl signals of cis and trans 1. Variable temperature nmr studies at 100 MHz. with both isomers of 1 showed no broadening of the methyl-group signals down to -90°C , indicating an upper limit on the flipping barrier of about 9 kcal/mole. The low barrier (< 9 kcal) to the flipping of the aromatic rings of 1 from side to side of the naphthalene plane and the higher barrier (~ 24 kcal) to ring rotation provides an interesting contrast to the recent study of 1,8-di-tert-butyl-

naphthalene, 2.⁵ For 2, the barrier to flipping of the tert-butyl groups to opposite sides of the naphthalene plane was reported to be > 25 kcal, while rotation of the tert-butyl groups was set at < 6.5 kcal. These results are not unreasonable. The relatively flat phenyl rings slide past each other easily (flipping), while the transition state for rotation involves a large increase in crowding with both the adjacent phenyl ring and the nearby naphthyl proton. The tert-butyl group may be viewed as relatively spherical, but more bulky and more crowded in the ground state. Rotation does not involve a substantial change in crowding, while flipping of tert-butyl groups through the ring plane forces these bulky groups closer together.

The nmr spectra of the phenyl-ring protons of isomers 1a and 1b are strikingly different, while the naphthyl-ring regions are essentially superimposable. 1a gives a sharp singlet for the phenyl-ring protons as does 1,8-diphenylnaphthalene, while the phenyl protons of 1b give a multiplet. Figure 1 shows the phenyl ring and methyl signals for each isomer.

For cis-1,8-di-o-tolyl-naphthalene, the meta phenyl-ring proton adjacent to the methyl substituent must be positioned over the plane of the adjacent phenyl ring 50% of the time (in), and outside the plane of the adjacent phenyl ring 50% of the time (out); the same is true of the ortho and meta protons on the side of the phenyl ring opposite the methyl group. For the trans rotamer, the two flipping isomers are expected to be of unequal energy, and, as a result, the meta proton adjacent to the methyl group must spend a different amount of time over the plane of the adjacent phenyl ring than the ortho and meta protons opposite the methyl group, and these protons must therefore experience different diamagnetic ring current shifts. The non-equivalent protons of the trans rotamer must give rise to the observed multiplet. The phenyl-ring protons of the cis rotamer must give rise to a single peak, as do the phenyl-ring protons of unsubstituted 1,8-diphenyl-naphthalene. We therefore assign the trans configuration to isomer 1b and the cis configuration to isomer 1a. This assignment is consistent with the observation that isomer 1a is less favorable than isomer 1b, because the cis conformation would be expected to be more crowded. With rapid flipping of the phenyl rings at room temperature, the trans rotamer must exist as a racemic mixture, while the cis rotamer must be non-symmetric. We have not attempted to resolve the rotamers.

It has previously been reported^{3b} that dramatic temperature-dependent changes occur in the phenyl-ring portion of the proton nmr spectra of 1-phenyl-8-(3-chlorophenyl)naphthalene, 3, and 1,8-di-

(3-chlorophenyl)naphthalene, 4, while the naphthyl-ring portion of the spectrum was nearly independent of temperature. The phenyl-ring region of 1,8-diphenylnaphthalene shows only a small temperature dependence. It is now apparent that these phenomena must arise from chemical-shift differences due to unequally populated rotamers and flipping conformers of 4 and unequally populated flipping conformers of 3 which are present when phenyl ring rotation becomes frozen out on the nmr timescale as the temperature is lowered.

The isomers 1a and 1b must be rotamers having rapid flipping. It is not possible that 1 has fast ring rotation and that the isomerism observed is due to a slow flipping of the phenyl rings from one side of the naphthalene plane to the other, because rotation interconverts all isomers. It is also not possible that 1a and 1b are non-rotating flipping isomers, since slow flipping on the nmr timescale would make the two meta protons highly non-equivalent in the proton nmr spectrum; a singlet phenyl proton peak should not be obtained. The same is true of 1,8-diphenylnaphthalene: ring flipping must be rapid. By making use of the ring-current shift tables of Bovey and the X-ray coordinates for 1,8-diphenylnaphthalene, we have calculated the shift difference between the two meta protons of this compound to be about 0.65 ppm in the absence of interconversion by flipping.

Isomerism in 1,8-Diarylnaphthalenes

Derivatives of 1,8-diphenylnaphthalene can be grouped into four classes according to the number of isomers which they must have. The four classes are outlined in Table I. 1,8-Di-o-tolyl-naphthalene is seen to be an example of Class III. The most simple member of each class is described in the Table. All other possible 1,8-diaryl-naphthalenes more highly substituted in the phenyl rings fall into one of these four isomerism classes. For example, derivative 5 would have Class IV isomerism properties and the derivative 6 would show Class I isomerism.

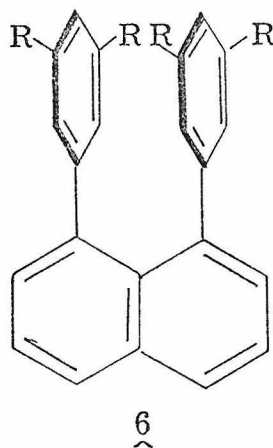
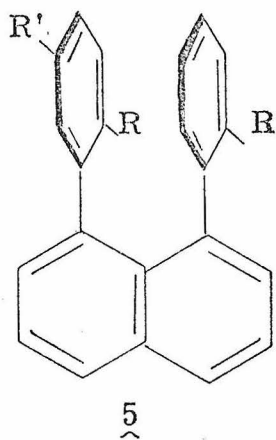


TABLE I
Isomerism in the 1, 8-Diarylnaphthalenes.

| Class | Phenyl ring
Substitution | Total Number of
Isomers Possible | Total Number of Rotamers
(assuming fast flipping). |
|-------|--|---|---|
| I | None | No geometric isomers;
one pair of <u>d, l</u> -isomers. | None |
| II | One <u>ortho</u> or
<u>meta</u> substit-
uent on one
phenyl ring. | 2 isomers: in and out.
Each isomer will be
a <u>d, l</u> -pair. | No geometric rotamers.
One pair of <u>d, l</u> -rotamers. |
| III | One <u>ortho</u> sub-
stituent or one
<u>meta</u> substituent
in each phenyl
ring, with the
substituents
identical. | 3 isomers: <u>cis</u> ,
<u>trans</u> -in, <u>trans</u> -
out. Each isomer
will be a <u>d, l</u> -
pair. | 2 rotamers: <u>cis</u> and <u>trans</u> .
The <u>trans</u> rotamer will be
a <u>d, l</u> -pair. |
| IV | One <u>ortho</u> sub-
stituent or one
<u>meta</u> substit-
uent on each
ring, where
the substituents
are not equiva-
lent; or one <u>ortho</u>
substituent on one
ring and one <u>meta</u>
substituent on the
other ring. | 4 isomers: <u>trans</u> -in,
<u>trans</u> -out, <u>cis</u> -R-in-
R'-out, <u>cis</u> -R'-in-R-
out. All isomers will
be <u>d, l</u> -pairs. | 2 rotamers: <u>cis</u> and <u>trans</u> .
Both rotamers will be <u>d, l</u> -
pairs. |

Experimental.

1,8-di-o-tolynaphthalene was prepared using an organo-nickel-catalyzed coupling reaction.⁶ Thus, 4.4g (20 mmol) o-tolyl-magnesium iodide was added to a solution containing 0.76g (2 mmol) of 1,8-diiodonaphthalene⁶ and 0.01g nickel acetylacetonate in 20 ml 1:1 ether-benzene at -15° to -10°C during 1½ hrs. After an additional 2 hrs. the cooling bath was removed, and the stirred mixture allowed to warm to room temperature overnight. After shaking with a saturated solution of ammonium chloride, the organic layer was reduced to about 3 ml volume and subjected to column chromatography on silica gel with hexane as eluent to give 1 as a mixture of isomers (0.06g, 10%). The yield of this reaction was considerably lower than for other peri-phenylnaphthalenes obtained by the same procedure, presumably because of the increased steric crowding of 1. Chromatography on a 16" x ½" column of alumina with 7½% benzene in hexane as eluent gave a separation of 1a and 1b.

1a: nmr δ (CDCl₃); 6.8 (s, 6), 1.85 (s, 6).

mass spec. 308.1566, 308.1565 calcd. for C₂₄H₂₀

Anal.⁷ Calcd. for C₂₄H₂₀: C 93.51, H 6.49.

Found: C 93.20, H 6.61.

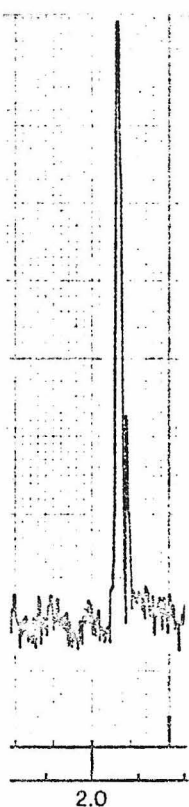
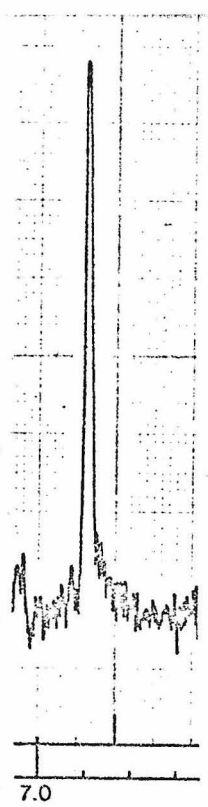
1b: nmr δ (CDCl₃); 6.7-7.0 (m, 6), 1.85 (s, 6).

mass spec. 308.1566, 308.1565 calcd. for C₂₄H₂₀.

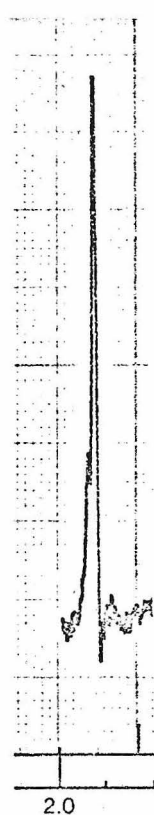
The nmr spectra were obtained on a Varian Associates XL-100 nmr spectrometer. Kinetics were obtained by equilibration of one isomer of 1 in the probe at $40^{\circ}\text{C} \pm 1^{\circ}$ during a period of 24 hrs. Rate constants were obtained by using an expression for a first order reversible reaction.⁸ The rotational barrier at 40°C was calculated using the expression $\Delta G^{\ddagger} = 4.575T(10.32 + \log T - \log k_r)$. The low temperature spectra were obtained in CD_2Cl_2 as a solvent.

FIGURE 1

Proton nmr spectra of the two rotational isomers of 1,8-di-o-tolyl-naphthalene. a) Compound 1a with the singlet phenyl-ring peak.
b) Compound 1b. The phenyl-ring protons are non-equivalent; several small peaks are observed in place of the singlet of isomer 1a. The small sharp peak at the side of the methyl singlets of both 1a and 1b is due to the persence of a small percentage of the other isomer.



a)



b)

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PART V

Determination of the Strain Energy of 1,8-Diphenylnaphthalene

Determination of the Strain Energy of
1, 8-Diphenylnaphthalene.

Summary

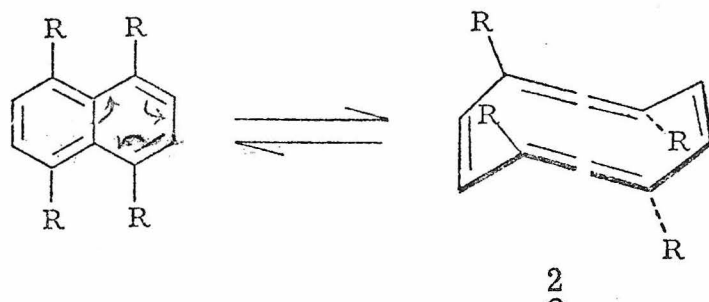
The forced proximity of the phenyl substituents results in considerable steric overcrowding in 1, 8-diphenylnaphthalene 1 as evidenced by X-ray analysis. We have undertaken a study to obtain a quantitative measurement of the energy due to overcrowding by comparison of the heat of formation of this compound with that of the isomer 1, 5-diphenylnaphthalene, and with the value calculated by group additivity for a hypothetical strain-free diphenylnaphthalene. A value for ΔH_c for 1 has been obtained by combustion calorimetry, and a total strain energy of 13-14 kcal/mol has been determined. Some implications of steric interactions in peri-substituted naphthalene derivatives are discussed.

Introduction

While fairly extensive studies have been made on the strain energy resulting from the distortion of bond angles, especially in small-ring compounds, little data is available on strain due to crowding interactions. Non-bonded interactions are, on the whole, not well understood, and a variety of equations, mostly empirical, are currently in use for calculation of the shapes of interaction-potential curves. Quantitative measurements of ground-state strain energy in molecules for which the geometry has been precisely determined should facilitate better understanding of the nature and magnitude of non-bonded forces.

Because the distance between C1 and C8 in naphthalene is about $2.44 \text{ \AA}^{\circ 1}$, and because the exocyclic bonds at these positions are parallel, placement of two substituents other than hydrogen (van der Waals radius $1.2 \text{ \AA}^{\circ 2}$) at these sites must introduce a state of stress into the molecule. Peri-substituted naphthalenes have been employed in many studies³ on the effects of molecular crowding, but no determination of the size of the strain energy of any derivative of this system has yet been made.

The question of the magnitude of the strain in this system is of special interest for another reason. The transition between naphthalene and the valence tautomer 2 would be an orbital-symmetry allowed disrotatory process.



From an examination of molecular models, the cyclic framework of $\underline{2}$ is expected to be essentially strain free. Note that in $\underline{2}$ the overcrowding of peri substituents should be completely relieved. If the total strain energy from the two sets of peri sites could be made sufficiently large as to approach the aromatic resonance energy of naphthalene (usually cited⁴ as 61 kcal/mol), it should be possible to push the naphthalene structure into equilibrium with $\underline{2}$.

It is of significance that recent X-ray studies⁵ on peri-substituted naphthalene derivatives show that the crowding interactions find relief by substantial distortions which are seen to lie along the reaction coordination to $\underline{2}$. These distortions include especially out-of-plane splaying of the peri substituents, a large increase in the naphthalene C1-C9-C8 angle, and a stretching of the C9-C10 bond. Furthermore, unexpectedly low barriers to rotation about naphthyl-peri-substituent bonds have been interpreted⁶ as indicating that these naphthalene-ring distortions increase in magnitude during the intramolecular rotational process. There is evidence that progress over the pathway connecting naphthalene with $\underline{2}$ is in fact facile. An attempted preparation of $\underline{2}$ in which all substituents were hydrogen

gave immediately naphthalene, even at low temperatures.⁷

The solution and crystal geometry of 1,8-diphenylnaphthalene 1 and several closely related derivatives have been studied;^{5c,d,e} we report here the strain energy of 1 as determined by combustion calorimetry. The crowding energy is expected to be given by the difference between the heat of formation of 1 and that of the isomer 1,5-diphenylnaphthalene, or, alternatively, by the difference between the heat of formation of 1 and that calculated for an uncrowded diphenylnaphthalene by group additivity methods.

Experimental

1,8-Diphenylnaphthalene 1 was prepared in a quantity of 1.8 g by scaling up the reaction described elsewhere.⁸ The product was subjected to column chromatography on silica gel with hexane as eluent and recrystallized twice from hexane to yield large needles which were placed in a vacuum desiccator for three days before calorimetric analysis.

1,5-Diiodonaphthalene was prepared in a yield of 20% by the Sandmeyer reaction. Purification was accomplished by shaking an ether solution of the product with aqueous sodium thiosulfate, filtration of the organic layer through silica gel, and by boiling the solution with activated charcoal. Crystallization from isopropyl alcohol gave tan needles, mp 143-146° (lit⁹ mp 147°).

1,5-Diphenylnaphthalene 3. Addition of 50 mmol of phenylmagnesium iodide to a solution of 2.95 g (7.8 mmol) of 1,5-diiodonaphthalene and 0.02 g of nickel acetylacetonate in 45 ml of 2:1 benzene-ether held at -15 to -11° was carried out over a period of 1.5 hours. After being stirred an additional 2.5 hours at -10°, the mixture was allowed to warm to room temperature overnight. After hydrolysis, the organic solvent was evaporated and the residue triturated with ether, recrystallized once from hexane, and subjected to chromatography on silica gel with hexane as the eluent. After six successive recrystallizations from hexane, the white needles (mp 222-223.5, lit¹⁰ mp 220-222°) were placed in a vacuum desiccator for three days.

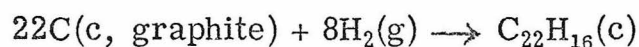
Combustion measurements were carried out¹¹ in an oxygen-bomb calorimeter. The compound was pelletized, weighed into a platinum crucible, and wetted with a few drops of mineral oil having a heat of combustion of -10.995 ± 0.81 cal/g. A cotton fuse was used to ignite the compound. The combustion was initiated by an electrical discharge through a platinum wire. The combustion was performed under an oxygen pressure of 450 psi. In some experiments, a small amount of unburned carbon was observed. This was weighed and a correction based on the heat of formation of CO_2 from graphite was applied. The combustion data for 1,8-diphenylnaphthalene is summarized in Table I. Thermodynamic values¹² are given below.



$$\Delta E_{\text{c}}^{\circ}/\text{m} = -9533.66 \pm 1.80 \text{ cal/g}$$

$$\Delta E_{\text{c}}^{\circ} = -2672.95 \pm 0.50 \text{ kcal/mol}$$

$$\Delta H_{\text{c}}^{\circ} = -2675.32 \pm 0.50 \text{ kcal/mol}$$



$$\Delta H_{\text{f}(\text{c})}^{\circ} = 59.68 \pm 0.50 \text{ kcal/mol}$$

The combustion of 1,5-diphenylnaphthalene is still in progress.

In order to make meaningful comparisons, $\Delta H_{\text{f}}^{\circ}(\text{g})$ must be obtained. Measurements of $\Delta H_{(\text{sub})}$ are still in progress. Molar heats of crystallization, per carbon atom, of polycyclic aromatic hydrocarbons have been found to fall within a relatively narrow

TABLE I

Combustion Data for 1,8-Diphenylnaphthalene

| Run | 1 | 2 | 3 | 4 |
|---|----------|----------|----------|----------|
| m(compound)/g | 0.20433 | 0.23255 | 0.21463 | 0.21504 |
| m(oil)/g | 0.10530 | 0.09255 | 0.09772 | 0.11039 |
| m(cotton)/g | 0.00373 | 0.00312 | 0.00333 | 0.00310 |
| $\Delta t/K = (t_f - t_i) + \Delta t_{\text{corr}}/K$ | 0.87255 | 0.90925 | 0.67450 | 0.91202 |
| E(calor)/(- Δt_c)/cal | -3118.14 | -3249.29 | -3125.11 | -3220.64 |
| $\Delta E(\text{contents})/\text{cal}$ | -4.06 | -4.20 | -4.07 | -4.24 |
| $\Delta E(\text{ign})/\text{cal}$ | 0.78 | 0.78 | 0.78 | 0.72 |
| $\Delta E(\text{correction})/\text{cal}$ | 1.17 | 1.21 | 1.18 | 1.18 |
| $\Delta E(\text{cotton})/\text{cal}$ | 15.12 | 12.89 | 13.50 | 12.89 |
| $\Delta E(\text{oil})/\text{cal}$ | 1159.18 | 1022.02 | 1074.42 | 1219.29 |
| $\Delta E(\text{soot})/\text{cal}$ | -4.69 | 0.0 | -6.65 | 0.0 |
| m' $\Delta E_c^\circ/M$ (compound)/cal | -1950.67 | -2216.60 | -2045.96 | -2050.75 |
| $\Delta E_c^\circ/M$ (compound)/cal g ⁻¹ | -9537.79 | -9527.75 | -9532.50 | -9536.61 |

range.¹³ We have used the averaged values for biphenyl and naphthalene (1.62 kcal/carbon atom and 1.73 kcal/carbon atom) to provide an estimate of 37 kcal/mol for $\Delta H_{(\text{sub})}$ for diphenylnaphthalene. This gives a $\Delta H_f^\circ(\text{g})$ for 1 of 97 kcal/mol. The error in the estimation of the $\Delta H_{(\text{sub})}$ could be as high as 3-4 kcal/mol.

Results

The group increment for the change from aryl-H to aryl-phenyl may be calculated¹⁴ from the difference in the heats of formation of benzene and biphenyl. The value is 23.7 kcal/mol.

$\Delta H_f^\circ(g)$ for an unstrained diphenylnaphthalene is obtained by summing the heat of formation of naphthalene (36.25 kcal/mol)¹⁵ with twice the phenyl-group increment to give 83.6 kcal/mol. The strain energy of 1,8-diphenylnaphthalene is thus calculated to be about 13-14 kcal/mol.

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PART VI

C-13 NMR. Steric Effects in 1,8-Diphenylnaphthalene

C-13 NMR. Steric Effects in 1, 8-DiphenylnaphthaleneSummary

The C-13 nmr spectrum of the sterically crowded 1, 8-diphenylnaphthalene 1 is reported. Partial shift assignments for 1-phenylnaphthalene 2 are also made.

The chemical shifts are found to be a good indicator of dihedral angle in diphenyl-type compounds. Thus, the C2 naphthyl and ortho-phenyl carbon resonances of 1 show substantial steric-related downfield shifts which are consistent with the near-perpendicular character of the naphthyl- and phenyl-ring planes. An upfield shift of the para-phenyl carbon atom of 1 is also correlated with this perpendicular conformation, and apparently results from steric inhibition of resonance. Substantial distortions in the naphthalene framework of 1, found by X-ray analysis, have no appreciable effect on the spectrum.

Introduction

The imposed proximity of the substituents of 1,8-disubstituted naphthalenes gives rise to unusual conformational and chemical properties for derivatives of this system.¹ X-ray analysis has shown² that in the crystal the phenyl rings of the 1,8-diarylnaphthalenes are face to face, splayed apart, and twisted somewhat away from being perpendicular to the naphthalene nucleus. Significant distortions occur throughout the naphthalene framework in 1,8-diphenylnaphthalene. These include bond lengthening near the peri substituent (compared with an unsubstituted naphthalene molecule) and bond shortening at the end opposite the substitution. The overall result appears to be a redistribution of electrons whereby the electron density is reduced at the overcrowded, distorted 1,8 carbon atoms, and increased towards the opposite peri carbons.^{2a,3}

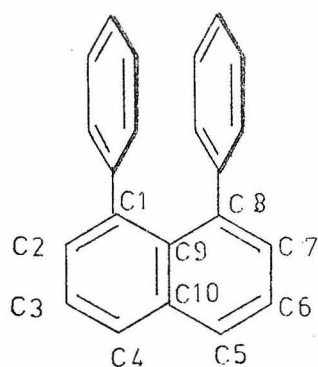
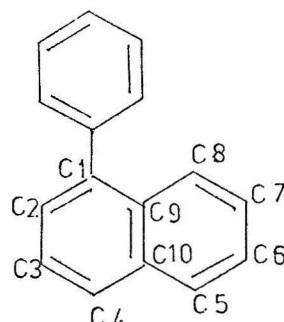
Many investigations have shown that C-13 nmr is a sensitive tool for the study of steric crowding. Steric-induced C-13 shifts (the "gamma" effect) have been observed with a variety of crowded systems⁴ and have been ascribed to electronic perturbations in C-H bonds which result from non-bonded interactions at the hydrogen atom.⁵ The effect is accentuated in cyclic hydrocarbons.⁶ It is also clear that C-13 chemical shifts reflect π -electron densities.⁷ We have undertaken to study the C-13 shifts of 1,8-diphenylnaphthalene to see what influences result from crowding effects in this system, including possible evidence for electronic redistribution in the naphthalene and/or phenyl rings.

Peak Assignments

The proton-bearing phenyl-ring carbons of 1 were readily distinguished from those of the naphthyl ring by selective proton decoupling which takes advantage of the fact that the phenyl protons are shifted 0.5 ppm upfield from the naphthyl protons because of the ring-current effect of the adjacent phenyl ring. The signal from the para-phenyl carbon is distinguishable from those of the ortho and meta carbons by its lower intensity. Deuterium labeling at the meta position allowed differentiation between the ortho and meta carbons. Atoms C2, C3 and C4 of the naphthyl ring were assigned by a series of selective proton decoupling experiments. The quaternary carbon atoms were identified by their intensity and shift range, and were grouped into two pairs.

Limited peak assignments, sufficient for useful comparisons with the 1,8-diphenylnaphthalene system, were made on 1-phenylnaphthalene 2. Because the phenyl proton peaks of 2 are superimposed on those of the naphthyl protons, selective decoupling experiments on this molecule were not possible. 1-(Phenyl-d₅)-naphthalene was prepared to allow a classification of the C-13 peaks as either phenyl or naphthyl. The para - phenyl peak was again distinguishable from the ortho and meta peaks by its intensity.

Spectral assignments for 1 and 2 are summarized in Table I. Assignments for biphenyl and naphthalene, which were determined previously by deuterium-labeling studies,⁸ are also shown.

TABLE IC-13 Chemical Shifts in ppm Relative to TMS11,8-diphenylnaphthalene 12

| | <u>phenyl ring</u> | <u>naphthyl ring</u> | <u>quaternary</u> |
|-------|--------------------|----------------------|------------------------|
| ortho | 129.7 | C2 131.0 | C9, C10 135.4
129.3 |
| meta | 127.0 | C3 125.1 | |
| para | 125.6 | C4 128.4 | C1, Ph1 143.0
140.4 |

1-phenylnaphthalene 2

| | <u>phenyl ring</u> | <u>naphthyl ring</u> | <u>quaternary</u> |
|------|--------------------|----------------------|------------------------|
| | 128.2 | 128.1 | C9, C10 133.8
131.6 |
| | 130.0 | 127.6 | |
| | | 126.9 | C1, Ph1 143.0
140.4 |
| para | 127.1 | 126.0 (X 2) | |
| | | 125.7 | |
| | | 125.4 | |

TABLE I (cont'd)

| | <u>Biphenyl</u> | <u>Naphthalene</u> | <u>Benzene</u> |
|-----------------|-----------------|--------------------|----------------|
| ortho | 127.6 | C1 128.3 | 128.7 |
| meta | 129.2 | C2 126.1 | |
| para | 127.7 | C9 133.9 | |
| qua-
ternary | 141.7 | | |

Discussion

The C3 and C4 naphthyl carbon atoms of 1 do not show large shift differences compared with the corresponding atoms of naphthalene; if an electronic redistribution has taken place in the naphthalene framework it apparently is not evidenced in the C-13 spectrum.

The chemical shifts of the phenyl ring hydrogens of 1 are dominated by the effect of the ring current of the adjacent phenyl ring; application of the anisotropy tables given by Bovey⁹ and the coordinates from the crystal geometry of 1^{2c} allow accurate calculation of the shift of the phenyl protons of 1 compared with those of 1-phenylnaphthalene. However, the C-13 shifts of the phenyl rings of 1 do not correlate well with calculations based on ring-current effects. (The calculated ring-current shifts are: C-ortho, -0.75 ppm; C-meta, -0.75 ppm; C-para, -0.65 ppm). This lack of correlation stems from the fact that the ring-current effect should be the same for any nucleus at a given spatial position, and C-13 has a relatively much larger range of shifts due to other factors than does H-1. This overshadowing of the ring-current effect for the carbon chemical shifts is consistent with expectation based on previous reports.^{10, 11, 12}

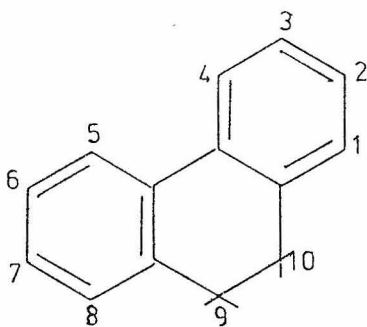
Two striking downfield shifts are observed in the C-13 spectrum of 1. The naphthyl C2 carbon comes into resonance 4.9 ppm downfield compared with C2 in the unsubstituted naphthalene molecule, and is downfield by 2.9 ppm from the lowest field naphthyl-ring resonance of 1-phenylnaphthalene. The ortho-phenyl carbon in 1 is shifted downfield by 2.1 ppm compared with the corresponding atom in bi-

phenyl; the shift is 2.85 ppm downfield from that expected for the ortho peak when an allowance is made for the ring-current effect. These shifts may be interpreted in terms of the relatively perpendicular arrangement of the naphthyl- and phenyl-ring planes of this system, for which an angle of 57° has been determined in the crystal,^{2c} and for which uv¹³ and proton evidence indicates a similar solution conformation.

The dihedral angle of biphenyl in solution has been under controversy: measurements obtained by several techniques^{14a,b} including uv^{14b} gave values of 20° - 31° , while estimates using other methods^{14c,d} indicated a smaller value. An increase in the dihedral angle increases the distance, and consequently decreases the nonbonded interactions, between the ortho protons of biphenyl-type compounds. Furthermore, this change affects the angle made by the force vector between these two hydrogen atoms and the C2-H2 bond. Both of these factors are expected to result in a more downfield shift of the ortho carbon atom. The formula due to Grant⁵ for sterically induced C-13 shifts is $\delta = 1680 \cos \theta \exp (-2.671r)$, where r is the distance between two nonbonded hydrogen atoms, and θ is the angle between the C-H bond axis and a line drawn between the two interacting hydrogens. We have calculated the change in distance between ortho hydrogens, and in θ , as a function of the dihedral ring angle, ϕ , in biphenyl. The results are shown in Figure 1. Relative steric shifts as a function of ϕ obtained by using Grant's⁵ formula, are shown in Figure 2. The shift difference predicted to accompany a change in dihedral angle from about 20° or 30° to about 60° falls in

the range of 2-4 ppm downfield, in line with the differences found between biphenyl and 1.

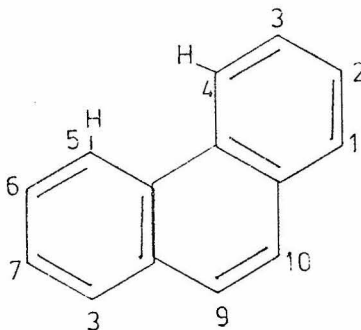
In light of this calculation of a correlation of dihedral angle and ortho C-13 shift, it is of interest to compare the chemical shift of the ortho carbon of biphenyl with that of C4 in 9,10-dihydrophenanthrene, 3. The situation with 3 is just opposite that of 1; instead of the aryl rings being constrained from varying by more than a small amount away from perpendicularity, the rings of 1 cannot exceed a dihedral angle of about 16° away from coplanarity.



3

The C4 peak¹⁵ is shifted in the direction expected, falling upfield by about 3.7 ppm compared with the biphenyl ortho resonance.

Another model compound is phenanthrene, 4, for which the rings must be coplanar.



4

The C4 shift in this molecule¹⁶ lies > 5 ppm upfield compared with the α - carbon resonance in naphthalene.

The chemical shift of the para-phenyl carbon of 1 is upfield by 2.1 ppm compared with the corresponding peak in biphenyl, and 1.5 ppm upfield from the para-phenyl peak of 2. This shift is interesting. Steric effects at this site can be ruled out, because the phenyl-phenyl splaying places C4 too far from the adjacent phenyl ring for it to experience crowding. The ring-current effect calculated for this atom accounts for only a part of the shift. The phenyl rings in 1 exhibit no appreciable warping,^{2c} indicating that the induced shift is not due to structural distortions.

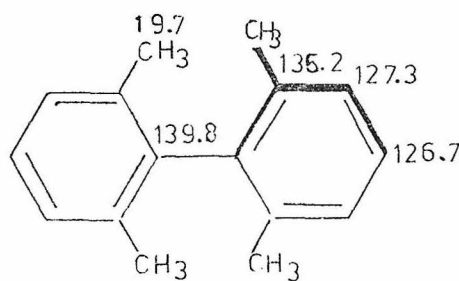
Previous studies have demonstrated that para carbon shifts reflect closely the electronic character of ring substituents: a Hammett plot shows a good correlation between σ_{para} and $\Delta\text{C-13}$.¹⁷ Furthermore, para C-13 shifts have been shown to provide a measure of steric inhibition of resonance. For example, in derivatives of aniline and nitrobenzene, the substituent additivity relationship breaks down for calculation of the shift of the para carbon atom, when applied to derivatives having substitution ortho to the amino or the nitro group.¹⁸ The para carbon shifts in a series of ortho -substituted phenyl ketones have been correlated with the size of the substituent, with the observed shifts being taken as a measure of the twist angle of the carbonyl group.¹⁹

The para-phenyl C-13 shift induced in 1 most likely results from an inhibition of resonance due to the inability of the rings to

approach coplanarity. The relatively perpendicular arrangement of the rings in 1 as well as in o-terphenyl and cis-diphenylethylene was observed^{2a} to simulate the effect of an alkyl group in the proton nmr spectrum. The C-13 peak of 1 is shifted upfield into the region of the para resonances of the alkylbenzenes.²⁰ The dihedral ring angle of 2 would be expected to be smaller than that of 1, while interactions with the peri hydrogen atom should make the angle larger than that of biphenyl. The shift of the para-phenyl carbon in 2 lies between those of 1 and biphenyl.

We have measured the para-phenyl carbon resonance of hexaphenylbenzene, which, like 1, should have a large dihedral angle along with a ring-current shift. The para peak lies upfield from that of the para carbon of biphenyl by 2.7 ppm. We have also obtained the spectrum of 2,2',6,6'-tetramethylbiphenyl, 5, which is expected to have a larger dihedral angle than biphenyl, but no ring-current shift.

Assignments are shown below.



5

Based on group-additivity values²¹ for two meta-methyl groups, the para carbons of 4 are predicted to give a signal 0.38 ppm upfield from those of biphenyl. The observed shift is upfield by 1.0 ppm, indicating an induced shift of about 0.6 ppm, which may be attributed to inhibition of resonance.

Experimental.

Carbon-13 nmr spectra were obtained with a Varian Associates XL-100 NMR Spectrometer, with the exception of the spectrum of 1,8-di-(3-deuteriophenyl)-naphthalene, which was measured with a Varian Associates HR-220 NMR Spectrometer. Selective decoupling experiments were performed using 0.5 watts decoupling power at a bandwidth of 10 Hz. The naphthyl carbons of 1 were assigned by a series of decoupling experiments in which the decoupling frequency was centered first on the phenyl ring protons, and then moved downfield by steps of 10 Hz. for each of 11 successive runs. All spectra were obtained at a concentration of 0.5 M in CDCl₃. However, it was observed that varying the concentration of 1 between 0.1 M and 1.0 M had no appreciable effect on shift values. All shifts were measured relative to TMS as an internal standard.

1,8-Diphenylnaphthalene 1 was prepared by an organonickel-catalysed Grignard-halide coupling as described elsewhere.²²

1-(Phenyl-d₅)naphthalene 2 was prepared by a Grignard-halide coupling reaction.²² Thus, 4.9 g (30 mmol) of bromobenzene-d₅ (Aldrich Chemical Company) was allowed to react with 0.73 g of magnesium turnings, and the resultant reagent was added dropwise to a stirred solution of 1.3 g (5 mmol) of 1-iodonaphthalene and 0.1 g of nickelacetylacetonate at -15° to -10°. After a reaction time of 4 hours, the mixture was hydrolysed and subjected to column chrom-

atography on silica gel with hexane as eluent and gave 0.86 g (82%) of 2 as a clear, viscous oil. Mass spec. 209.1251, 209.1253 calcd. for $C_{16}H_7D_5$.

1,8-Di-(3-deuteriophenyl)naphthalene. 1,8-Di-(3-chlorophenyl)-naphthalene 3 was obtained by an organonickel-catalysed coupling reaction.²² The product 3 reacted readily with lithium using conditions recommended for hindered chloro groups.²³ Thus, when 0.35 g (1 mmol) of 3 in 5 ml of ether was stirred at reflux under argon with lithium dust (Alfa, 140 mesh) which had been activated by addition of 1 drop of bromobenzene, the solution turned to a deep chocolate brown. After 20 minutes, the solution was added to D_2O , and the organic layer evaporated to dryness, and the white residue recrystallized from hexane to give 0.24 g (84%) of the di-deuterio compound: mass spec 282.1377, 282.1377 calcd. for $C_{22}H_{14}D_2$.

The C-13 spectrum of this molecule showed a decrease in the intensity of the peak at 127.0 compared with the spectrum of the completely protonated molecule, and this peak was assigned to the meta carbon atom. Consistent with this assignment, the peak due to the ortho carbon, situated adjacent to the deuterated site, was shifted 0.1 ppm upfield compared with the peak due to the non-adjacent ortho carbon. The direction and magnitude of this shift are in accord with previous observations²⁴ of C-13 isotope shifts of phenyl carbons β to a site of deuterium incorporation. The para-phenyl carbon peak was also shifted 0.1 ppm upfield, compared with the shift observed for the protonated analog.

FIGURE 1

Ortho H - H distance and angle θ as a function of dihedral ring angle, ϕ ,
in biphenyl-type compounds.

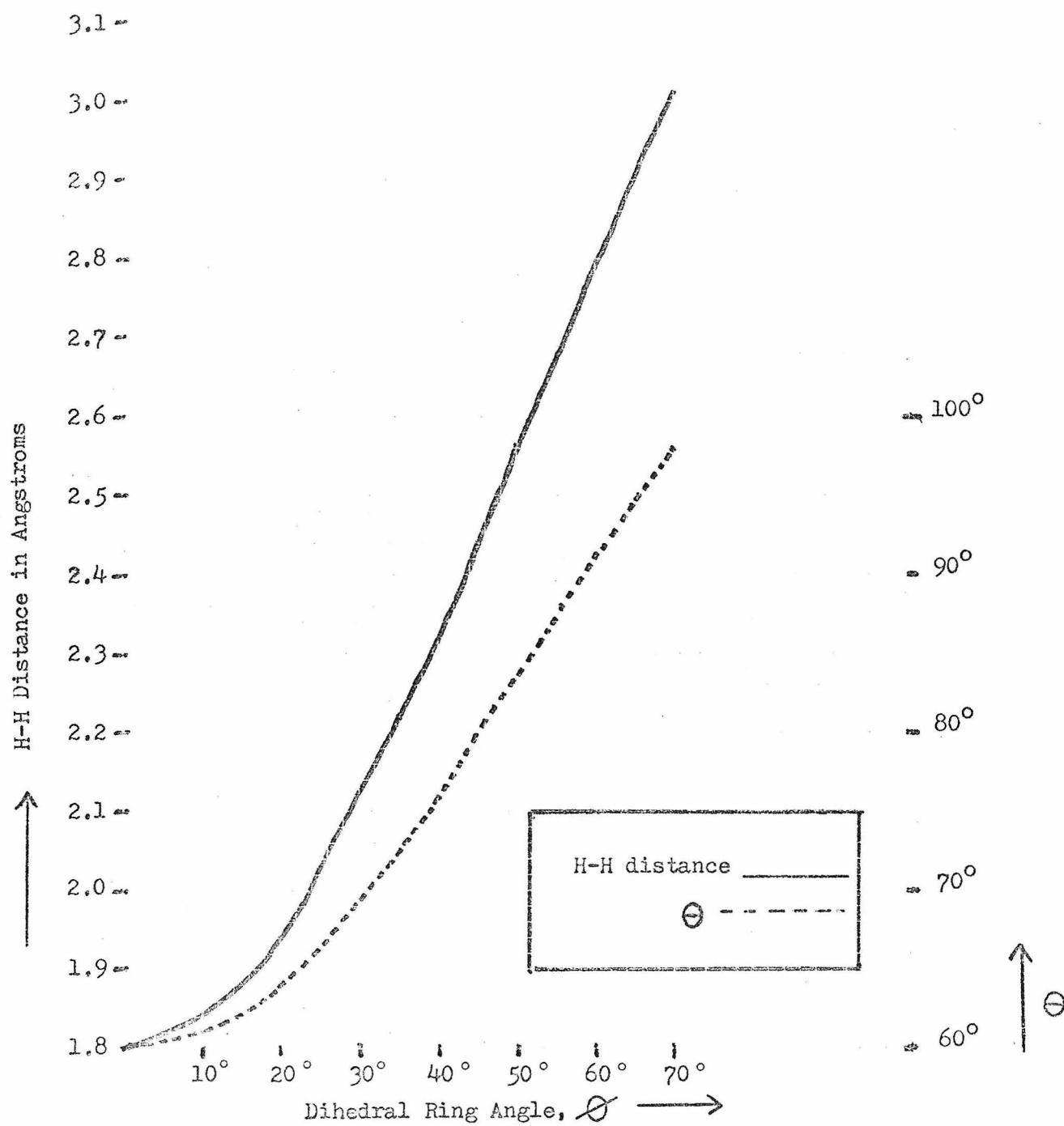
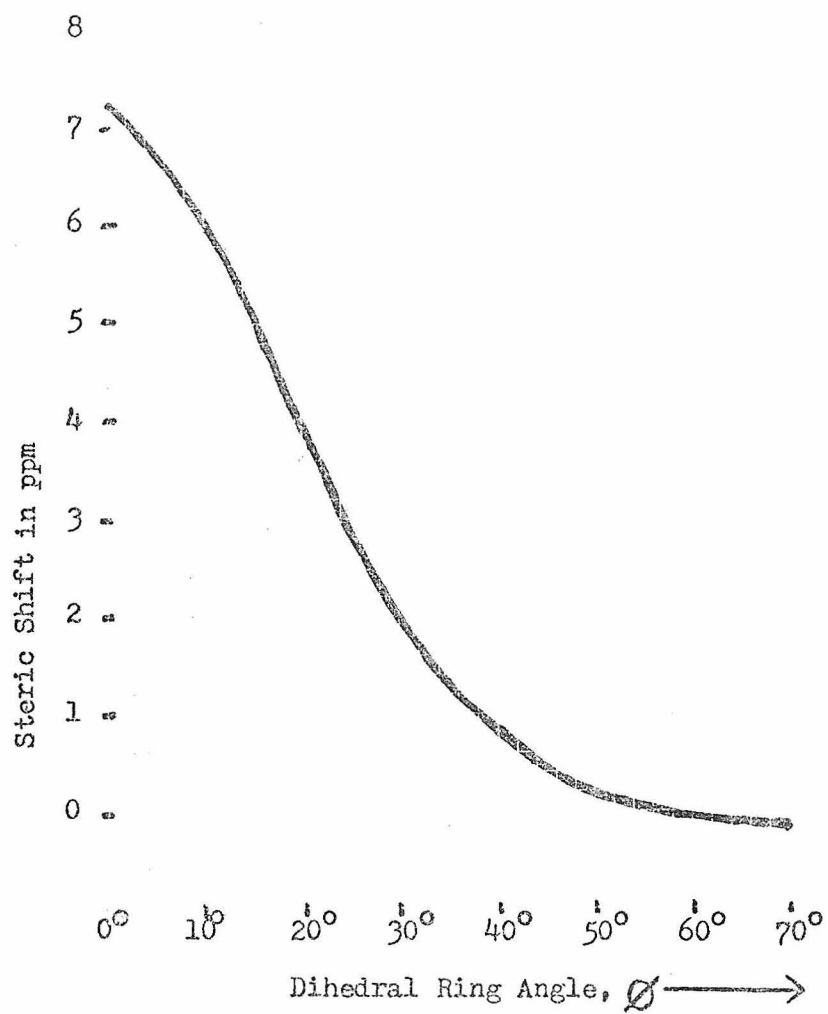


FIGURE 2

C-13 ortho steric shift calculated as a function of dihedral ring angle, θ ,
in biphenyl-type compounds.



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PROPOSITIONS

Abstracts of the Propositions

I. Synthesis with Metal Carbynes. Unique transition metal complexes having a carbon-metal triple bond have been reported. Spectroscopic and other evidence lead me to suggest that the carbyne carbon should be a powerful electrophile. Investigation of the chemistry of these complexes aimed at evaluation of their potential as organic synthetic reagents according to several basic reaction sequences is proposed.

II. Soft Ligand Cages. The ability of crown ethers and the related cryptates to strongly complex, and to discriminate between alkali metal cations has been recently discovered. Preparation of a series of cage compounds having "soft" ligands (especially sulfur and phosphorus) is proposed. It is predicted that these molecules will have a high affinity for the noble transition metals, and that selectivity in binding will be possible by matching charge, coordination geometry, and internal cavity size of the ligand to the requirements of the metal.

III. C_2O_3 . Several decomposition mechanisms, including one having the presently unknown cyclic carbon oxide C_2O_3 as a free intermediate, are suggested for the hydrolysis of oxalic acid derivatives to CO and CO_2 . A labeling experiment designed to establish the existence of C_2O_3 , which is capable of distinguishing between all four proposed mechanisms is described.

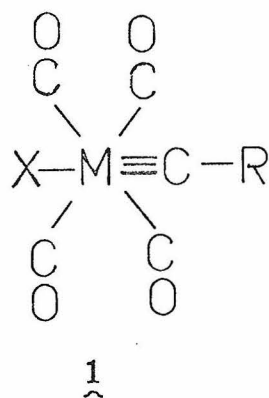
IV. N-15 NMR: Protein Conformational Changes. An evaluation of the effects on the N-15 spectra of polypeptides, due to changes in the microscopic atomic environment resulting from molecular conformational changes, is proposed. Examination of simple helix-coil transitions in polyamino acids is suggested, and an application to a conformational study of an octapeptide is discussed.

V. Systematic Adsorption Resolution. It is proposed that a series of polymers, each possessing a single type of asymmetric center, be prepared, and their potential as adsorbents for optical resolution using high-pressure liquid chromatography be evaluated. The goals of the work are design of effective chiral adsorbents and eventual development of a standard series of columns for resolution work.

PROPOSITION I

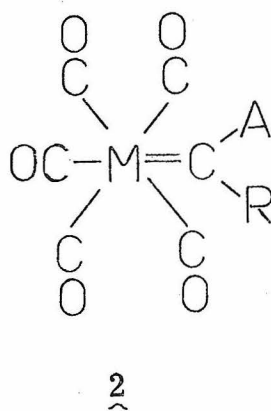
Synthesis with Metal Carbynes

E.O. Fischer has recently reported¹ the preparation of a unique type of transition metal complex having a carbon-metal triple bond 1.



(R = methyl, phenyl; X = I, Br, Cl; M = Cr, W)

Compounds 1 are formed directly from methoxy carbenes (2, A = OCH₃) by reaction with a boron trihalide.

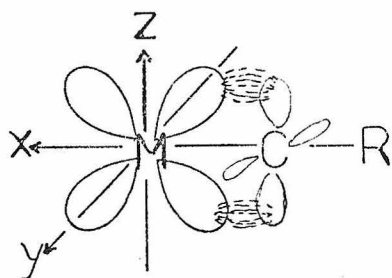


(A = OR', NR₂')

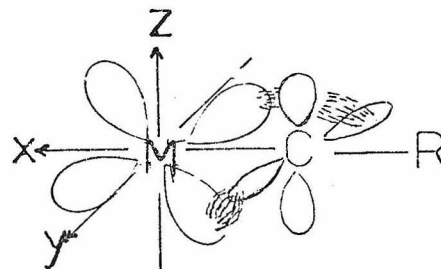
The metal carbynes are relatively stable in the absence of oxygen and have been well characterized, including an X-ray structure analysis. The complexes are nearly linear about the carbyne carbon; they are diamagnetic and are monomeric both in solution and in the solid phase.¹ They are fairly soluble in organic solvents and have dipole moments ranging between 4 and 6 D.

Nearly nothing is presently known about the chemistry of these complexes. A consideration of the unique carbon-metal triple bonding suggests that they will prove valuable and potent reagents for organic synthesis and it is proposed to conduct an investigation of the triply bound carbon specifically aimed at developing their synthetic utility.

The modes of reaction expected for the carbyne complexes may be derived from their bonding structure. It seems not unreasonable to consider the complexes as having the metal-bound ligands: X^- and $:\overset{+}{C}-R$, with electron delocalization from the metal d orbitals to the unoccupied p orbitals on the sp-hybridized carbon atom. The electron delocalization in these compounds must involve two sets of metal d orbitals, one in the XZ plane and one in the XY plane.

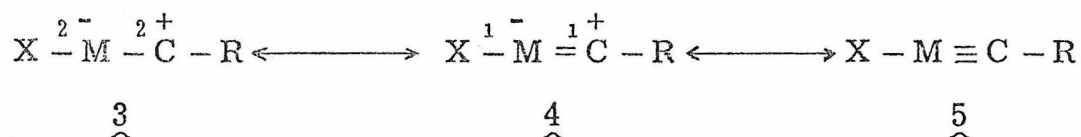


XZ overlap



XY overlap

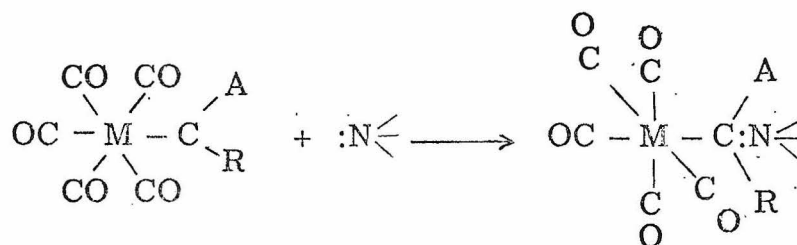
Formal valence bond structures corresponding to a coordinated sp carbon with no metal back-bonding, 3; back-bonding in one plane only, 4; and full back-bonding, 5, are shown below. Structures 4 and 5 are expected to be most important.



The C-13 spectrum¹ of 1 is indicative of the low electron density at the carbyne carbon atom. The acetylenic carbon atoms in most carbon-containing organic molecules absorb in the range of 65-90ppm downfield from TMS.² The chemical shifts of alkynes substituted with a heteroatom have been explained in terms of the relative electron densities at the acetylenic carbon atoms.² The shifts of organo-nitrile carbon-atoms fall in the range of 112-126ppm.³ The carbyne carbon atom in complexes 1 resonates between 286.3 and 288.8ppm. The methyl C-13 shifts in 1 are also indicative of the low electron density of the carbyne carbon. They resonate at 38.0-38.8ppm compared with 13-14ppm for the methyl group of linear alkanes and 4.9ppm for the methyl group of phenylmethylacetylene. It is interesting to compare the chemical shifts of carbynes 1 to the shifts observed by Olah⁴ for carbonium ions in superacid media. Thus, for example, the trimethylcarbonium ion has a peak at 330.0ppm for the cationic carbon, and another at 48.3ppm for the methyl carbons. Methylcyclopropylcarbonium ion, which is said to be stabilized by electron don-

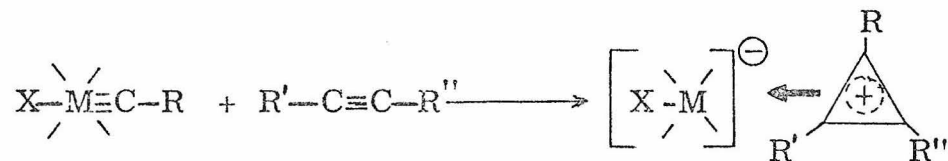
ation from the cyclopropyl ring, gives a shift of 253.7ppm for the cationic carbon and 35.0ppm for the methyl carbon.⁴ The proton nmr spectrum is less sensitive to such charge effects but also indicates a low electron density for the methyl protons. Thus, for the derivatives of 1 with R = methyl, the methyl protons give in each case a singlet, with chemical shifts 1.9-2.2 δ compared with the spectrum of propyne which has a methyl singlet at 1.8 δ .⁵

Spectroscopic evidence shows a very high electron demand of the carbyne carbon. Thus, withdrawal of electron density away from the metal toward the carbyne carbon results in electron withdrawal from the CO ligands to the metal, giving rise to an increased CO bond order. Thus, the CO stretching frequencies are shifted 150cm⁻¹ to higher frequency in the IR as compared with the CO frequencies of the corresponding carbene complexes, 2.¹ It is known that the carbene complexes 2 themselves show considerable electrophilic behavior in their chemistry. Thus, they are able to form Lewis-type adducts with amines and phosphines at the carbene carbon.⁶



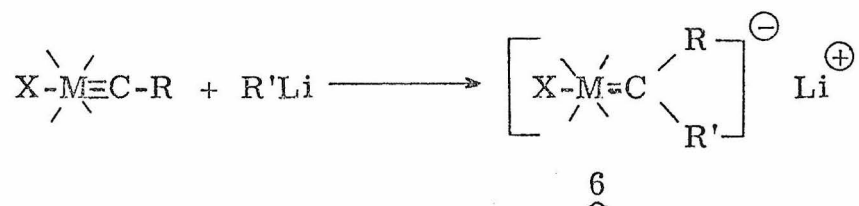
The carbyne carbon may be expected, then, to have the properties of both a bound carbene and a cation. It might be of interest to attempt the simultaneous use of these two properties. For

example, a reaction with an alkyne to produce the stabilized cyclopropenyl cation may be envisioned.

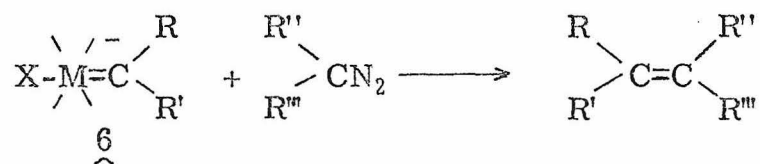


It might be possible to displace this cyclopropenyl cation from the metal by reaction with an anionic species. It is also possible that the reaction might be reversed to give back a metal carbene and an alkyne; this would make possible exchange of an R group on the alkyne. Such a metal carbene-mediated reaction has been postulated by Katz as a mechanism for the alkyne metathesis reaction.⁷

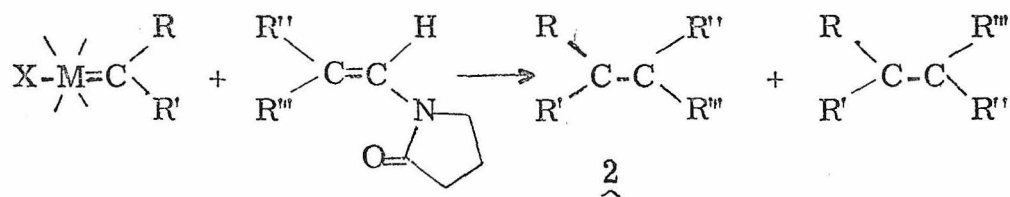
The most important synthetic potential of these compounds may lie in separate, stepwise utilization of the cation and carbene characteristics. It should be possible to carry out reactions at the bound carbyne carbon using its cationic character, followed by use of its carbene nature with a reaction involving a release of the ligand. The addition of a carbanion, for example a lithium alkyl or lithium aryl, to the metal-bound carbyne carbon should proceed readily to give a complex (6) as shown below.



The carbene character of (6) could then be used by carbon-metal bond cleavage. Those reaction schemes shown below are modeled on known reactions^{8, 9, 10, 11} of the extensively studied neutral transition metal carbene complexes (2) which have a heteroatom alpha to the bound carbene carbon. Ligand exchange at the metal⁸ by carbon monoxide or a tertiary amine should yield the free carbene, which should then undergo the typical reactions such as addition to a double bond, or alpha-hydrogen migration to give an alkene. A displacement reaction at the bound carbon atom might be effected, for example with a diazo compound,⁹ to give an olefin.

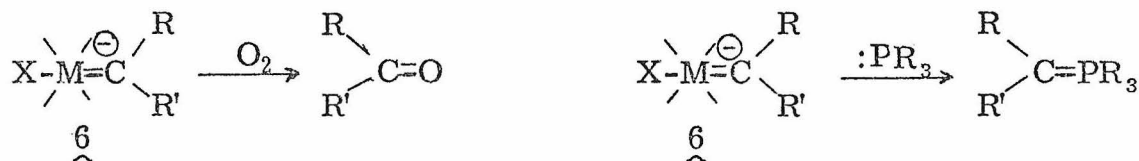


The displacement reaction shown below would also give rise to an olefin. When this reaction was carried out on the heteroatom neutral carbenes, 2, a selectivity in the formation of the two possible isomeric olefins was observed.¹⁰



Note that in the case of the known heteroatom carbenes, 2, the

above reactions yield products having an alpha O or alpha N (R' in each product is alkoxy or amino). If the reactions proceed for carbyne adducts, 6, tetrasubstituted olefins would be formed having all carbon substituents as R groups. Reaction of adducts 6 with oxygen or sulfur in a manner analogous to the reaction of the carbenes 2 with these elements¹¹ would yield ketones and thiones. If displacement in 6 can be effected with a phosphine, an ylide will result.¹²



It might be possible to vary the electrophilicity of the carbyne carbon by exchanging the halogen atom trans to the carbyne with other ligands having different sigma donor strengths and different π acidities. Such electronic interactions of ligands situated trans to each other in transition metal complexes are well known.¹³ This could prove an important means for varying and controlling the chemistry of the carbynes.

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PROPOSITION II

Soft-Ligand Cages

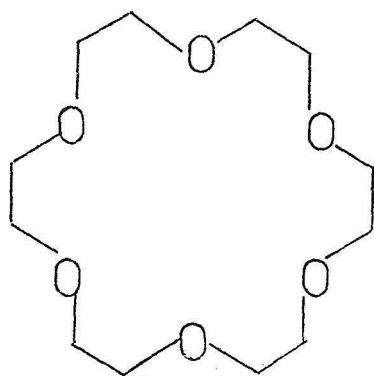
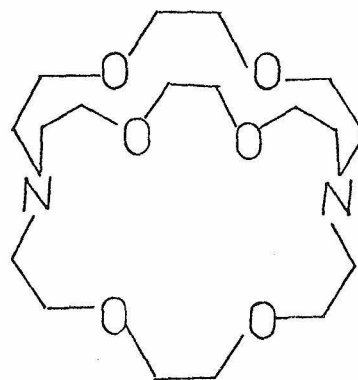
Surface deposits of high grade ores are rapidly being depleted. An oncoming chemical challenge of considerable economic and technological importance will be the efficient recovery of rare metals at extremely low concentrations.

The ocean is one potential source of numerous metals. For example, it has been estimated¹ that the seas contain 7×10^7 tons of gold. There is currently no commercially feasible process for recovery of elements in concentrations as low as from ocean water. Agents capable of binding transition metals are available, and some workers have succeeded in extracting gold from samples of sea water.¹ A central problem has been development of agents which not only have a high metal affinity but which also have a high specificity and do not extract a whole group of metal cations. It has been pointed out that certain living systems are in fact capable of efficient, specific metal concentration. For example, the tunicate Phallusia mamillata concentrates vanadium in its blood cells by a factor of 10^6 compared with sea water.¹

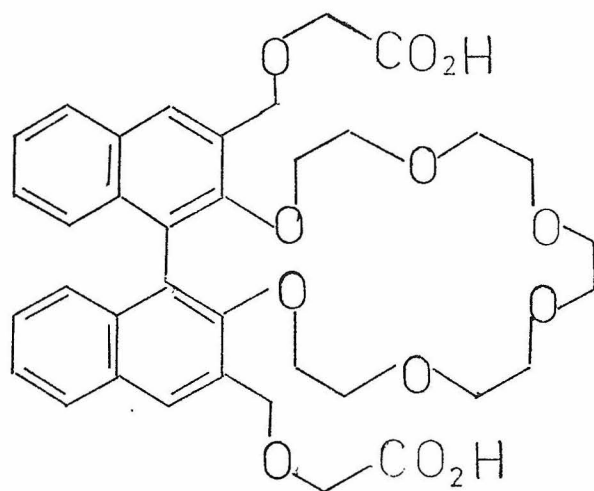
Stable complexes of transition metals with organic ligands which have heteroatoms with non-bonded electron pairs have been extensively studied. It has been generally observed that the stability of chelated complexes is greater than that of monodentate analogues and the stability increases steadily with increasing chelation number.² Ligands which are bidentate, tridentate, tetradentate and higher are known.³ Examples of geometric selectivity

of transition metal ligands have been known for some time. Thus, while 1,10-phenanthroline complexes both Fe^{++} and Cu^+ , introduction of alkyl substituents at positions 2 and 9 suppresses the interaction with Fe^{++} while Cu^+ is still strongly bound.⁴ Similarly, introduction of a substituent into the 2-position of 8-hydroxyquinoline hinders complexation with Al^{+++} but not with other cations including Mg^{++} .⁴

Recently, Pederson⁵, Lehn⁶, Cram^{7,8} and others reported on the ability of cyclic polyethers 1 and the three-dimensional cryptates 2 to complex and lyophilize alkali metal cations.

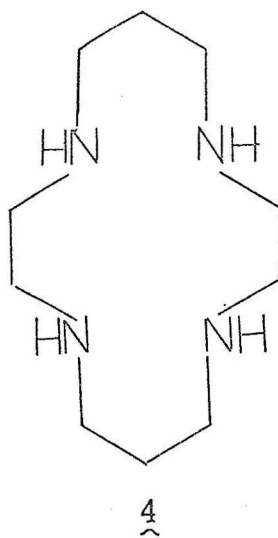
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High association constants have been observed. It appears that ligands with a pre-organized shape gain another substantial degree of stability compared with open chain chelates. Cram has designed and prepared an extensive series of crown ethers. By varying the geometry of these cyclic ligands it was possible to achieve considerable selectivity. Compound 3 has a built-in -2 charge and a pocket which matches well the ionic radius of Sr^{++} . It was found that 3 extracted strontium ion from a solution of barium hydroxide and this was attributed to a less favorable fitting of the larger barium ion into the cavity of 3.⁸



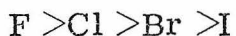
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Some complexation of cyclic polyethers and polyamines with transition metals has been reported.⁵ It was recently reported⁹ that the cyclic amines of the type 4 complex cobalt and nickel, and that the 14-membered cycle complexes cobalt best, while the 15-membered cycle was best for nickel.

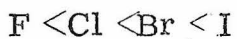


(ring size 12-16 atoms)

It has been observed that transition metals at the right of the chart are capable of forming much stronger complexes than the other metals.¹⁰ It has been noted that complexes of Rh, Pd, Ir, Ag(II) and Au(III) are especially stable.¹¹ Most important, substantial differences are found in the type of donor ligand preferred by different metals for complexation. Experimentally the metals fall into two categories.¹² It is observed that for the alkali metals, the transition metals at the left of the chart, and many rare earth metals, the complexing preference closely parallels the basicity of the ligand. Thus, donor atoms of the second period are markedly superior in their ability to complex with these metals compared with donors from the third and later periods. The order of complex stabilities is:



In marked contrast, transition metals to the right of the chart strongly prefer donors from the third and later periods. The order of stabilities for complexes of these metals is:



The differences in behavior have been discussed¹² in terms of the high mutual polarizability of the later group of metals and ligands which have been termed "soft" metals and "soft" ligands. Members of the first set are termed "hard" ligands and "hard" metals. The remaining metals fall into a borderline class and complex with both ligand types. The periodic chart is shown below; classification of the metals according to hard and soft behavior is indicated.¹³

The periodic table is classified into three categories based on the legend below:

- hard**: Represented by a box with diagonal lines from top-left to bottom-right.
- soft**: Represented by a box with diagonal lines from top-right to bottom-left.
- borderline**: Represented by a box with a cross-hatch pattern.

The classification is as follows:

- Hard metals** (diagonal lines \): H, He, Li, Be, B, C, N, O, F, Ne, Na, Mg, Al, Si, P, S, Cl, Ar, K, Ca, Sc, Ti, V, Cr, Mn, Fe, Co, Ni, Cu, Zn, Ga, Ge, As, Se, Br, Kr, Xe, Rn, Cs, Ba, La, Hf, Ta, W, Re, Os, Ir, Pt, Au, Hg, Tl, Pb, Bi, Po, At, Fr, Ra, Ac, Th, Pa, U.
- Soft metals** (diagonal lines /): Ag, Cd, In, Sn, Sb, Te, I, Pt, Au, Hg, Tl, Pb, Bi, Po, At.
- Borderline metals** (cross-hatch): All transition metals (Groups 3-10), including Sc, Ti, V, Cr, Mn, Fe, Co, Ni, Cu, Zn, Ga, Ge, As, Se, Br, Kr, Xe, Rn, Cs, Ba, La, Hf, Ta, W, Re, Os, Ir, Pt, Au, Hg, Tl, Pb, Bi, Po, At.

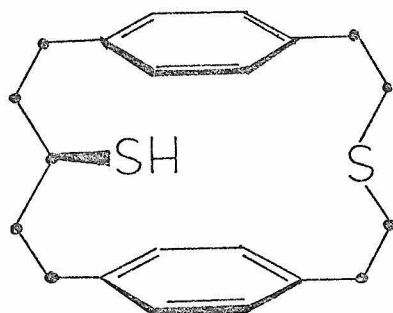
* Lanthanides
† Actinides

Because of their strong complexing abilities and strictly controlled geometries, organic "cage" ligands seem especially promising as potential agents for specific complexation of metals. It is proposed to prepare a series of soft-ligand cages for complexation of "soft" and "borderline" transition metals. Use of soft ligands should impart a high affinity for "soft" metals. Several main parameters are available to achieve specificity among the soft metals. Matching of binding site size with the diameter of the metal ion should prove an important parameter. Matching of the built-in charge of the ligand with the valence charge of the metal is another parameter and both of these have been used successfully in designing crown ethers as cages for alkali metals. Transition metals have strong preferences in coordination geometry; building rigid cages to match the coordination type of the metal, (i.e. square planar, trigonal bipyramidal etc.) should be a third important parameter.

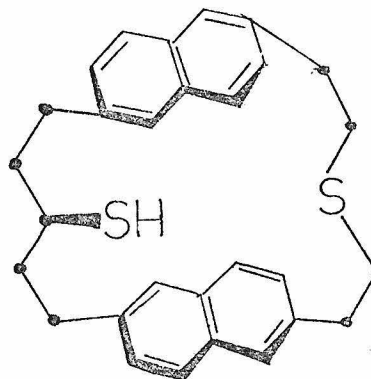
Because of their ease of preparation from organic halides, organo-sulfur linkages seem a good first choice for wide use in the construction of soft-ligand cages. Phosphines may be employed to some extent. Mercaptans are oxidized to disulfides even by molecular oxygen; more than one -SH site per cage may not prove feasible unless they are held rigidly apart. Several examples of cages to be prepared are discussed below.

Silver has an ionic diameter¹⁴ of 2.52A (Ag^+) and forms linear coordination complexes. Soft cages having charge one, with linear coordination are shown below. The ether linkages of 8 are

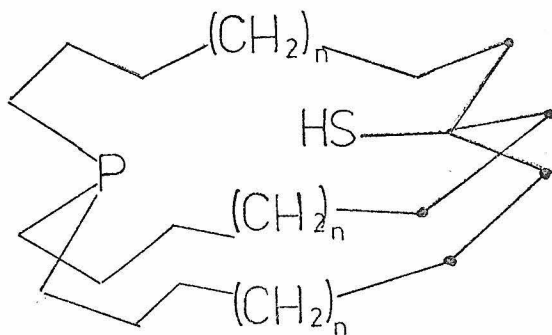
provided for increased water solubility of the cage should this be desired. A series of cages which vary stepwise in cavity size, as for 7, could be readily prepared for screening on metal ions.



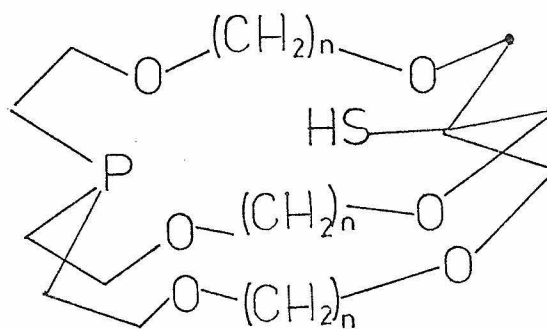
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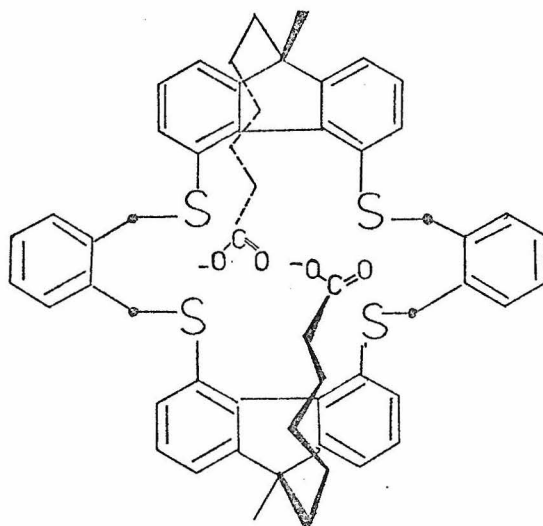


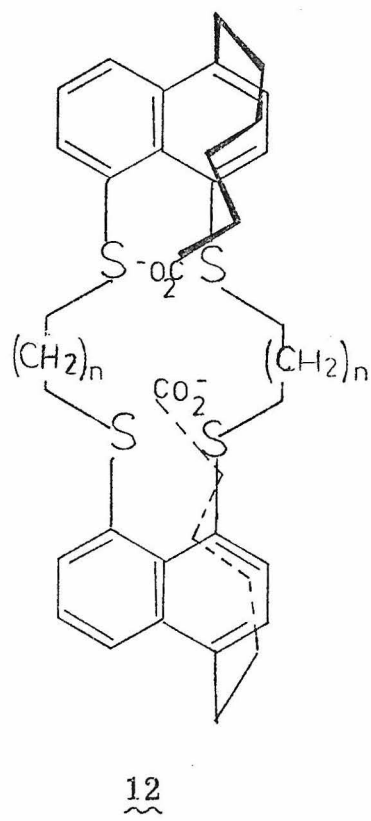
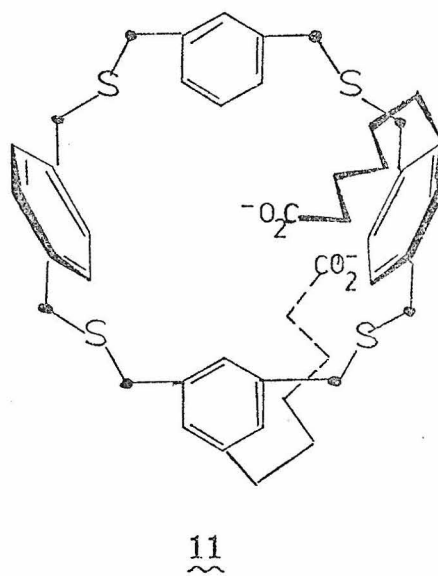
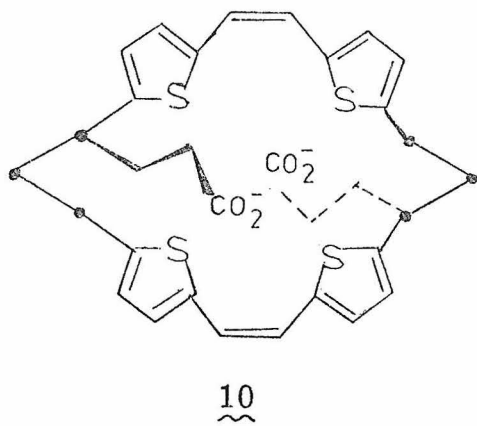
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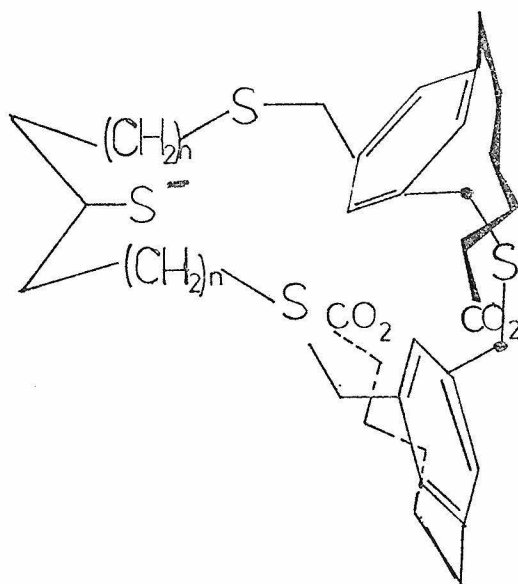
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Octahedral complexes are quite common for transition metals, as are square planar complexes. The square planar complexes often have additional weaker solvent binding interactions above and below the plane of the complex giving them pseudo-octahedral shape (for example, Pt^{++} and Pd^{++}). Numerous linkages can be envisioned to provide a ring having four planar (or non-planar) donor atoms. Carboxylate groups above and below the plane would provide the built-in charge.





The comparatively small diameter, 1.70A , and the +3 valence of Au^{+++} ion should be helpful in effecting separation of this metal with a cage complex. One structure type which should fit Au^{+++} is shown below.



13

Though the primary interest in the soft-ligand cages is in their potential for extracting transition metals, there are two other important uses which should stem from their expected solubility in organic solvents. First, transition metal ions bonded by cages which have one or more coordination sites which are vacant or which are loosely bound to a readily displaced cage "arm" may prove valuable as soluble catalysts for organic reactions. Second, it is reasonable to expect that soft-ligand cages may be prepared which will have the

ability, like their hard-ligand analogues, of passing membranes, allowing selective introduction of transition metal ions into cells or selective metal ion removal from cells. Biological activity of certain metal chelates has been reviewed; the highest activity was generally found with chelates having some lipid solubility.¹⁵

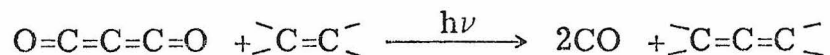
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PROPOSITION III

$$\underline{\text{C}_2\text{O}_3}$$

Hydrocarbons and boron hydrides each comprise large systems of binary compounds which have been extensively studied. The catenation ability of carbon, combined with the stability of carbon-oxygen bonds potentially permits preparation of a large and diverse system of carbon oxides, expected to be of varying stability. A few are presented in Figure 1. Of the examples shown, compounds 1, 2, 4, 6, 8, and 18 are known, and several of these have interesting properties. CO and CO₂ are familiar to every chemist. CO₃ has been observed spectroscopically, by irradiation of solid CO₂ with simultaneous scanning of the infrared spectrum. It exists as a closed 3-membered ring species as drawn in Figure 1.¹ C₂O₄ (8, Figure 1) has been proposed as an intermediate in the oxidation of oxalyl chloride and oxalyl esters by hydrogen peroxide.² The compound has not been isolated, but is believed to decompose to give two molecules of CO₂, one in an excited state. There is mass spectral and other evidence for its existence.^{3,4} C₃O₂ can be generated by dehydration of malonic acid with P₂O₅.⁵ This compound has been referred to as carbon suboxide, though in light of the present text, this must be considered a misnomer, since many carbon oxides containing fewer oxygen atoms than carbon atoms may be envisioned. Infrared studies show that the molecule is completely linear.⁶ Photolysis of this compound in the presence of an olefin gives insertion reactions of the type shown below.⁷



Tricarbon dioxide has been thought to be present in the atmosphere of Venus.⁸ The recent discovery of the excellent matching of the infrared spectrum of polymers of C_3O_2 with the spectrum of the light reflected from Mars has provided evidence that the reddish hue of that planet is a consequence of the presence of C_3O_2 polymers.⁹

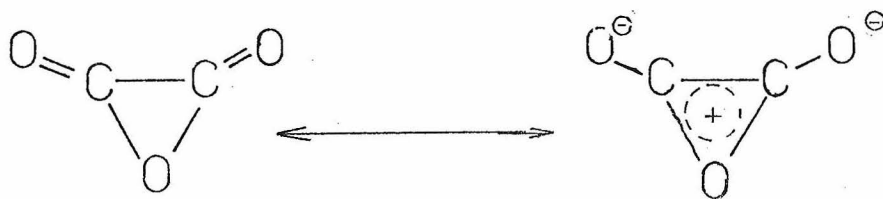
C_3O_2 may be considered in the context of a series of carbon oxides having the general formula C_nO_2 , of which the familiar carbon dioxide is the simplest member. A simple molecular orbital analysis of this series yields a prediction similar in form to the familiar Hückel rule for cyclic alternate unsaturated compounds: all odd members of the C_nO_2 series should have a stable, spin-paired configuration, while even members are expected to have a diradical groundstate.¹⁰

We now focus attention on another simple member of the carbon dioxide family, C_2O_3 (compound 7, Table I). This molecule has not yet become a subject of theoretical discussion, and there has to date been no published account of any concerted attempt at isolating it. There is one account of molecular orbital calculations¹¹ on the photochemical decomposition of acid anhydrides which indicates that 7 does not lie on the reaction coordinate. The three-membered ring of C_2O_3 would be expected to have an especially high angle strain. Some related structures merit discussion.

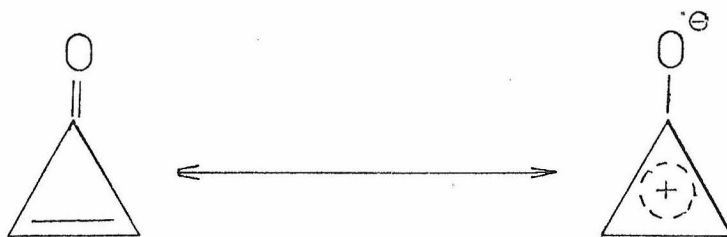
A simple α -lactam should have less angle strain than C_2O_3 , as the former has only one sp^2 hybridized carbon (preferred angle = 120°) incorporated into a three-membered ring, and one sp^3 hybridized carbon (preferred angle 109.5°), while C_2O_3 has two

sp^2 carbon atoms in the ring. There is evidence for the existence of α -lactams, as reactive species. For example by low temperature ozonolysis of a ketene, Bartlett generated a species on which an nmr spectrum was obtained. Addition of methanol gave the corresponding ester, while warming the sample caused formation of the polymeric anhydride.¹² Cyclopropanone and related derivatives have been observed but are of low thermal stability. Cyclopropanone decarbonylates readily to yield ethylene and carbon monoxide.¹³

Dipolar aromatic character could be of importance for C_2O_3 . A contribution from a cyclic 2-electron system could enhance the stability of this compound.



This resonance form is analogous to that invoked for cyclopropenone.



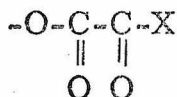
A relatively high thermal stability of cyclopropenone as compared with cyclopropanone has been noted, despite the expected higher

angle strain of cyclopropenone, which incorporates three sp^2 hybridized carbons in the three-membered ring.¹⁴ The high dipole moment (5D), and the carbonyl stretching frequency (1350 cm^{-1}) of diphenylcyclopropenone, and the proton chemical shift (9δ) of cyclopropenone have been cited to indicate the importance of the dipolar cyclopropenone structure.¹⁴ Aromatic character of oxygen-containing rings has been observed.¹⁵ It has been pointed out that the high electronegativity of oxygen inhibits its ability to participate in extended π systems.¹⁶ The dipolar character of the aromatic resonance form for C_2O_3 may be advantageous to inducing a release of the non-bonded oxygen electrons, compared with "neutral" aromatic oxygen-containing systems.

It was found by the author that P_2O_5 reacts immediately with oxalic acid to evolve a gas, which was identified as a mixture of CO and CO_2 by the infrared spectrum. Similarly, it was reported by Staudinger in 1908 that oxalyl chloride, $C_2O_2Cl_2$, decomposes immediately on contact with water to yield CO and CO_2 .¹⁷ A reasonable mechanism for the decomposition of the oxylates is through C_2O_3 . Such a pathway is analogous to the α -lactam-mediated mechanism proposed by Winstein for the solvolysis of α -bromopropionate.¹⁸ There are three other possible reaction routes envisioned and these are outlined in detail below. An experiment is described which will attempt to establish the existence of C_2O_3 and which is capable of distinguishing between all of the four mechanisms proposed.

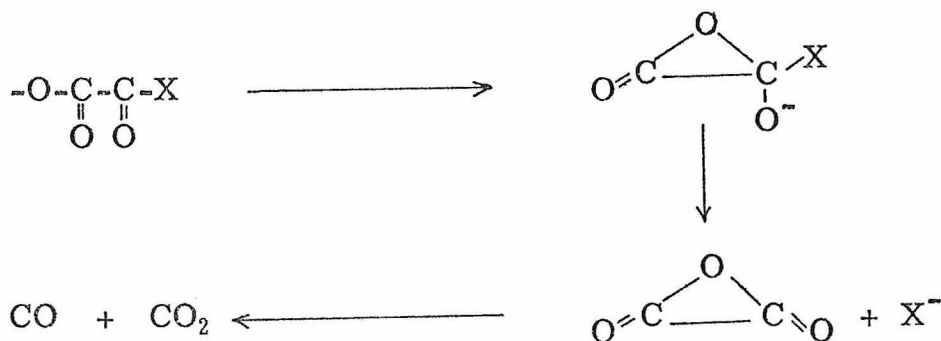
Decomposition Mechanisms.

A first step which is common to all the mechanisms outlined here is formation of a monofunctionalized oxalic acid derivative:

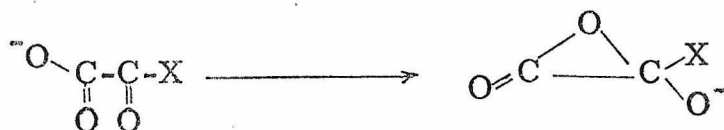


In the case of the oxalyl chloride, this is the hydrolysis of one of the halves of the molecule. For the reaction of the diacid with P_2O_5 this step is the formation of the phosphate anhydride.

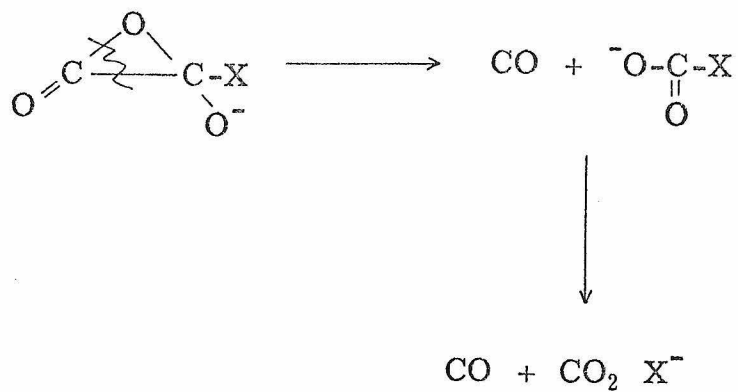
Mechanism I: Ring Closure with Subsequent Formation of C_2O_3 .



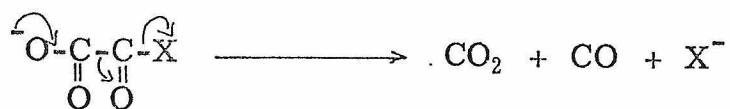
Mechanism II : Ring Closure with Decomposition of the Intermediate Ionic Species



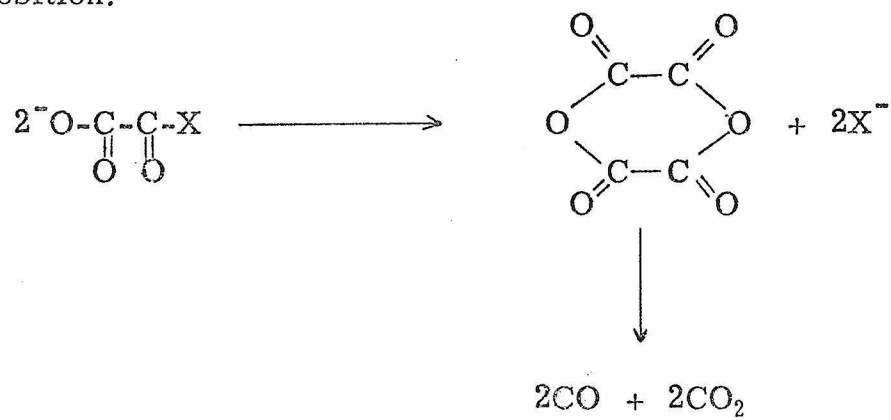
II. (cont'd).



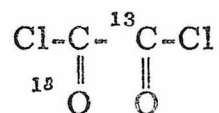
Mechanism III: Non-cyclizing Decomposition.



Mechanism IV: Formation of Dimeric Anhydride Followed by Decomposition.

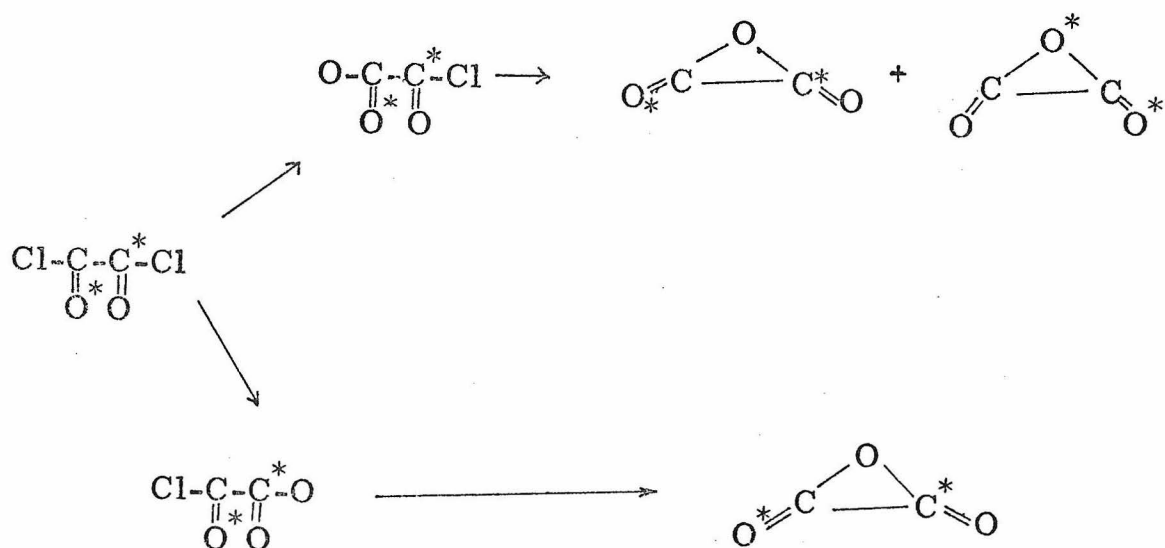


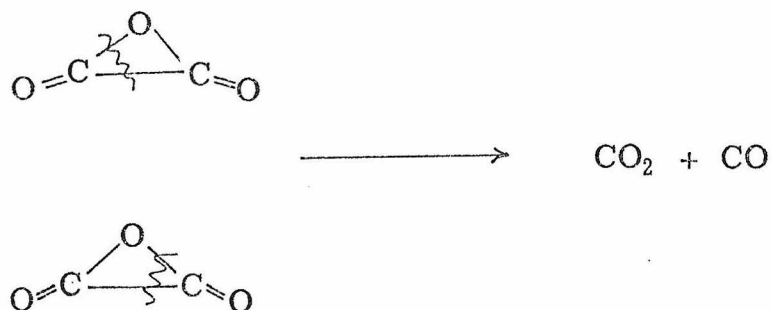
It is proposed that an oxalyl chloride having the following labeling be prepared:



The two carbon isotopes in this molecule differ by one mass unit while the two oxygen isotopes differ by two mass units. Mass spectral analysis of the isotope distribution for the CO and CO₂ formed on hydrolysis will allow a very exacting analysis of the reaction route.

Assume first that once one end of the molecule is hydrolyzed, the two carboxylate oxygens at that end become chemically equivalent and have equal probabilities of ending up in the lactone bridge in mechanisms I-II. For mechanism I, either half of the molecule may be hydrolyzed first and there are two chemically equivalent pathways for decomposition of the C₂O₃:





The following isotope distribution is predicted by this mechanism:

| | | | | | |
|---------------|--------------------------------|--------------------------------|---|---|-----------------|
| Species: | $^{12}\text{C}^{16}\text{O}$ | $^{13}\text{C}^{16}\text{O}$ | $^{12}\text{C}^{18}\text{O}$ | $^{13}\text{C}^{18}\text{O}$ | |
| MW: | 28 | 29 | 30 | 31 | CO |
| Relative | 1 | 4 | 3 | 0 | |
| Distribution: | | | | | |
| Species: | $^{12}\text{C}^{16}\text{O}_2$ | $^{13}\text{C}^{16}\text{O}_2$ | $^{12}\text{C}^{16}\text{O}^{18}\text{O}$ | $^{13}\text{C}^{16}\text{O}^{18}\text{O}$ | |
| MW: | 44 | 45 | 46 | 47 | CO ₂ |
| Relative | 0 | 3 | 4 | 1 | |
| Distribution: | | | | | |

For mechanism II the predicted ratio is:

| | | | | | |
|---------------|--------------------------------|--------------------------------|---|---|-----------------|
| Species: | $^{12}\text{C}^{16}\text{O}$ | $^{13}\text{C}^{16}\text{O}$ | $^{12}\text{C}^{18}\text{O}$ | $^{13}\text{C}^{18}\text{O}$ | |
| MW: | 28 | 29 | 30 | 31 | CO |
| Relative | 1 | 2 | 1 | 0 | |
| Distribution: | | | | | |
| Species: | $^{12}\text{C}^{16}\text{O}_2$ | $^{13}\text{C}^{16}\text{O}_2$ | $^{12}\text{C}^{16}\text{O}^{18}\text{O}$ | $^{13}\text{C}^{16}\text{O}^{18}\text{O}$ | |
| MW: | 44 | 45 | 46 | 47 | CO ₂ |
| Relative | 0 | 1 | 2 | 1 | |
| Distribution: | | | | | |

For mechanism III there would be no label scrambling. The following ratios are predicted:

| Species: | $^{12}\text{C}^{16}\text{O}$ | $^{13}\text{C}^{16}\text{O}$ | $^{12}\text{C}^{18}\text{O}$ | $^{13}\text{C}^{18}\text{O}$ | |
|---------------|------------------------------|------------------------------|------------------------------|------------------------------|----|
| MW: | 28 | 29 | 30 | 31 | CO |
| Relative | 0 | 1 | 1 | 0 | |
| Distribution: | | | | | |

| Species: | $^{12}\text{C}^{16}\text{O}_2$ | $^{13}\text{C}^{16}\text{O}_2$ | $^{12}\text{C}^{16}\text{O}^{18}\text{O}$ | $^{13}\text{C}^{16}\text{O}^{18}\text{O}$ | |
|---------------|--------------------------------|--------------------------------|---|---|-----------------|
| MW: | 44 | 45 | 46 | 47 | CO ₂ |
| Relative | 0 | 1 | 1 | 0 | |
| Distribution: | | | | | |

Mechanism IV would yield a very complex ratio. It would be readily distinguishable by two criteria. It is the only mechanism which allows formation of CO₂ doubly labeled in oxygen : $^{12}\text{C}^{18}\text{O}^{18}\text{O}$ (MW 48). Also, for this mechanism only, running the reaction in the presence of excess unlabeled oxalyl chloride would alter the observed molecular weight ratios, reducing all doubly labeled species.

It is possible that the two geminal carboxylate oxygens of the partially hydrolyzed acid chloride do not become equivalent. Beginning formation of epoxide bonding simultaneously with hydrolysis would have this effect. This will introduce a factor, p , for the relative probability of oxygen from the water ending up in the epoxide position where $0.0 < p < 1.0$. (For $p = 0.5$, the initial equivalence assumption holds).

A new set of relative isotope ratios can be written in terms of p for mechanisms I and II. These ratios are given below:

Mechanism I

| Species: | $^{12}\text{C}^{16}\text{O}$ | $^{13}\text{C}^{16}\text{O}$ | $^{12}\text{C}^{18}\text{O}$ | $^{13}\text{C}^{18}\text{O}$ | |
|---------------|------------------------------|------------------------------|------------------------------|------------------------------|----|
| MW: | 28 | 29 | 30 | 31 | CO |
| Relative | $1 - p$ | 2 | $1 + p$ | 0 | |
| Distribution: | | | | | |

| Species: | $^{12}\text{C}^{16}\text{O}_2$ | $^{13}\text{C}^{16}\text{O}_2$ | $^{12}\text{C}^{16}\text{O}^{18}\text{O}$ | $^{13}\text{C}^{16}\text{O}^{18}\text{O}$ | |
|---------------|--------------------------------|--------------------------------|---|---|-----------------|
| MW: | 44 | 45 | 46 | 47 | CO ₂ |
| Relative | 0 | $1 + p$ | 2 | $1 - p$ | |
| Distribution: | | | | | |

Mechanism II

| Species: | $^{12}\text{C}^{16}\text{O}$ | $^{13}\text{C}^{16}\text{O}$ | $^{12}\text{C}^{18}\text{O}$ | $^{13}\text{C}^{18}\text{O}$ | |
|---------------|------------------------------|------------------------------|------------------------------|------------------------------|----|
| MW: | 28 | 29 | 30 | 31 | CO |
| Relative | $1 - p$ | 1 | p | 0 | |
| Distribution: | | | | | |

| Species: | $^{12}\text{C}^{16}\text{O}_2$ | $^{13}\text{C}^{16}\text{O}_2$ | $^{12}\text{C}^{16}\text{O}^{18}\text{O}$ | $^{13}\text{C}^{16}\text{O}^{18}\text{O}$ | |
|---------------|--------------------------------|--------------------------------|---|---|-----------------|
| MW: | 44 | 45 | 46 | 47 | CO ₂ |
| Relative | 0 | p | 1 | $1 - p$ | |
| Distribution: | | | | | |

Hydrolysis of completely unlabeled oxalyl chloride, in ^{18}O water followed by mass spectral analysis of the product gas will provide the data from which a p value may be calculated to fit the correct

mechanism. If mechanism I is operable, $p = \frac{1 - \text{CO}^{18} / \text{CO}^{16}}{1 - \text{CO}^{18} / \text{CO}^{16}}$.

If mechanism II is operable, $p = \frac{1}{1 + \text{CO}^{18} / \text{CO}^{16}}$.

If mechanisms III or IV are operable, the present hydrolysis reaction will yield only unlabeled CO, with all ^{18}O ending up in the CO_2 .

FIGURE 1
Carbon oxides.



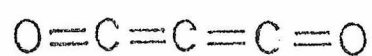
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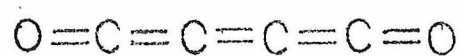
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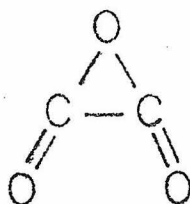
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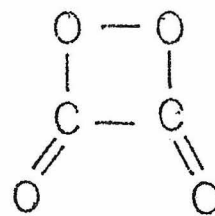
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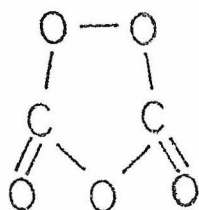
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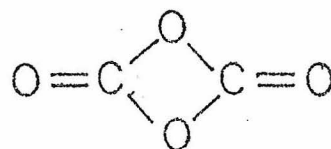
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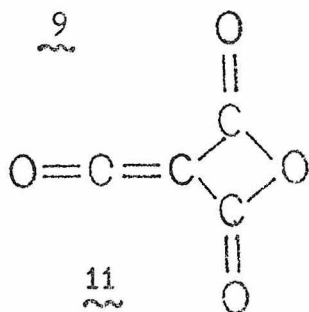
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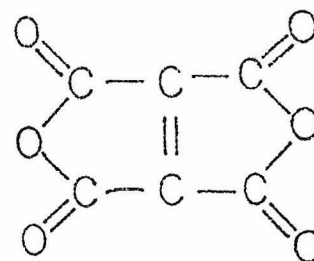
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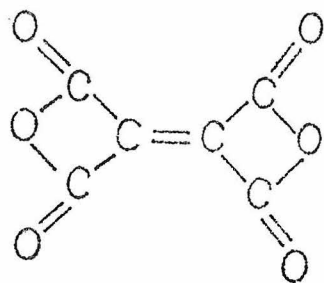
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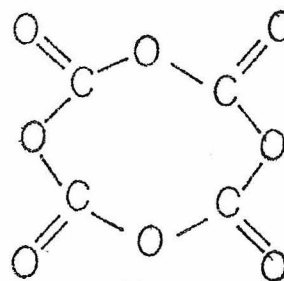
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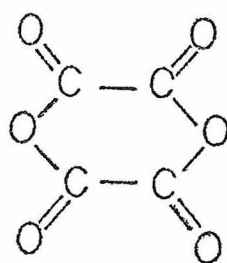
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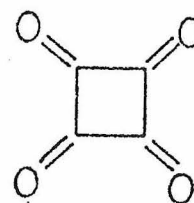
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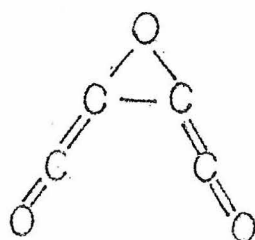
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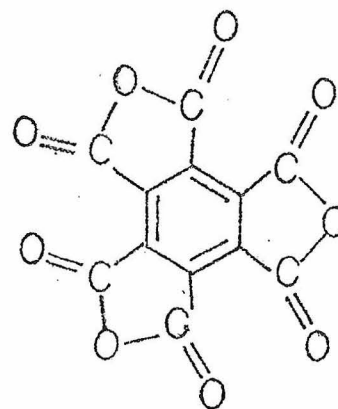
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PROPOSITION IV

N-15 NMR: Protein Conformational Changes

Structural studies utilizing nmr of nuclei other than protons have become a major branch of research in chemistry. NMR studies of nitrogen have been severely hampered by experimental difficulties. The N-14 isotope has spin number 1 and an abundance of 99.64% but unfortunately has an electric quadrupole moment. The N-15 isotope has the more convenient spin number of $\frac{1}{2}$ and no quadrupole moment. However, the gyromagnetic ratio is -0.1013 relative to protons and the natural abundance (NA) is 0.365%; the natural abundance nmr sensitivity relative to proton $((\text{NA})(\gamma)^3/99.98)$ is thus 3.8×10^{-6} . Until recently, this low sensitivity factor made N-15 studies possible only with molecules specially enriched with this isotope. Some natural abundance work has now been possible with neat liquids and compounds with very high solubility factors. The Bruker WH-180, which combines the pulse-fourier transform technique with a superconducting magnet having a high field strength corresponding to 180MHz. for proton resonance and which is designed to hold sample tubes of 30mm. diameter, now makes natural abundance N-15 studies down to a concentration of 0.1M feasible.

My central interest in this newly available technique is to examine and develop its potential for detecting and characterizing conformational changes in proteins in solution. N-15 nmr seems well suited to this task. The N-15 spectra of proteins will be much simplified compared with the proton spectra: the number of nitrogen atoms is much reduced compared with the number of protons, homo -

nuclear coupling is not observed because of the low natural abundance of N-15, heteronuclear decoupling is easily accomplished, and the shift range of organo-nitrogen compounds is of the order of 800ppm. The nitrogen atoms are spaced like markers all along the length of the peptide backbone. Because of the complexity of the protein structure, other techniques available for solution studies are usually capable of giving much less precise information than nmr. By observation of the amide nitrogens, it should in principle be possible to simultaneously follow specific conformational changes along the entire peptide chain. Initial experiments have indicated that the amide signals of small polypeptides are reasonably well separated at the 180MHz. field strength. Correlation of peptide nitrogen shifts with the structure of the amino acid residue and nearest neighbor residues in the chain is in progress.

This proposition is aimed at laying the foundation for studying conformational changes in more complex proteins, particularly changes associated with biological action. Effects on the N-15 spectrum are expected to be produced primarily by shifts directly induced by interaction with bound substrate or metal ions, by changes in hydrogen bonding of the amide proton and by movement of residues between hydrophobic "inside positions" and hydrophilic "outside positions". The interest, then, is not in N-15 spectral effects arising from structural changes in the molecule, but in effects resulting from changes in the microscopic environment of a nucleus located at a given site in the molecule.

Some initial work on N-15 spectral effects resulting from changes in the macroscopic molecular environment (solvent effects) is of interest. That N-15 shifts are, in fact, quite solvent dependent has been demonstrated.¹ Changes in hydrogen bonding are seen to play a large role in shift changes, but other environmental effects which are not well understood apparently have substantial influence. Shift changes on dilution are strongly dependent on the solvent employed. It is interesting that dilution with the relatively "inert" CCl_4 can induce substantial shift changes. Shifts of alkyl ammonium ions have been found to be sensitive to halide concentration. High field dilution shifts for amide nitrogen in dioxane have been interpreted as the breaking up of H-bonded associations. Shifts of methyl formamide extrapolated to infinite dilution² indicate a range of environment-shifts possible.

| | |
|-------------|-----|
| acetone | 272 |
| methanol | 267 |
| dioxane | 278 |
| neat liquid | 266 |

(Shifts relative to external NO_3^- , 4.5M in NH_4NO_3 in 1M HCl)

Initial studies would evaluate the effect of a well understood conformational change on the N-15 spectrum. Subsequent work will attempt to elucidate conformational information from simple peptides.

An important type of secondary structure in proteins is the

well known α -helix. The uncoiling of the helix can be induced by changes in temperature, solvent, or pH. Polyamino acids will be examined first for several reasons. Since they are built of repeating units, the helix structure along the chain is regular, and contains no disruptions or angular bends. The conformation at the identical repeating units can be unambiguously seen from molecular models. Because of the structural uniformity, the helix-coil transformation occurs very sharply as a function of pH and the point of transformation can be readily observed by polarimetry, since the α -helix is itself chiral and has a marked effect on the total optical rotation.³ Many polyamino acids are available commercially.

Poly-l-glutamic acid exists as an α -helix at low pH but near pH 6 the ionic repulsion between titrated carboxyl groups becomes great enough to overcome the hydrogen bonding and the chain uncoils. Poly-l-lysine exists as a helix at high pH but protonation of the side chain amine causes uncoiling at pH 10.5.³ Helix-coil transformations may be induced in a number of polyamino acids such as poly-l-leucine⁴ and poly-l-alanine⁵ which have neutral side chains, on dilution with solvents which compete with intramolecular hydrogen bonding.

An example of a somewhat more complex peptide problem to be examined is outlined below. The naturally occurring polypeptide angiotensin is a powerful pressor agent currently in clinical use. The amino acid sequence is Asp-Arg-Val-Tyr-Val-(or Ile)-His-Pro-Phe. The solution conformation of the molecule has been under study by a wide range of techniques for the past ten years with the hope that

conformation will be a key to physiological activity. The conformation(s) of this molecule have not been elucidated with certainty. That the molecule in fact has definite solution conformational preferences rather than random conformation has been demonstrated by circular dichroism⁶ and is consistent with other results.^{7,8} Numerous models have been proposed, including an α -helix,⁹ a β turn,¹⁰ a γ turn,¹⁰ an antiparallel sheet¹¹ and others. It has been suggested that because of the small size of this polypeptide, it is in equilibrium between several conformations of similar energy.

A pH-induced conformational change has been observed.⁶ Biological assay tests have shown that certain cations, including ammonium, sodium and potassium, potentiated the blood pressure activity of angiotensin. Thin film dialysis studies indicate that addition of small amounts of ammonium ion caused the protein to become more extended.¹²

After assigning the N-15 spectrum, it should be possible to investigate the conformation and conformational changes. Gain or loss of hydrogen bonding at any amide nitrogen should be apparent. The β turn model has a pair of intramolecular amide bonds between Val₃ and His₆. Cation or pH induced changes in the relative contribution of a β turn model are expected to be manifested by changes in the resonance positions of the two corresponding amide nitrogen signals. The γ turn model has hydrogen bonding between Val₃ and Val₅; changes in concentration of this conformation should be indicated by shifts in these two resonances. Changes in α -helix conformation concentration should shift all hydrogen bonded amide signals

in the same direction. If analogous to observations on amides discussed above, decreased hydrogen bonding should result in down-field shifts. Changes in relative contribution of a structure which has three hydrophobic hydrocarbon side chains of Val₃, Val₅ and Phe₈ folded into the center and surrounded by the ionic groups of the molecule should be reflected by the shifts in these three nitrogen signals that result from solution changes in their local environment.

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PROPOSITION V

Systematic Adsorption Resolution

During the 126 years since Louis Pasteur effected the first enantiomeric resolution by picking apart crystals of d- and l- sodium ammonium tartrate with a pair of tweezers, work on the separation of optical isomers has remained in an Edisonian state. The work on resolution has been characterized largely by efforts directed toward separations of individual compounds of interest rather than toward development of reliable general techniques of enantiomeric separation which could be chosen a priori and applied with some confidence. Thus even today, when faced with the problem of separation of optical isomers, the chemist must rely heavily upon trial and error and upon the application of esoteric techniques.

The most common approach to resolution is by reaction with an available pure optical isomer followed by separation of the resultant diastereomers by physical techniques such as fractional crystallization. It is often necessary to try different combinations of resolving agents and solvents.

Numerous other approaches have been described. Selective crystallization of a single enantiomer is sometimes successful when a supersaturated solution of the racemate is seeded with crystals of that enantiomer. One worker resolved glutamic acid by seeding an aqueous solution with small crystals of the L isomer and larger crystals of the R isomer simultaneously and separating the crystals by screening.¹ Some resolutions have been effected by clathrate formation in an asymmetric lattice² while others have been achieved

by fractional crystallization of organic charge transfer complexes formed with chiral molecules.³ There is a report of a partial resolution by diffusion through an optically active membrane.⁴ Some selectivity in solubility in chiral solvents is known.⁵ Kinetic resolutions, the result of unequal rates of reaction of enantiomers with an optically active reagent, have been described.⁶ Resolution due to the preferential digestion of one optical isomer by a living organism or by an isolated enzyme are known.⁷ Preferential adsorption on chiral sorbents has been employed.⁵ In addition to the fact that the procedures referred to above are specific to isolated cases, it should be noted that most resolutions actually consist of isolation of only a single isomer, usually in non-quantitative yield.

One method which shows considerable promise is that of chromatography utilizing selective adsorption on asymmetric sorbents. The procedure is relatively simple and is potentially capable of allowing quantitative isolation of both isomers. Early efforts in this field involved use of naturally available sorbents, such as proteins and carbohydrates. Thus, for example, Bradley found that wool showed selective sorption of asymmetric α -hydroxy acids.⁸ Troger's base, an asymmetric diamine, was partially resolved on a column of lactose.⁹ Starch columns have been used in a number of instances: Krebs¹⁰ has had some success resolving amino acids and camphor derivatives, isolating some fractions with 100% optical activity. Complexes of chromium have been partially resolved by chromatography on optically active quartz.¹¹ Dagliesh observed separation of racemic mixtures of

amino acids by paper chromatography, which resulted from the asymmetry of the cellulose.¹² There have been several recent papers by Gil-Av and coworkers¹³ describing the successful resolution of N-trifluoroacylamino acids by gas chromatography utilizing capillary columns. There are reports of partial resolutions using inert materials such as SiO₂ which have been impregnated with a solution of an optically active compound.¹⁴

Some recent reports have dealt with the use of synthetic polymers for chromatography. Several workers have prepared chiral ion exchange resins, especially by binding readily available alkaloids, and have had some success with the partial resolution of amino acids and other highly polar molecules. Manecke, for example, partially resolved mandelic acid using 1-ephedrine bound to a polystyrene matrix.¹⁵ Workers at Dow have reported partial resolution of methionine by elution with water through a column of 1-methionine bound to a polymer matrix.¹⁶ Some success has also been realized with chiral, polymer-bound transition metal complexes. Thus, matrix-bound (N-carboxymethyl-L-valine)copper(II) showed some selectivity towards amino acids.¹⁷

There is clearly a need for development of more reliable methods of optical resolution. Chromatography on chiral adsorbents holds some promise, but the work in this area has suffered from a number of problems. While paper chromatography is reportedly capable of complete resolution, this technique is restricted to use for qualitative analysis. Though Gil-Av has reportedly achieved total

resolution of acylated amino acids by gas chromatography, the technique is limited to relatively stable, low molecular weight compounds. Separations have been carried out on exceedingly small scale, typically employing columns 70 m. x 0.25 mm. Even if resolution can be improved to allow use of larger capacity columns, preparative gas chromatography is tedious and highly restrictive in terms of quantity. Column chromatography has given only partial separations of enantiomers, despite the use of high sorbent to substrate ratios and slow elution.

The recently available technique of high pressure liquid chromatography has provided a substantial boost in resolution capability compared with other chromatographic techniques. Present instruments use columns packed with adsorbents with a particle size of the order of 75 microns. They are capable of automatically recycling the fractions back through the column, so that a single 3' column may be effectively extended to a 30' column by using ten cycles. Present instruments interchangeably use columns with capacity varying from 100 mg to around 40 g of sample. An example of the use of high pressure chromatography for resolution has just been reported. By attaching chiral crown ethers to silica, a support capable of resolution of racemic mixtures of certain amino acids was obtained.¹⁸ It should be noted that the zwitterionic character of amino acids results in strong intermolecular interactions, and makes them especially suited for this chromatographic resolution.

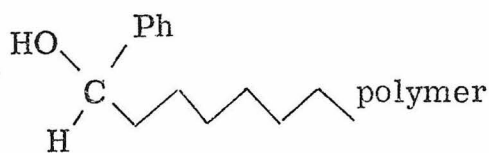
The work on chiral chromatographic resolution has follow-

ed the same course as other methods of enantiomeric separations: experiments have been conducted on a hit or miss basis, using whatever asymmetric sorbents (natural proteins, polymer-bound alkaloids and amino acids) where readily available. Pauling suggested that for every asymmetric substrate, a corresponding sorbent could be designed which would specifically bind it.⁵ While this is clearly an impractical undertaking, it may be possible to develop a series of columns for effective optical resolution, one of which could be selected for resolution of a given compound based on an understanding of its previous performance in resolution of other related compounds.

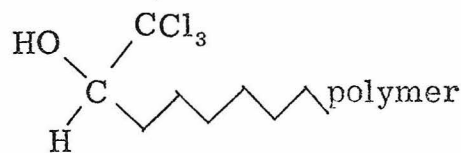
It is proposed that systematic studies on a series of closely related asymmetric polymers of regular conformation, each of which possesses a single type of asymmetric center, be initiated. Asymmetric units would be attached to a polystyrene matrix, and the resolving power of the resins evaluated using high pressure liquid chromatography.

The adsorption of optical isomers on asymmetric sorbents results in the formation of adsorbates which are diastereomeric and hence should be of different stability. The isomer which gives the adsorbate of lowest stability passes through the column most rapidly. The sites of asymmetry for the polymers to be prepared here are chosen to have a single functional group (OH, NH₂, OCH₃, carbonyl, carboxyl) potentially capable of a strong interaction such as hydrogen bond formation with a functionality in the molecule to be adsorbed. The strong binding group is positioned near the chiral carbon. The

differing stabilities of the adsorbates then depend upon weaker intermolecular interactions between the other substituents on the asymmetric sites of the adsorbent and the adsorbate, such as dipolar and steric interactions. The three other substituents of the chiral carbon are chosen to be as different from each other as possible in electronic properties and in physical size and shape. Two alcohol examples are shown below:

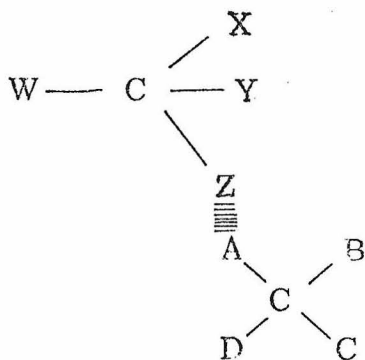


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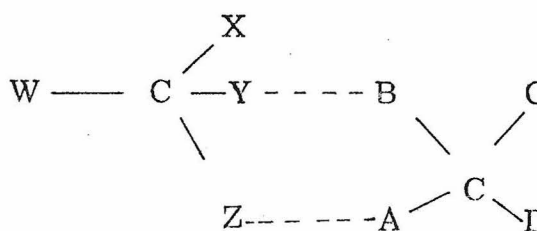


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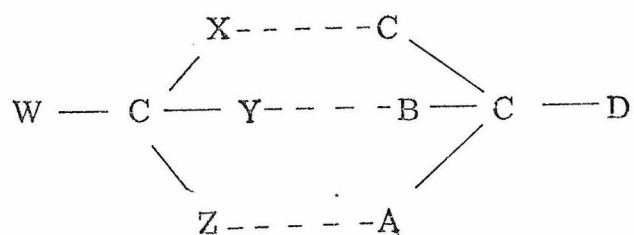
By a simple picture, there are three types of contact possible between the adsorbent and the adsorbate: one point contact, two point contact and three point contact.



One point contact



Two point contact



Three point contact.

For a substrate bound at the "strong-binding" polar site of the adsorbent, there are 9 possible two point contacts and 9 possible three point contacts, in addition to the single one point contact. Only the three point interaction will give rise to chiral recognition. Determination of relative chromatographic retention times of d- and l- components of a series of structurally similar compounds on an adsorbent having chiral centers of known stereochemistry should make possible an evaluation of geometries of the intermolecular interactions responsible for the differences in d- and l- sorbent-sorbate stabilities. Further design of chiral centers for chromatography would be based on initial studies; design of effective chiral adsorbents would be the first goal of this work. The long range goal would be development of a series of chiral adsorbents which would be tested against a wide variety of racemic mixtures. A column to be used for resolution of a newly prepared racemic mixture would be selected by knowledge of its effectiveness in resolution of related substances.

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