I. AN INVESTIGATION OF REARRANGEMENT IN 2-PHENYLETHYL ORGANOMETALLIC COMPOUNDS

II. SKELETAL INTERCONVERSION IN ALLYLCARBINYL, CYCLOPROPYLCARBINYL AND CYCLOBUTYL GRIGNARD REAGENTS

Thesis by

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ABSTRACT

I. AN INVESTIGATION OF REARRANGEMENT IN 2-PHENYLETHYL ORGANOMETALLIC COMPOUNDS

The Grignard reagent formed by 2-phenylethyl-1-^{14}C chloride has been shown not to undergo significant isotope-position rearrangement. Attempts to prepare 2-phenylethyllithium are discussed.

II. SKELETAL INTERCONVERSION IN ALLYLCARBINYL, CYCLOPROPYLCARBINYL AND CYCLOBUTYL GRIGNARD REAGENTS

The Grignard reagents have been prepared from allylcarbinyl, cyclopropylcarbinyl, and cyclobutyl chlorides in the presence of proton donors, and rearrangement of all three skeletons has been observed. It has been established that allylcarbinylmagnesium chloride exists in equilibrium with cyclopropylcarbinylmagnesium chloride, the former being very much favored. Evidence for the existence of a non-classical homoallyl free radical is presented.

ACKNOWLEDGMENTS

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This thesis is dedicated to the memory of my father.

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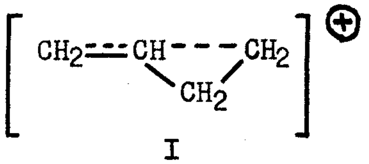
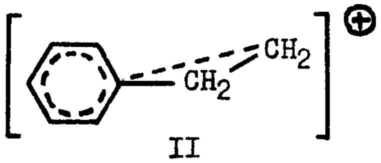
I. AN INVESTIGATION OF REARRANGEMENT IN 2-PHENYLETHYL ORGANOMETALLIC COMPOUNDS

Introduction

Participation in the formation and reactions of carbonium ions by the π-electrons of vinyl and phenyl groups *beta* to the ionic centers has been well demonstrated. The effects of such interaction range from increases of reaction rate (1, 2, 3) and steric control (1, 3, 4, 5) to actual molecular rearrangement (1, 3, 5, 6, 7), which is the case of interest here. Simonetta and Winstein (1) have made calculations of the considerable energetic advantage gained by electron delocalization in the *homoallyl* and *homobenzyl* cations, I and II, pointing out the possibility for still further delocalization which could, under favorable circumstances, lead to


I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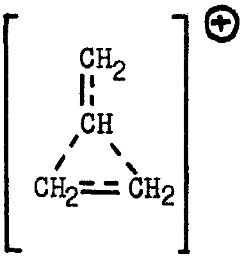
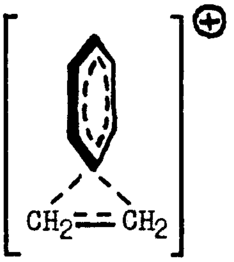
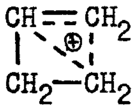
symmetrical species such as III and IV, and rearrangement.


III


IV

The structure formulated as III is, in actuality, less stable than the isomeric bicyclobutonium ion V (8), the several forms of



V

which account for the carbonium ion rearrangements observed in the cyclopropylcarbinyl-cyclobutyl-allylcarbinyl system (9). Thus the simplest homoallyl cation does take advantage of the opportunity for maximum delocalization, although in a manner somewhat different from a priori predictions. Analogously, rearrangement of the simplest homobenzyl cation has been shown to occur; a combination of the intermediates II and IV has been invoked to explain the partial isotope scrambling observed in the products of the deamination of 2-phenylethylamine-1-^{14}C (7).

The hypothesis that double-bond participation leading to rearrangement occurs in the allylcarbinyl Grignard reagent (vide infra) suggests the possibility of similar behavior in the homobenzyl anion.* Migration of a phenyl group to a beta anionic center is not unknown. Cope (10) has observed the base-catalyzed rearrangement

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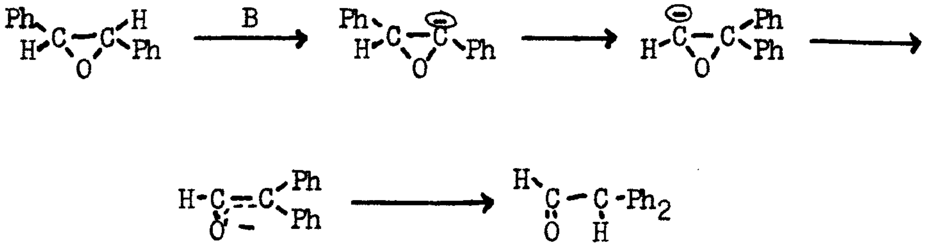
*The designation anion or carbanion, as used in this thesis, does not necessarily imply that the species so called exists as a free negatively charged moiety -- close association with a cation is highly likely, particularly in relatively non-polar organic solvents.

of trans-1,2-diphenylethylene oxide to diphenylacetaldehyde, and has suggested the sequence of equation 1 as a possible mechanism.



(1)

Treatment of 1,1,1-triphenyl-2-chloroethane with sodium produces 1,1,2-triphenylethylsodium (11, 12). The rearrangement may take place by way of the carbanion, but the possibility that it occurs in a radical intermediate cannot be excluded (11, 13). In this connection, it is of interest that the 2,2,2-triphenylethyl radical (generated by the decarbonylation of β,β,β-triphenylpropionaldehyde (14) and the thermal decomposition of di-(3,3,3-triphenylpropionyl)-diimide (15)) undergoes, among other reactions, rearrangement to the 1,1,2-triphenylethyl skeleton. Decarbonylation of 3-phenylpropionaldehyde-2-^{14}C proceeds with 3-5% rearrangement of the 2-phenylethyl radical (16).

Zimmerman and Zweig (17) have observed phenyl migration in 2,2-diphenylpropyllithium, producing 1,2-diphenyl-1-methylethyllithium. A preference for phenyl shift in 2-phenyl-2-(p-tolyl)-propyllithium was among the arguments used to reach the conclusion that rearrangement of a carbanion was indeed taking place. However, the findings of Rüchardt and co-workers (18) that phenyl migrates in preference to p-tolyl in authentic free-radical rearrangements removes much of the force of the argument.

In the present research, some organometallic derivatives of ^{14}C-labeled 2-phenylethyl halides were chosen as likely sources of the homobenzyl anion, in which rearrangement might be observed.

Results and Discussion

Evidence for phenyl migration in the 2-phenylethyl anion was first sought in the Grignard reagent prepared from 2-phenylethyl-1-${}^{14}C$ chloride (VI). The labeled starting material was synthesized by lithium aluminum hydride reduction of commercially available phenylacetic-1-${}^{14}C$ acid, followed by conversion of the resultant 2-phenylethanol-1-${}^{14}C$ to the chloride by treatment with thionyl chloride. The intermediates in this scheme were not checked for

$$\mathrm{PhCH_2{}^{14}COOH} \xrightarrow{\mathrm{LiAlH_4}} \mathrm{PhCH_2{}^{14}CH_2OH} \xrightarrow{\mathrm{SOCl_2}} \underset{\mathrm{VI}}{\mathrm{PhCH_2{}^{14}CH_2Cl}}$$

isotope-position rearrangement; later results eliminated the necessity for such precautions.

The Grignard reagent was prepared from VI and refluxed for two days before carbonation to yield hydrocinnamic-x-${}^{14}C$ acid (VII) with an activity of 1.84 microcuries per millimole (C_1 plus C_2). To determine the distribution of radioactivity between C_1 and C_2, VII was degraded to benzoic acid (VIII) by potassium permanganate oxidation. The activity in VIII (C_2) amounted to 3.23×10^{-3} microcuries per millimole, corresponding to 0.2% rearrangement, hardly a significant amount.

$$\underset{\mathrm{VI}}{\mathrm{PhCH_2{}^{14}CH_2Cl}} \xrightarrow[\mathrm{2.)\ CO_2}]{\mathrm{1.)\ Mg,\ Et_2O}} \underset{\mathrm{VII}}{\underset{(2)}{\mathrm{PhCH_2}}\underset{(1)}{\mathrm{{}^{14}CH_2}}\mathrm{COOH}} \xrightarrow{\mathrm{KMnO_4}} \underset{\mathrm{VIII}}{\mathrm{PhCOOH}}$$

The lack of rearrangement in the 2-phenylethyl Grignard reagent is not surprising. Nor is it necessarily indicative that the 2-phenylethyl anion is incapable of such isomerization. A good deal of evidence has been cited in support of the view that no appreciable concentration of carbanions exists in a solution of Grignard reagent. The carbon-magnesium bond is essentially covalent, possessing only 34% ionic character as calculated from Pauling's electronegativities (19), and may be expected to cleave with difficulty in a medium which cannot solvate the resulting carbanion (20, 21). Evans and Pearson (22) have proposed that such ionization does occur, and that the carbanions are "solvated" by magnesium-containing species in the Grignard aggregate. The resulting ions (23) are the same as would be formed by ionization of the magnesium-halogen bond and complexing of the halide with magnesium (21). If carbanions are formed, then, they would most likely be transitory states within the complex aggregate, never really free of strong binding forces. That free carbanions do not find their way into the solution is borne out by the general failure of Grignard reagents to cleave ethers, behavior exhibited by many of the more ionic organometallic compounds (20, 21).

Previous experimental evidence would indicate that the homobenzyl anion (or incipient anion) must be less constrained than in a Grignard reagent before rearrangement can take place. While phenyl migration could be induced in the sodium derivative of 1,1,1-triphenyl-2-chloroethane (11, 12), hydrolysis of the corresponding Grignard reagent afforded only 1,1,1-triphenylethane (24). Likewise, 2,2-diphenylpropylmagnesium chloride failed to rearrange after twenty hours at room temperature; the corresponding lithium compound was stable at 0°, but underwent phenyl migration when the solution was refluxed (17). These compounds represent especially favorable conditions for rearrangement, in that the products have their charge (or partial charge) located in a benzylic position and should be of lower energy than the unrearranged molecules, and the intermediate bridged anions (fig. 1) are predicted to be considerably stabilized with respect to the unbridged anions (17).* Even in

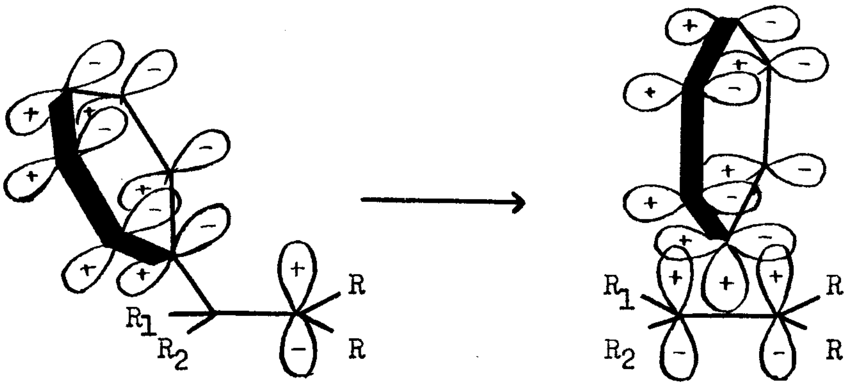


Fig. 1

these cases, more energy is required to ionize the carbon-magnesium bond and provide the electrons necessary for rearrangement-producing

---

*Calculations made by Zimmerman and Zweig (17) of the energy change expected on transformation of the free unbridged anions to the half-migrated species (see fig. 1) give values of $-0.52\ |\beta|$ for cases in which R_1 and R_2 are groups other than phenyl, $-0.88\ |\beta|$ where R_1 is phenyl and R_2 is non-phenyl, and $-1.35\ |\beta|$ where $R_1 = R_2 =$ phenyl.

delocalization than is available to the system. Lowering these requirements (*i.e.* providing a carbon-metal bond with more ionic character) allows the migration to proceed.

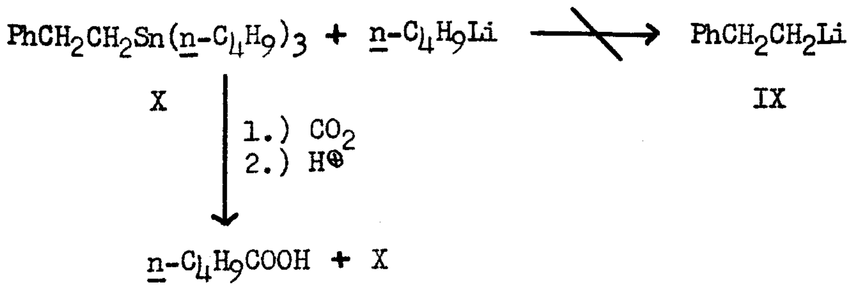
Since rearrangement of the 2-phenylethyl anion lacks the "push" provided by a lower energy product and an extra-stabilized intermediate state, the ionic nature of the carbon-metal bond is expected to be quite important in determining whether or not migration will occur. Accordingly, the attempt was made to prepare 2-phenylethyllithium (IX). Treatment of 2-phenylethyl bromide with lithium metal was carried out under a wide variety of conditions (see Experimental) with little success. The apparent low reactivity of the halide was in part responsible for the difficulties encountered, as demonstrated by the consistent recovery of most of the starting material despite increases in the reaction temperature and use of high-speed stirring. The formation of ethylbenzene and styrene suggested that *beta*-elimination of hydrogen bromide from the phenylethyl bromide was consuming any organometallic compound formed.

Treatment of 2-phenylethyl bromide with a solution of *n*-butyllithium effected a small amount of metal-halogen exchange. No styrene was obtained, and the only evidence of attack by the butyllithium on the halide was formation of a high-boiling phenyl-containing hydrocarbon, which could be accounted for by unrecovered phenylethyl bromide. Most of the butyllithium was consumed, presumably by attack on the bromide and in initiating polymerization of the resulting styrene. A material balance in the experiment could not be obtained, however, due in part to partial oxidation of the butyllithium solution (see Experimental) before its use, and conclusions based on the results can only be regarded as tentative.

The largest yield of hydrocinnamic acid (still less than 2%) obtained on carbonation of a 2-phenylethyl bromide-lithium reaction mixture was accompanied by coupling product, 1,4-diphenylbutane, and a tertiary alcohol (possibly tris-(2-phenylethyl)-carbinol). The ratio of acid to diphenylbutane to alcohol was approximately 1:3:1.5. No ethylbenzene or styrene was detected in this reaction, which was run in ether at -10° using lithium pieces and ordinary stirring, nor was any starting halide recovered.

It seemed advisable to try to prepare 2-phenylethyllithium in an environment which did not contain 2-phenylethyl bromide to undergo elimination or coupling. Displacement of an allyl group from allyltriphenyltin has been used to good advantage in the preparation of allyllithium (25), so two tetrasubstituted tin compounds were prepared as possible intermediates from which the lithium compound IX might be derived (26).

(2-Phenylethyl)-tri-*n*-butyltin (X) and (2-phenylethyl)-triphenyltin (XI) were prepared from phenethylmagnesium bromide and the corresponding trisubstituted tin chloride (25, 26). Treatment of X with *n*-butyllithium, followed by carbonation, gave *n*-valeric acid in 72% yield (based on butyllithium) and 80% recovery of X. The reaction of phenyllithium with the tin compound XI afforded a 27% yield (based on phenyllithium) of benzoic acid upon carbonation.

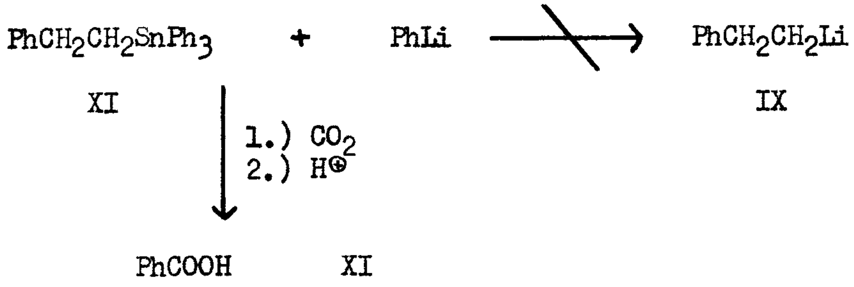


$$PhCH_2CH_2Sn(\underline{n}\text{-}C_4H_9)_3 + \underline{n}\text{-}C_4H_9Li \not\longrightarrow PhCH_2CH_2Li$$

X IX

1.) CO_2
2.) $H^{\oplus}$

$\underline{n}\text{-}C_4H_9COOH + X$



$$PhCH_2CH_2SnPh_3 + PhLi \not\longrightarrow PhCH_2CH_2Li$$

XI IX

1.) CO_2
2.) $H^{\oplus}$

PhCOOH XI

The remaining products were XI (41% recovered), tetraphenyltin (13% based on XI) and a large amount of unidentified oil.

The order of removal of groups in cleavage of unsymmetrically substituted tin compounds by bromine or iodine, and to some extent by hydrogen chloride, is as follows (27):

> o-tolyl, m- and p-tolyl, phenyl, benzyl, methyl, ethyl, n-propyl, n-butyl, n-hexyl, n-heptyl

Benzyl (28), allyl (25), and vinyl (29) groups are removed before phenyl on reaction with phenyllithium; insufficient data are available to predict the direction of cleavage of unsymmetrical organotin compounds by strong base. Clearly n-butyl is cleaved more easily than the 2-phenylethyl group. If the latter behaves as a large alkyl group, the order may parallel somewhat that for halogen cleavage, and removal of phenyl before phenylethyl would be expected. That the 2-phenylethyl group is not displaced by phenyllithium, while the benzyl group is, is also consistent with the behavior of substituents with alpha and beta cyano and carbalkoxy groups (29). Cyanomethyl and carbalkoxymethyl groups in unsymmetrically substituted tin compounds react with aqueous base and lithium aluminum hydride with carbon-tin cleavage, but when the ester or cyano group is beta to the tin atom, these reagents afford the usual products of reaction with the substituted alkyl groups. Treatment of (2-cyanoethyl)-tri-*n*-propyltin with methylmagnesium iodide gives mostly addition product, with a small amount of cleavage, while similar reaction of tri-*n*-butyl-(2-carbomethoxyethyl)-tin proceeds with addition only.

The formation of tetraphenyltin during the reaction of the tin compound XI and phenyllithium was most likely due to the tendency of phenyl-substituted tin compounds to undergo facile disproportionation and symmetrization. In the synthesis of triphenyl-4-pentenyltin by interaction of 4-pentenyllithium and triphenyltin chloride (30), for example, a large quantity of tetraphenyltin resulted. Use of 4-pentenylmagnesium bromide prevented initial disproportionation, but distillation of the product again brought about the formation of tetraphenyltin. Similarly, reaction of triphenyltin hydride and strong base (31) led to formation of tetraphenyltin even at room temperature.

Incidental to the work carried out on tin compounds, it was observed that the infrared spectrum of each phenyl-substituted tin compound encountered contained a strong, sharp band at 1428 cm^{-1}. as well as the absorption at 1075 cm^{-1}. which had previously been attributed to the tin-phenyl linkage (29, 32). The 1428 cm^{-1}. band did not seem to be characteristic of any of the substituent groups present. It has been reported that absorption characteristic of the linkage between silicon and unsubstituted phenyl groups lies in the region between 1430 and 1435 cm^{-1}. (33). In view of the many similarities observed between silicon and tin in organic compounds, it is suggested that the absorption at 1428 cm^{-1}. is, in addition to that at 1075 cm^{-1}., characteristic of the tin-phenyl bond.

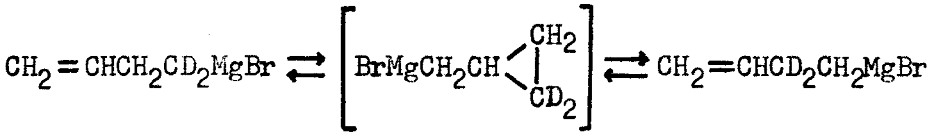
II. SKELETAL INTERCONVERSION IN ALLYLCARBINYL, CYCLOPROPYLCARBINYL AND CYCLOBUTYL GRIGNARD REAGENTS

Introduction

The ease of interconversion of carbonium ions arising from cyclopropylcarbinyl, cyclobutyl, and allylcarbinyl derivatives has received extensive study (9). The recent discovery (34) that the *alpha* and *beta* methylene groups in allylcarbinylmagnesium halides are slowly interchanged, coupled with the fact that Grignard reagents derived from cyclopropylcarbinyl halides give rise to products with the allylcarbinyl skeleton only (6), suggests that this mobility extends in some measure at least to the related anionic systems.

The organic radical of the Grignard reagent from allylcarbinyl chloride or bromide has been shown by n.m.r. spectra to possess the allylcarbinyl structure to the extent of at least 99% (34). The rearrangement of 3-butenyl-1,1-$^2H_2$-magnesium bromide (XII) to 3-butenyl-2,2-$^2H_2$-magnesium bromide (XIII) has been followed by n.m.r.; the half-times for establishment of equilibrium between the two forms are thirty hours at 27° and forty minutes at 55.5°, corresponding to an activation energy of about 23 kcal. (34).

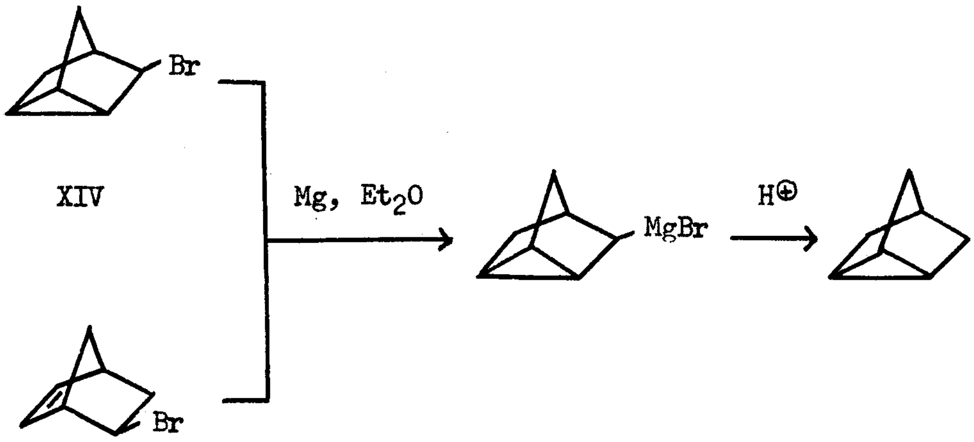
One may delve further into the nature of the equilibrium between the isotope-position isomers of the allylcarbinyl Grignard reagent. The Grignard reagent prepared from a cyclopropylcarbinyl halide has an n.m.r. spectrum which is the same as that of the reagent derived from an allylcarbinyl halide (34), in addition to forming open-chain products upon reaction (6). Conversely, the Grignard reagents from both 3-bromonortricyclene (XIV) and 5-bromonorbornylene (XV) react to give products with the nortricyclene skeleton (35) and possess a common n.m.r. spectrum, which is best explained by the nortricyclyl structure (20). In each isomer pair the structure predominating is that expected to be the most thermodynamically stable (20). A definite relationship between the allylcarbinyl and cyclopropylcarbinyl



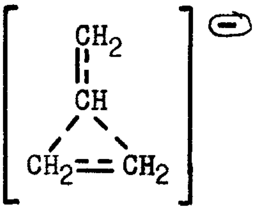
$$CH_2{=}CHCH_2CD_2MgBr \rightleftarrows \left[BrMgCH_2CH\left\langle \begin{array}{l} CH_2 \\ | \\ CD_2 \end{array} \right. \right] \rightleftarrows CH_2{=}CHCD_2CH_2MgBr \qquad (2)$$

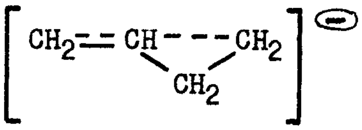
XII XVI XIII

configurations in suitably constituted Grignard reagents may be inferred from this information; it is reasonable to postulate intervention of a cyclopropylcarbinyl species (XVI) in the allylcarbinyl equilibrium (equation 2).



Alternatively, the bridged anionic structure XVII could lie between the two isomers, XII and XIII, but this would not be the most economical of intermediate states. A pathway between the cyclopropylcarbinyl and allylcarbinyl skeletons clearly exists (vide supra), and would be more likely to proceed through a homoallyl anion XVIII, which simple molecular orbital theory predicts to have significant delocalization energy (36), than through XVII, in which two sigma bonds must be broken at the expense of energy gained by delocalization. The symmetrically bridged ion would have to be involved in the allylcarbinyl equilibrium in a process independent of the transition between the allylcarbinyl and the cyclopropylcarbinyl structure.

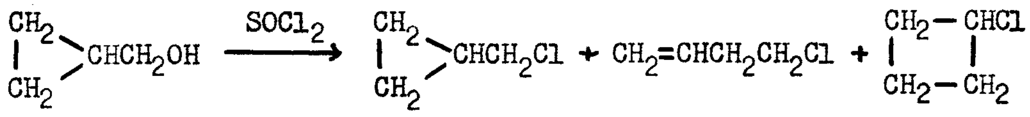

XVII


XVIII

It remains to be decided whether XVI plays the role of a relatively stable intermediate or is just a transition state. The behavior of the Grignard reagent prepared from a cyclopropylcarbinyl halide might be expected to provide some insight into this problem. The cyclic halide could react with magnesium to give a cyclic organometallic compound which would rearrange rapidly to the open-chain isomer, or the latter could be formed directly as the halide combined with the metal. If the former case obtains, it would be reasonable to expect that a cyclopropylcarbinylmagnesium halide would be a structure of lower energy than a transition state. It was of interest, then, to determine if the cyclopropylcarbinyl Grignard reagent is capable of discrete existence; it was decided to try to trap the reagent prepared from cyclopropylcarbinyl chloride very early in its existence and see if cyclic products could be isolated.

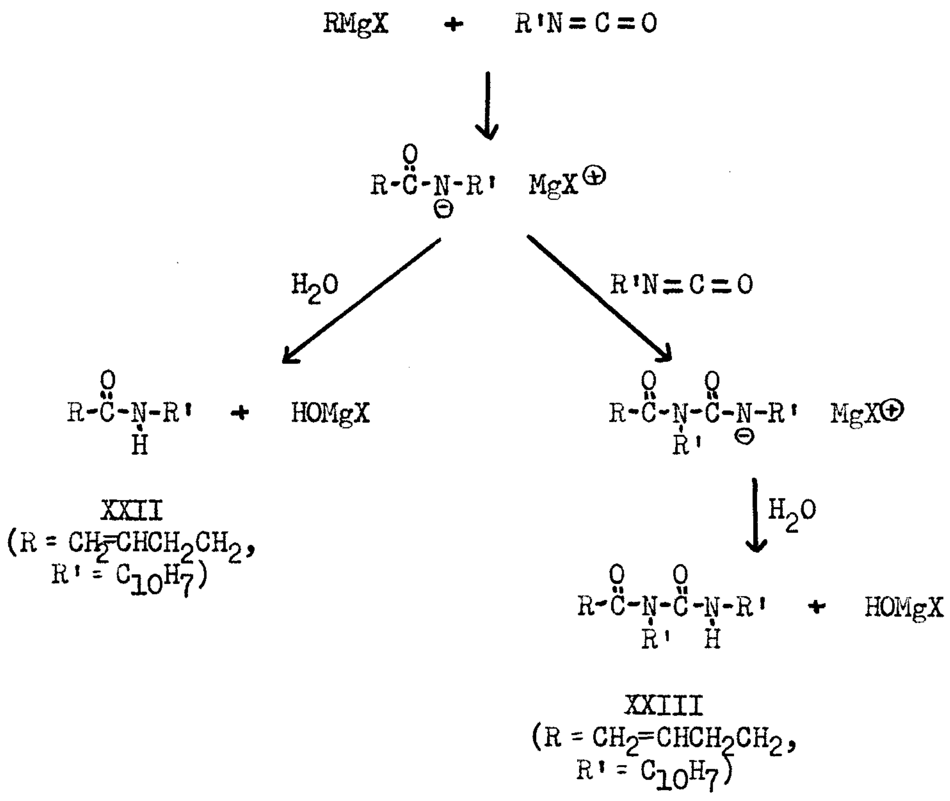
Results

Cyclopropylcarbinyl chloride (XIX) was prepared by treatment of cyclopropylcarbinol with thionyl chloride under conditions carefully controlled to prevent carbonium ion formation and rearrangement (37). The product was still contaminated with allylcarbinyl chloride (XX) and cyclobutyl chloride (XXI), and could not be completely purified by distillation. The cyclopropylcarbinyl chloride used as starting material in most of the experiments described was contaminated with 2-7% of cyclobutyl chloride.



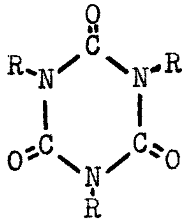
XIX XX XXI

One attempt at trapping the cyclopropylcarbinyl Grignard reagent involved allowing the corresponding chloride to react with magnesium in a cyclic reactor (20), in which the newly formed organometallic compound was swept into a refluxing solution of α-naphthyl isocyanate at a rate determined by the vigor of reflux. N-(1-Naphthyl)-3-butenecarboxamide (XXII) was first prepared by addition of the Grignard reagent made from cyclopropylcarbinyl chloride in the normal manner to a solution of α-naphthyl isocyanate. A significant amount of a side product, XXIII, which had an infrared spectrum and elemental analysis consistent with the structure of N-allylacetyl-N,N'-bis-(1-naphthyl)-urea, was also isolated. An analogous compound was obtained occasionally from the reaction of cyclobutylmagnesium chloride with phenyl isocyanate (6), and was presumed to have originated from attack by the Grignard reagent-isocyanate condensate on a second molecule of isocyanate (see equation 3).



(3)

When a trial reaction was run in the cyclic reactor, no XXII or XXIII was produced; the major product (XXIV) was a high-melting white crystalline solid. Its infrared spectrum (see Experimental) contained bands which might be indicative of a secondary amide, disubstituted urea, or related structure; no cyclopropyl absorption was observed (33). It has been reported that, in the reaction of the Grignard reagent of a sulfone with phenyl isocyanate, triphenyl isocyanurate (XXV, R = C_6H_5) was formed (38). In fact, as weak a base as potassium acetate is capable of catalyzing the trimerization of phenyl isocyanate (39). The analogous tris-(1-naphthyl) isocyanurate (XXV, R = $C_{10}H_7$) has been prepared (39a). This compound possesses a melting point somewhat higher than that of XXIV (335° as



XXV

compared to 312-313°) and in a Nujol mull exhibits a single carbonyl peak in the infrared at 1713 cm^{-1}. A suspension of XXIV in hexachloro-1,3-butadiene shows strong absorption at 1610 cm^{-1}. and medium absorption at 1635 cm^{-1}. Difficulty was encountered in the trimerization of α-naphthyl isocyanate (39a), in that traces of moisture caused the formation of sym.-bis-(1-naphthyl)-urea (m.p. 298°) which, like XXIV and unlike XXV (R = $C_{10}H_7$), was insoluble in acetone and soluble in dimethylformamide. Identification of XXIV cannot be made with certainty from this data; the properties of the material are more consistent with those of the urea than those of the isocyanurate, though trimer could also be present. The evidence does indicate that α-naphthyl isocyanate is not an effective trapping agent for Grignard reagents under the experimental conditions used.

The reaction of cyclopropylcarbinyl chloride with magnesium in the presence of a suitable proton donor provided a more fruitful approach to the problem of trapping the cyclopropylcarbinyl Grignard reagent. While the resulting hydrocarbons were quite soluble in ether, they could be removed by slow distillation, and vapor-phase chromatography provided a simple and sensitive means for their analysis. It was anticipated that variation of the proton donor might provide some measure of control over the time elapsing between formation of the Grignard reagent and its consumption. In the end, the technique was employed with all three of the isomeric halides, and revealed much more than whether or not cyclopropylcarbinylmagnesium chloride exists.

When cyclopropylcarbinyl chloride (containing 2% of cyclobutyl chloride) was allowed to react with magnesium in the presence of benzoic acid, a 52% yield of hydrocarbon, consisting of 92% 1-butene, 6% methylcyclopropane, and 2% cyclobutane, was obtained. If the Grignard reagent was prepared from cyclopropylcarbinyl chloride and refluxed for 5-42 hr. before addition to an ether solution of benzoic acid, the amount of methylcyclopropane dropped to a trace (roughly 0.1 ± 0.1% of the hydrocarbon fraction*), but it was still present.

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*In the vapor-phase chromatograms of the hydrocarbon mixtures, the peaks due to methylcyclopropane appeared at slightly longer retention times than those of 1-butene, and the two were incompletely resolved. When a very small amount of methylcyclopropane was present, precise measurement of the area of its peak could not be made.

To investigate the possibility that the trace of methylcyclopropane observed was due to a radical reaction independent of Grignard reagent formation and decomposition (13), the reagent from cyclopropylcarbinyl chloride (containing 7% of cyclobutyl chloride) was prepared and refluxed for 42 hr., during which time all volatile substances produced were trapped. At the end of this period, most of the liquid from the Grignard solution was distilled into the same trap. The combined material was found to contain a mixture of 86% 1-butene, 3% methylcyclopropane, and 11% cyclobutane; acidolysis of the Grignard reagent produced about ten times as much hydrocarbon, consisting of 92% 1-butene, a trace of methylcyclopropane, and 8% cyclobutane. Although a small amount of hydrocarbon seems to arise from processes other than reaction of the Grignard reagent with acid, it would not have effected greatly the product composition obtained in the reaction of cyclopropylcarbinyl chloride in benzoic acid solution (if it was formed that rapidly), and apparently was distilled from the system before the acidolysis step in the long-term experiment.

The same series of experiments was carried out using allylcarbinyl chloride as the starting material. In the synthesis of this chloride by treatment of allylcarbinol with thionyl chloride, a small amount of the cyclobutyl isomer was formed; some of the samples of allylcarbinyl chloride contained as much as 0.5% of this material. When the Grignard reagent prepared from the unsaturated chloride was decomposed with benzoic acid after a reflux period of 8-42 hr., hydrocarbon mixtures were produced which were $>99\%$ 1-butene, but contained again traces of methylcyclopropane. The hydrocarbons formed during one reflux period (amounting to ca. 4% of the hydrocarbons formed upon acidolysis of the Grignard reagent in the same experiment) were composed of 97% 1-butene, 1% methylcyclopropane, and 2% cyclobutane. The reaction of allylcarbinyl chloride with magnesium in the presence of benzoic acid resulted in hydrocarbons containing an unexpected 1-3% of methylcyclopropane.

The above experiments revealed the composition of the products of acidolysis of the Grignard reagents from cyclopropylcarbinyl and allylcarbinyl chlorides very soon after their formation and after they had reached what seemed to be their equilibrium constitution. Supplementary information on the product compositions arising from decomposition at an intermediate time was then sought. It was expected that phenylacetylene, which takes 30 min. to react with 0.25 mole quantities of methyl- or ethylmagnesium halides at the temperature of refluxing ether (40), would allow the Grignard reagents a somewhat longer lifetime than would benzoic acid, depending on the rate of reaction of the halide with magnesium. The results of experiments in which phenylacetylene was included in the reaction mixtures are listed in Tables I and II, along with those from the reactions described above.

With cyclopropylcarbinyl chloride as the starting material, the Grignard reaction in the presence of phenylacetylene produced a hydrocarbon mixture containing 0.5-0.7% of methylcyclopropane, while only a trace of that compound resulted from the reaction of

Table I

GRIGNARD REACTIONS OF CYCLOPROPYLCARBINYL CHLORIDE*

Composition of Starting Material[a]	Lifetime[b]	Hydrocarbon Composition (Mole Percent)			Percent Composition of Recovered Starting Material		
					XX[a]	XIX[a]	XXI[a]
98% XIX, 2% XXI	PhCOOH	92	6	2	-	ca. 98	ca. 2
93% XIX, 7% XXI	PhCOOH	91	6	3			
95% XIX, 5% XXI	5 hr.[c]	96.3	0.1	3.6			
93% XIX, 7% XXI	5 hr.[c]	91.2	0.1	8.7			
95% XIX, 5% XXI	42 hr.[c]	95.8	0.2	4.0			
93% XIX, 7% XXI	42 hr.[c]	92.4	<0.1	7.6			
93% XIX, 7% XXI	PhC≡CH	94.1	0.7	5.3			
93% XIX, 7% XXI	PhC≡CH	90.9	0.5	8.6			
96% XIX, 4% XXI	t-BuOH	80	15	6			

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*See Table III, p. 26 for footnotes.

Table II

GRIGNARD REACTIONS OF ALLYLCARBINYL CHLORIDE*

Composition of Starting Material^{a}	Lifetime^{b}	Hydrocarbon Composition (Mole Percent)			Percent Composition of Recovered Starting Material		
					XX^{a}	XIX^{a}	XXI^{a}
100% XX	PhCOOH	99	1	...^{d}	ca. 100	-	-
XX, <0.1% XXI	PhCOOH	97	3	0			
XX, <0.1% XXI	PhCOOH	98	2	0			
100% XX	8 hr.^{c}	99.8	0.2	...^{d}			
XX, <0.1% XXI	24 hr.^{c}	99.8	0.1	0.1			
XX, 0.4% XXI	24 hr.^{e}	99.8	tr	tr			
XX, 0.4% XXI	24 hr.^{f}	99.9	0	tr			
100% XX	42 hr.^{c}	99.6	0.2	0.2			
XX, <0.1% XXI	PhC≡CH	96.4	0.2	3.4			
XX, <0.1% XXI	PhC≡CH	93.8	0.2	6.0			
XX, 0.4% XXI	_t_-BuOH	99.8	tr	0.2			

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*See Table III, p. 26, for footnotes.

allylcarbinyl chloride under the same conditions. However, in the latter case, a significant amount of cyclobutane was formed, although the starting material was contaminated with less than 0.1% of cyclobutyl chloride (see Table II). Decomposition of the Grignard reagent from allylcarbinyl chloride with phenylacetylene after 24 hr. yielded the same hydrocarbon mixture as did acidolysis of the day-old reagent with benzoic acid. It made no difference whether the Grignard reagent was filtered and added to the alkyne solution or the latter was added to the solution of organometallic compound with excess magnesium still present.

Cyclobutyl Grignard reagents made in the usual manner have been shown to react normally, giving cyclobutyl derivatives free of the open-chain unsaturated isomer (6). The appearance of the cyclobutyl skeleton in the products of the Grignard reaction of allylcarbinyl chloride in phenylacetylene solution prompted an investigation of the behavior of cyclobutyl chloride with magnesium in an environment containing proton donors. The Grignard reagent prepared from cyclobutyl chloride reacted with benzoic acid, either immediately or after 24 hr. of reflux time,* to produce a mixture of 99% cyclobutane, 1% 1-butene, and no methylcyclopropane (see Table III). When phenylacetylene was used as an addend, however, the hydrocarbons formed consisted of 74% 1-butene and 26% cyclobutane.

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*The volatile fraction isolated during the reflux period consisted of a trace of 1-butene, 67% of cyclobutane, and 33% of a compound corresponding in retention time to one of the often-observed unidentified products (vide infra).

Table III

GRIGNARD REACTIONS OF CYCLOBUTYL CHLORIDE

Composition of Starting Material[a]	Lifetime[b]	Hydrocarbon Composition (Mole Percent)			Percent Composition of Recovered Starting Material		
					XX[a]	XIX[a]	XXI[a]
XXI, 0.5% XX	PhCOOH	1	0	99			
XXI, 0.5% XX	24 hr.[c]	1	0	99			
XXI, 0.5% XX	PhC≡CH	74	0	26	8.1	0	91.9
XXI, 0.5% XX	*t*-BuOH	55	14	29	0.6	0	99.4

[a] XX = allylcarbinyl chloride, XIX = cyclopropylcarbinyl chloride, XXI = cyclobutyl chloride. [b] Lifetime is designated either by the period between the start of reaction and addition of the hydrolyzing agent or by the included hydrolyzing agent. [c] Hydrolysis accomplished by adding Grignard reagent to benzoic acid solution. [d] Analysis for cyclobutane was not made. [e] Hydrolyzed by adding Grignard reagent to phenylacetylene solution. [f] Hydrolysis by phenylacetylene, inverse addition.

In the face of the apparently anomalous behavior of the C_4H_7 Grignard reagents in a phenylacetylene solution, it was decided to examine the product compositions resulting from formation of the organometallic compounds in the presence of another proton donor comparable in acidity to the alkyne. The compound selected was t-butyl alcohol, which has a pK_a of about 20 (41), in the same general range as that of phenylacetylene ($pK_a \sim 21$) (42). This addend led to formation of hydrocarbon mixtures which were quite different from those arising in the reaction of the corresponding halides in the presence of phenylacetylene. The results are included in Tables I-III. No more cyclobutane was produced than could be accounted for by the amount of cyclobutyl chloride present when allylcarbinyl chloride was used as the starting material. In the reaction of cyclopropylcarbinyl chloride, however, the hydrocarbon mixture contained 15% of methylcyclopropane. The Grignard reagent from cyclobutyl chloride was decomposed by the t-butyl alcohol present to yield a mixture of 55% 1-butene, 14% methylcyclopropane, and 29% cyclobutane.

All of the experiments described so far were carried out with approximately a four-fold excess of magnesium over halide. When an excess of halide (5:2) was used, the results listed in Table IV were obtained. The relative amount of magnesium had a significant effect on the hydrocarbon composition only in the reactions of cyclopropylcarbinyl and cyclobutyl chlorides, when t-butyl alcohol was present.

Table IV

MAGNESIUM EFFECT ON HYDROCARBON PRODUCT MIXTURES

Composition of Starting Material[a]	Lifetime[b]	Excess Reagent	Hydrocarbon Composition (Mole Percent)			Percent Recovered	Composition of Starting Material	
						XX[a]	XIX[a]	XXI[a]
98% XIX, 2% XXI	PhCOOH	Mg	92	6	2	-	ca. 98	ca. 2
96% XIX, 4% XXI	PhCOOH	RCl	91.3	8.2	0.5	tr	91	9
84% XIX, 14% XXI, 2% XX	PhC≡CH	Mg	96	1	3	19	7	74
84% XIX, 14% XXI, 2% XX	PhC≡CH	RCl	95	2	3	17	27	56
96% XIX, 4% XXI	*t*-BuOH	Mg	78	17	5	-	-	tr
96% XIX, 4% XXI	*t*-BuOH	RCl	41	58	1	20	44	37
99.5% XXI, 0.5% XX	*t*-BuOH	Mg	55	14	29	0.6	0	99.4
93% XXI, 7% XIX	*t*-BuOH	RCl	70	18	12	tr	2	98
Mixed C_4H_7Cl[c]	*t*-BuOH	RCl	62.5	26.6	10.9	25.6	26.2	48.2
Mixed C_4H_7Cl[c]	PhC≡CH	RCl	93.9	1.5	4.6	31.6	9.2	59.2

[a] XX = allylcarbinyl chloride, XIX = cyclopropylcarbinyl chloride, XXI = cyclobutyl chloride.

[b] Lifetime is designated by the hydrolyzing agent included in the reaction mixture.

[c] Mixture contained 20% XX, 42% XIX, and 38% XXI.

In order to meaningfully assess the significance of the hydrocarbon mixtures afforded by the Grignard reactions of the various halides, it is necessary to know if the starting materials themselves undergo rearrangement during the course of the experiments. Tables I-IV contain the compositions of the halide fractions recovered from several of the reaction mixtures. This data, along with the results of control experiments, is enumerated for convenient reference below, in terms of the conditions under which C_4H_7Cl has or has not been observed to isomerize. Net rearrangement has been demonstrated not to occur under the following circumstances:

(a.) When an equimolar solution of cyclopropylcarbinyl chloride and benzoic acid in ether is refluxed for five hours.

(b.) When a chloride mixture is refluxed overnight, or when cyclobutyl bromide (6) is refluxed for four hours in ether with nearly an equivalent amount of magnesium bromide.

(c.) When an ether solution of cyclopropylcarbinyl and cyclobutyl chlorides is refluxed for three hours with magnesium chloride and magnesium.

(d.) During the Grignard reaction of either allylcarbinyl or cyclopropylcarbinyl chloride in the presence of benzoic acid and excess magnesium.

(e.) During the Grignard reaction of cyclobutyl chloride in the presence of t-butyl alcohol, whether magnesium was in excess or not.

(f.) During the Grignard reaction of excess allylcarbinyl chloride in a solution of t-butyl alcohol in ether.

Net rearrangement does occur:

(a.) To a slight extent during the Grignard reaction of cyclobutyl chloride in the presence of phenylacetylene and excess magnesium.

(b.) To a slight extent in the reaction of excess cyclopropylcarbinyl chloride with magnesium in the presence of benzoic acid.

(c.) During the Grignard reaction of a chloride mixture in the presence of phenylacetylene, whether magnesium was in excess or not.

(d.) During the reaction of excess cyclopropylcarbinyl chloride in the presence of t-butyl alcohol.

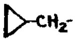
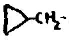
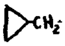
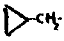
Metal-halogen interchange, although not expected to occur with Grignard reagents (42), would provide one means by which the starting halides could be rearranged in the course of an experiment. It was repeatedly observed that allylcarbinyl chloride was considerably less reactive in Grignard reagent formation than cyclopropylcarbinyl chloride or cyclobutyl chloride; of the latter two, cyclopropylcarbinyl chloride probably reacted more rapidly. If metal-halogen exchange were to take place, it would involve transfer of magnesium to the more electronegative of the isomeric alkyl groups (43).

Assuming that ease of reaction with metallic magnesium parallels the electronegativity of the alkyl groups, one would predict that the allylcarbinyl Grignard reagent would undergo exchange with one or the other of the cyclic chlorides. The Grignard reagent was prepared from allylcarbinyl chloride (containing 0.2% of cyclobutyl chloride) and refluxed for 24 hr. with a mixture of 95% cyclopropylcarbinyl and 5% cyclobutyl chlorides. After acidolysis with benzoic acid, the C_4H_7Cl recovered consisted of 41% cyclopropylcarbinyl, 53% allylcarbinyl, and 7% cyclobutyl chlorides. Correction for the amount of unsaturated chloride present in the Grignard solution showed that the composition of the added C_4H_7Cl had been changed to 64% cyclopropylcarbinyl, 26% allylcarbinyl, and 10% cyclobutyl chloride. The hydrocarbon fraction obtained from the decomposition step consisted mostly of 1-butene, a little cyclobutane, and possibly a trace of methylcyclopropane.

At this point it should be brought out that the data presented here do not represent the total course of the reactions studied. Table V shows the material balance obtained by consideration of only the C_4H_8 formed and the C_4H_7Cl recovered in several experiments. Analysis by vapor-phase chromatography of the ether solutions remaining after decomposition of a few of the Grignard reagents showed the presence of as many as six or seven high-boiling compounds, none of which were identified. Small amounts (up to 2-3 mole percent) of three compounds with v.p.c. retention times in the same range as the C_4H_8 isomers were observed regularly. Two of these appeared to be

Table V

YIELDS OF HYDROCARBON AND RECOVERED CHLORIDE

Starting Material	Addend	Yield C_4H_8[a]	C_4H_7Cl Recovered[b]
 Cl^c	PhCOOH	52	6
 Cl^d	PhCOOH	7 (18)	6
 Cl^c	PhCOOH	39	14
 Cl^c	PhC≡CH	. . .	27
 Cl^d	PhC≡CH	. . .	44
 Cl^c	*t*-BuOH	80	tr
 Cl^d	*t*-BuOH	0.8 (2)	10

[a] Percent based on chloride used. Value in parentheses is based on magnesium, when that reactant was not in excess. [b] Percent of original amount. [c] Magnesium in excess. [d] Chloride in excess.

unsaturated, as their peaks disappeared after bromination of the hydrocarbon fraction. Comparison of v.p.c. retention times with authentic compounds for two typical hydrocarbon mixtures and their bromination products showed that none of the unidentified volatile products were *cis*- or *trans*-2-butene, and also confirmed that the peaks due to methylcyclopropane were not likely to be augmented by the presence of these compounds, which have retention times quite close to that of methylcyclopropane.

A final experiment was carried out to help establish the nature of the processes giving rise to the hydrocarbon mixtures observed in this study. The decomposition of Grignard reagents with cobaltous halides is considered to proceed with the formation of free alkyl radicals (44, 45); it was of interest to see if the volatile hydrocarbons generated in such a reaction with the Grignard reagents from cyclopropylcarbinyl and allylcarbinyl chlorides were similar in composition to any of the product mixtures obtained when those reagents were prepared in the presence of proton donors. The halides were allowed to react with magnesium and a slight excess of anhydrous cobaltous chloride, and the volatile products were trapped and analyzed as in all of the Grignard reactions in which an addend was included (see Experimental). From a mixture of 95% cyclopropylcarbinyl and 5% cyclobutyl chlorides was obtained 68% 1-butene, 18% trans-2-butene, 10% cis-2-butene, and 4% cyclobutane. When the starting material was allylcarbinyl chloride containing 0.4% of cyclobutyl chloride, the low-boiling hydrocarbons formed consisted of 50% 1-butene, 29% trans-2-butene, 20% cis-2-butene, and ca. 0.3% cyclobutane. Removal of the unsaturated components from the products of the reaction of cyclopropylcarbinyl chloride by bromination and vapor-phase chromatography of the residue suggested that some methylcyclopropane was also formed.

Discussion

At the outset, this research involved investigation of the nature of cyclopropylcarbinylmagnesium chloride and its equilibrium with allylcarbinylmagnesium chloride, based on analysis of a selected segment of the products derived from these Grignard reagents under controlled conditions. The study was extended to include the behavior of the cyclobutyl Grignard reagent in similar circumstances. The assumption was made in this work that the hydrocarbons formed upon treatment of a Grignard reagent with a proton donor reflect in their structure the nature of the organic portion of the organometallic compound at the time of reaction. We shall attempt to evaluate this assumption with the idea of establishing that a valid correlation between the Grignard reagents and the products analyzed exists.

Evaluation of Product Mixtures.- First, it should be noted that evidence has been presented for the formation of hydrocarbons in Grignard reaction mixtures by some process not involving the organometallic compounds themselves. Thus, when (γ,γ-diphenylallyl)carbinyl bromide was allowed to react with magnesium and the resulting solution was treated with a reagent such as carbon dioxide, oxygen, or mercuric bromide, a hydrocarbon fraction was isolated in addition to the expected derivative (13). In each case, this fraction was made up of 1,1-diphenyl-1-butene and diphenylcyclopropylmethane only; the absence of the corresponding diene suggests that the hydrocarbon mixture was not likely to have arisen from disproportionation of the Grignard reagent. It was proposed (13) that these hydrocarbons were formed from free-radical intermediates during the reaction of the bromide with magnesium.

The occurrence of such a side reaction in the preparation of the Grignard reagents investigated here could affect interpretation of the results obtained, since the process could afford the same products as decomposition of the organometallic compounds, almost certainly in different proportions. The fact that some C_4-hydrocarbons were indeed produced prior to the benzoic acid decomposition of C_4H_7MgCl solutions when these were refluxed for extended periods has been demonstrated, and it will be necessary to determine if corrections of the experimental data for the effect of material originating from non-Grignard precursors are warranted.

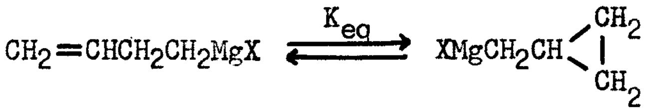
The hydrocarbon mixtures under discussion here arose in two main types of experimental situation. In one, the Grignard reagents were refluxed for some time, usually about 24 hours, before they were added to the solutions of benzoic acid or phenylacetylene which were used as decomposing agents. When allylcarbinyl chloride or cyclopropylcarbinyl chloride was used as the starting material under these conditions, the hydrocarbon products formed from acidolysis were consistently of the same composition as those from like experiments in which a special effort was made to distill the radical-derived hydrocarbons from the Grignard solutions before the decomposition step. It would seem, then, that normal treatment of the reaction mixture brought about removal of the radical-derived hydrocarbons before the reaction of the organometallic compound with acid took place. Examination of the amount and composition of the hydrocarbon fractions trapped during the reflux periods reveals that even if they were combined with the products of acidolysis the composition of the latter mixtures would remain unchanged. In any case, it is reasonable to conclude that no correction need be applied to the compositions of the hydrocarbon mixtures analyzed as products in the long-term experiments.

The second type of experiment involved allowing the alkyl chlorides to react with magnesium in the presence of a proton-donating addend (expressed more concisely, the Grignard reagents were prepared with the addend in situ). In the runs falling into this category, a neat separation into radical-derived and Grignard-derived fractions could not be made. Any products due to non-Grignard intermediates could be neglected, however, if in the presence of the proton donors used they were formed in the same small relative amounts (4-10% of the material arising from acidolysis) as in the long-term experiments. That this was the case when benzoic acid was used as the addend is evidenced by the behavior of cyclobutylmagnesium chloride when prepared with this reagent in situ. The same mixture of hydrocarbons was produced as when a cyclobutyl Grignard solution, from which the radical-derived hydrocarbons had been removed, was decomposed with the acid. The radical-derived product mixture obtained from cyclobutyl chloride was unique in that it contained a large proportion of an unidentified compound found only in small amounts in other experiments. The appearance of very little of this material (a maximum of 2%) when the cyclobutyl Grignard reagent was prepared in the presence of phenylacetylene or *t*-butyl alcohol can be taken to mean that the radical pathway does not operate to any great extent when these reagents are included in the reaction mixtures.

Interconversion of Cyclopropylcarbinylmagnesium Chloride and Allylcarbinylmagnesium Chloride.- Having reached the decision that the hydrocarbon mixtures obtained in either the long-term or short-term experiments were not likely to have been contaminated with material arising independently of Grignard formation, we may examine the data for information about the cyclopropylcarbinylmagnesium chloride-allylcarbinylmagnesium chloride interconversion. Of primary interest is the fate of cyclopropylcarbinyl chloride in its reaction with magnesium. This chloride could first form the cyclopropylcarbinyl Grignard reagent, which would then rearrange to the open-chain isomer. Alternatively, it could react to form allylcarbinylmagnesium chloride directly, or it could form a mixture of both organometallic compounds.

The preparation of the Grignard reagent from the cyclic halide with benzoic acid *in situ* resulted in the formation of methylcyclopropane and 1-butene in the ratio 6:100, which is 60 times greater than that obtained by acidolysis of the day-old organometallic compound. This behavior can be attributed to formation of cyclopropylcarbinylmagnesium chloride followed by rearrangement to allylcarbinylmagnesium chloride; it can also be explained by saying that the allylcarbinyl Grignard reagent was produced directly and, in order to give the cyclic hydrocarbon, a portion of it was attacked at the terminal carbon atom by benzoic acid adsorbed on the magnesium surface. Such "tail-end" attack could take place by a process similar to the cyclic mechanism proposed for addition reactions of allylic Grignard reagents (20, 21), and might conceivably be highly favored at the metal surface compared with the same process in solution. If, however, the methylcyclopropane observed were indeed derived from terminal-carbon attack on an initially-formed open-chain organometallic compound, it would be expected that the ratio of methylcyclopropane to 1-butene found would be the same whether allylcarbinyl chloride or cyclopropylcarbinyl chloride was used as the starting material. Actually, the ratio resulting from the reaction of the open-chain halide was only about one-third that obtained in the reaction of the cyclic chloride. The possibility that allylcarbinylmagnesium chloride is the sole Grignard species formed is therefore unlikely, and the logical alternative is that cyclopropylcarbinylmagnesium chloride is actually produced in the Grignard reaction of cyclopropylcarbinyl chloride and is capable of existence for a measurable time. This, in turn, suggests that the equilibrium between position-isomers in the allylcarbinyl Grignard reagent involves cyclopropylcarbinylmagnesium chloride as a relatively stable intermediate rather than as a transition state.

The fact that traces (ca. 0.1% of the total C_4H_8) of methylcyclopropane are found in the products of acidolysis of the day-old Grignard reagents prepared from both cyclopropylcarbinyl and allylcarbinyl chloride supports the formulation of the organometallic compound as an equilibrium mixture of the two structures. Since the equilibrium would be slowly established relative to the rate at which the Grignard reagents react with acid*, differences in the reaction rates of the two isomers should not affect the product composition. From the ratios of methylcyclopropane to 1-butene obtained, the equilibrium constant, K_{eq}, is calculated to be about 10^{-3}. However,



$$CH_2{=}CHCH_2CH_2MgX \underset{}{\overset{K_{eq}}{\rightleftharpoons}} XMgCH_2CH\langle\begin{smallmatrix}CH_2\\|\\CH_2\end{smallmatrix}$$

the possibility remains that the rearrangement of cyclopropylcarbinylmagnesium chloride to allylcarbinylmagnesium chloride is negligibly reversible and that the methylcyclopropane observed in the long-term experiments arises solely from terminal-carbon attack on the open-chain Grignard reagent.

It is interesting that methylcyclopropane is formed in relatively large amounts (ca. 2% of the total C_4H_8) in the Grignard reaction of allylcarbinyl chloride in the presence of benzoic acid. Considering the resulting Grignard reagent as an equilibrium mixture of two isomers, one might naïvely predict that the steady-state composition could only be approached from either side by proper choice of starting material. From this, the inference might be made that trapping the

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*The half-time for equilibration of the position-isomers of allylcarbinylmagnesium chloride is thirty hours at 27° (34).

reagent before equilibrium was attained (as in its preparation with benzoic acid in situ) would afford hydrocarbons with a greater-than-equilibrium percentage of methylcyclopropane when the starting halide was cyclopropylcarbinyl chloride, and at most the steady-state percentage when allylcarbinyl chloride was used.

The formation of more than the expected amount of methylcyclopropane from the reaction of allylcarbinyl chloride might then be construed as evidence that terminal-carbon attack on the open-chain Grignard reagent does take place to some extent on the magnesium surface, by the mechanism mentioned on p. 38. It must be pointed out, however, that the prediction of products on the basis of the hypothetical direction of approach to equilibrium is not warranted. For example, the deamination of either cyclopropylcarbinylamine or cyclobutylamine gives a mixture of roughly equal proportions of cyclopropylcarbinol and cyclobutanol, along with only a small amount of allylcarbinol (6), even though, at equilibrium, allylcarbinol is highly favored. When allylcarbinylamine was deaminated, a mixture containing significant amounts of the cyclic alcohols was isolated instead of the pure allylcarbinol which would have been expected considering that approach to the steady-state condition should have been from the side opposite to that in which the cyclic ions were involved. It may be supposed that the allylcarbinyl carbonium ion, which is difficult to form and of high energy (6), rearranges partly to the more favorable bridged ion; this gives mainly cyclic alcohols, so that the system proceeds toward equilibrium from the opposite side from the starting halide.

Radical Intermediates in Grignard Reagent Formation.- In attempting to explain the formation of more than the equilibrium percentage of methylcyclopropane in the reaction of allylcarbinyl chloride in the presence of benzoic acid, it would be useful at this point to examine more closely the mechanism by which the Grignard reagents are formed from C_4H_7Cl. Since it is likely that free-radical intermediates are involved (46)*, knowledge of the behavior of the radical derived from a particular chloride would be helpful in gaining insight into the nature of the Grignard reagent produced from that chloride. Little is known about the unsubstituted allylcarbinyl and cyclopropylcarbinyl radicals, but the information available combined with what may be inferred from the behavior of substituted allylcarbinyl and cyclopropylcarbinyl systems provides a basis from which Grignard formation may be viewed.

Howden (13) has observed the formation of both 1,1-diphenylbutene and diphenylcyclopropylmethane in the thermal decomposition of t-butyl (γ,γ-diphenylallyl)peracetate in the presence of hydrogen donors and, although the relative amount of diphenylcyclopropylmethane was found to increase with the reactivity of the donor, it was also found to be almost independent of the donor concentration. The rate of decomposition of t-butyl (γ,γ-diphenylallyl)peracetate was only 1.4 times that

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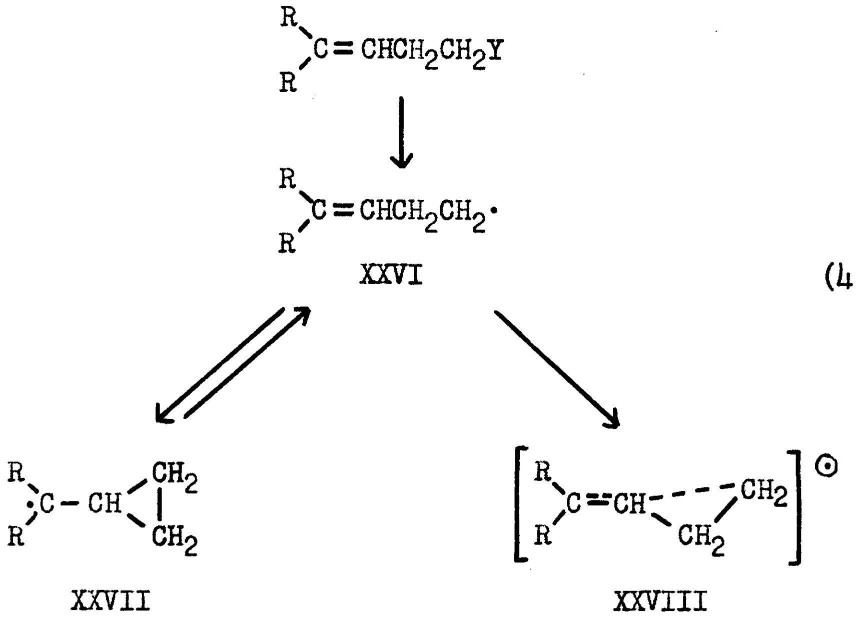
*The precursors of the non-Grignard-derived hydrocarbons discussed earlier (pp. 34-36) could reasonably be those radicals which escape reaction with magnesium-containing species and diffuse away from the metal surface to react with solvent.

of the non-olefinic analog, t-butyl 5,5-diphenylperpentanoate, which precludes a rate-determining step with substantial assistance provided by formation of a delocalized non-classical radical. Howden therefore concluded that the (γ,γ-diphenylallyl)carbinyl radical (XXVIa) was formed initially and, in a subsequent rapid step, either equilibrated with the diphenylcyclopropylmethyl radical (XXVIIa) or isomerized to a non-classical homoallyl radical XXVIIIa (see equation 4), which



(4)

(a.) $R = Ph, Y = -\overset{O}{\overset{\|}{C}}OOC(CH_3)_3$

(b.) $R = H, Y = Cl$

could react at either end to form cyclic or open-chain products directly. The lack of a temperature effect on the percentage of diphenylcyclopropylmethane obtained supported his preference for the latter explanation (13).

Considering the non-classical diphenylhomoallyl radical XXVIIIa as the species produced in the substituted case, one might conclude that the lower energy cyclic structures (<u>vide infra</u>) would make the greatest contribution to the whole. Molecular orbital treatment of the similarly delocalized (γ-vinylallyl)carbinyl system predicts the hybrid structure to possess 72% cyclic character (1). The non-classical radical XXVIIIa likewise may be postulated to be quite similar to the classical diphenylcyclopropylmethyl radical; it will be of lower energy than the classical radical by an amount determined by the expected homoallyl resonance stabilization. Despite its predominantly cyclic character, preferential hydrogen abstraction by the diphenylhomoallyl radical to form the more stable open-chain hydrocarbon is clearly predicted. The enthalpy changes for some hydrogen abstractions by methyl radicals range from -13 kcal. per mole for reaction with acetaldehyde (47) to an estimated -25 kcal. per mole for R_3SnH (48); these ΔH values would be slightly smaller for a classical (γ,γ-diphenylallyl)carbinyl radical, and still smaller (by about 25 kcal.) for the delocalized diphenylhomoallyl radical. Hydrogen abstractions by the diphenylhomoallyl radical XXVIIIa would be expected to be more or less endothermic, then, and their course would be less influenced by factors governing the nature of the radical and more dependent on the characteristics of the possible products.

Treatment of the diphenylsubstituted radical as a rapidly equilibrating mixture of classical allylcarbinyl and cyclopropylcarbinyl structures would also predict preferential formation of 1,1-diphenylbutene on reaction with hydrogen donors, if it be assumed that the barrier to hydrogen abstraction by the diphenylcyclopropylmethyl radical is somewhat higher than that involved in its isomerization to the open-chain radical XXVIa and the subsequent reaction of that species with a hydrogen donor. The cyclic species XXVIIa would be expected to be less reactive than the open-chain radical XXVIa because of steric hindrance and stabilization due to the phenyl groups on the carbon atom carrying the odd electron. The difference in activation energies for production of open-chain and cyclic products according to this line of reasoning would be small, consistent with the lack of temperature effect on the relative amounts of these isomers formed on reaction with a given hydrogen donor (13). Howden predicted an appreciable temperature effect, arguing that the activation energy accompanying hydrogen abstraction by the diphenylcyclopropylmethyl radical would be little different from that involved in hydrogen abstraction by the (γ,γ-diphenylallyl)carbinyl radical, and that, therefore, the difference in the activation energies leading from the bulk of the radical intermediate mixture to open-chain and to cyclic products would be comparable to the enthalpy difference between the two isomeric radicals, i.e. 24.5 kcal. (13). If this were so, one would expect hydrogen abstraction to lead consistently to a mixture of products of the same composition as the equilibrium radical mixture, contrary to the behavior actually observed.

Behavior analogous to that of the (γ,γ-diphenylallyl)carbinyl radical might conceivably be ascribed to the allylcarbinyl radical (as in equation 4, series b), a conclusion which is supported by similarities between free-radical reactions of unsubstituted cyclopropylcarbinyl compounds and those of (γ,γ-diphenylallyl)carbinyl derivatives. Decarbonylation of cyclopropylacetaldehyde leads exclusively to 1-butene, even in the presence of benzyl mercaptan (47), while the vapor-phase chlorination of methylcyclopropane affords a monochlorinated fraction containing cyclopropylcarbinyl chloride and allylcarbinyl chloride in equal amounts (6). This increase in amount of cyclic product with the reactivity of the trapping agent parallels the behavior observed in the decomposition of t-butyl (γ,γ-diphenylallyl)peracetate, and is consistent with the existence of the non-classical intermediate XXVIIIb.

It would be reasonable to expect that the unsubstituted cyclopropylcarbinyl derivatives would react, as in carbonium ion formation (8), to give the non-classical radical (homoallyl rather than "bicyclobutyl") directly; the cyclopropylcarbinyl radical could be formed first, however, and rapidly rearrange to the more stable delocalized species. The non-classical radical is expected, from simple molecular orbital calculations, to be lower in energy than even the allylcarbinyl radical by 2.0-2.8 kcal. (assuming the overlap integral β to be 20 kcal.) (36). Simonetta and Winstein have calculated, from the coefficients of the atomic orbitals making up the bonding molecular orbital in the most stable configuration of the homoallyl carbonium ion, that this ion represents a 56% contribution from the allylcarbinyl structure and a 44% contribution from the cyclopropylcarbinyl structure (1). These workers, however, used in this computation the value 66.6 kcal. per mole for the normal carbon-carbon bond energy. The currently accepted value of 82.6 kcal. per mole (36, 49) means considerable amendment is required of their results. The predicted charge distribution in the homoallyl cation was calculated anew, using the secular determinant and energy levels determined by Howden (13, 36), who incorporated the higher carbon-carbon bond energy, for the homoallyl system in its most stable configuration. This particular calculation neglects 1,4-overlap (as is implicit in the designation "homoallyl"), but this interaction is not excluded by the geometry of the system. However, further calculations made by Howden (36) reveal that inclusion of 1,4-overlap in the computation has little effect on the delocalization energy obtained for the radical. According to the revised figures, the homoallyl cation would possess 79% open-chain character and 21% cyclic character. Since electrons added to the system would fall into a non-bonding orbital (36), the configuration of the homoallyl radical should be the same as the cation, neglecting the effect of interelectronic repulsion. The Coulson free-valence index (50) was also calculated for the homoallyl radical; it was half again as large for the α-carbon as for the δ-carbon, suggesting that the delocalized radical would be more likely to react to produce open-chain products. Formation of allylcarbinyl derivatives would also be favored thermodynamically (6). All factors combine to produce a selectivity for formation of open-chain products from the unsubstituted homoallyl radical which evidently can be overcome only by extremely reactive and indiscriminate trapping agents (e.g. chlorine).

The possibility that the classical radicals XXVIb and XXVIIb exist in equilibrium may be discounted more concretely than in the substituted case. While the diphenylcyclopropylmethyl radical was calculated to be more stable than the (γ,γ-diphenylallyl)carbinyl radical by 24.5 kcal. per mole, it was predicted that the allylcarbinyl radical would be favored over its cyclic isomer by 16.5 kcal. (13). Thus, in radical reactions of allylcarbinyl derivatives, unassisted rearrangement of an initially-formed allylcarbinyl radical to a cyclopropylcarbinyl radical and equilibration between the two would seem unlikely; by this reasoning we are forced to accept the alternative isomerization to a delocalized homoallyl radical as the most probable succeeding step.

The nature of the organometallic compounds initially obtained in the formation of the Grignard reagents from cyclopropylcarbinyl and allylcarbinyl chlorides might, then, depend upon how voraciously the alkyl radical intermediates discussed above were consumed in subsequent steps. A postulated reaction sequence is illustrated in equation 5.*

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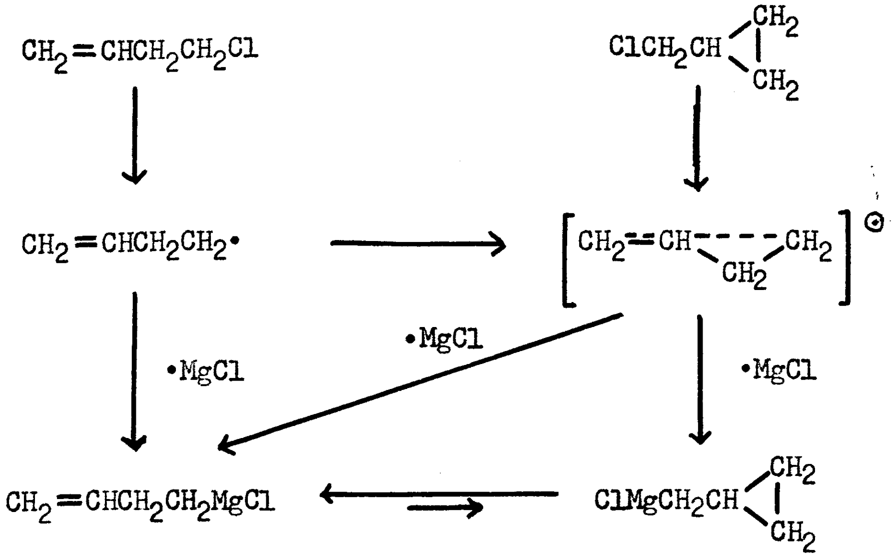
*The alkyl radicals are pictured, for simplicity, as reacting with ·MgCl to form the Grignard reagents. The actual situation is undoubtedly much more complex (46).


(5)

From cyclopropylcarbinyl chloride would arise the non-classical homoallyl radical, either directly or by rapid isomerization of the classical radical structure; this would give a mixture of cyclopropylcarbinylmagnesium chloride and allylcarbinylmagnesium chloride whose initial composition would be a function of the reactivity of the species with which the radical reacted. Allylcarbinyl chloride would give rise to the open-chain radical, which could either collapse to allylcarbinylmagnesium chloride or rearrange to the non-classical structure, from which it would react further to produce a mixture of Grignard reagents. Thus, it could be expected that the open-chain halide would produce cyclic Grignard reagent, but probably to a somewhat lesser extent than would the cyclopropylcarbinyl halide. This is precisely what is indicated by the products of the Grignard reactions of the two chlorides when they are carried out in the presence of benzoic acid. After formation, the Grignard reagent mixtures derived from allylcarbinyl and cyclopropylcarbinyl chlorides would proceed to the equilibrium state described earlier.

Experiments with Phenylacetylene and *t*-Butyl Alcohol.- Attempts to gain further information about the equilibrium between cyclopropylcarbinylmagnesium chloride and allylcarbinylmagnesium chloride by trying to catch the two species at intermediate lifetimes, using phenylacetylene and *t*-butyl alcohol as trapping agents, were unsuccessful. The volatile hydrocarbon mixtures formed in the Grignard reactions of C_4H_7Cl in the presence of these addends cannot be satisfactorily explained in terms of the model presented above, and in some respects the data obtained are not internally consistent. Although the phenylacetylene and *t*-butyl alcohol experiments contributed little toward answering the initial question posed by this research, they revealed some unexpected and interesting behavior.

An outstanding feature of the Grignard reaction of allylcarbinyl chloride in the presence of phenylacetylene was the appearance in the product mixture of 3-6% of cyclobutane along with the expected steady-state concentration (*ca.* 0.1%) of methylcyclopropane. Conceivably, the cyclobutane could have arisen from rearrangement of the allylcarbinyl Grignard reagent to the cyclobutyl structure, but interconversion of the two organometallic compounds would not be expected on the basis of previous observations (6, 20). It is likely that whatever process led to conversion of the allylcarbinyl to the cyclobutyl skeleton took place before the formation of the alkylmagnesium chloride. Decomposition of day-old allylcarbinyl Grignard reagent with the alkyne failed to produce cyclobutane, even when excess magnesium was present.

Alternatively, isomerization of the starting material to a mixture containing cyclobutyl chloride may have been responsible for the cyclobutyl product in the allylcarbinyl chloride-phenylacetylene experiments. When cyclobutyl chloride was allowed to react in the presence of phenylacetylene, however, the hydrocarbons isolated indicated extensive isomerization to the allylcarbinyl structure (none to the cyclopropylcarbinyl skeleton), while the chloride recovered showed little net rearrangement. The apparent lack of rearrangement in the starting material might be the result of compensation for actual isomerization by the relative reaction rates of the chlorides produced. For this to occur, however, allylcarbinyl chloride would have to undergo Grignard reaction at a rate much greater than cyclobutyl chloride; the open-chain chloride was observed throughout this work to be the slowest of the three isomers used in reacting with magnesium. This objection could be removed by postulating that the cyclobutyl chloride rearranged to cyclopropylcarbinyl chloride, which would react rapidly to give 1-butene. Since the equilibrium ratio of cyclobutyl to cyclopropylcarbinyl chloride is about 36:1 (37), it would have to be assumed that equilibration between the two be fast compared with reaction with magnesium and that cyclopropylcarbinyl chloride display a rate significantly greater than that of cyclobutyl chloride in Grignard reagent formation. If cyclopropylcarbinyl chloride and the corresponding Grignard reagent were involved in the cyclobutyl chloride-phenylacetylene experiment, one would expect a trace of methylcyclopropane to appear in the hydrocarbon products and a small amount of cyclopropylcarbinyl chloride to be found in the recovered halide mixture. Neither appeared to be present, but failure to observe the predicted trace components does not provide sufficient grounds for elimination of this possibility. It is of interest that a mixture containing mostly cyclopropylcarbinyl chloride has been observed to rearrange during Grignard reaction in the presence of phenylacetylene to a mixture containing a large amount of cyclobutyl chloride (see Table IV).

The possibility also remains that rearrangement of free-radical intermediates in the formation of the Grignard reagent is responsible for the production of cyclobutane when allylcarbinyl chloride reacts with magnesium in the presence of phenylacetylene. However, products containing a four-membered ring have not been observed in other free-radical reactions of compounds with the allylcarbinyl or cyclopropylcarbinyl skeletons (13, 47), and the vapor-phase chlorination of cyclobutane gives cyclobutyl chloride as the only monochlorinated product (6).

Discrepancies appear in the data from both the phenylacetylene and the t-butyl alcohol experiments when the starting materials consist of mixtures of all three chlorides (see Table IV). When a mixture of 20% allylcarbinyl chloride, 42% cyclopropylcarbinyl chloride, and 38% cyclobutyl chloride reacted with a deficit of magnesium in the presence of phenylacetylene, the hydrocarbons produced consisted of 93.9% 1-butene, 1.5% methylcyclopropane, and 4.6% cyclobutane. From the behavior of the chlorides separately under the same conditions, a mixture containing about 0.5% methylcyclopropane and 11% cyclobutane would have been predicted. Similarly, the mixture of 84% cyclopropylcarbinyl chloride, 14% cyclobutyl chloride, and 2% allylcarbinyl chloride produced methylcyclopropane in an amount over three times the predicted 0.5%, while giving about the expected quantity of cyclobutane. As may be seen in Table IV, the halide to magnesium ratio had no effect on the composition of the hydrocarbons produced from the latter mixture of chlorides in the presence of phenylacetylene, but it did affect the composition of the recovered halide fraction. Treatment of a mixture of allylcarbinyl, cyclopropylcarbinyl, and cyclobutyl chlorides in the proportions 20:42:38 with less than an equivalent amount of magnesium in the presence of _t_-butyl alcohol (Table IV) gave rise to hydrocarbons containing 62.5% of 1-butene, 26.6% of methylcyclopropane, and 10.9% of cyclobutane. The mixture predicted for this reaction on the basis of the separate chlorides is 64% 1-butene, 31% methylcyclopropane, and 4% cyclobutane.

The behavior exhibited by C_4H_7MgCl when prepared in the presence of _t_-butyl alcohol was generally more complex than when phenylacetylene was used as the addend. The hydrocarbon mixtures produced are more suggestive of carbonium ion rearrangement than of the Grignard reagent or free-radical interconversions discussed earlier. Except when allylcarbinyl chloride was used as the starting material, the amount of methylcyclopropane formed was greater than observed with any other addend, and more nearly comparable with the quantity of cyclobutane. For example, starting with cyclopropylcarbinyl chloride, 15% of methylcyclopropane and 6% of cyclobutane were produced, while 14% of methylcyclopropane and 29% of cyclobutane arose when the starting halide was cyclobutyl chloride. The magnesium to alkyl chloride ratio had a marked effect on the compositions of both the C_4H_8 obtained and the C_4H_7Cl recovered, which was not observed in experiments with the other addends. When cyclopropylcarbinyl chloride was used in excess over magnesium in the presence of t-butyl alcohol the amount of methylcyclopropane formed was increased by a factor of 3.5 over that obtained with excess metal, at the expense of both 1-butene and cyclobutane. Excess cyclobutyl chloride produced about half as much cyclobutane, half again as much 1-butene and the same amount of methylcyclopropane when in excess as when it was treated with more than an equivalent amount of metal. Metal-halogen interchange, which brought about only about 30% isomerization of cyclopropylcarbinyl chloride in 24 hr., would be too slow to account for any gross magnesium effects due to rearrangement of the starting materials before reaction when an addend was present to consume the Grignard reagents as they were formed. It is apparent that the results obtained in the experiments involving the addition of phenylacetylene and t-butyl alcohol to the Grignard reaction mixtures reflect a process or processes entirely different from those which seem to be involved in "normal" Grignard reagent formation, rearrangement, and reaction.

The results of the experiment to test for metal-halogen exchange present somewhat of an anomaly in themselves. Treatment of a mixture of chlorides with allylcarbinylmagnesium chloride should have resulted in a decrease in the amount of the more reactive chlorides and an increase in the allylcarbinyl chloride if exchange were the only reaction taking place. In the actual experiment, after a chloride mixture was refluxed with allylcarbinyl Grignard reagent for 24 hr., the amount of cyclopropylcarbinyl chloride was reduced from 95% to 64% of the total halide fraction, the percentage of allylcarbinyl chloride was raised from zero to 26%, and the amount of cyclobutyl chloride, instead of falling, increased from 5% to 10% of the mixture. Isomerization of cyclopropylcarbinyl to cyclobutyl halides occurs in the presence of zinc chloride (see Experimental) and at temperatures above 40° with magnesium bromide, but a mixture of cyclopropylcarbinyl, cyclobutyl, and allylcarbinyl chlorides remains unaffected by treatment with magnesium bromide at the temperature of refluxing ether.

<u>Effect of Cobaltous Chloride</u>.- One method of seeking understanding of the events which have been observed in this study is comparison of the products with those from a reaction whose mechanism is better understood. The decomposition of Grignard reagents with cobaltous halides has been extensively studied (44, 51). Although disagreement exists as to the exact manner in which the cobalt is involved in the process (52, 53, 54), it is generally accepted that organic free

radicals are generated. When stoichiometric amounts of cobaltous bromide are added to refluxing ether solutions of methyl Grignard reagent, the theoretical volume of gaseous products is obtained. Of the gas generated, 94% is methane and the remainder is roughly equal amounts of ethane and ethylene. When ethylmagnesium halide is used, ethylene and ethane are formed in proportions of about 2:1 along with a trace of butane, and butyl Grignard reagent gives rise to butane and an equivalent amount of mixed 1- and 2-butenes accompanied by a small amount of n-octane (45). These results were attributed to formation of alkyl free radicals from the organic portion of the organometallic compounds and their subsequent reaction with the solvent or each other.

When the Grignard reagents were prepared from allylcarbinyl and cyclopropylcarbinyl chlorides in the presence of cobaltous chloride, hydrocarbon mixtures were formed which were quite different in composition from any previously observed. Therefore, it seems reasonable to conclude that none of the experiments in which Grignard reagents were prepared from C_4H_7Cl with proton donors in situ led to formation of free radicals other than at the magnesium surface. A distinguishing characteristic of the products of the cobaltous chloride experiments was the presence of 2-butene. The reaction of n-butyl bromide with magnesium and cobaltous bromide has been observed to result in a mixture of 55% butane, 21% 1-butene, and 24% 2-butene (55). Treatment of 1-bromoöctane with various Grignard reagents and cobaltous bromide produced a relatively constant amount of 2-octene regardless of the nature of the Grignard reagent (56). It was concluded that the 2-octene was formed by isomerization of the 1-octene resulting from disproportionation of the *n*-octyl free radical. Analogous behavior may be proposed for the formation of 2-butene in the reaction of *n*-butyl bromide; under the very similar conditions of the cobaltous chloride experiments performed in this work, it is reasonable to conclude that 1-butene was the source of the 2-butene observed. No information was available in the bromoöctane experiments to distinguish between a radical mechanism and a polar one for isomerization of 1-octene to 2-octene (56). The fact that, in the experiments described here, 1-butene was not rearranged to 2-butene in reaction mixtures identical except for the presence of the cobaltous halide to those in which the isomerization took place provides evidence in favor of radical attack away from the magnesium surface.

EXPERIMENTAL

All boiling and melting points are uncorrected. The latter were taken in a capillary tube heated in an oil bath or with a Reichert Koffler Block. Most of the infrared spectra were taken using a Beckman IR-7 infrared spectrometer; some were made with a Perkin-Elmer double-beam recording spectrophotometer, Model 21. Vapor-phase chromatograms, unless otherwise stated, were obtained using a Perkin-Elmer Model 154-C Vapor Fractometer. Radioactivity determinations were made by converting the compound to carbon dioxide (57) and measuring the activity of the gas with an Applied Physics Corporation Vibrating Reed Electrometer, Model 30. Nuclear magnetic resonance spectra were made using a Varian Associates V-4300 B high resolution spectrometer with a 12-in. magnet, equipped with flux stabilizer, constant-temperature water for magnet cooling, field homogeneity controls, and operating at 60 Mc. Also used was a Varian Associates A-60 high resolution nuclear magnetic resonance spectrometer. Elemental analyses were performed by Elek Microanalytical Laboratories, Los Angeles, and Spang Microanalytical Laboratories, Ann Arbor, Michigan.

2-Phenylethanol-1-^{14}C.- Phenylacetic-1-^{14}C acid (17.1 mg., 500 microcuries) was recrystallized from a mixture of ethanol and water along with 34.02 g. of unlabeled phenylacetic acid (Matheson, Coleman, and Bell). The material recovered amounted to 32.40 g. and had m.p. 76.4-77.4°; the calculated activity was 2 microcuries per millimole.

A portion of the acid was reduced with lithium aluminum hydride, using standard techniques. Distillation of the product at reduced pressure gave 2-phenylethanol-1-^{14}C, b.p. 59-67° (0.3-1.0 mm.), in 58% yield.

2-Phenylethyl-1-^{14}C chloride was prepared by treatment of 2-phenylethanol-1-^{14}C with thionyl chloride using the method of Roberts and Mazur (6). The product, b.p. 42-45° (0.5-1.0 mm.), was obtained in 82% yield.

2-Phenylethyl-x-^{14}C-magnesium Chloride.- The Grignard reagent was prepared under nitrogen from 2.00 g. (14 mmole) of 2-phenylethyl-1-^{14}C chloride and 0.50 g. (20 mg.-atom) of magnesium in anhydrous ether. Addition of methyl iodide and application of heat were necessary to initiate the reaction. The Grignard mixture was refluxed for 46 hr., then carbonated by pouring onto ca. 10 g. of powdered Dry Ice. Isolation of the acid fraction yielded 0.89 g. (42%) of hydrocinnamic acid, m.p. 44.5-48.5°. Recrystallization, once from ethanol-water and three times from hexane, gave material, m.p. 48.4-49.0°, which had an activity of 1.84 microcuries per millimole.

Degradation of Hydrocinnamic-x-^{14}C Acid.- The acid formed by carbonation of 2-phenylethyl-x-^{14}C-magnesium chloride was oxidized with alkaline potassium permanganate (58), and the resulting benzoic acid was isolated in 68% yield. Two recrystallizations from hexane gave material, m.p. 122.4-122.9°, with an activity of 3.23×10^{-3} microcuries per millimole.

Reaction of 2-Phenylethyl Bromide and Lithium Metal.- Several attempts were made to prepare 2-phenylethyllithium in the traditional manner from lithium metal and the corresponding bromide. Ether and 70:30 benzene-ether were used as solvents; all reactions were carried out under nitrogen or helium at temperatures ranging from -78° to 50°. Either freshly cut metal pieces or lithium sand, always in excess of the stoichiometric amount, were employed. The rate of agitation was varied from moderate (using an ordinary Herschberg stirrer) to high speed stirring at rates up to about 15,000 r.p.m. The time taken for addition of the bromide solution to the reaction mixture and the period between completion of the addition step and carbonation of the mixture were both varied over a wide range.

The largest yield of hydrocinnamic acid obtained in any one experiment was less than 2%. In most cases, a large proportion of the starting bromide was recovered. A small amount of 1,4-diphenylbutane was observed in one reaction; otherwise, the only products identified were ethylbenzene and styrene. No correlation between reaction conditions and products formed was noted.

2-Phenylethyl Bromide and n-Butyllithium*.- n-Butyllithium was prepared (43) from 6.9 g. (0.05 mole) of n-butyl bromide (Matheson, Coleman, and Bell reagent grade) and 0.87 g. (0.125 g. atom) of lithium metal in 75 ml. of dry ether. After storage overnight under nitrogen, the solution was filtered and cooled to slightly below 0°. A solution of 4.5 g. (0.024 mole) of 2-phenylethyl bromide (Eastman Organic Chemicals) in 25 ml. of ether was added with vigorous stirring over a period of 45 min., and the mixture was stirred at 0° for 30 min., longer. Carbonation yielded 0.1 g. of base-soluble material which was shown by its infrared spectrum to be hydrocinnamic acid contaminated with a trace of n-valeric acid. From the neutral fraction were isolated 0.4 g. of a butanol-water azeotrope, 2.8 g. (62% recovery) of 2-phenylethyl bromide, and 0.6 g. of a high-boiling phenyl-containing hydrocarbon which was not further characterized. Product identifications were made by vapor-phase chromatography (v.p.c.) and by comparison of infrared spectra with those of authentic materials.

(2-Phenylethyl)-tri-n-butyltin.- The procedure of Seyferth and Weiner (25) was employed. A solution of 9.25 g. (0.050 mole) of 2-phenylethyl bromide and 10.57 g. (0.0325 mole) of tri-n-butyltin chloride (26) in 20 ml. of purified tetrahydrofuran** was added over a period of 1.25 hr. to 2.56 g. (0.105 g. atom) of magnesium turnings

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*This experiment was done in part as a portion of a special project by Kerry L. Donovan

**Tetrahydrofuran was refluxed over potassium hydroxide pellets for 12 hr., then distilled from lithium aluminum hydride.

in 40 ml. of vigorously stirred refluxing ether under a nitrogen atmosphere. After 8 hr. of refluxing, during which time 25 ml. of benzene were added, the mixture was left overnight at room temperature; it was then worked up to yield 6.70 g. (52.4%) of a colorless liquid, b.p. 132-133° (0.5-1.0 mm.). The infrared spectrum of the material contained bands characteristic of monosubstituted phenyl groups as well as aliphatic C-H stretching and bending absorptions.

Anal. Calcd. for $C_{20}H_{36}Sn$: C, 60.77; H, 9.12. Found: C, 61.15; H, 9.25.

Reaction of n-Butyllithium and (2-Phenylethyl)-tri-n-butyltin.- A solution 0.665 N in *n*-butyllithium (26 ml., 0.0173 mole) was added rapidly, under nitrogen, to 6.70 g. (0.0170 mole) of (2-phenylethyl)-tri-*n*-butyltin in 50 ml. of dry ether (25). After being stirred at room temperature for 30 min., the mixture was carbonated. The acid isolated was identified by its infrared spectrum as *n*-valeric acid; 1.27 g. (72.2% yield) of material were obtained. No infrared absorption indicating the presence of hydrocinnamic acid was observed. Neutral material with an infrared spectrum identical to that of (2-phenylethyl)-tri-*n*-butyltin amounting to 5.37 g. (80.2%) was recovered.

(2-Phenylethyl)-triphenyltin.- This compound was prepared by the same procedure used for (2-phenylethyl)-tri-*n*-butyltin. From 9.25 g. (0.050 mole) of freshly distilled 2-phenylethyl bromide, 12.50 g. (0.0325 mole) of triphenyltin chloride (26), and 2.56 g. (0.105 g. atom) of magnesium were obtained 6.88 g. (46.5% yield) of

a white crystalline solid, m.p. 126-128° after recrystallization from 95% ethanol. (Lit. for (2-phenylethyl)-triphenyltin 127.0-127.5° (29, 59, 60).) The n.m.r. spectrum of the product consisted of a doublet in the phenyl region and a weak pair of unsymmetrical triplets in the methylene region. An infrared spectrum was obtained containing bands characteristic of monosubstituted phenyl and aliphatic $-CH_2-$ groups, as well as a strong band at 1075 cm^{-1}. which has been attributed to the tin-phenyl linkage (29, 32). Another strong absorption, at 1428 cm^{-1}., was noted; this band was found in the spectra of all of the phenyl-substituted tin compounds used in this study and did not seem to be characteristic of the individual substituent groups. A satisfactory elemental analysis was not obtained, perhaps as a result of the presence of tin in the molecule, which is known to interfere with carbon-hydrogen combustion analyses (61, 62).

In a previous preparation run using tetrahydrofuran which had not been recently purified and commercial 2-phenylethyl bromide which was not further purified, a low yield of white crystals, m.p. 122-124°, was obtained. This substance gave an n.m.r. spectrum containing a single peak in the phenyl region; in the infrared it exhibited absorption attributable to aromatic substituents, plus the tin-phenyl bands at 1075 cm^{-1}. (29, 32) and 1428 cm^{-1}. It was assigned the identity of bis-(triphenyltin) oxide (lit. m.p. 124° (29)).

Anal. Calcd. for $C_{36}H_{30}Sn_2O$: C, 60.38; H, 4.23. Found: C, 59.59; H, 4.09.

Reaction of Phenyllithium and (2-Phenylethyl)-triphenyltin.- As in the reaction of *n*-butyllithium and (2-phenylethyl)-tri-*n*-butyltin (*vide supra*), 10 ml. (98 mmole) of 0.980 N phenyllithium was added under helium to 4.46 g. (98 mmole) of (2-phenylethyl)-triphenyltin in 60 ml. of benzene. Carbonation of the mixture after a reflux period of 2 hr. yielded 0.32 g. (26 mmole) of benzoic acid; no hydrocinnamic acid could be detected. Also isolated were 0.57 g. (13 mmole) of tetraphenyltin and 1.82 g. (40 mmole, 41% recovery) of (2-phenylethyl)-triphenyltin. An oily residue amounting to 1.41 g. was not identified.

Part II

Cyclopropylcarbinol.- Lithium aluminum hydride reduction of cyclopropanecarboxylic acid (Columbia Organic Chemicals, Inc.) after the method of Nystrom and Brown (63) gave cyclopropylcarbinol, b.p. 121.5-122.5° (745 mm.), n_D^{25} 1.4300 ± 0.0006, in 75-78% yield.

Allylcarbinol.- Vinylacetic acid was reduced in the same manner as cyclopropanecarboxylic acid (63) to give a 70% yield of allylcarbinol, b.p. 111.5-112.5° (744 mm.), n_D^{25} 1.4191.

Cyclopropylcarbinyl chloride was prepared by the method of Caserio, Graham and Roberts (37) from cyclopropylcarbinol, tri-n-butylamine, and thionyl chloride. The product mixture obtained was fractionated through a center-rod column. In a typical preparation, a 74% yield of material, b.p. 82.5-86.2° (745 mm.) was collected; of this, 37% had b.p. 85.9-86.2° and consisted of 98% cyclopropylcarbinyl chloride and 2% cyclobutyl chloride. The composition of fractions was determined by quantitative vapor-phase chromatography (v.p.c.).

Allylcarbinyl Chloride.- Allylcarbinol and thionyl chloride were allowed to react in the presence of pyridine according to the procedure of Roberts and Mazur (6). Distillation of the product through a 45-cm. Vigreux column gave a 72% yield of material, b.p. 71.5-74.2° (744 mm.), 86% of which had b.p. 74.0-74.2° and was composed of 98.9% allylcarbinyl chloride and 1.1% cyclobutyl chloride. Upon refractionation using a center-rod column, the product was collected in three fractions, the least pure of which contained 0.4% of cyclobutyl chloride as determined by v.p.c. analysis.

Cyclobutyl chloride was prepared by treatment of cyclopropylcarbinyl chloride with zinc chloride (37). A mixture of 3% allylcarbinyl chloride, 34% cyclobutyl chloride and 63% cyclopropylcarbinyl chloride, when stirred at room temperature with approximately five weight percent of zinc chloride, was isomerized in about 2 hr. to the composition 17% allylcarbinyl chloride, 69% cyclobutyl chloride, and 14% cyclopropylcarbinyl chloride. When the isomerization, which was followed by v.p.c., reached this stage, the mixture was taken up in pentane and washed with a 10% potassium hydroxide-10% sodium bicarbonate solution. After the organic layer had been dried over potassium carbonate, the pentane was removed by distillation. The remaining halide mixture was separated on a Carbowax column in a Beckman Megachrom preparative vapor-phase chromatograph. The main fraction collected proved to consist of 10.3% allylcarbinyl chloride and 89.7% cyclobutyl chloride when checked by analytical v.p.c. The percentage of allylcarbinyl chloride was reduced to 0.5 by repeated extraction of an ether solution of the fraction with ice-cold saturated potassium permanganate solution. From time to time, the resulting manganese dioxide deposits were removed by washing the ether layer with cold sodium bisulfite solution. When the oxidation was complete, the ether layer was washed with water and dried over potassium carbonate; most of the solvent was removed by distillation, leaving a concentrated ether solution of the halides. Of the cyclobutyl chloride present in the isomerized mixture, ca. 33% was recovered after the purification procedure.

Reaction of Grignard Reagent from Cyclopropylcarbinyl Chloride with α-Naphthyl Isocyanate.- The Grignard reagent was prepared under helium from cyclopropylcarbinyl chloride (*ca.* 85% pure) and magnesium turnings and was refluxed for 2 hr. The mixture was then poured through a glass-wool plug into a stirred solution of α-naphthyl isocyanate in ether. Two products were isolated, which were separable by trituration with methanol at room temperature.

N-(1-Naphthyl)-3-butenecarboxamide, after sublimation at 110° (0.3-1.0 mm.), was recrystallized from hexane-benzene to give white filaments, m.p. 120.0-120.5°. The infrared spectrum of this product was similar to that of allylacetanilide (64) in all gross features.

Anal. Calcd. for $C_{15}H_{15}NO$: C, 79.96; H, 6.72; N, 6.22. Found: C, 80.00; H, 6.67; N, 6.22.

The methanol-insoluble material, N-allylacetyl-N,N'-bis-(1-naphthyl)-urea, crystallized from a hot solution of that solvent as colorless needles, m.p. 143.2-143.9°. In the infrared, it showed strong absorption at 1720 cm^{-1}. and weaker absorption at 1667 cm^{-1}., behavior characteristic of carbonyls in an imide-type group (33). Also present in the spectrum was a strong band at 1555 cm^{-1}., supporting the assignment of a symmetrically substituted urea structure (33).

Anal. Calcd. for $C_{26}H_{22}N_2O_2$: C, 79.15; H, 5.63; N, 7.10. Found: C, 78.80; H, 5.80; N, 7.08.

When the Grignard reagent was prepared in a cyclic reactor (20) and allowed to drip into a refluxing solution of α-naphthyl isocyanate, the major product was a white crystalline solid, m.p. 312-313° after sublimation at 170° (0.3-1.0 mm.). The infrared spectrum of this substance contained outstanding bands at 3280, 1635, 1610 and 1563 cm^{-1}., and no evidence of a cyclopropyl group.

Grignard Reactions.- All of the Grignard experiments performed were variations of the general procedure described below. The apparatus used is illustrated in fig. 2.

Helium was passed through gas washing bottles containing Fieser's solution (65) and concentrated sulfuric acid into a bypass system with which the gas stream could be diverted through the trapping train or allowed just to flow past the connection to the train. The gas line was protected from moisture by a calcium-chloride-filled drying tube at the outlet.

At the outset of an experiment, the components of the train were plugged with absorbant cotton and dried in an oven at 100-110° for at least 3 hr. The cotton plugs were left in place until the apparatus was assembled, as soon as it was cool enough to handle.

Magnesium turnings (0.5 g., 20 mg.-atom) were amalgamated by treatment in several portions with a solution of 0.3 g. of mercuric bromide in 15 ml. of ether (20), washed well with ether and placed in the reaction flask of the train. The apparatus was flushed with helium and the flask was charged with 0.50 g. (5.5 mmole) of C_4H_7Cl, a drop or two of methyl iodide, any addend desired, and 5-7 ml. of dry ether. Liquid reagents were added from a 1-ml. hypodermic syringe graduated to 0.01 ml.

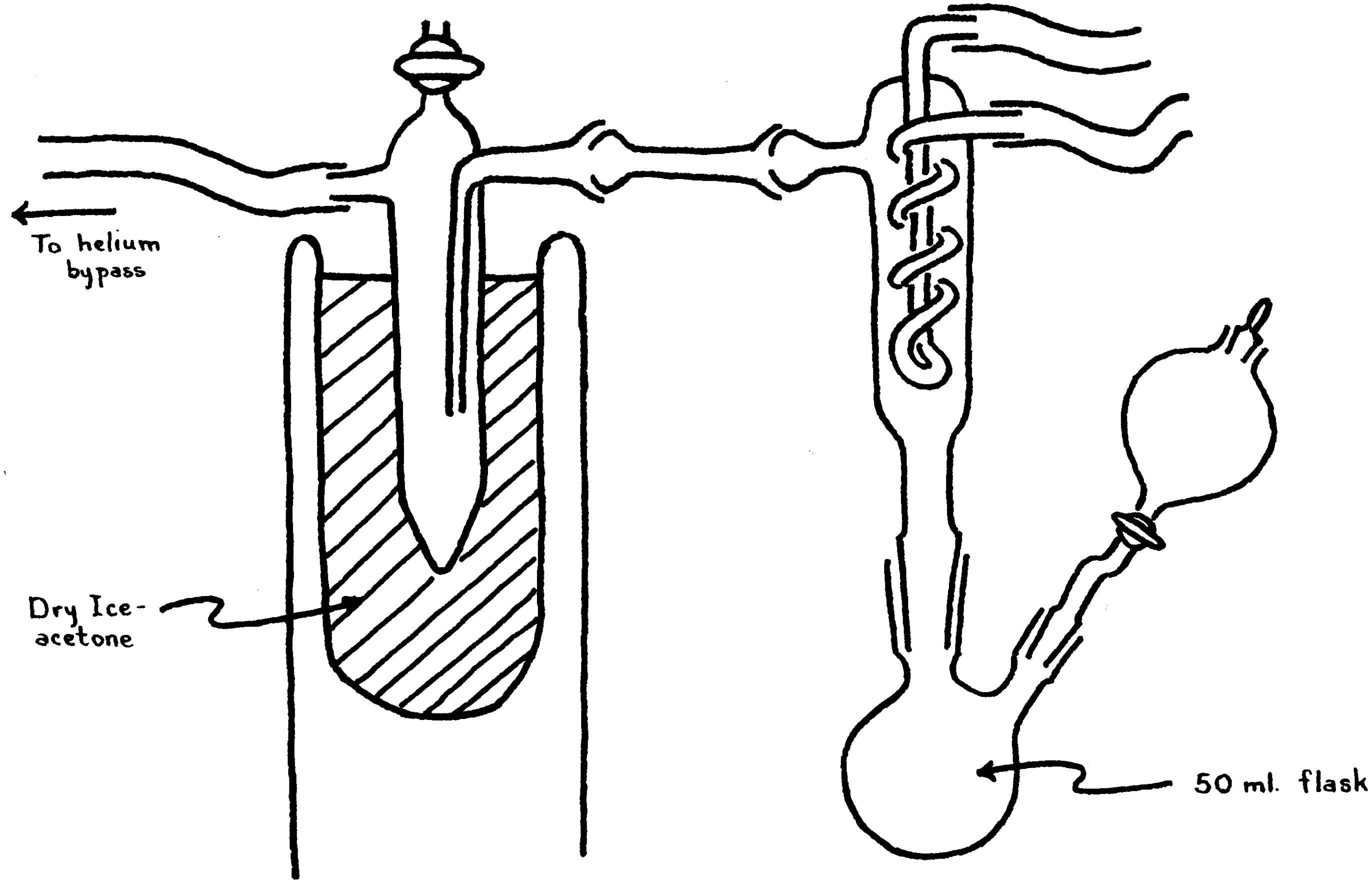

Fig. 2

When the Grignard reaction had been initiated, the mixture was heated until the ether barely refluxed. If an addend was used, the reflux period extended for 48-72 hr., or until all hydrocarbon products had been distilled into the Dry Ice trap. The contents of the trap were analyzed by v.p.c. on a Perkin-Elmer Column D (tetraisobutylene on diatomaceous earth packing). Peak areas were estimated by multiplying the heights by peak width at half-height. The peaks were identified by comparison with the chromatograms of known 1-butene (Matheson C. P. grade) and methylcyclopropane.

If an addend was not used, the Grignard mixture was heated for the desired time, then transferred through a glass-wool plug to a nitrogen-filled dropping funnel. This was attached to another trapping train containing an ether solution of the hydrolyzing agent under helium. The Grignard solution was added to the hydrolyzing agent and the hydrocarbon products were distilled and analyzed as above.

The composition of unreacted chloride was determined by v.p.c. analysis of the liquid which was flash distilled from the hydrolyzed Grignard mixture into a Dry Ice trap at room temperature (aspirator pressure). This mixture was separated on Perkin-Elmer type A packing (diisodecyl phthalate on diatomaceous earth).

Methylcyclopropane was prepared in 98% yield by reduction of 1,3-dibromobutane with zinc dust in ethanol (66).

Cyclopropylcarbinyl Chloride and Magnesium Bromide.- A mixture of 5% allylcarbinyl chloride, 21% cyclobutyl chloride, and 74%

cyclopropylcarbinyl chloride was refluxed in ether for 18 hr. with freshly prepared magnesium bromide (6). V.p.c. analysis of the chloride mixture recovered at the end of this time showed the presence of 6% allylcarbinyl chloride, 18% cyclobutyl chloride, and 75% cyclopropylcarbinyl chloride.

Cyclopropylcarbinyl Chloride and Magnesium Chloride in the Presence of Grignard Reagent.- Magnesium chloride was formed by the reaction of magnesium turnings with ethylene dichloride in ether. To this mixture, which contained unreacted magnesium, was added halide of the composition 95% cyclopropylcarbinyl chloride and 5% cyclobutyl chloride; the magnesium was totally consumed within 0.5 hr. After a reflux period of 3 hr., the unreacted halide was isolated and, upon v.p.c. analysis, was found to consist of 94% cyclopropylcarbinyl chloride, 6% cyclobutyl chloride, and a trace of allylcarbinyl chloride.

Cyclopropylcarbinyl Chloride and Benzoic Acid.- Cyclopropylcarbinyl chloride was allowed to reflux with an equimolar solution of benzoic acid in ether for 5 hr. During this time, no observable isomerization of the halide took place, as determined by v.p.c. analysis.

Bromination of Hydrocarbon Products.- The hydrocarbon products from the Grignard reactions of cyclopropylcarbinyl chloride and cyclobutyl chloride were combined and brominated by dropwise addition of bromine at -78°. The remaining hydrocarbons were distilled from the solution and analyzed by v.p.c. 1-Butene and two hitherto unidentified components had been removed.

After a washing with sodium thiosulfate solution, the distillation residue was subjected to v.p.c. analysis. The major component was 1,2-dibromobutane, identified by comparison of its retention time with that of material prepared by bromination of commercial 1-butene. Two unidentified peaks were observed, neither of which could be attributed to either of the 2,3-dibromobutanes. Bromination of commercial *cis*-2-butene (Phillips Petroleum Co., research grade) provided *d,l*-2,3-dibromobutane for comparison; like treatment of the products of a reaction in which both *cis*- and *trans*-2-butene were formed* provided a retention time for *meso*-2,3-dibromobutane.

Metal-Halogen Interchange.- The Grignard reagent was prepared from 0.45 g. (5.0 mmole) of allylcarbinyl chloride and 0.10 g. (4.1 mg.-atom) of magnesium turnings and refluxed for 4 days. In this time all of the magnesium was not consumed. A 1.5 ml. aliquot of the Grignard solution was hydrolyzed with benzoic acid, and the unreacted halide was recovered and measured by v.p.c. It was found that 100 mg. of allylcarbinyl chloride was present in the aliquot.

The remaining Grignard solution (0.5 ml.) was added to 50 mg. (0.55 mmole) of 95% cyclopropylcarbinyl - 5% cyclobutyl chloride in 1 ml. of ether and refluxed for 24 hr. This mixture, when hydrolyzed with benzoic acid, gave a mixture of hydrocarbons consisting of 1-butene, a small amount of cyclobutane, and possibly a trace of

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*The reaction was the formation of the Grignard reagent from cyclopropylcarbinyl chloride in the presence of cobaltous chloride.

methylcyclopropane. The chloride mixture recovered was found to consist of 48 mg. of allylcarbinyl chloride, 6 mg. of cyclobutyl chloride, and 37 mg. of cyclopropylcarbinyl chloride.

All steps were carried out under helium or nitrogen. Quantitative measurements were made by v.p.c. and were not corrected for variations in thermal conductivities or volatilization.

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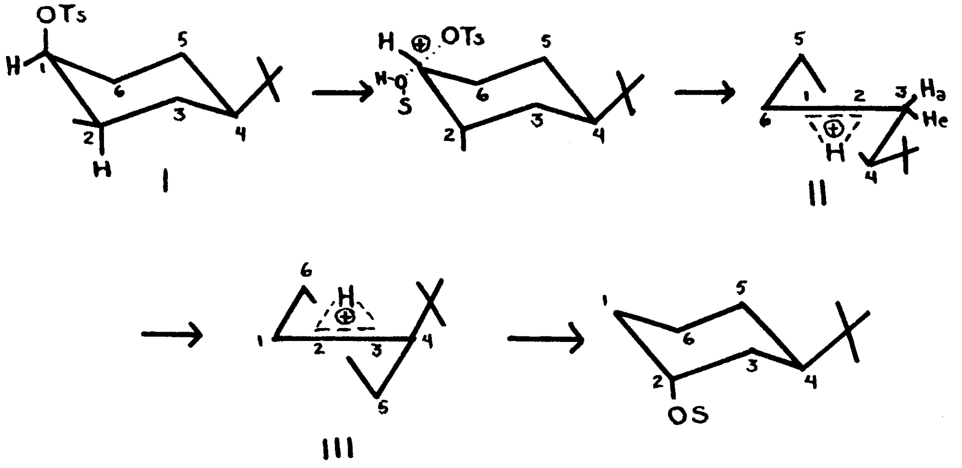
PROPOSITION 1

The solvolysis of *cis*-4-*t*-butylcyclohexyl *p*-toluenesulfonate has been found by Winstein and Holness to yield, as well as olefin and a mixture of *cis*- and *trans*-4-*t*-butylcyclohexanol, *trans*-3-*t*-butylcyclohexanol. Analogous treatment of *trans*-4-*t*-butylcyclohexyl *p*-toluenesulfonate gives little or no rearranged solvolysis product (1).

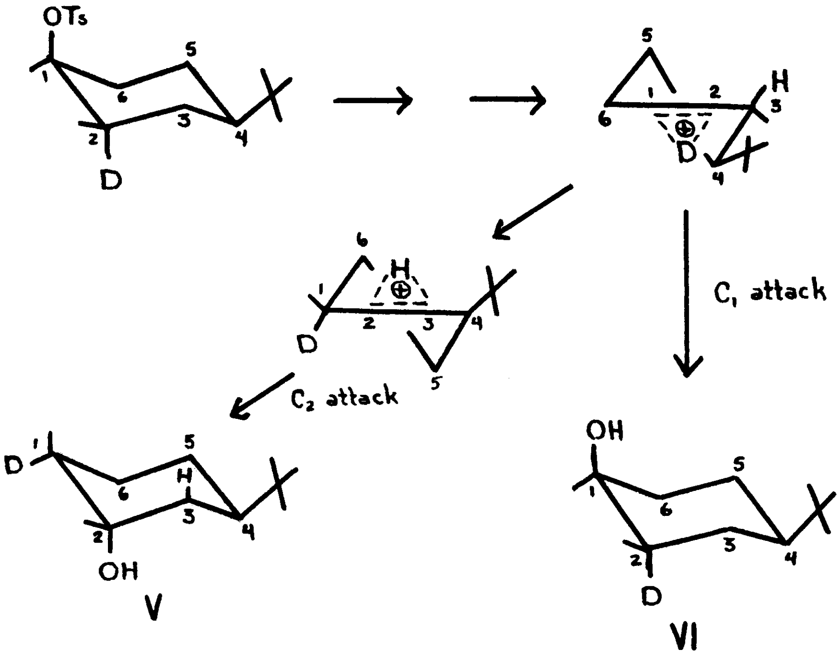
In a consideration of the mechanism involved in formation of the observed products, it was proposed that hydrogen-bridged carbonium ions are formed, in conjunction with intimate ion pairs. In the cyclohexyl carbonium ion displaying the least modification of the chair structure, the vacant p-orbital is in a more favorable position for overlap with an adjacent axial C-H bond than with an equatorial one. The reaction of *cis*-tosylate I should, therefore, lead to ion II. On the basis of behavior observed in epoxide ring opening and halogen additions (2), one would expect that attack on



(1)

the hydrogen-bridged species would occur so as to result predominantly in axial alcohol (1). Such attack at C_2 of ion II would afford cis-3-t-butylcyclohexanol, instead of the trans-isomer actually obtained.

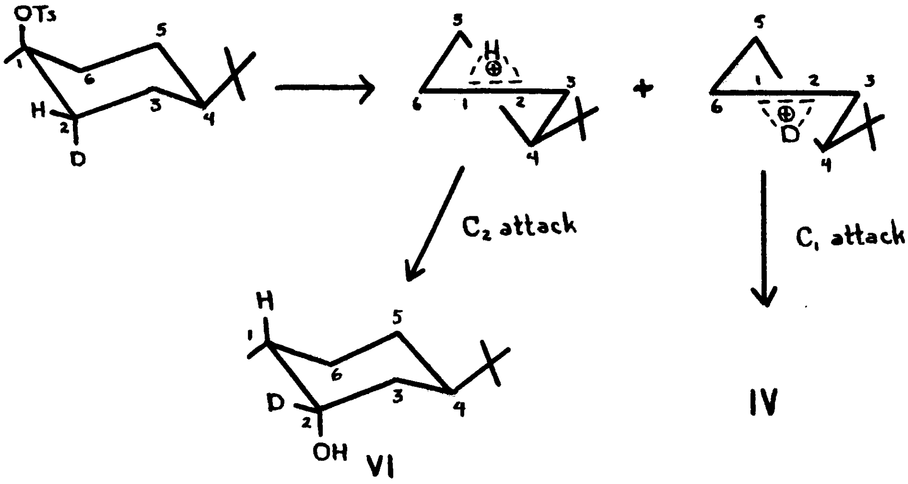
The appearance, then, of trans-3-t-butylcyclohexanol requires either that the equatorial β-hydrogen bridge to some extent or that two successive shifts of axial hydrogen take place (1). On the strength of the occurrence of hydrogen shifts noted in other cyclohexane reactions (3) and on the basis of the predicted preference for bridging by axial hydrogen, Winstein chose to regard the appearance of trans-3-t-butylcyclohexanol as a consequence of a double hydrogen shift resulting in ion III, the sequence illustrated in equation 1.



(2)

It is proposed that examination of the products obtained on solvolysis of *cis*-4-*t*-butylcyclohexyl *p*-toluenesulfonate-*trans*-2-d would give excellent evidence as to the nature of hydrogen migration taking place. To illustrate, if only axial hydrogens shifted (equation 2), the products would be *cis*-4-*t*-butylcyclohexanol-*trans*-2-d (IV) and *trans*-5-*t*-butylcyclohexanol-*cis*-2-d (V).

If, however, an equatorial hydrogen were able to migrate, equation 3 would describe the reaction and one would expect to isolate IV plus *trans*-3-*t*-butylcyclohexanol-1-d (VI).

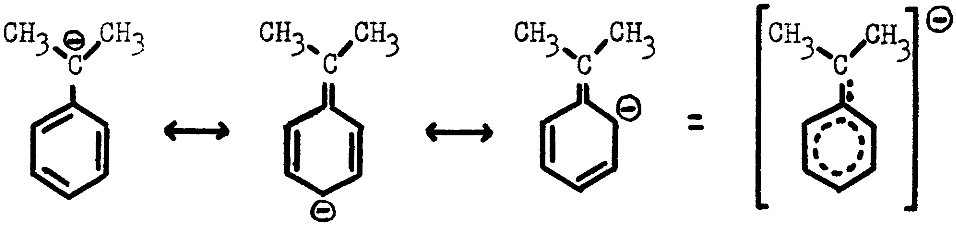


(3)

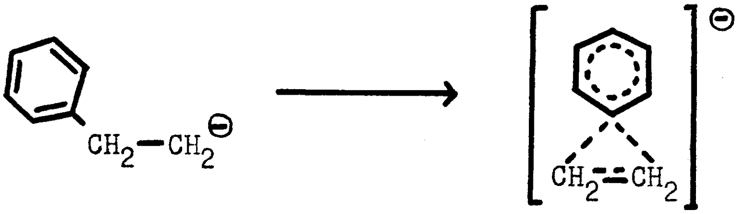
All of the deuterated products should be distinguishable from one another by means of infrared spectra, as in the case of 2-deuterated cyclohexanols (4).

PROPOSITION 2

In a recent experiment performed by Russell, results were obtained which were interpreted as chemical verification of the commonly written resonance forms of the benzyl anion. The work



involved the hydrolysis of the cumyl anion (as cumyl potassium) with deuterium chloride (5). Deuterium was found not only at the α-carbon in the resulting cumene but also in the ortho and para positions on the benzene ring. It is suggested that Russell's technique might prove to be a useful tool in seeking evidence for the existence under favorable conditions of the delocalized 2-phenylethyl anion, which has been discussed in some detail in this thesis (see pp. 6-8).

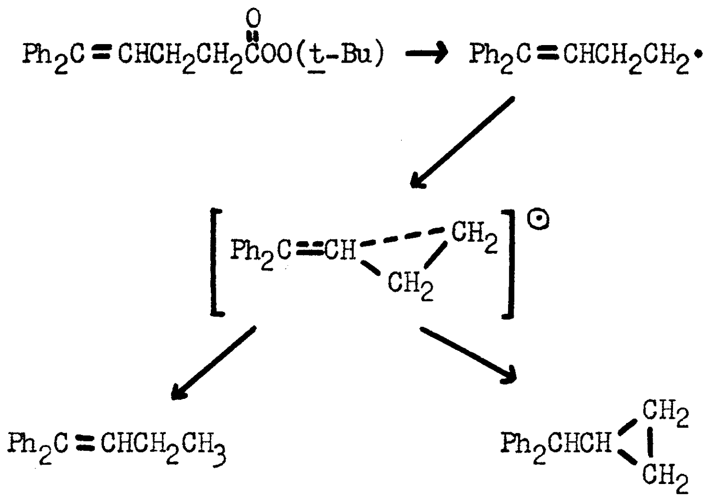


Solutions of 2-phenylethyl potassium should contain appreciable concentrations of the alkyl anion (6). If the phenyl-bridged structure is, as predicted by molecular orbital calculations (7), more stable than its classical counterpart, its presence in solution may well be detected by deuterium chloride hydrolysis of the organometallic compound. The appearance of deuterium in the phenyl group of the resulting ethylbenzene as well as on the side chain would provide good evidence that the 2-phenylethyl anion existed in a delocalized form.

In view of the difficulties encountered in formation of 2-phenylethyllithium (see pp. 8-11), it may be anticipated that the corresponding potassium derivative might not be easily obtainable. If the more conventional methods for its preparation should fail, cleavage of bis-(2-phenylethyl)-mercury with potassium metal might be successful. This procedure has been effective in the synthesis of several alkyl and aryl sodium and lithium derivatives (8). Another intriquing method would involve adaptation of the recently developed technique of reduction of alkynylmetallic compounds, in which $RC \equiv CMgBr$ and $RC \equiv CLi$ have been catalytically hydrogenated to $RCH = CHMgBr$ and $RCH = CHLi$ (9).

PROPOSITION 3

The thermal decomposition of t-butyl (γ,γ-diphenylallyl)peracetate (I) has been postulated to proceed with generation of the (γ,γ-diphenylallyl)carbinyl free radical, which rapidly isomerizes to a non-classical diphenylhomoallyl radical capable of reaction at either end to form either olefinic or cyclopropylcarbinyl products (10).



A portion of the discussion in this thesis rests upon the assumption that analogous behavior may be predicted in free-radical reactions involving the allylcarbinyl skeleton. The main basis for this assumption lies in the comparison of the effect of reactant selectivity on the product mixtures obtained in hydrogen abstractions by the radical species generated in decomposition of the phenyl-substituted perester I with the selectivity effect displayed in decarbonylations of cyclopropylacetaldehyde and chlorination of methylcyclopropane (see pp. 41, 45). Clearly, the data leading to the proposed analogy between the substituted and unsubstituted allylcarbinyl radical systems are meager, and more concrete experimental support for the idea should be sought.

Information on the product mixtures arising from both systems under like reaction conditions might be useful in verifying or disproving the analogy, and, since delocalized intermediates possessing cyclic character are supposedly involved, it would be of interest to observe the behavior of corresponding open-chain and cyclic starting materials in the same reactions.

First, the experimental situations for which product mixtures are known should be reviewed. t-Butyl (γ,γ-diphenylallyl)peracetate has been decomposed in the presence of the hydrogen donors (in ascending order of reactivity) tetralin, benzhydrol, cumene, and tri-n-butyltin hydride (10). Cyclopropylacetaldehyde has been decarbonylated with aldehyde and benzyl mercaptan to act as hydrogen donors (11). Decarbonylation of (γ,γ-diphenylallyl)acetaldehyde produces no hydrocarbons, presumably because abstraction of a hydrogen atom from aldehyde by the highly stabilized diphenylhomoallyl radical is strongly endothermic (10). The only data available on the effect of an extremely reactive radical trap is for the vapor-phase chlorination of methylcyclopropane (12). Attempts to generate radicals from diphenylcyclopropylmethyl derivatives have been unsuccessful (10), due to the ease with which these compounds undergo carbonium ion rearrangement.

It is proposed, in order to supplement the information already available for the diphenylhomoallyl radical, that t-butyl allylperacetate and t-butyl cyclopropylperacetate be decomposed in the presence of tri-n-butyltin hydride and the products examined. In addition, a radical reaction is suggested in which a reactant of relatively high reactivity is involved and which should be applicable to the study of all three of the starting structures already examined as well as, perhaps, the diphenylcyclopropylcarbinyl skeleton.

The value of the decomposition of tertiary alkyl hypochlorites as a source of free radicals has recently been emphasized (13). This reaction may be initiated easily by weak irradiation, heat, or added radicals (14), and proceeds by the following chain process (15):

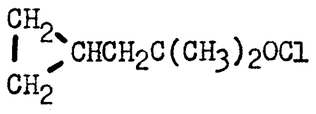
$$RC(CH_3)_2OCl + R\cdot \longrightarrow RCl + RC(CH_3)_2O\cdot$$
$$RC(CH_3)_2O\cdot \longrightarrow R\cdot + (CH_3)_2C\ O$$

The possible competing reactions of inter- and intramolecular hydrogen abstraction (14, 16, 17) and addition to double bonds (16) may be controlled by working in dilute solutions at relatively high temperatures. Since the O-Cl bond energy is comparable to that of the Cl-Cl bond (18), an alkyl hypochlorite should be quite reactive toward free radicals.

The decomposition of the hypochlorites II, III, and IV seems, therefore, to be an excellent method for comparing the behavior of

$R_2C{=}CHCH_2CH_2C(CH_3)_2OCl$

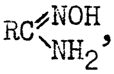
II; R = Ph
III; R = H

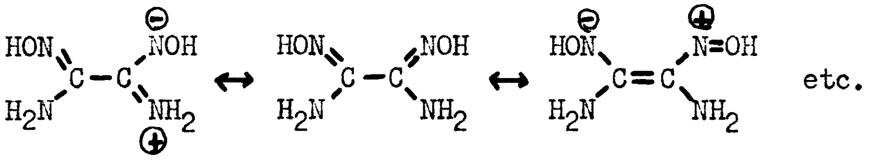


IV

the radicals they produce on reaction with a reagent of low selectivity. As the reaction would involve a starting material from which a carbonium ion could not easily be derived, it may be possible also to include the diphenylcyclopropylmethyl skeleton in the study. The reactions are carried out in carbon tetrachloride with no added reagents, so the resulting chlorides should be stable; the products could be analyzed without isolation by vapor-phase chromatography.

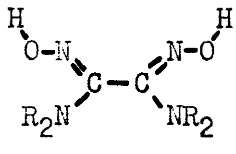
PROPOSITION 4

A great deal of work has been done on the chemistry of the class of compounds designated as amidoximes,  $RC\begin{smallmatrix}\nearrow NOH \\ \searrow NH_2\end{smallmatrix}$, but little physical study of these molecules has been performed (19). A particularly interesting question is posed by the molecule oxamidedioxime (I) and its N-substituted derivatives. Examination of the structure of

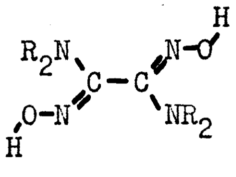


I

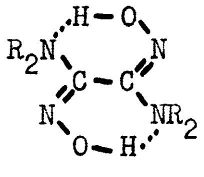
I suggests that the molecule would be essentially planar to take advantage of resonance interactions, and that it could exist in a cis or a trans configuration about the carbon-carbon bond, with a substantial barrier to interconversion of the rotamers. Picturing the molecule in its trans configuration raises the additional possibility of internal hydrogen-bonding, providing three forms (II, III, and IV) in which oxamidedioxime derivatives might be found.



II



III



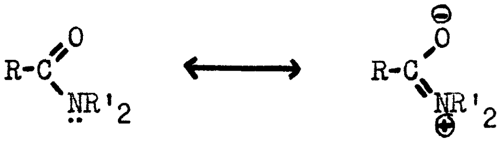
IV

An investigation of the structure of N,N,N',N'-tetramethyloxamidedioxime (II-IV, R = Me) in solution, utilizing dipole moment measurements supplemented by infrared spectra, is proposed. The structures III and IV would not be expected to possess any dipole moment. An appreciable moment would be displayed by II, however, unless this species were intermolecularly hydrogen-bonded in such a way that the moments would cancel. Such hydrogen bonding would be disrupted by use of dioxane as the solvent (20), and the apparent dipole moment of the solute would increase over that measured in a hydrocarbon solvent. Thus the cis and trans configurations may be distinguished; mixtures of the rotamers should possess temperature-dependent dipole moments, since III and IV are likely to be of lower energy than II.

The distinction would remain to be made between structures III and IV. In the simplest instance, IV would provide an infrared spectrum with hydrogen-bonded OH absorption only, and II and III would show a free OH band. Characteristic infrared spectra of amidoximes have been described, however, with the notation that the OH stretching band is broad, with maximum absorption at 3.2μ (19); no mention was made of the conditions under which the spectra were taken. The shape and position of the OH absorption are indicative of hydrogen bonding. Its occurrence in "plain" amidoximes would suggest that it could be expected to occur in II and III as well as in IV. Evidence for the existence of forms II and III would have to be sought in the spectra of dilute solutions of the substituted oxamidedioxime in solvents not amenable to hydrogen bonding. The OH absorption of the internally hydrogen-bonded structure IV should be independent of concentration and solvent. Combination of the characteristics which may be inferred from infrared spectra with those elucidated by dipole moment data may be expected to result in a more or less comprehensive picture of the nature of the N,N,N',N'-tetramethyloxamidedioxime molecule in solution.

PROPOSITION 5

The existence of a resonance hybrid with appreciable contribution from canonical structure I has been established for N,N-disubstituted amides by nuclear magnetic resonance studies (21).



I

It was shown that a substantial barrier (7 ± 3 kcal. for N,N-dimethylformamide (22)) to rotation about the carbon-nitrogen bond exists, as manifested by the appearance in n.m.r. spectra of two N-methyl resonances.

The interesting question arises as to whether or not similar interaction is possible in sulfonamides. Theoretically, the π-electrons of the sulfone group occupy two molecular orbitals, only one of which contains electrons weakly bonding enough to enter into conjugation. This orbital has one nodal plane through the sulfur and oxygen atoms and another bisecting the O-S-O angle, and can overlap with *p*-orbitals whose axes are perpendicular to the plane in which the sulfur and attached carbon atoms lie (figure 1). Conjugation involving these orbitals will occur only if the sulfone is flanked by two unsaturated substituents. Charge transfer conjugation (figure 2) involving *p*-orbitals perpendicular to the carbon-sulfur plane and vacant sulfur *d*-orbitals can also be expected (23).

Regarding the sulfonamide group itself experimentally, dipole moment measurements indicate that in sulfanilamide a small (about 3%) contribution is made by the structure II (24). The sulfonamide group <u>para</u> to a -COOH or -$NH_3^{\oplus}$ affects the acidity constants in a manner consistent with operation of the mesomeric effect (25). Also noteworthy is the well-known acidity of the N-hydrogens in unsubstituted and monosubstituted sulfonamides (26), testifying to the ability of the sulfone grouping to stabilize a full-fledged negative charge on nitrogen.

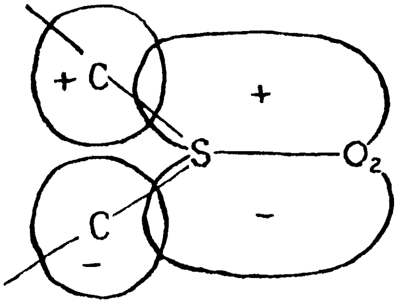


Fig. 1

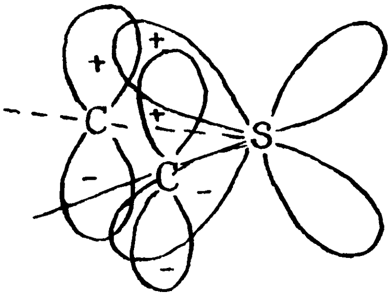
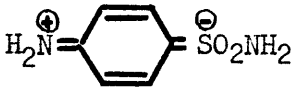


Fig. 2



$H_2\overset{\oplus}{N}=C_6H_4=\overset{\ominus}{S}O_2NH_2$

II

Apparently, then, the means for resonance interaction between nitrogen and the sulfonyl grouping is available; the extent to which such interaction would operate is difficult to predict <u>a priori</u>. In order to gain some idea as to how much nitrogen-sulfonyl conjugation is possible in the system, it is proposed to look at the n.m.r. spectrum of N,N-dimethyl-p-nitrobenzenesulfonamide and see if two N-methyl peaks are produced, at lowered temperatures if not at room temperature. The p-nitro substituent should eliminate any effect of electron donation from the ring side of the sulfonyl group.

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