C H E M 8 0 T H E S I S

THE PHOTOSENSITIZED CIS-TRANS ISOMERIZATION OF ETHYLIDENE CYCLOHEXENE

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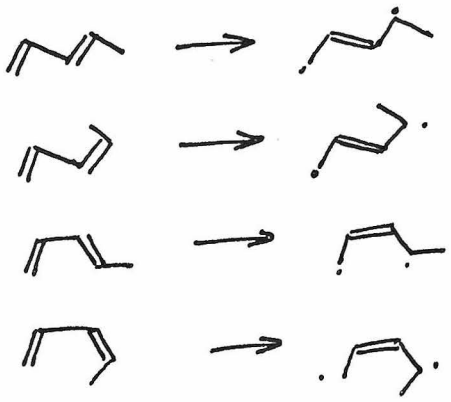
I N T R O D U C T I O N

The photosensitized cis-trans isomerization of the piperylenes has been reported.[1] Variation in photostationary states with different sensitizers has been attributed to differences in singlet-triplet excitation energies of the two isomeric piperylenes with cis-piperylene being lower. However, the study of the photosensitized dimerization of isoprene[2] suggests that for piperylenes instead of two there are four modes of excitation possibly with unequal excitation energies:



To avoid the inherent complexity of having the ground state S-cis and S-trans equilibration, we have synthesized 3-ethylidene cyclohexene and studied the photosensitized cis-trans isomerization:

It is evident that in this system only excitations from S-trans diene units are possible.

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[1] G.S.Hammond, P.A. Leermaker, N.J. Turro, "Photosensitized Cis-Trans Isomerization of the Piperylenesm" JACS 83, 2396 (1961)

[2] G.S. Hammond, R.S.H. Liu, "Stereoisomeric Triplet States of Conjugated Dienes," JACS 85, 477 (1963)

EXPERIMENTAL

MATERIALS

Solvents--

Benzene--Matheson, Coleman and Bell reagent grade distilled over Sodium.

Cyclohexane--Matheson, Coleman and Bell Spectroquality Reagent grade used without further purification.

Anhydrous Ether--Mallenkrodt Reagent grade.

Sensitizers-- All sensitizers were provided by Mr. A. A. Lamola

Synthesis Reagents

Ethyl Bromide--M., C., & B. reagent grade.

Cyclohexenone--Synthesized by Mr. D. Valentine and distilled.

Lithium Aluminum Hydride--

Acetic Acid Anhydride--

Ethylidene Cyclohexanone--Aldrich research grade distilled over a vigreaux column.

SYNTHESIS

Wittig Reaction

200 g. of ethyl phosphonium bromide was prepared from triphenyl phosphine and ethyl bromide by the standard Wittig method described in Wittig and Wittenberg, Liebig's Ann. Chem. 606(1957). (M.P. 206.6-208.3) .16 M of Phenyl lithium was prepared by dripping 70 g. (.45 MO of bromobenzene into a flask containing 6.5 g. of Lithium wire in 50 ml of anhydrous ether with stirring. After the addition was completed the solution was refluxed for $3\frac{1}{2}$ hours using a 300 ml round bottomed flask equipped with a reflux condenser and heating mantle.

.16 M (60 g) of triphenyl ethyl phosphonium bromide was slowly poured into a 500 ml rb flask containing .16 M of stirring phenyl lithium solution (prepared above). The flask was equipped with a stirrer and reflux condenser. 25 ml of anhydrous ether was added and the reaction mixture was allowed to stir for four hours.

16 g. of cyclohexenone in 25 ml of ether was slowly dripped into the solution and the solution was allowed to reflux overnight.

After neutralization with 4-75 ml portions of water the ether was

evaporated off leaving 3 ml of a colorless liquid. Separation of this material using the autoprep equipped with an 8 foot x $\frac{1}{4}$" Carbowax (10%) column yielded only a few drops of product. NMR spectra of the second autoprep fraction were in good agreement with the predicted spectra.

FINAL SYNTHESIS VIA REDUCTION OF ETHYLIDENE CYCLOHEXANONE

REDUCTION OF ETHYLIDENE CYCLOHEXANONE--

15g. (.395 M) of lithium aluminum hydride was ground to a powder and placed in a 2-liter three-necked flask equipped with a mechanical stirrer and reflux condenser. 300 ml of anhydrous ether was placed in the flask. The mixture was allowed to stir for about 15 minutes. 49 g (.395 M) of 3-ethylidene cyclohexanone dissolved in 75 ml of anhydrous ether was dripped slowly into the stirring lithium aluminum hydride solution. This addition proceeded for four hours. After completion of the addition, the solution was warmed slightly and stirred for an additional four hours. 60 ml of distilled water was then added (slowly!) to remove the rest of the lithium aluminum hydride.

500 ml of a 10% sulfuric acid solution was then added and the ether layer was removed via a separatory funnel. The aqueous layer was extracted twice with 40 ml portions of ether. After drying over anhydrous magnesium sulfate, the ether solution was concentrated over a steam bath. Distillation over a spinning band column yielded 39.0 g (80%) of a colorless liquid (B.P. 98° C at 2-3 mm). NMR spectra indicated that it was the desired ethylidene cyclohexanol.

DEHYDRATION OF ETHYLIDENE CYCLOHEXANOL--

39.0 g (.31 M) of ethylidene cyclohexanol and 44 ml of acetic anhydride (.6M) were placed in a 200 ml one-neck round bottom flask equipped with a reflux condenser. The material was allowed to reflux for 48 hours. After refluxing, the acetic acid and acetic acid anhydride were neutralized with 200 ml of distilled water and about 30 g of solid sodium bicarbonate. The organic layer was separated with a separatory funnel and the aqueous layer was extracted twice with 30 ml portions of anhydrous ether. After drying the ether solution over anhydrous magnesium sulfate, the ether was driven off over a steam bath and the mixture was distiooed. Yield 18.6 g (55 %) (b.p. 68-70°C. 5-8mm). Note: This was then combined with 5.1 g of the diene mixture from a previous synthesis to make a total of 23.7 g.)

REMOVAL OF THE 1-VINYL CYCLOHEXENE--

23.7 g. of the ethylidene cyclohexene-vinyl cyclohexene mixture (.19 M) was mixed with 7.5 g. of maleic anhydride (.076 M) in 50 ml of reagent grade spectroquality cyclohexane. The mixture was slowly refluxed for 12 hours in a 100 ml flask equipped with an upright condenser. The cyclohexane was then distilled over at room pressure and the 3-ethylidene cyclohexene was distilled over under reduced pressure. Total yield 5.68 g. (b.p. 49° C at 2-3 mm).

The NMR spectrum agreed with the theoretical spectrum of ethylidene cyclohexene and an IR spectrum showed no marked deviations from the

predicted spectrum. VPC runs showed that the product had very little impurities in it.

Overall yield--11.8%

GENERAL PROCEDURE

Each sample consisted of about 3 ml of a .05 M solution of ethylidene cyclohexene in a suitable solvent. To this was added some form of photosensitizer and the entire solution was sealed (after degassing) in a tube made from a 13x100 mm pyrex test tube. A total of three or four tubes were prepared for each photosensitizer. The original cis to trans ratio of the ethylidene cyclohexene was about 0.6.

The pyrene, acridine, eosin, anthracene and cyclopropylphenyl ketone sensitized isomerizations were carried out in an ether solution .05 M in ethylidene cyclohexene for increased solubility. The other tubes used a .05 M solution of ethylidene cyclohexene dissolved in reagent spectro-quality cyclohexane. (Cyclohexane was used as solvent in preference to benzene becasue it left a shorter "tail" when shot through the VPC.) In general the concentration of the sensitizer was .05 M except when availability (e.g beta-Naphthylphenyl ketone) or solubility (e.g. Michler's ketone) made such a high concentration impossible. For sensitizers with a very low solubility, a saturated solution of the sensitizer was used.

Concentration dependent runs were carried out using beta Aceto-naphthone, pyrene, and acridine as sensitizers, using sensitizer concentrations that varied from about .005 M to 0.1 M.

The samples were irridiated either with an immersion apparatus (pyrex) equipped with a 200 watt Hanovia lamp or with the "merry-go-round," a rotating immersion apparatus equipped with a 450 watt Hanovia lamp. In general no filters were used although filters should not

appreciably affect the photostationary state of the molecule. But since the test tubes were made of pyrex, the light was effectively cut off at about 2900 Å.

DETERMINATION OF THE PHOTOSTATIONARY STATE

To determine whether the samples had reached photostationary state, sample tubes were opened and investigated after varying lengths of irradiation until two tubes of different irradiation times had about the same cis/trans ratio (to about 10 %). Then it was assumed that the photostationary state had been reached. (The average irradiation time was about 50 hours per tube.)

(Note: During all the runs it was assumed that equal amounts of the cis and trans configurations would produce equal peak areas. This assumption is reasonable because of the very great similarity between the two isomers.)

For preliminary runs to see if the photostationary state had been reached, the samples were run through a 12 foot x $\frac{1}{4}$" tris 1,2,3 cyanoethoxylpropane column in a Loenco Model 70 Chromatograhh. Separation was not very good but estimates of the peak heights and areas could be made for the two isomers and from them the photostationary state could be detected. Much better separation (but still not complete) was obtained with a 32 foot tris 1,2,3 cyanoethoxylpropane column in a Loenco Model 15 B Chromatograph and all final runs were preformed on it.

RESULTS AND DISCUSSION

The synthesis of ethylidene cyclohexene was attempted in a number of ways but only two methods yielded any of the desired product: The standard Wittig Reaction between cyclohexenone and triphenyl ethyl phosphonium bromide.[1,2] and secondly via the reduction and dehydration of

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[1] The general method used was from Hauser, Brooks, et.al., J. Org Ch., 372 (1963), 28, and from S. Trippett, The Wittig Reaction, Adv. in Org. Chem., I, 83, (1960).

[2] Production of triphenyl ethyl phosphonium bromide according to a synthesis of Wittig's, Wittig and Wittenberg, Liebig's Ann. Ch., 606,1 (1957).

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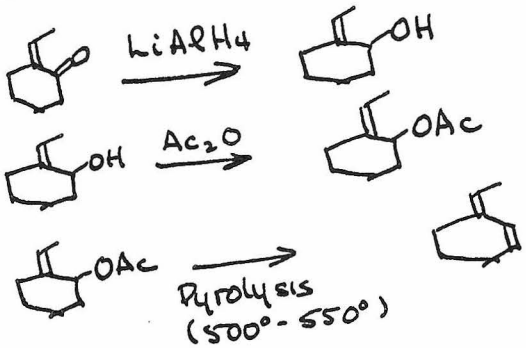
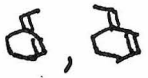
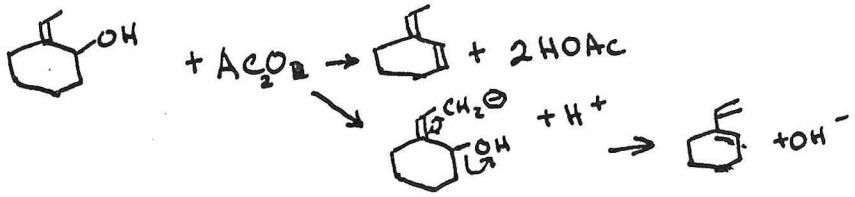
ethylidene cyclohexanone. The Wittig reaction was abandoned because of the poor yield of the product it gave.

The original prupose of the ethylidene cyclohexanone reduction reaction was first the production of the ethylidene cyclohexanol, then the acetylation of the alcohol followed by a pyrolysis of the material to give acetic acid and the desired olefin. via the following mechanism:



But instead, in the attempts to form the acetate by refluxing the alcohol with acetic acid anhydride, the alcohol instead was dehydrating to form the conjugated diene. The product of this dehydration was passed through a 6 foot (10%) Carbowax column and two adjacent peaks were noted on the VPC charts. Conceivably these could be the two desired isomers

of the ethylidene cyclohexene  . But a Carbowax column should not be capable of resolving the two dienes. Further analysis by NMR revealed that the second peak was the desired ethylidene cyclohexene while the first peak was 1-vinyl cyclohexene. This seem reasonable if we consider the two possible dehydration reactions taking place.



The mixture of 1-vinyl cyclohexene and ethylidene cyclohexene could not be separated on a Beckman Megachrom equipped with columns so chemical means were employed. The vinyl cyclohexene can react in a Diels Alder reaction with maleic anhydride while the ethylidene cyclohexene cannot because it can never assume the cis-configuration necessary for the reaction. Thus by refluxing the mixture with an excess of maleic anhydride (in a suitable solvent) the 1-vinyl cyclohexene was removed as a solid maleic anhydride cross adduct.

A better synthesis which was not tried would be the preparation of a xanthate derivative which would selectively form the ethylidene cyclohexene since elimination is done via a cyclic mechanism.

Our identification of the compound was based on four criteria:

1) NMR spectra agreed very closely with the predicted spectra of the product. There was an unequal doublet centered at about 1.3 ppm from tetramethylsilane of area 5. This could be the once split ethylidene methyl group masking the ring methylene group. A broad peak at 1.9 ppm of area 4 could be the ring allyl methylene groups and a broad width of many peaks with area 3 between 4.8 and 6.2 ppm could be the three

vinyl protons split by adjacent protons. This anaylsis is very consistent with the predicted spectrum of the desired compound.

2) The same product (identical NMR spectra) was obtained by two separate synthetic procedures--The Wittig reaction and the reduction and dehydration of ethylidene cyclohexanone.

3) Infrared spectra also agreed well with predicted spectra although very little accurate information could be drawn drom it.

4) Lastly some type of equilibrium was observed between two components of the system which implied some type of interconversion between the two species present in the system does in fact take place. This is in agreement with the expected cis-trans isomerization of the ethylidene cyclohexene.

More work must of course be done to verify the structure of the compound. A more exact verification should include an elemental analysis, hydrogenation to ethyl cyclohexane and possibly ozonolysis.

The results of the cis-trans isomerization are shown in Tables I and II and graphs I and II.

From the graphs of the cis to trans ratio versus sensitizer energy we can see that as the energy of the sensitizer decreases from very high energy sensitizers, the cis to trans ratio remains approximately constant down to sensitizers with energies of about 59 kcal. per mole. Then the ratio decreases as the sensitizer energy drops down to about 55 kcal. per mole. Then as the sensitizer energy is dropped even lower the ratio again increases.

The isomerization obviously occurs through excitation of the ground state molecule to an excited state: 

Since conjugated dienes do not absorb light above 3000 Angstroms, the

excitation must proceed via the excitation of a ground state photosensitizer molecule to an excited triplet and then transfer of the triplet energy to the ground state diene molecule. (Under the conditions of the experiment, light was effectively cut out at about 2900 Å.)

Judging by the curve shown in graph I, the constant photostationary state produced by high energy sensitizers indicates that in this region energy transfer to both species are equally efficient, probably diffusion controlled. But as the triplet energy of the sensitizer gets below about 60 kcal. per mole the cis to trans ratio drops appreicably. This implies that excitation from the trans 3-ethylidene cyclohexene to its excited triplet becomes less efficient. $S_g \rightarrow T_1$ of the trans diene therefore appears to occur at about 59 kcal. per mole and the corresponding transition for the cis diene occurs at some energy below 59 kc./m.

From the studies of the ethyl iodine absorption and photosensitized dimerization of isoprene[1] and butadiene, we believe that the $S_0 \rightarrow T_1$

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[1] G.S.Hammond, R.S.H.Liu, "Stereoisomeric Triplet States of Conjugated Dienes," JACS 85, 477 (1963).

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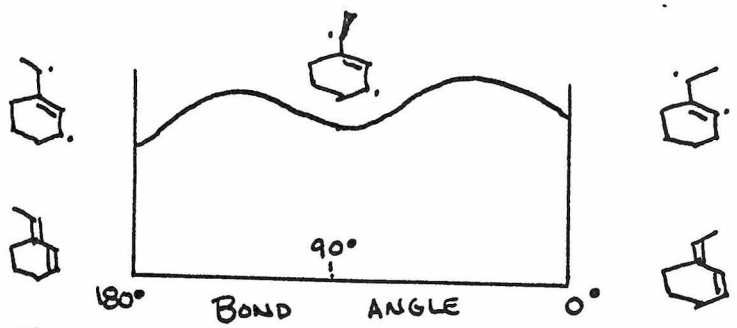
excitation of S-trans conjugated dienes is about 59 kcal. and that of S-cis is below 53 kcal. Since the ethylidene cyclohexene isomers both possess transoid conjugated diene units, the triplet energies of the two species should be close and probably between 57 and 60 kcal. per mole.

But sensitized isomerization is seen to occur with photosensitizers of energies below 57 kcal. and even down as low as 40.2 kcal. for 9,10 Dibromoanthracene. This suggests that some other means of excitation besides direct excitation to the normal cis and trans triplets (energy transfer with preservation of nuclear positions of the dienes) must be occuring. These excitation paths are now known as non-vertical excitation. Thus there is the possibility of excitation directly to the

"relaxed" cis and trans triplets from the respective dienes, or even direct excitation to a "perpendicular" triplet with the ethylidene group perpendicular to the plane of the ring.



These processes should be observable only with low energy sensitizers. With higher energy sensitizers these excitation are probably maskedby the normal cis to cis* and trans to trans* Franck-Condon excitation, but with low energy sensitizers, this non-vertical excitation could become the predominant reaction taking place. However, without more extensive data, it is even premature to speculate about the relative importance of these stable triplets.

The effects of sensitizer concentration was also investigated in the case of pyrene (E_T = 48.5 kcal. per mole) and β-acetonaphthone (E_T = 59.3 kcal per mole.).

When β-acetonaphthone was used as sensitizer, a slight increase in cis to trans ratio could be seen as the concentration of sensitizer decreased. But this effect is very small and could well be with experimental error. With relatively high energy sensitizers no concentration effect is expected since the sensitizer should have sufficient energy to excite the molecule to both the excited trans and excited cis form with equal efficiency.

When pyrene was used as sensitizer there was a marked increase in cis to trans ratio as the concentration of the sensitizer decreased. This marked concentration dependence with pyrene seems to indicate that there

is already a reversible energy transfer taking place between the sensitizer and the diene.

The decrease in the cis to trans ratio with increasing concentration of sensitizer may indicate the presence of selective quenching of the excited triplet by the sensitizer to give the trans ground state while with spontaneous decay, large amounts of the cis isomer are formed. Azulene experiments done in the photosensitized dimerization of isoprene[1] indicate

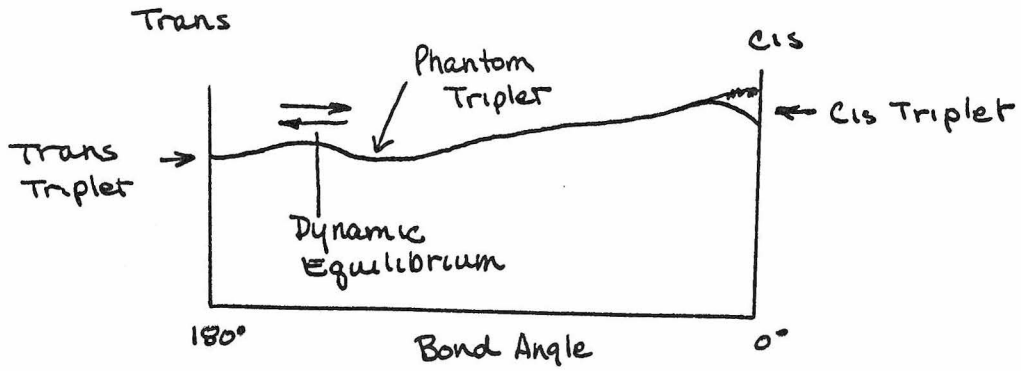
[1]Private communication with R.S.H. Liu.

that quenching of conjugated dienes does in fact take place and it is not unreasonable to suspect that quenching to one ground state may be more efficient than quenching to the other. Theoretically this concentration dependence could by explained by the existence of excited cis and trans triplets with the trans form having a longer lifetime than the corresponding cis excited state and thus being more completely quenched. But this theory is not compatible with our observations of low energy sensitization.

Another hypothesis that has recently been put forward to explain the cis-trans equilibriums is the existence of a phantom triplet "p" which is in dynamic equilibrium with the trans excited state,[2] the trans excited

[2] G.S. Hammond; et.al., Mechanisms of Photochemical Reactions in Solution XXI. Photochemical Cis-Trans Isomerization, JACS, (1964), xxxx.

triplet selectively decaying to the trans ground state and the phantom triplet decaying to both the cis and trans ground states. Unfortunately, this is not consistent with our other experimental data. For the phantom state to exist in dynamic equilibrium with the trans excited state, it should have approximately the same energy as the trans excited state of about 57-60 kcal per mole. But as mentioned previously, photosen-



sitization has been seen to occur at sensitizer energies below 45 kcal. per mole. Obviously a phantom state at this energy could not be in dynamic equilibrium with the trans triplet!

Another problem that was observed during the experiment was the appearence of a third anomolous peak right before the appearence of the two isomer peaks of the ethylidene cyclohexene. This third peak appears after long irradiation (about 160 hours with a 200 watt Hanovia immersion lamp) with low energy photosensitizers such as pyrene and acridene. After long irradiation the third peak's area was about $\frac{1}{4}$ that of the largest isomer peak. The position of the peak was approximately the same as that of the 1-vinyl cyclohexene formed during the synthesis of the material. This brings in the possibility that some additional type of isomerization takes place during irradiation. This may occur via a Schenk-type addition of the sensitizer to the diene and subsequent rearrangement and removal. (Rearrangement probably does not take place via direct hydrogen abstraction by the sensitizer since a compound like pyrene should not be expected to abstract hydrogens very readily.) Further work must be done to clarify this problem.

TABLE I

SENSITIZER	E_T	CONCENTRATION	CIS/TRANS AT EQUILIBRIUM
9,10 Dibromoanthracene	40.2 KC	Saturated	1.87
Anthracene	42.5	Saturated	0.90
Eosin	43.0	Saturated	0.88
Acridine	45.3	Saturated	0.76
	45.3	0.00 M (extrapolated)	0.86
Pyrene	48.7	0.05 M	0.67
	48.7	0.00 M(extrapolated)	0.81
Fluorenone	53.3	0.05 M	0.47
Biacetyl	54.9	0.05 M	0.46
α-Naphthaldehyde	56.3	0.05 M	0.74
α-Acetonaphthone	56.4	0.05 M	0.78
β-Acetonaphthone	59.3	0.05 M	0.98
	59.3	0.00 M(extrapolated)	1.01
β-Naphthaldehyde	59.5	0.05 M	0.87
Michler's ketone	61.0	Saturated	1.02
Anthraquinone	62.4	Saturated	1.06
4-Acetyl Biphenyl	64.1	Saturated	1.09
Benzophenone	68.5	0.05 M	1.03
Acetphenone	73.6	0.05 M	1.08

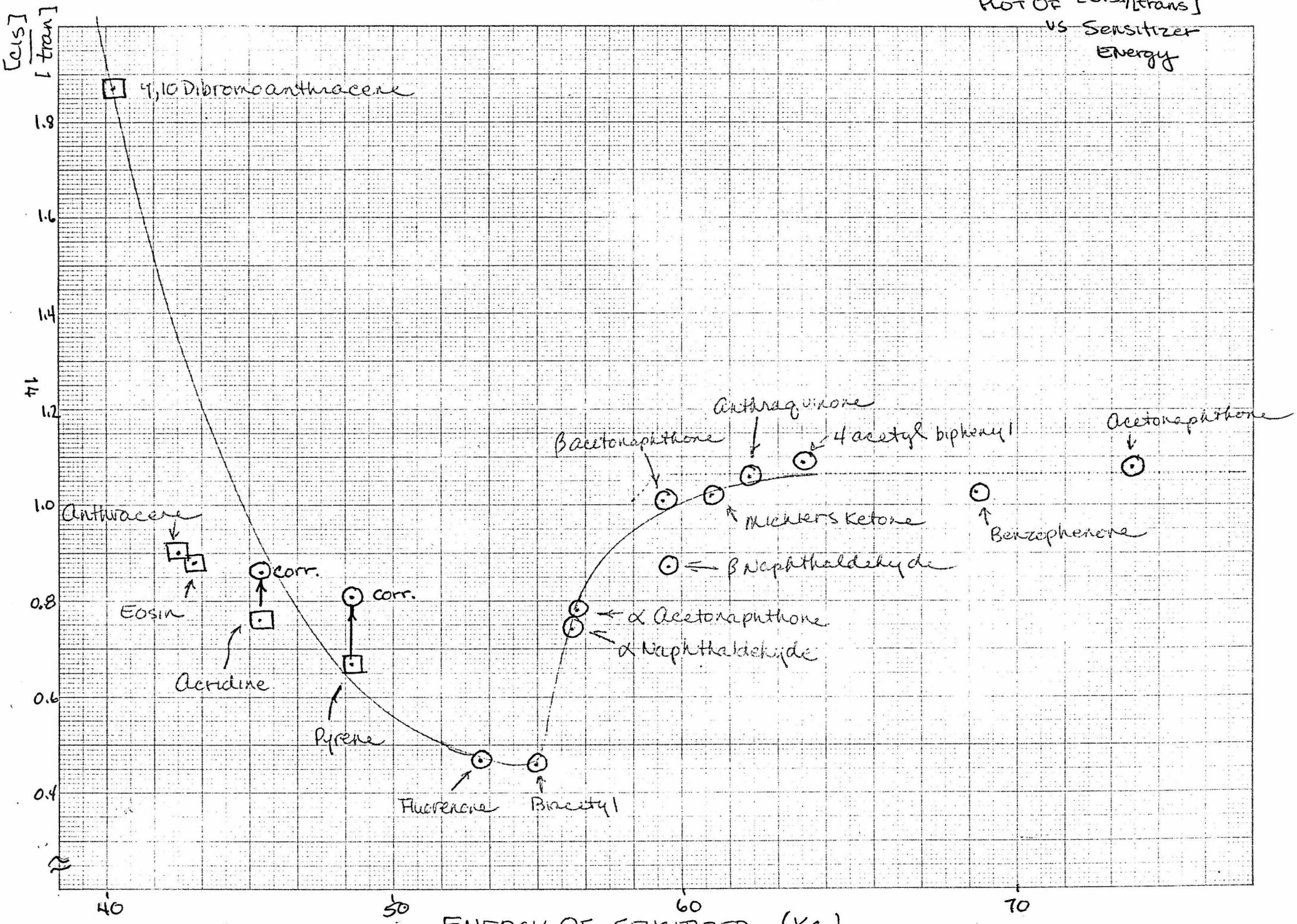
TABLE II

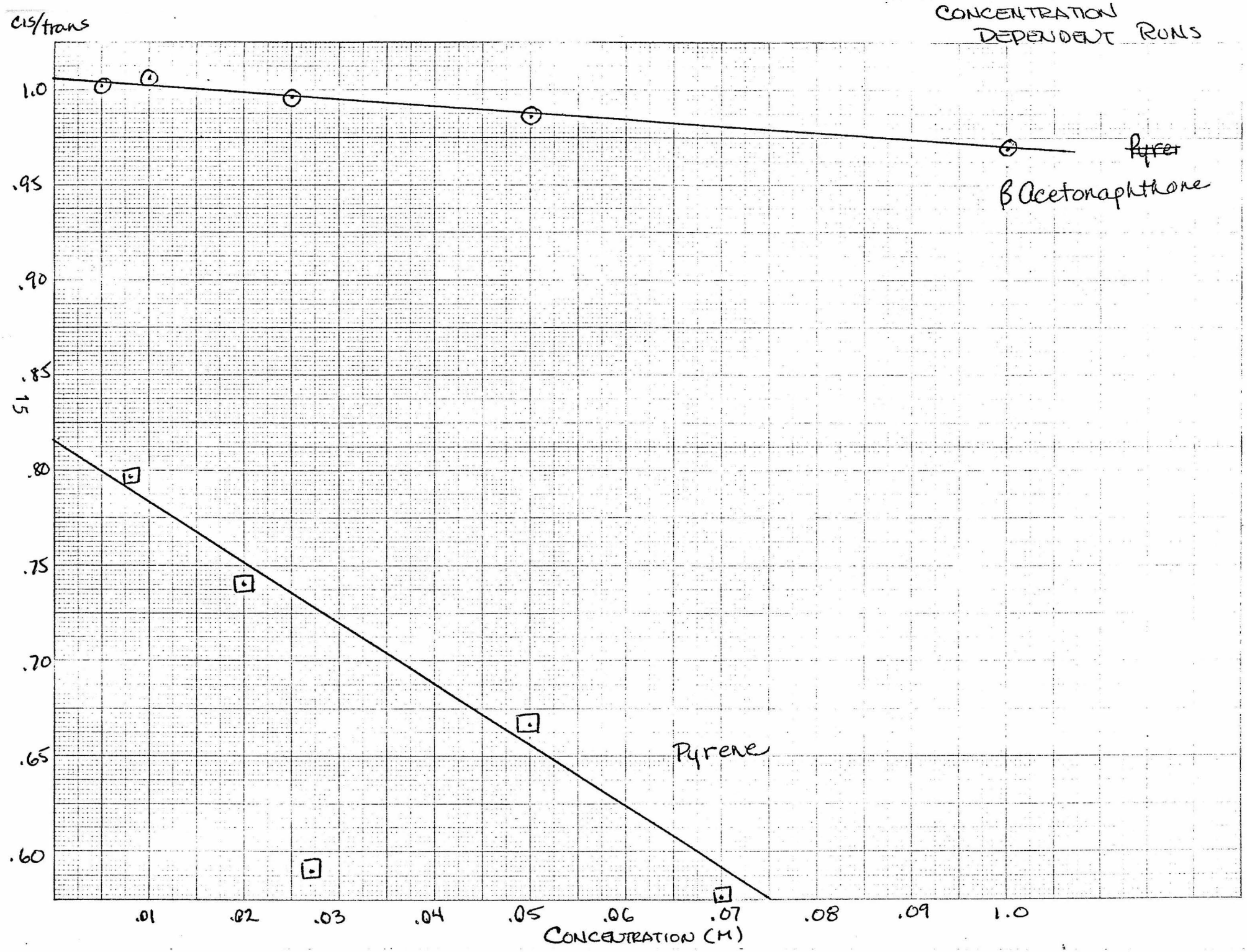
CONCENTRATION DEPENDENT RUNS

SENSITIZER	E_T	CONCENTRATION	CIS/TRANS AT EQUILIBRIUM
β-Acetonaphthone (Solvent-cyclohexane)	59.3 KC	.1 M	.969
		.05 M	.985
		.025 M	.996
		.01 M	1.006
		.005 M	1.002
		Zero Con.	1.01
Pyrene (Solvent-ether)	48.7 KC	.07 M	.576
		.05 M	.667
		.027 M	.587
		.020 M	.740
		.008 M	.796
		Zero Con.	.81
Acridine (Solvent-ether)	45.3 KC	Sat. Soln.	.76
		.001 M	.84
		Zero Con	~ .86

GRAPH 1

PLOT OF [cis]/[trans] VS SENSITIZER ENERGY




CONCENTRATION DEPENDENT RUNS
cis/trans
1.0
.95
.90
.85
.80
.75
.70
.65
.60
.01
.02
.03
.04
.05
.06
.07
.08
.09
1.0
CONCENTRATION (M)
β Acetonaphthone
Pyrene