and δ used. Values of δ are indicated which give approximately the right ratios of splitting constants. The values at $K = -2.60$ and $\delta = 0.990$ are in excellent agreement with experiment if we assume $Q = 25$. Unfortunately we have no way to determine the spin densities on the sulfone group and on the 1 positions. Little is known about the interactions of a free spin with a sulfur–carbon bond, nor with a sulfur nucleus in a sulfone linkage. Therefore even if we had ^{13}C coupling constants and those for ^{33}S, interpretation would be difficult.

In order to exclude the possibility that direct 1,1′ interactions were responsible for the conjugation between the two rings, we calculated a theoretical spectrum assuming only this interaction, *i.e.*, in direct analogy to biphenyl. Using the same procedure as described above and varying $\beta_{1,1'}$ from 0 to $0.40\beta_{C-C}$, we found that we could not approach the observed spectrum. This was also noted by McLachlan[15] who pointed out that $\beta_{1,1'}$ had to be larger than $0.5\beta_{C-C}$ to approach the observed spectrum for the biphenyl radical. Overlap of that extent was considered unlikely.

Conclusions

The calculations we have done demonstrate that the spin densities observed for the diphenyl sulfone anion radical can be adequately accounted for by proposing that an orbital of A_1 symmetry on the sulfone group is available for effective conjugation with the two phenyl rings. The exact nature of the orbital is not implied in a simple Hückel calculation, but if we wish to use LCAO language, it would seem that the orbital is mainly the sulfur $3d_{(3z^2-r^2)}$ orbital.

Nucleophilic Dequaternization of Condensed Azetidinium Salts

Gabor Fodor

Contribution from the National Research Council, Pure Chemistry Division, Ottawa, Ontario, Canada. *Received September 20, 1965*

Abstract: Complete reversal of quaternization by nucleophilic C substitution occurs with [1.5]methylenequinolizidinium tosylate and brosylate on reaction with nucleophiles, *e.g.*, sodium iodide, lithium bromide, sodium cyanide, and sodium methoxide in aprotic solvents (methylene chloride, or chloroform, and acetone). The homolog [1.5]ethylenequinolizidinium ion is not susceptible to this reaction, hence (1) steric compression in the condensed nonplanar azetidinium system, (2) the relative nucleophilicity of the reactants, and (3) the relative nucleophilicity of the solvents seem to determine whether internal quaternization or dequaternization takes place.

The quaternary salt[1] obtained from tosyllupinine[2] (IIa) has been shown[3] to have the condensed azetidinium ring structure I, as opposed to a diazaoctane ring (1) by osmometric molecular weight determination, (2) by infrared and nmr spectra, and (3) by X-ray crystallography[4] (this latter revealed noncoplanarity of the four-membered ring). It was also found that *quantitative ring opening* occurred when the tosylate Ia was dissolved in dichloromethane and treated with lithium bromide in acetone. "Bromolupinane,"[5,6] *i.e.*, (−)-1-bromomethylquinolizidine (IIc), was formed as the only product according to vpc; an authentic sample was prepared from lupinine with phosphorus tribromide.

Similarly, sodium iodide in acetone gave (−)-1-iodomethylquinolizidine (IId), while sodium cyanide in methanol, when added to the solution of the quaternary tosylate in dichloromethane, led to homolupinic nitrile (IIf).

Brosyllupinine was prepared. This is crystalline (mp 107°) but when heated to 85° for 3 hr is quantitatively isomerized during the operation to I brosylate (mp 155°) without melting. The brosylate has the same nmr signals as the tosylate (except for methyl protons) and undergoes the same substitution reactions in methylene chloride.

The brosylate gave, with sodium methoxide, lupinine methyl ether (IIg) and no trace of an olefinic Hofmann degradation product. In view of these facts, the alkali hydrolysis of I tosylate into lupinine (IIh) might also be considered as a nucleophilic substitution on the ring methylene carbon 11.

The conversion of I brosylate into II iodide was followed by nmr; it proved to be a very fast reaction as was the cleavage by lithium bromide to IIc.

Curiously enough, I picrate gave with aqueous hydrobromic acid a crystallized bromide, obviously Ic. The tetraphenylborate Ie is stable as well. In alcohol the iodide Id was formed from the tosylate along with iodomethylquinolizidine (IId). The ratio salt:covalent compound is much smaller in an acetone–alcohol mixture than in pure alcohol, but larger than in dichloromethane. It seems that the weak nucleophilicity of the tosylate, brosylate, and tetraphenylborate ion stabilizes those salts while bromide, iodide, and methoxide ions as stronger nucleophiles afford ring opening to the halogenomethyl and methoxy compounds (II), respectively.

(1) N. J. Leonard in "The Alkaloids," Vol. 7, R. H. F. Manske, Ed., Academic Press Inc., New York, N. Y., 1961.
(2) F. Galinovsky and H. Nesvadba, *Monatsh. Chem.*, 85, 1300 (1954).
(3) O. E. Edwards, G. Fodor, and L. Marion, *Can. J. Chem.*, 44, 13 (1966).
(4) C. Saunderson, unpublished.
(5) G. R. Clemo, W. M. Morgan, and R. Raper, *J. Chem. Soc.*, 965 (1939).
(6) F. Bohlmann, E. Winterfeldt, and U. Friese, *Chem. Ber.*, 96, 2251 (1963).

Quaternary ammonium salts usually undergo Hofmann elimination but not substitution when treated with bases, except for cases where methanol is eliminated.[7] There is a single analogy to an interionic nucleophilic attack: that of the alleged intermediates of the von Braun degradation, *i.e.*, N-cyano-N-trialkylammonium bromides, giving rise to N-cyano-N-dialkyl-ω-haloalkylamines as by-products. However, the N-cyano group is extremely strongly electron withdrawing; so there is no close parallelism with the compounds reported here. The observation of Leonard, *et al.*,[8] on the other hand, that methylene adducts of 5,10-dehydroquinolizidinium salts give 10-halomethyl derivatives by ring opening, is relevant to ours. However, simple azetidinium salts are much more stable than ethylenimines.

On the other hand, there is a similarity with the case of N^a-gelsemine norcarbinol methohydroxide trihydrate with the nitrogen in the five-membered ring which becomes dequaternized by an internal alkoxide ion into a volatile anhydro base. This reaction is reversible.[9]

The reason for this easy reaction of I may be sought in the high steric strain and the noncoplanarity of the azetidinium ring. This assumption was verified by synthesis of [1.5]ethylenequinolizidinium brosylate (Vb) *via* 1-cyanomethylquinolizidine (IIf), alcoholysis to methyl homolupininate (III) followed by lithium aluminum hydride (LAH) reduction to homolupinine (IVa), brosylation to IVb, and internal quaternization thereof to Vb. This latter compound with sodium iodide in acetone gave no trace of a covalent haloethyl compound but the corresponding crystalline iodide Vc.

Accordingly, this nucleophilic ring opening seems to be limited primarily to a sterically compressed and distorted azetidinium salt. The scope and limitations of this curious transformation are under investigation.[10,10a]

Quantitative information as to the kinetics and energetics of cyclization and dequaternization are expected from a more systematic nmr study of I with different nucleophiles and in a variety of solvents.

Experimental Section

Melting points were determined under the microscope and are uncorrected.

[1.5]Methylenequinolizidinium *p*-toluenesulfonate (Ia) was described by Galinovsky[2] and by us.[3]

***p*-Bromobenzenesulfonyllupinine (IIb).** Lupinine (3.38 g, 0.02 mole) and brosyl chloride (2.557 g, 0.01 mole) were dissolved in 28 ml of acetone, and the solution was stirred magnetically for 3 hr. Crystallization of lupinine hydrochloride (1.4763 g) set in within a few minutes. The filtrate was then evaporated and the residue taken up in ether (100 ml) and 5 ml of 0.5 *N* NaOH. The ethereal layer was dried over sodium carbonate, the solvent removed, and the remaining solid recrystallized from ether–hexane (1:1), yield 3.2 g (IIb) (81%), mp 107°.

Anal. Calcd for $C_{16}H_{22}O_3NSBr$: C, 49.50; H, 5.68; Br, 20.6. Found: C, 49.28; H, 5.81; Br, 20.42.

[1.5]Methylenequinolizidinium brosylate (Ib) was obtained by heating the ester (2 g) on a rotatory evaporator for 5 hr in an oil bath of 95° without transitory melting. The product was washed with ether to give 1.72 g (86%) of colorless tetragonal crystals, mp 145°, which was raised on recrystallization from ethanol–ether (1:1) to 155°.

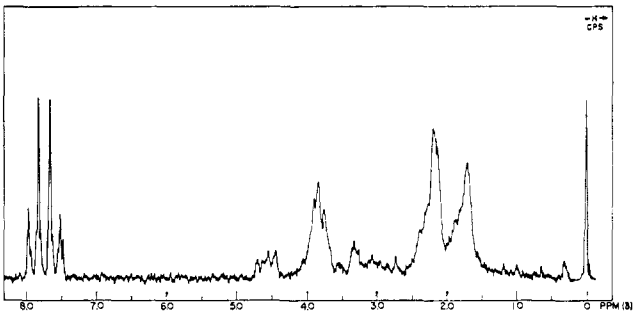


Figure 1. Nmr spectrum of [1.5]methylenequinolizidinium brosylate (Ib) in $CDCl_3$.

Anal. Calcd for $C_{16}H_{22}O_3NSBr$: C, 49.50; H, 5.68; Br (ionic), 20.6. Found: C, 49.38; H, 5.81; Br (ionic), 20.77.

The nmr spectrum (Figure 1) in chloroform-*d* (TMS as internal standard) shows a quartet at δ 7.95, 7.80, 7.65, and 7.53 (aromatic protons); one α-proton resonates at δ 4.85, 4.58, and 4.46; five α-protons resonate at δ 3.95, 3.85, and 3.77; and twelve remote protons resonate at δ 2.18, 2.13, and 1.72. This may be compared with the nmr spectrum of Ia in the previous paper.[3]

(−)-Bromomethylquinolizidine (IIc). (a) From [1.5]Methylenequinolizidinium Tosylate. To a solution of the tosylate Ia (530 mg, 1.64 m*M*) in 5 ml of methylene chloride, lithium bromide (142.6 mg, 1.64 m*M*) in 60 ml of acetone was added. The precipitated lithium *p*-toluenesulfonate, 236.1 mg (81%), was removed by filtration and washed with methylene chloride; the mother liquor was evaporated in a rotatory evaporator at 30° to give 400 mg of a yellowish oil containing some crystals. It was distilled from a microdistilling set equipped with a cold finger (acetone–Dry Ice). The distillate, 197.2 mg (51%) of II, bp 80–100° (0.02 mm), was a colorless oil (the solid residue weighed 82.8 mg).

Anal. Calcd for $C_{10}H_{18}NBr$: C, 51.70; H, 7.75; Br, 34.40. Found: C, 51.58; H, 7.56; Br, 34.21.

A vapor-phase chromatogram (15% diethylene glycol succinate on Chemosorb, 60–80 mesh; 2 m × 0.5 in. column) showed a single peak; infrared peaks: 2960, 2790, 1650, 1450, 1285, 1125, and 695 cm^{-1}.

(b) From Lupinine. To lupinine (1.75 g, 103 m*M*) in 20 ml of carbon tetrachloride, phosphorus tribromide (2.5957 g, 0.96 m*M*) in 15 ml of carbon tetrachloride was added with cooling. A brownish precipitate appeared at once and the reaction mixture was refluxed for 3 hr. Then 5 g of ice and 10 ml of 0.5 *N* sodium hydroxide were added, the aqueous layer was extracted with 15 ml of chloroform, and the combined extracts were dried over potassium carbonate. Removal of the solvent left an oil behind which was distilled under 0.0001 mm, bp 80°, yield 2 g of 1-bromomethylquinolizidine (IIc). Clemo, *et al.*,[5] reported bp 120° (10 mm) for their product obtained from 4-(2-piperidyl)-1,5-pentanediol with hydrobromic acid.

Anal. Calcd for $C_{10}H_{18}NBr$: Br, 34.40. Found: Br, 34.23.

The vpc showed one single peak; infrared peaks: 2960, 2790, 1440, 1280, 1125, and 690 cm^{-1}.

Attempted Internal Quaternization of IIc. 1-Bromomethylquinolizidine (IIc) (from method b) (340 mg) was heated in a thermostated oil bath to 100–102° for 16 hr. Apart from a tar (5 mg), the rest gave the same unique peak in the vpc. It was then heated an additional 32 hr to 100°; 302.7 mg of the substance was unchanged, while 25.7 mg polymerized. 1-Tosyloxymethyl- and 1-brosyloxymethylquinolizidine both gave a nearly quantitative yield of the internally quaternized product under the same conditions.

(−)-1-Iodomethylquinolizidine (IId). (a) In Dichloromethane–Acetone. To tosylate Ia (1.075 g, 3.34 m*M*) dissolved in 15 ml of methylene chloride, a solution of sodium iodide (0.4997 g, 3.34 m*M*) was added, and the sodium *p*-toluenesulfonate (0.6173 g, 96.2%) was removed by filtration. The solvents were removed under atmospheric pressure to give an oil, which was distilled from an oil bath of 70–80° (0.005 mm), affording 0.6874 g (76.2%) of pure iodomethyl compound IId. The nmr spectrum is shown in Figure

(7) W. Hanhard and C. K. Ingold, *J. Chem. Soc.*, 997 (1927).

(8) N. J. Leonard, K. Jann, J. V. Paukstelis, and C. K. Steinhardt, *J. Org. Chem.*, 28, 1499 (1963).

(9) A. M. Roe and M. Gates, *Tetrahedron*, 11, 148 (1960).

(10) Quaternary ammonium salts are known to be alkylating agents but not toward alkali halides and methoxides.

(10a) Note Added in Proof. A. Ebnöther and E. Jucker reported [*Helv. Chim. Acta*, 47, 745 (1964)] that N-methylpyrrolidino- and -piperidino-1,2-azetidinium chlorides undergo ring opening on heating with strong bases such as 10% NaOH, benzylamine, and benzhydrylsodium, respectively.

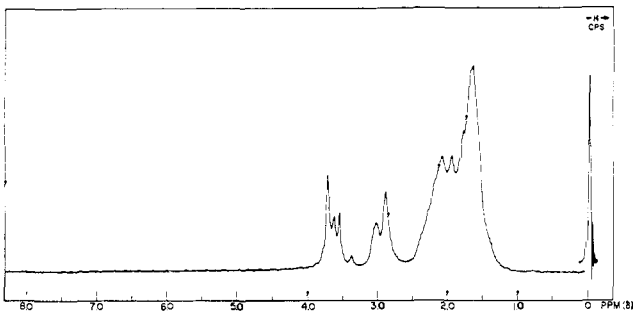


Figure 2. Nmr spectrum of 1-iodomethylquinolizidine (IId) (homogeneous).

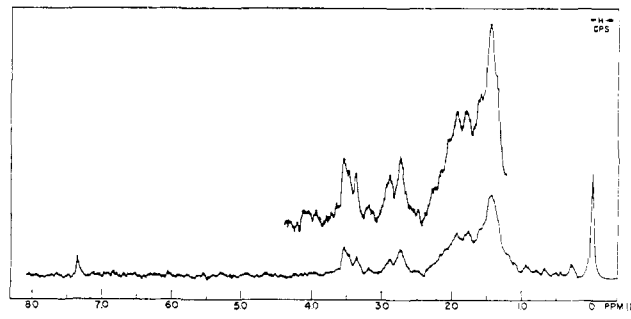


Figure 3. Nmr spectrum of the product from Ib in $CDCl_3$, 4 hr after NaI has been added.

2. It gave one single peak in the vpc using the same column as with the bromomethyl compound; infrared absorption: 2920, 2740, 1460, 1442, 1380, 1347, 1310, 1278, 1270, 1210, 1178, 1152, 1100, 1072, 1050, 995, 975, 365, and 920 cm^{-1}.

Anal. Calcd for $C_{10}H_{18}NI$: C, 43.03; H, 6.45. Found: C, 43.12; H, 6.53.

(b) In Pure Acetone. Freshly dried NaI (244.9 mg, 1.68 m*M*) was dissolved in 10 ml of dry acetone, and a hot solution of tosylate Ia (447 mg, 1.68 m*M*) in 30 ml of acetone was added. After removing the sodium tosylate (257 mg, 82%), the mother liquor was evaporated in a Rotavapor at 30° and distilled as under part a, *in vacuo*, to give iodomethylquinolizidine (IId), 153 mg; the residue weighed 20.5 mg. Accordingly, no salt was formed; the losses in IId are due to its volatility.

(c) In Ethanol–Acetone. The tosylate (349.6 mg, 1.08 m*M*) was dissolved in 10 ml of dry ethanol, and a solution of 162 mg of NaI (1.08 m*M*) in 10 ml of acetone was added. The filtrate from sodium tosylate (150.5 mg, calculated 195 mg) gave on evaporation at reduced pressure a solid (249.5 mg, calculated 299 mg) of impure I iodide, mp 140–180°.

Anal. Calcd for $C_{10}H_{18}NI^-$: I (ionic), 45.5. Found: I (ionic), 38.8.

Methiodide-d_3. A few drops (0.1 ml) of IId reacted instantaneously with excess (0.5 ml) CD_3I giving white crystals. These were washed with ether and acetone, mp 229°.

Anal. Calcd for $C_{10}H_{18}D_3NI_2$: C, 29.30; H + D, 5.83; I, 67.95. Found: C, 29.39; H + D, 5.26; I, 67.23.

Conversion of Brosylate Ib into 1-Iodomethylquinolizidine (IId). The brosylate Ib (42.5 mg) was dissolved in an nmr tube in 0.3 ml of $CDCl_3$ and the spectrum taken; then a solution of dry sodium iodide (16.5 mg) in 0.1 ml of acetone-d_6 was added. The resulting solution was filtered from sodium tosylate through cotton-wool into another nmr tube. After 10 min the spectrum was taken again, then checked at regular intervals. After 4 hr at 25°, the signals of iodomethylquinolizidine were not disturbed by overlapping signals of the methylenequinolizidinium ion (see Figure 3).

Lupinine Methyl Ether (IIg). The brosylate Ib (388 mg, 1 m*M*) was dissolved in 15 ml of methylene chloride, and sodium methoxide (80 mg, 1.6 m*M*) in 5 ml of dry methanol was added. The sodium brosylate was filtered off and the solution evaporated. Distillation afforded 154 mg of a colorless liquid, bp 100–110° (0.001 mm) nmr signal δ 3.37 (OCH_3). No olefin signal appeared in the lower field.

1-Cyanomethylquinolizidine (IIf). To [1.5]methylenequinolizidinium tosylate (Ia) (3.23 g, 0.01 mole) in 20 ml of methylene chloride, a solution of sodium cyanide (0.54 g, 0.011 mole) in 10 ml of methanol was added. The sodium tosylate (1.87 g, 96%) was filtered off and the solvents were removed at 80° on a steam bath. The residue was taken up in 30 ml of ether, the last traces of sodium tosylate were filtered off, and the filtrate was evaporated again and distilled, 90–100° (0.001 mm), yield 2.283 g. Another distillation gave 1.228 g (total yield 69%) of a colorless liquid, which had the typical CN stretching at 1285 cm^{-1} and was proved pure by vpc.

Anal. Calcd for $C_{11}H_{18}N_2$: N, 15.65. Found: N, 15.16.

Methyl Homolupininate (Methyl 1-Quinolizidylacetate) (III). The pure cyanomethyl compound IIf (1.22 g, 6.87 m*M*) was taken up in 10 ml of absolute methanol. The solution was saturated under cooling (Dry Ice) with hydrogen chloride; then more hydrogen chloride was bubbled through while refluxing the solution for 16 hr, at which time crystals separated. The crude product gave no CN absorption but showed a strong carbonyl band. The methanol was driven off and the oily residue treated with ether and 50% potassium carbonate. The ethereal extract left 1.1154 g of a yellowish oil, which was then distilled under 0.0001 mm from a 100° oil bath, yielding 1 g of methyl homolupininate (III).

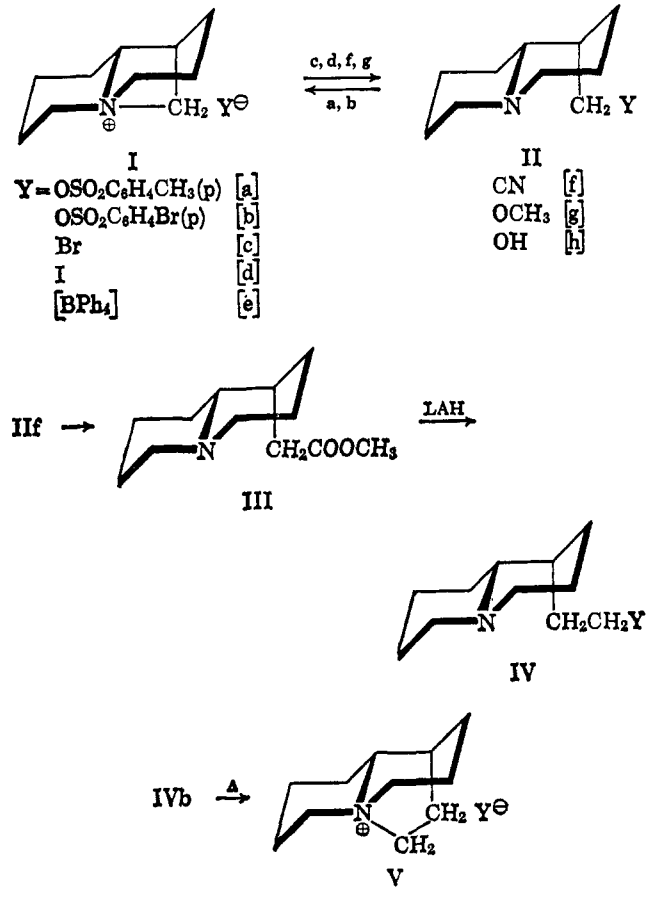
Anal. Calcd for $C_{12}H_{22}NO_2$: C, 68.2; H, 9.98. Found: C, 67.96; H, 10.16.

In another experiment, the cyano compound from 5.6 g of tosylate Ia was subjected to alcoholysis without distillation of the nitrile IIf, giving 2.2949 g of methyl 1-quinolizidylacetate with the same infrared spectrum.

(−)-Homolupinine 2-(1-Quinolizidyl)ethanol) (IVh). A solution of methyl homolupininate (III) (2.034 g, 0.00965 mole) was added dropwise to a stirred solution of excess LAH (0.8 g) at 25°. Stirring was continued for 3 hr, then 5 ml of water added drop by drop. The precipitated metal hydroxides were filtered off and washed thoroughly with a total of 30 ml of ether. Evaporation gave 1.526 g of hygroscopic homolupinine IVh as a viscous oil: $[\alpha]^{20}D$ −17.95° (*c* 9.04 acetone; ν_{max} 3400, 2950, 2900, 2780, 1640, 1438, and 1120 cm^{-1}.

Anal. Calcd for $C_{11}H_{21}ON$: C, 72.2; H, 11.48. Found: C, 70.56; H, 11.96.

[1.5]Ethylenequinolizidinium Brosylate (Vb). Homolupinine (IVa) (1.8737 g, 0.0103 mole) and brosyl chloride (1.30 g) in 15 ml of dry acetone was worked up as the lower homolog. The crude



O-*p*-bromobenzenesulfonylhomolupinine ester was not purified but converted by heating to 90° in a rotatory evaporator for 2 hr into 250 mg of the internal quaternary salt, mp 138°.

Anal. Calcd for $C_{17}H_{24}O_3NSBr$: C, 50.7; H, 5.97; N, 3.48; Br, 19.80. Found: C, 50.56; H, 5.83; N, 3.39; Br, 19.79.

Iodide (Vd). The brosylate (44.5 mg) was dissolved in 5 ml of methylene chloride; then sodium iodide (20 mg) in 2 ml of acetone was added and the sodium brosylate filtered. The residue after evaporation, 30 mg, was crystalline. Recrystallization from ethanol–ether gave leaflets, mp 332–333° dec.

Anal. Calcd for $C_{11}H_{20}NI$: C, 45.02; H, 6.82. Found: C, 44.91; H, 6.90.

Nmr spectra were recorded on a Varian A-60 spectrometer using chloroform-*d*.

The **infrared data** were obtained on a Perkin-Elmer grating spectrophotometer.

Acknowledgment. This research was carried out during the tenure of the author's stay as a visiting scientist with the Pure Chemistry Division of the National Research Council in Ottawa, Canada. Grateful acknowledgment is hereby made to the Council, in particular to Dr. Léo Marion, former Vice-President, to Dr. W. G. Schneider, Vice-President, and to Dr. O. E. Edwards, Organic Chemistry Section. Thanks are due to Mr. H. Seguin for the microanalyses.

Photochemical Synthesis. XI. On the Mechanism of the Maleate–Cyclohexene Cycloaddition

A. Cox, P. de Mayo, and R. W. Yip

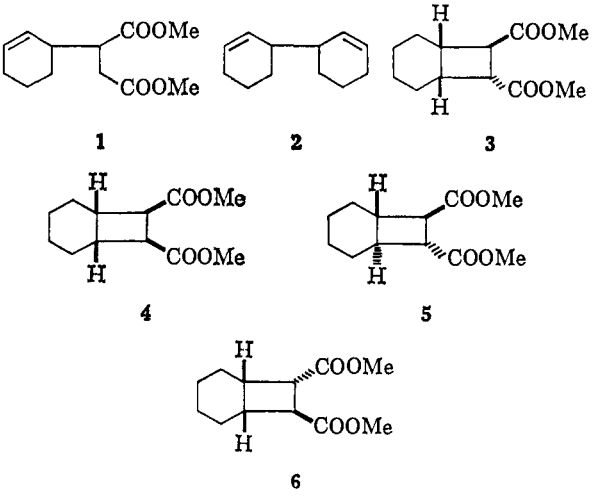
Contribution from the Department of Chemistry, University of Western Ontario, London, Canada. *Received October 1, 1965*

Abstract: The composition of the bicyclo[4.2.0]octane dicarboxylic ester mixture produced by the irradiation of dimethyl maleate in cyclohexene varies with the temperature of irradiation. Since the intervention of excited cyclohexene molecules is improbable, this and the formation of *trans*-fused products requires that part of the product, at least, be formed through a discrete diradical intermediate. The sensitized reaction, using sensitizers of E_T from 40 to 84 kcal/mole, shows a similar, but different, temperature dependence and the product analysis is independent of the E_T. A triplet–triplet energy transfer mechanism is indicated for this process, and at least part of the directly formed product appears to be formed through the singlet.

In a previous paper in this series[1] the products obtained in the photochemical addition of dimethyl maleate to cyclohexene and to cyclopentene were described.[3] It was found that, in addition to the allylic addition products, such as cyclohex-2-enyl succcinic ester (**1**) and bicyclohexenyl (**2**), a number of saturated dicarboxylic esters, formed by cycloaddition, were obtained. Those isolated in the cyclohexene series were bicyclo[4.2.0]octane derivatives and included members of both the *cis*- and *trans*-fused systems, specifically esters **3**–**6**.

The *cis,cis,endo* isomer, isolated in a small amount by Barltrop,[4] was present in our system in too small quantities for investigation: its exiguousness is probably to be attributed to the steric compression in this molecule. No obvious explanation for the absence of the *trans,cis* isomer is available unless it be present as an unseparated very minor component of the peak containing **3**.

Present detailed knowledge concerning the photochemical cycloaddition process is comparatively sparse, though presently attracting attention,[4,5] and the present instance appeared suitable for further study as regards the nature of the species involved.



Results

A. Ground-State Charge-Transfer Complexes. No indication of additional or modified absorption was found with dimethyl maleate in cyclohexene (as distinct from that of the components) although complex

(1) P. de Mayo, S. T. Reid, and R. W. Yip, *Can. J. Chem.*, **42**, 2828 (1964); see also ref 2.

(2) P. de Mayo, R. W. Yip, and S. T. Reid, *Proc. Chem. Soc.*, 54 (1963).

(3) The addition of maleic anhydride to cyclohexene has also been reported recently.[4]

(4) R. Robson, P. W. Grubb, and J. A. Barltrop, *J. Chem. Soc.*, 2153 (1964); see also J. A. Barltrop and R. Robson, *Tetrahedron Letters*, 597 (1963).

(5) (a) S. J. Cristol and R. L. Snell, *J. Am. Chem. Soc.*, **76**, 5000 (1954); (b) P. E. Eaton, *ibid.*, **84**, 2454 (1962); (c) P. de Mayo and H. Takeshita, *Can. J. Chem.*, **41**, 440 (1963); (d) H. J. F. Angus and D. Bryce-Smith, *J. Chem. Soc.*, 4791 (1960); (e) E. Grovenstein, Jr., and D. V. Rao, *Tetrahedron Letters*, **No. 4**, 148 (1961); (f) E. J. Corey, J. D. Bass, R. Le Mahieu, and R. B. Mitra, *J. Am. Chem. Soc.*, **86**, 5570 (1964); (g) G. O. Schenck and R. Steinmetz, *Tetrahedron Letters*, **No. 21**, 1 (1960); (h) G. O. Schenck, W. Hartmann, and R. Steinmetz, *Chem. Ber.*, **96**, 498 (1963).