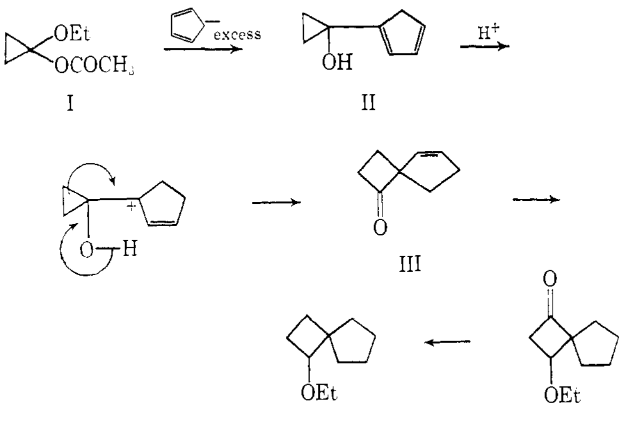
Cyclopropanone Reactions of 1-Ethoxycyclopropyl Alcohol and Acetate[1]

Sir:

In view of current interest in the chemistry of cyclopropanes[2-5] we are reporting certain novel reactions of 1-ethoxycyclopropyl alcohol (VII) and acetate (I) which appear to involve intermediate cyclopropanone formation.



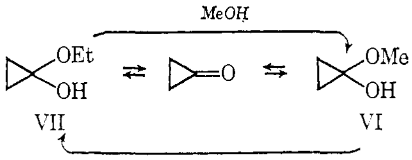
I II III IV V

With excess cyclopentadienylmagnesium bromide, I yielded the cyclopentadienylcyclopropanol (II) as an unstable, easily polymerized oil; nmr, τ 3.47 (multiplet), 7.27 (doublet), 9.13 (multiplet); infrared peak at 3600 cm^{-1}; $\lambda_{\max}^{\mathrm{EtOH}}$ 247 mμ. *Anal.* Calcd for $C_8H_{10}O$: C, 78.65; H, 8.25. Found: C, 78.88; H, 8.05. When shaken briefly with 10% aqueous H_2SO_4 in ether, II readily isomerized to III (20%, from I); infrared bands at 1780 and 1057 cm^{-1}; nmr, τ 4.33 (multiplet, 2 H), 6.95–7.26 (multiplet, 2 H), 7.75–8.44 (multiplet, 6 H). *Anal.* Found: C, 78.63; H, 8.29; mol wt (mass spectrum), 122. The mass spectral cracking pattern shows peaks at 94 (loss of CO) and 80 (loss of ketene).

Assignment of structure III to the isomerization product is supported by its conversion to the ethoxyspirooctane IV by the following sequence:[6] catalytic hydrogenation, $LiAlH_4$ reduction of the saturated ketone, and reaction of the alcohol (sealed tube at 175°) with KOH and EtBr. The ether IV was independently prepared[6] from V, the cycloaddition product of ethyl vinyl ether and cyclopentanecarboxylic acid chloride in the presence of triethylamine.[7] Reduction of V by $LiAlH_4$, tosylation, and further $LiAlH_4$ reduction yielded IV.

As pictured above, addition of a proton to II produces a stable cyclopropylcarbinyl carbonium ion, providing the driving force for the novel cyclopropanol rearrangement to III.

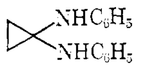
Reaction of I with excess methanol at 25° yielded cyclopropanone methyl hemiketal (VI, 64%) along with methyl acetate and methyl propionate. With ethanol, the ethyl hemiketal VII, bp 63–65° (50 mm), was obtained (35%). This product could also be formed by the reaction of ketene and diazomethane in the presence of ethanol;[8] nmr, τ 4.94 (singlet, 1 H), 6.23 (quartet, 2 H), 8.80 (triplet, 3 H), 9.17 (singlet, 4 H). *Anal.* Calcd for $C_5H_{10}O_2$: C, 58.80; H, 9.87; mol wt, 102. Found: C, 58.60; H, 9.98; mol wt (mass spectrum), 102. The ethyl hemiketal rearranges above 65°, or on standing in inert solvents, to form ethyl propionate. It is readily converted to I with ketene.



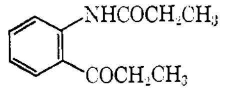
VII VI

On standing at 25° for 1 week with methanol, *ca.* 65% of VII was converted to VI as shown by glpc retention times and infrared spectral comparison. Conversion appeared to be complete after 15 days. In like manner, VI was slowly transformed to VII by excess ethanol. These changes are pictured, as shown above, in terms of a cyclopropanone–hemiketal equilibrium.[9]

Reaction of aniline with cyclopropanone ethyl hemiketal (VII) at 25° yielded 1,1-dianilinocyclopropane (VIII; 48%). At higher temperatures (125° in a sealed tube) *o*-propionylaminopropiophenone (IX) was isolated in addition to VIII. The same two products were isolated in low yield from the reaction of I with aniline at 125°.



VIII



IX

The dianilino derivative (mp 144–144.5°. *Anal.* Calcd for $C_{19}H_{16}N_2$: C, 80.32; H, 7.19; N, 12.49; Found: C, 80.49; H, 7.30; N, 12.23) shows nmr absorption at τ 2.70–3.50 (10 H), 5.13 (singlet, 2 H), and 8.85 (singlet, 4 H), and is converted to N,N-diphenylpropionamidine on heating. The keto amide IX (*Anal.* Calcd for $C_{12}H_5NO_2$: C, 70.22; H, 7.37; N, 6.82. Found: C, 70.10; H, 7.23; N, 7.01) was identified by comparison with an authentic sample prepared by the ozonolysis of 2,3-diethylindole; nmr, τ −1.98 (singlet, 1 H), 1–3.2 (multiplet, 3 H), 7.03 (quartet, 2 H), 7.61 (quartet, 2 H), and 8.83 (multiplet, 6 H).

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(1) See H. H. Wasserman and D. C. Clagett, *Tetrahedron Letters*, 341 (1964), for the preparation of I by the addition of methylene to ethoxyvinyl acetate and for earlier studies on this system.

(2) (a) Cyclopropanone has never been isolated in a pure state although the hydrate and methyl hemiketal were prepared some years ago by P. Lipp, J. Buchkremer, and H. Seeles (*Ann.*, **499**, 1 (1932)); (b) A. S. Kende (Ph.D. Thesis, Harvard University, 1956) obtained spectral evidence for the formation of this ketone in the reaction of ketene with diazomethane; (c) very recently, N. J. Turro and W. B. Hammond (*J. Am. Chem. Soc.*, **88**, 3672 (1966)) clearly showed that synthetically useful methylene chloride solutions of cyclopropanone may be obtained in excellent yield from the above reaction at −78°.

(3) W. B. Hammond and N. J. Turro *ibid.*, **88**, 2880 (1966).

(4) N. J. Turro, W. B. Hammond, and P. A. Leermakers, *ibid.*, **87**, 274 (1965).

(5) S. E. Schaafsma, H. Steinberg, and Th. J. DeBoer, *Rec. Trav. Chim.*, 85, 70 (1966).

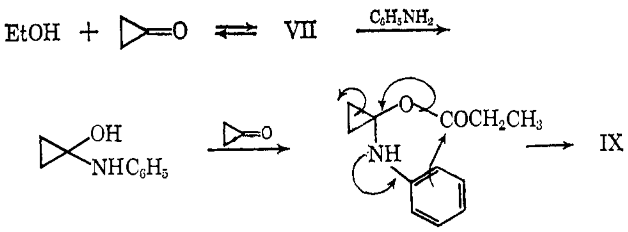
(6) All compounds in these conversions gave satisfactory elemental analyses, and all structural assignments are consistent with nmr and infrared spectra.

(7) See R. H. Hasek, P. G. Gott, and J. C. Martin, *J. Org. Chem.*, **29**, 1239 (1964), for related cycloaddition reactions.

(8) Lipp[2a] attempted to prepare VII in this manner, but observed isomerization to ethyl propionate.

(9) N. J. Turro and W. B. Hammond, *J. Am. Chem. Soc.*, 87, 3258 (1965), have provided evidence for this type of equilibrium in the case of tetramethylcyclopropanone and its methyl hemiketal.

The unusual formation of IX at high temperature may be explained by the following mechanism involving cyclopropanone as an intermediate.[10]



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(10) N,N-Dipropionylaniline or propionanilide failed to give IX under these reaction conditions.

(11) National Institutes of Health Predoctoral Fellow, 1962–1965.

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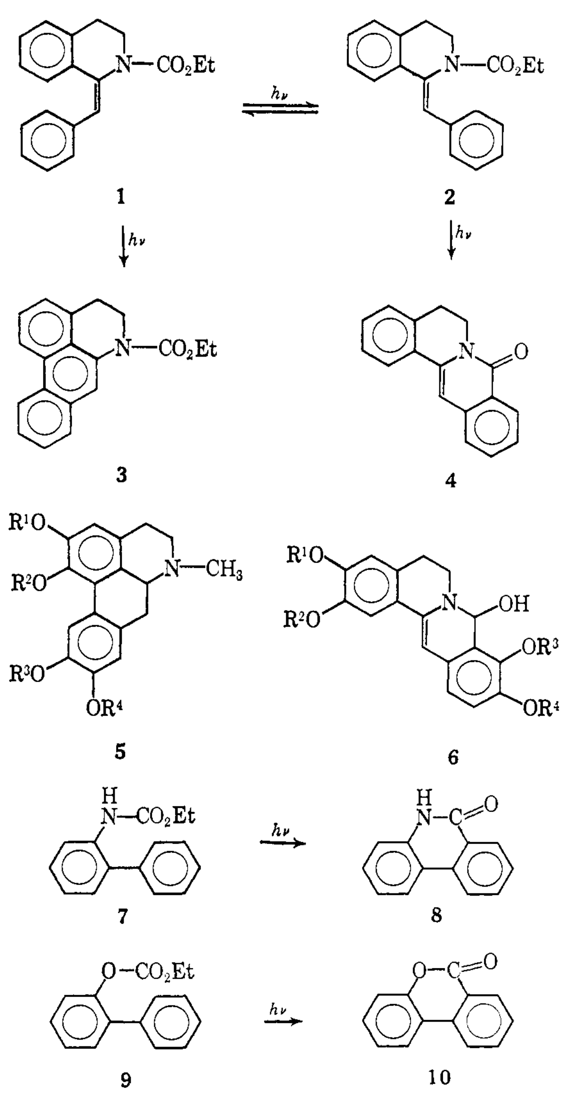
Intramolecular Photoacylation of Carbamates and Carbonates[1]

Sir:

In applying photochemical reactions to organic syntheses, we irradiated *cis*-1-benzylidene-2-carbethoxy-1,2,3,4-tetrahydroisoquinoline (**1**). After a rapid *cis–trans* isomerization, the *cis* isomer was converted into a dehydroaporphane (**3**) in 65% yield.[2] Another product was isolated from the reaction mixture by chromatography in 10–21% yield depending on the reaction conditions. The minor product was identified as dehydroprotoberberine (**4**, $C_{17}H_{13}ON$), mp 93–94° (ether–hexane), γ_{max} 6.08, 6.17, 6.26, and 13.05 μ; λ_{max} 233 mμ (log ϵ 4.32), 322 (4.17), 343 (4.08), and 358 (3.90); τ 6.95 (triplet, $J = 7$ cps, 2 H), 5.62 (triplet, $J = 7$ cps, 2 H), 3.01 (singlet, 1 H), 2.05–2.83 (multiplet, 7 H), and 1.55 (doublet, $J = 9$ cps, 1 H). *Anal.* Found: C, 82.47; H, 5.24; N, 5.60; mol wt (mass spectrum), 247.101. It is probable that irradiation of a common intermediate similar to compounds **1** or **2** will give two compounds simultaneously which may be readily converted into an aporphine alkaloid (**5**) and a berberine alkaloid (**6**). The application of this reaction to the synthesis of alkaloids is being investigated.



Dehydroprotoberberine (**4**) may be derived from an intramolecular photoacylation from compound **2**. It has been shown by molecular orbital calculation that there is localization of electron density at the *ortho* positions of stilbene in the excited state.[3] The aromatic system is thus activated in the excited state, and the intramolecular acylation occurs. On the basis of this hypothesis the reaction has been extended to another carbamate and a carbonate. Irradiation of ethyl N-*o*-biphenylylcarbamate (**7**) in methanol with a conventional Hanovia lamp yielded a crystalline residue which exhibited an infrared spectrum virtually identical with that of phenanthridone (**8**).[4] Recrystallization of the residue from ethanol yielded pure phenanthridone in 85% yield, mp 291–292°, and tlc of the mother liquor showed only the presence of phenanthridone contaminated with a small amount of **7**. Under similar conditions, ethyl *o*-biphenylyl carbonate (**9**) was converted into dibenz-α-pyrone (**10**)[5] in 85% yield. The scope and the mechanism of these reactions are being investigated.

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(2) N. C. Yang, G. R. Lenz, and A. Shani, *Tetrahedron Letters*, 2941 (1966); see also M. P. Cava, S. C. Havlicek, A. Lindert, and R. J. Spangler, *ibid.*, 2937 (1966).

(3) H. C. Ting, Ph.D. Thesis, University of Chicago, 1965.

(4) Sadtler Standard Spectra, Spectrum No. 21101.

(5) J. D. Brooks, *J. Appl. Chem.*, **5**, 250 (1955).

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