have confirmed that the bicyclic ether II is formed under these conditions and in addition have identified the major products of the reaction as the keto alcohols III and IV, the products to be expected by analogy with the solvolysis products of 9-decalyl p-nitroperbenzoate[2] and formed indeed on solvolysis of 1,3,3-trimethylcyclohexyl p-nitroperbenzoate (I, X = $O_2CC_6H_4NO_2$).[3]

I

II

III

IV
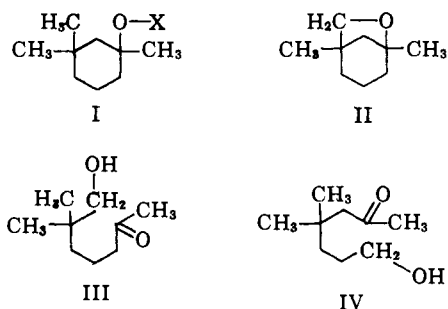
We wish to report here a related reaction of both synthetic and mechanistic interest which gives oxygen insertion products in far better yields and which proceeds by a process, almost certainly heterolytic in nature, involving a non-ion-paired cationic transition state. We have found that, when certain tertiary alcohols are treated with bromine in the presence of silver salts (nitrate, acetate, oxide) and in the absence of light, ring closure occurs directly to give cyclic ethers. Thus a pentane solution of 1,3,3-trimethylcyclohexanol (I, X = H), when treated with bromine and silver oxide at room temperature and in the absence of light, furnished the bicyclic ether II in 75% yield (based on recovered starting material).[4] Detectable amounts of the keto alcohols III and IV were not formed.

The reaction appears to be quite general for tertiary alcohols. Thus 6α-methylcholestan-6β-ol (V)[5] [m.p. 105–106.5°, $[\alpha]^{32}D$ +25.1° (chloroform). $Anal.$ Found: C, 83.38; H, 12.52] gives in 55% yield by the same procedure 6α-methyl-6,19-oxidocholestane (VI), m.p. 83–84°, $[\alpha]^{28}D$ +14.7° (chloroform). $Anal.$ Found: C, 83.84; H, 12.16.

V   VI
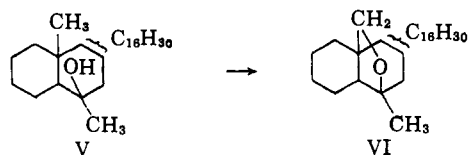
Even the straight-chain tertiary alcohol, 2-methyl-2-pentanol (VII), undergoes the reaction, furnishing 2,2-dimethyltetrahydrofuran (VIII) in 50% yield (by v.p.c.).

(2) R. Criegee and W. Schnorrenberg, $Ann.$, **560**, 141 (1948).

(3) N. P. Matheny, Ph.D. Thesis, Purdue University, 1964.

(4) A heterogeneous mixture of the alcohol I (2.75 g.), silver oxide (8.0 g.), and bromine (1.0 ml., 3.1 g.) in pentane (100 ml.) was stirred in the absence of light and at room temperature for 30 min. Chromatography on alumina furnished 1.50 g. of bicyclic ether 11 and 0.76 g. of recovered alcohol 1.

(5) Prepared by the addition of the methyl Grignard reagent to cholestan-6-one. Note that the success of the ring closure reation confirms the 6β orientation assigned to the alcohol function in V and, by analogy, that the configurations tentatively assigned by R. A. S. to the products of addition of various Grignard reagents to cholestan-3β-ol-6-one acetate are incorrect.[6] These adducts should be formulated as 6α-(R)-3β,6β-cholestandiols.[7]

(6) R. A. Sneen, $J. Am. Chem. Soc.$, **80**, 3971, 3982 (1958).

(7) This conclusion had earlier been reached by others: M. Davis and G. H. R. Summers, $J. Chem. Soc.$, 4707 (1960), and M. Shiota, $Chem. Abstr.$, **51**, 17,969 (1957).

VII   VIII
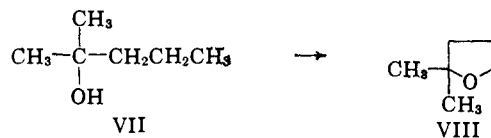
Our experiments indicate that the reaction takes place by way of an intermediate hypobromite[8] whose decomposition is silver ion catalyzed.[9]
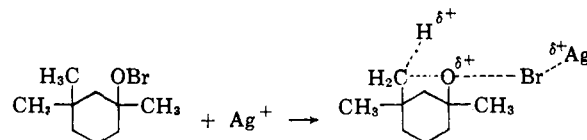
Mechanistically the decomposition of the hypobromite is similar to the reaction reported by Corey and White[i] in that a form of cationic oxygen is involved, but it differs in that the leaving group is effectively neutral silver bromide rather than sulfonate anion. To what extent the developing positive charge in the transition state is resident upon oxygen is a question requiring further experimentation.

Extensions of this new reaction to primary and secondary systems are currently under active investigation as are questions of any implications which it may have for the mechanism of the Hunsdiecker reaction.

(8) 1,3,3-Trimethylcyclohexyl hypobromite, prepared $in situ$ by the action of bromine and mercuric oxide on a pentane solution of the alcohol 1 in the absence of light, gave rise to the cyclic ether 11 when treated with silver oxide.

(9) The heterolytic nature of the reaction is evidenced by our observations that it takes place readily in the absence of light and is unaffected by the addition of known free-radical inhibitors.

DEPARTMENT OF CHEMISTRY   RICHARD A. SNEEN
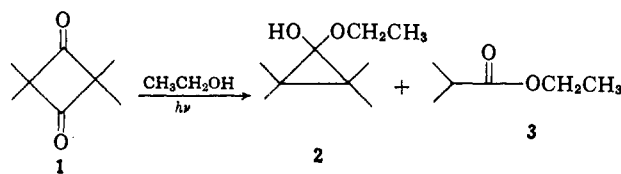PURDUE UNIVERSITY   NINA P. MATHENY
LAFAYETTE, INDIANA

Isolation of Tetramethylcyclopropanone Ethyl Hemiketal from Photolysis of Tetramethylcyclobutanedione

$Sir:$

Tetramethylcyclopropanone ethyl hemiketal (2) has been prepared by photolytic decarbonylation of tetramethylcyclobutanedione (1). Solutions of 5–15%

1   2   3

by weight of 1 in absolute ethanol were irradiated at 40–75° with a Hanau PL 321 immersion mercury lamp until little starting material remained. After removal of most of the solvent at reduced pressure, yields of up to 35% of 2, m.p. 20–26°, were obtained by crystallization and yields of up to 55% were isolated by gas-liquid chromatography (g.l.c.). The other major product was ethyl isobutyrate (3), obtained from the photolysis solutions by g.l.c. in yields[1] of 20–25%.

(1) Calculated on the assumption that one molecule of 1 furnished two molecules of 3.

Photolysis of 1 must form an acyclic intermediate, perhaps 4 (only one resonance structure is shown), a type of intermediate which has been considered for Favorskiĭ rearrangements and other reactions.[2] The intermediate can cyclize to tetramethylcyclopropanone (5) which in ethanol solution forms 2. Adduct 6, isolated by g.l.c. in 35% yield from a similar photolysis of 1 in refluxing furan, is formed most probably from addition of the same intermediate to furan. This

4   5   6
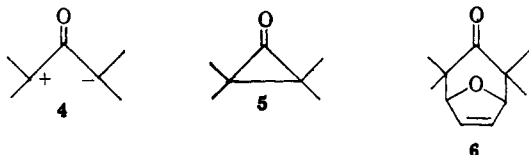
adduct was also obtained recently by Cookson, Nye, and Subrahmanyam.[3] Ethyl isobutyrate must arise from addition of ethanol to dimethylketene formed from an alternate photolytic cleavage of 1.

The structure proof for 2[4] is based on spectral evidence and on the preparation of a p-nitrobenzoate derivative,[4] m.p. 117–118°. The highest nonisotopic peak in the mass spectrum of 2 was the parent peak, $m/e = 158$. The n.m.r. spectrum[5] of a carbon tetrachloride solution of 2 exhibited absorptions at 6.38 (quartet, $J = 7$, 2 protons) and 8.83 p.p.m. (triplet, $J = 7$, 3 protons) for the ethyl hydrogens, at 7.08 p.p.m. (singlet, 1 proton) for the hydroxyl hydrogen, and at 8.98 p.p.m. (singlet, 12 protons) for the methyl hydrogens. In dimethyl sulfoxide solution, 2 absorbed at 9.03 (6 protons) and 9.05 p.p.m. (6 protons), indicating that there are two types of methyl groups, and at 4.00 p.p.m. (1 proton), within the range characteristic[6] for hydrogens of hemiketal hydroxyls. A dichloromethane solution of the p-nitrobenzoate ester had absorptions at 1.68 (singlet, 4 protons), 6.28 (quartet, $J = 7$, 2 protons), 8.82 (triplet, $J = 7$, 3 protons), 8.80 (singlet, 6 protons), and 8.90 p.p.m. (singlet, 6 protons).

Isolation by g.l.c. also furnished combined yields of 10–15% of ethyl 2,2,3-trimethylbutyrate (7), 2-ethoxy-2,4-dimethyl-3-pentanone[4] (8), and ethyl 2,2,3-tri-

7   8

9
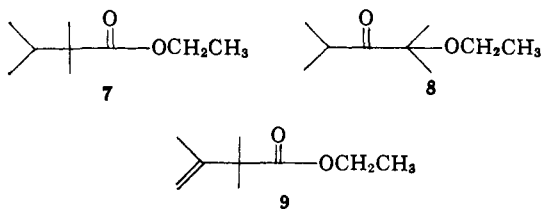
methyl-3-butenoate (9); distillation of photolysis solutions furnished combined yields of about 30% of the same components. It is possible that these are not initial products of photolysis but instead artifacts formed from 2. In fact, formation of these compounds was observed from the partial decomposition of 2 during its isolation by g.l.c. and by refluxing 2 in eth-

anol. The structure of 8, not previously reported, is consistent with the n.m.r. and infrared spectra; 8 formed a 2,4-dinitrophenylhydrazone derivative,[4] m.p. 110–112°, and was reduced with lithium aluminum hydride to an alcohol[4] which was reoxidized to 8 with chromic anhydride–pyridine. It was reported recently that photolysis of 1 in methanol and 2-propanol gave esters corresponding to 3 and 7 as the major products.[7]

Further investigations of the formation and reactions of intermediates such as 4 and of the reactions of cyclopropanone derivatives are in progress.[8]

(7) N. J. Turro, G. W. Byers, and P. A. Leermakers, *ibid.*, **86**, 955 (1964).
(8) Carbon tetrachloride solutions of **2** after heating and concentration have sometimes exhibited strong absorption at 1800 cm.⁻¹ that may be due to **5**.
(9) Alfred P. Sloan Research Fellow.
(10) Part of this work was done by D. C. C. in partial fulfillment of the requirements for a B.S. degree, The Pennsylvania State University, 1961.

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RECEIVED JUNE 24, 1964

The Biosynthesis of Anabasine.   Origin of the Nitrogen of the Piperidine Ring[1]

Sir:

In the past decade much information has been obtained on the biosynthesis of alkaloids by administering isotopically labeled compounds, especially α-amino acids, to alkaloid-producing plants. However, in most of these investigations the tracer used has been carbon-14, and there is very little direct knowledge concerning the origin of the nitrogen in alkaloids.[2]

The biosynthesis of anabasine (I), a major alkaloid of *Nicotiana glauca*, has now been investigated using N^{15}-labeled precursors. We have previously shown that the administration of lysine-2-C^{14} to intact *N. glauca* plants leads to the formation of anabasine labeled

I
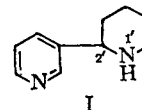
solely at C-2' of the piperidine ring.[3] A similar result was obtained when lysine-C^{14} was fed to a sterile culture of excised roots.[4] In the present work we fed a mixture of lysine-2-C^{14} and lysine-ϵ-N^{15} to sterile cultures of excised *N. glauca* roots cultivated by the method of Dawson and co-workers.[4] In a second experiment a mixture of lysine-2-C^{14} and lysine-α-N^{15} was administered. One month after feeding the tracers the roots were harvested and extracted with chloro-

(2) J. G. Aston and J. D. Newkirk, *J. Am. Chem. Soc.*, **73**, 3900 (1951); J. G. Burr, Jr., and M. J. S. Dewar, *J. Chem. Soc.*, 1201 (1954); E. F. Ullman, *J. Am. Chem. Soc.*, **82**, 505 (1960); H. O. House and W. F. Gilmore, *ibid.*, **83**, 3972, 3980 (1961); A. W. Fort, *ibid.*, **84**, 2620, 2625, 4979 (1962); R. C. Cookson and M. J. Nye, *Proc. Chem. Soc.*, 129 (1963).
(3) R. C. Cookson, M. J. Nye, and G. Subrahmanyam, *ibid.*, 144 (1964).
(4) Satisfactory analyses were obtained for all new compounds.
(5) Chemical shifts are in p.p.m. relative to tetramethylsilane as 10.00.
(6) O. L. Chapman and R. W. King, *J. Am. Chem. Soc.*, **86**, 1256 (1964).

(1) This investigation was supported by a research grant (GB-363) from the National Science Foundation.
(2) A notable exception was the formation of ephedrine-N^{15} from phenylalanine-N^{15}: S. Shibata and I. Imaseki, *Pharm. Bull.* (Tokyo), **4**, 277 (1956).
(3) E. Leete, *J. Am. Chem. Soc.*, **78**, 3520 (1956).
(4) M. L. Solt, R. F. Dawson, and D. R. Christman, *Plant Physiol.*, **35**, 887 (1960).