

**Table I.** Relative Intensity of Some Characteristic Fragment Ions of *n*-Alkyl Vinyl Ethers (ROCH=CH<sub>2</sub>) at 70 and 12 eV<sup>a</sup>

R	M - C <sub>2</sub> H <sub>3</sub> O	M - C <sub>2</sub> H <sub>4</sub> O	M - C <sub>2</sub> H <sub>5</sub> O	M - C <sub>2</sub> H <sub>6</sub> O
C <sub>4</sub> H <sub>9</sub>	37.3 (10.7)	55.0 (89.3)	7.7 (0)	0
C <sub>5</sub> H <sub>11</sub>	25.0 (21.9)	67.6 (73.0)	4.2 (1.5)	1.3 (3.6)
C <sub>6</sub> H <sub>13</sub>	16.8 (7.8)	21.9 (17.7)	16.4 (12.1)	39.2 (62.4)
C <sub>7</sub> H <sub>15</sub>	5.9 (11.6)	27.9 (16.1)	18.3 (12.9)	47.6 (59.3)
C <sub>8</sub> H <sub>17</sub>	10.3 (6.0)	9.7 (10.3)	15.5 (11.8)	64.5 (73.5)
C <sub>9</sub> H <sub>19</sub>	5.0 (2.1)	25.0 (16.4)	7.0 (10.7)	62.0 (70.8)
C <sub>10</sub> H <sub>21</sub>	10.7	8.9	10.3	70.0

<sup>a</sup> Nominal 12-eV values are given in parentheses.

was lost in this fragmentation, it followed that three hydrogen atoms had to migrate from the alkyl chain (C<sub>5</sub>>). In order to establish the origin of these itinerant hydrogens, *n*-heptyl vinyl ether (I) was labeled with deuterium in every position of the alkyl chain. The results, summarized in Table II, demonstrate the absence

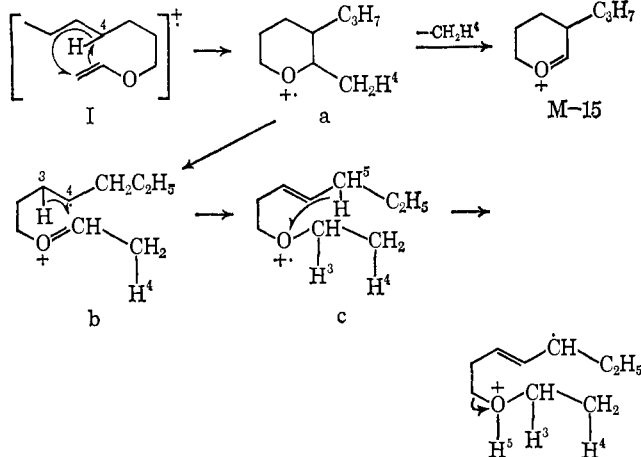
**Table II.** Origin of Hydrogen Transfer in M - C<sub>2</sub>H<sub>6</sub>O Fragment in *n*-Heptyl Vinyl Ether at 70 eV<sup>a,b</sup>

	1-d <sub>2</sub>	2-d <sub>2</sub>	3-d <sub>2</sub>	4-d <sub>2</sub>	5-d <sub>2</sub>	6-d <sub>2</sub>	7-d <sub>3</sub>
M - C <sub>2</sub> H <sub>6</sub> O	99	96	32	47	28	61	97
M - C <sub>2</sub> H <sub>5</sub> OD	1	4	63	53	62	37	1
M - C <sub>2</sub> H <sub>4</sub> OD <sub>2</sub>			5		11	2	1

<sup>a</sup> Only minor changes were noted at low voltage (nominal 15 eV). <sup>b</sup> All values are %.

of hydrogen randomization in the alkyl chain, since essentially no hydrogen was lost from positions 1, 2, and 7. Since summation of all deuterium transfers in the labeled substrates (Table II) did not amount to 300%, a deuterium isotope effect had to operate, whose existence and magnitude is quite compatible with previously demonstrated<sup>10</sup> deuterium isotope effects in mass spectrometry.

The bulk of the hydrogen transfer involves positions 3, 4, and 5, which can be rationalized readily through postulating the intermediacy of ionized 2-methyl-3-propyltetrahydropyran (a) and is also completely consistent with our previous observation<sup>7</sup> that over 80% of the hydrogen lost in the important M - CH<sub>3</sub> ion of all



(10) J. K. MacLeod and C. Djerassi, *J. Amer. Chem. Soc.*, **89**, 5182 (1967).

*n*-alkyl vinyl ethers originated from C-4 of the alkyl chain (together with the methylene portion from the vinyl group).

We visualize the triggering reaction to be the firmly established<sup>7</sup> eight-membered hydrogen transfer from C-4 in *n*-heptyl vinyl ether (I) with concomitant cyclization to ionized 2-methyl-3-*n*-propyltetrahydropyran (a). The latter now undergoes the thoroughly documented<sup>11</sup>  $\alpha$  fission of tetrahydropyrans, which can lead either to the M - CH<sub>3</sub> ion<sup>7</sup> or to species b. Hydrogen transfer from C-3 of b is mechanistically attractive (six-membered transition and stabilization of C-4 radical site) and has in fact been demonstrated<sup>12</sup> in tetrahydropyran itself by deuterium labeling. The third required shift, from C-5, then occurs from an allylically activated position.

The proposed reaction scheme can also account for the observation (Table II) that C-6 is implicated in the triple hydrogen transfer, albeit to a lesser extent. If the hydrogen atom from C-5 rather than C-3 is transferred in the hypothetical intermediate b, then C-6 becomes an activated position and can participate in the hydrogen transfer in a manner analogous to the step c  $\rightarrow$  d. This qualitative rationalization of the triple hydrogen transfer in higher *n*-alkyl vinyl ethers is supported by the observation that the mass spectrum of the hitherto unknown 2-methyl-3-propyltetrahydropyran<sup>13</sup> exhibited the same features (M - CH<sub>3</sub>, M - C<sub>2</sub>H<sub>6</sub>O, etc.) as the vinyl ether I. The scheme also accounts for the fact (see Table I) that the M - C<sub>2</sub>H<sub>6</sub>O loss becomes significant only with an *n*-hexyl chain, since this is the first member of the series in which all three migrating hydrogens originate from secondary positions.

In view of their intrinsic interest as well as their significant mechanistic implications, we are continuing in our laboratory the examination of other triple hydrogen transfer processes.

**Acknowledgment.** We are indebted to Mr. C. E. Conover for performing the mass spectral measurements with an MAT CH-4 mass spectrometer equipped with a molecular beam inlet system, and to Mitsubishi Chemical Industries Co. for fellowship funds and leave of absence to M. K.

- (11) See ref 3a, p 253.  
 (12) R. Smakman and T. J. de Boer, *Org. Mass Spectrom.*, **1**, 403 (1968).  
 (13) Its synthesis will be described in our full paper dealing with the mass spectrometry of alkyl vinyl ethers.

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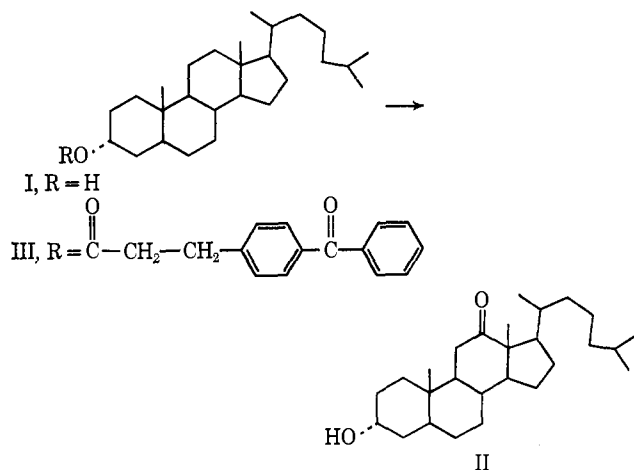
### Conversion of Cholesterol to 12-Ketocholesterol and to $\Delta^{14}$ - and $\Delta^{8(14)}$ -Cholesterol by Remote Oxidation

Sir:

A recent communication<sup>1</sup> from this laboratory described the conversion of straight-chain hydrocarbon alcohols such as hexadecanol to products of "remote oxidation" such as 14-ketohexadecanol. The sequence—esterification with *p*-benzoylbenzoic acid, photolysis, dehydration, ozonolysis, and hydrolysis—led to

- (1) R. Breslow and M. Winnik, *J. Amer. Chem. Soc.*, **91**, 3083 (1969).

products with the carbonyl group distributed over several carbon atoms. However, we suggested that if the substrate were a rigid steroid the reaction might be more highly selective. We now wish to report that when a sequence similar to that used previously is applied to 3- $\alpha$ -cholestanol (I), 12-keto-3- $\alpha$ -cholestanol (II) is formed as the exclusive ketonic product, albeit in only modest overall yield.



In contrast to the previously reported results with flexible substrates, photolysis of the *p*-benzoylbenzoic acid ester of I in  $\text{CCl}_4$  affords no lactone, but only monochlorinated steroids after hydrolysis ( $m/e = 422, 424$ ). The benzophenone triplet can remove a hydrogen atom but the system is too rigid to allow the thus created radical pair to form a carbon-carbon bond, so chlorine is abstracted from the solvent. The same observation is made for the ester of I with *m*-benzoylbenzoic acid or *p*-benzoylphenylacetic acid. However, with the *p*-benzoyl- $\beta$ -phenylpropionic acid ester (III) the link between the two rigid systems is flexible enough to permit ring closure after the hydrogen-transfer step.

Controlled basic hydrolysis of the crude product from photolysis<sup>2</sup> of a  $10^{-3}$  M solution of III in dry  $\text{CCl}_4$  (450-W medium-pressure lamp, uranium glass filter) affords 0.66 equiv of monochloro-I ( $m/e = 422, 424$ ) and 0.33 equiv of the unhydrolyzed lactone fraction derived by the insertion of the benzophenone carbonyl group in III into steroidal C-H bonds. This was reduced with lithium aluminum hydride, acetylated with acetic anhydride in pyridine, and dehydrated with thionyl chloride in pyridine. The resulting diphenylethylene derived from III, mixed with undehydrated material, was submitted to oxidation with ruthenium tetroxide and sodium periodate<sup>3</sup> (ozonolysis failed), followed by hydrolysis and chromatography. The only steroidal ketone detectable,<sup>4</sup> isolated in 16% yield based on the total lactone fraction, was the hitherto unreported 12-keto-3- $\alpha$ -cholestanol (II), mp 134–136° ( $m/e = 402$ ). *Anal.* Calcd: C, 80.54; H, 11.51. Found: C, 80.61; H 11.40.

(2) Controls indicate that at these dilutions intermolecular processes are negligibly slow compared with the observed rate of disappearance of the benzophenone chromophore.

(3) G. Stork, A. Meisels, and J. E. Davies, *J. Amer. Chem. Soc.*, **85**, 3419 (1963).

(4) The total simple steroid fraction was easily separated chromatographically from uncleaved material. It was homogeneous by thin layer chromatography, and the nmr spectrum showed that it was at least 95% II because of the absence of C-18 methyl signals higher than the uniquely shifted signal of II.

The structure is indicated by the finding that the ketone incorporates only two carbon-bound deuterium atoms under exhaustive exchange conditions;<sup>5</sup> thus the ketone group is either at C-1, C-4, or C-12. The assignment to C-12 is confirmed by the fact that the C-18 methyl resonance of II occurs at 62.0 cps (at 60 Mc), a downfield shift of 22.0 cps from the position in I. A downfield shift of this magnitude is uniquely diagnostic for 12-keto steroids.<sup>6</sup> This has been confirmed by oxidation of II to 3,12-cholestandione, mp 186–188°, which we have also prepared by Birch reduction of the known<sup>7</sup>  $\Delta^4$ -cholesten-3,12-dione.

The low yield of II results in part from losses during the five-step conversion of the photoproduct to II, but also from the fact that a significant part of the photoproduct does not undergo dehydration with  $\text{SOCl}_2$  and pyridine even under exhaustive conditions. It readily reacts with lead tetraacetate, however, to regenerate the benzophenone carbonyl and a still unidentified steroidal residue. This indicates that the site of attachment of the benzophenone carbon in this portion of the lactone photoproduct is at a steroidal carbon bearing no additional hydrogen atoms (e.g., C-14). Molecular models of ester III indicate that the benzophenone carbonyl oxygen can swing in an arc under carbons 12, 13, and 14 of the steroid, so that the axial  $\alpha$  hydrogens at carbons 12 and 14 should be most accessible to attack by the excited ketone.

In part the low yield of II results also from the fact that in  $\text{CCl}_4$  only *ca.* one-third of the diradicals from hydrogen transfer form a new carbon-carbon bond, while the remainder react with solvent to produce chlorinated steroid. As expected, photolysis of III in acetonitrile avoids this problem, and lactone is produced in high yield. However, the standard degradation of this lactone produced no detectable amounts (<1%) of any ketone, although again it was smoothly cleaved by lead tetraacetate to give the benzophenone and a modified steroid. Apparently this change in solvent affects the conformation, and thus site of attack, in ester III.

Direct lead tetraacetate cleavage of the crude product from photolysis of I in acetonitrile, followed by hydrolysis of the cleaved product with methanolic KOH, affords a mixture of two cholestanols in 35% overall yield. One of the products, mp 165–167°, has been identified as  $\Delta^{14}$ -cholesten-3 $\alpha$ -ol (V) from spectra and conversion to the known<sup>8</sup>  $\Delta^{14}$ -cholesten-3 $\beta$ -ol and the corresponding benzoate, for which physical constants are recorded. The other olefin, mp 141–145°, has been identified as  $\Delta^{8(14)}$ -cholesten-3 $\alpha$ -ol (VI) on a similar basis.<sup>9</sup> The olefins V (27% yield) and VI (8% yield) are the only detectable steroid products from this sequence, confirming that in acetonitrile the photoproduct is chiefly IV, the lactone from attack at C-14. Furthermore, *ca.* 10% of V is detectable from direct hydrolysis of the photoproduct, and this rises to 20%

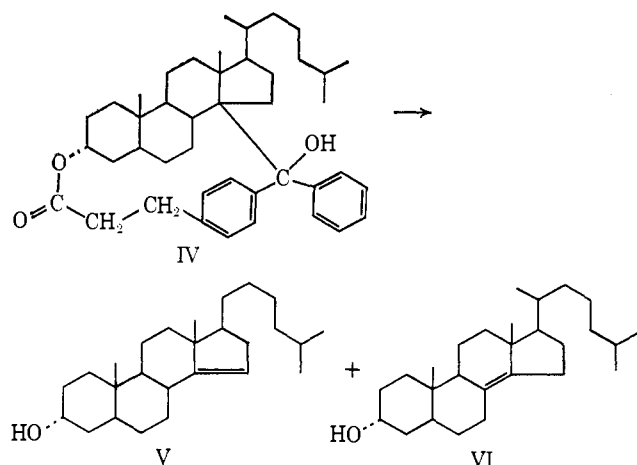
(5) The conditions used by D. H. Williams, J. M. Wilson, H. Budzikiewicz, and C. Djerassi, *J. Amer. Chem. Soc.*, **85**, 2091 (1963), for exhaustive deuteration of 5- $\alpha$ -androstan-11-one, followed by neutral  $\text{H}_2\text{O}$  washing to reconvert OD to OH, gave >98% II- $d_2$  and no II- $d_3$ .

(6) N. Bhacca and D. H. Williams, "Applications of Nmr Spectroscopy in Organic Chemistry; Illustrations from the Steroid Field," Holden-Day, San Francisco, Calif., 1964, Tables 2–3.

(7) D. N. Kirk and V. Petrow, *J. Chem. Soc.*, 1691 (1959).

(8) G. M. L. Cragg, C. W. Davey, G. D. Meakins, E. E. Richards, and T. L. Whately, *ibid.*, 1266 (1966).

(9) F. Schenk, K. Buchholz, and O. Wiese, *Ber.*, **69**, 2696 (1936).



when the photolysis of III is performed in acetone and 35% when benzene is used.

Obviously, it remains to elucidate the solvent effects, and as well to identify the other products of these reactions under various conditions, in particular the chlorinated steroids. However, even the present relatively inefficient conversion of cholestanol to 12-ketocholestanol, and the more efficient conversion to  $\Delta^{14}$ - and  $\Delta^{8(14)}$ -cholestenol, are indications of the synthetic potential of "remote oxidation" in performing transformations of a type hitherto restricted to enzymatic reactions.<sup>10</sup>

(10) Support of this work by the National Institutes of Health and a National Institutes of Health Postdoctoral fellowship to S. W. B. is gratefully acknowledged. We also wish to thank Dr. M. Winnik for some of the early work on remote oxidation in steroids. Part of the material in this communication was reported at the 158th National Meeting of the American Chemical Society, New York, N. Y., Sept 1969, Abstract ORGN-147.

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### The Photochemical Synthesis of Condensed Bridged Phosphines

Sir:

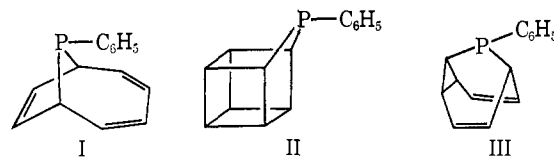
The bridged phosphine I is easily prepared from the cyclooctatetraene dianion and dichlorophenylphosphine.<sup>1</sup> We examined its behavior upon irradiation with ultraviolet light because it seemed likely<sup>2</sup> that highly condensed ring systems, such as II<sup>3</sup> and III,<sup>3c</sup> which would probably be difficult to prepare otherwise, might thereby be synthesized. This route would be considerably shorter than others that have given homocubanes<sup>4</sup> or barbaralanes.<sup>5</sup> In fact both compounds

(1) T. J. Katz, C. R. Nicholson, and C. A. Reilly, *J. Amer. Chem. Soc.*, **88**, 3832 (1966).

(2) However, irradiation of the parent hydrocarbon, bicyclo[4.2.1]nonatriene, in acetone solution is not reported to give either homocubane or barbaralane—the *exo* and *endo* cyclobutenes form—(cf. L. G. Cannell, *Tetrahedron Lett.*, 5967 (1966)), and no other derivative of bicyclo[4.2.1]nonatriene has been photolyzed.

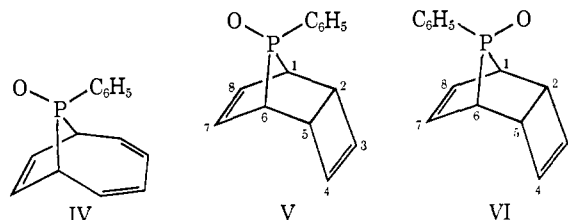
(3) (a) W. L. Dilling, *Chem. Rev.*, **66**, 384 (1966); (b) G. J. Fonken, *Org. Photochem.*, **1**, 197 (1967); (c) R. Steinmetz, *Fortschr. Chem. Forsch.*, **7**, 445 (1967).

(4) (a) P. E. Eaton and T. W. Cole, Jr., *J. Amer. Chem. Soc.*, **86**, 3157 (1964); (b) W. G. Dauben and D. L. Whalen, *Tetrahedron Lett.*, 3743 (1966); (c) K. V. Scherer, Jr., R. S. Lunt, III, and G. A. Ungefug, *ibid.*, 1199 (1965); (d) G. L. Dunn, V. J. DiPasquo, and J. R. E. Hoover, *ibid.*, 3737 (1966); (e) C. G. Chin, H. W. Cuts, and S. Masamune, *Chem. Commun.*, 880 (1966); (f) P. von R. Schleyer, J. J. Harper, G. L. Dunn,



II and III can be prepared from I, and in separate experiments, since photolysis through Corex<sup>6a</sup> of the phosphine oxide IV of I in benzene-acetone gives the oxide of II, while photolysis through Pyrex<sup>6b</sup> of the phosphine I itself in benzene gives III.

The route from IV to the oxide of II probably<sup>3</sup> proceeds *via* V, and this material can be isolated when IV is photolyzed through Pyrex in benzene solution without



added acetone (mp 175–177°, 28% yield), or in acetone solution for a short time (45% yield).<sup>7,8</sup> Simultaneously, cyclooctatetraene is formed, and the nmr spectrum of a photolyzed  $C_6D_6$  solution of IV indicates that the molar amount formed is half that of V. The structure of V was assigned on the basis of the nmr spectrum, which shows that (disregarding the phenyl) the molecule is tricyclic, has a plane of symmetry, and has two isolated double bonds.<sup>9</sup> The *endo* stereochemistry is indicated by the magnitude of  $J_{1,2}$ .<sup>2,9,10</sup> The *exo* isomer could not be found. The stereochemistry at the phosphorus atom in V is presumably the same as that in IV,<sup>1</sup> and when the phosphorus epimer<sup>1</sup> of IV is photolyzed in benzene through Pyrex it gives in 32% yield VI (mp 107.5–109°),<sup>8</sup> the epimer of V. The features of the nmr spectra of V and VI<sup>11</sup> are similar, indicating that the ring systems are the same. Again the *exo* isomer could not be found.

When benzene solutions containing acetone of IV, V, or VI are photolyzed through Corex, the nmr spectrum shows that the oxide of II is formed. In the case of IV the oxide<sup>8</sup> (mp 122–123°) can be isolated in 25–40% yield and is identified by its nmr spectrum (three

V. J. DiPasquo, and J. R. E. Hoover, *J. Amer. Chem. Soc.*, **89**, 698 (1967); (g) J. C. Barborak and R. Pettit, *ibid.*, **89**, 3080 (1967).

(5) (a) V. Biethan, H. Klusacek, and H. Musso, *Angew. Chem. Intern. Ed. Engl.*, **6**, 176 (1967); (b) W. von E. Doering, *et al.*, *Tetrahedron*, **23**, 3943 (1967); (c) M. J. Goldstein and B. G. Odell, *J. Amer. Chem. Soc.*, **89**, 6356 (1967); (d) H. Tsuruta, K. Kurabayashi, and T. Mukai, *Tetrahedron Lett.*, 3775 (1967); (e) J. Daub and P. von R. Schleyer, *Angew. Chem. Intern. Ed. Engl.*, **7**, 468 (1968).

(6) (a)  $\lambda \geq 280 \text{ m}\mu$ ; (b)  $\lambda \geq 300 \text{ m}\mu$ .

(7) First prepared in this laboratory by C. N. Lazaridis.

(8) Satisfactorily analyzed for C, H, P. Exhibits the required parent peak in the mass spectrum.

(9) Aromatics,  $\tau$  2.65 (5.14 H);  $H_7$ , 3.73 (1.97 H, doublet  $|J_{PH}| = 11 \text{ Hz}$ , triplet  $|J_{6,7}| = 3.2 \text{ Hz}$ );  $H_3$ , 4.50 (1.90 H, singlet);  $H_1$ , 6.77 (2.04 H);  $H_2$ , 7.10 (1.95 H, doublet  $|J_{1,2}| = 3.2 \text{ Hz}$ ); simultaneous irradiation at the resonance frequency of phosphorus and  $H_1$  collapses the olefinic resonances to two singlets.

(10) (a) T. J. Katz, J. C. Carnahan, Jr., and R. Boeckle, *J. Org. Chem.*, **32**, 1301 (1967), footnote 20; (b) L. Watts, J. D. Fitzpatrick, and R. Pettit, *J. Amer. Chem. Soc.*, **88**, 623 (1966).

(11) Aromatics,  $\tau$  2.6 (5.16 H);  $H_7$ , 4.0 (doublet,  $|J_{PH}| = 12.5 \text{ Hz}$ , triplet,  $|J_{6,7}| = 3.5 \text{ Hz}$ );  $H_3$ , 4.21 (singlet), total of  $H_7$  and  $H_3 = 3.92 \text{ H}$ ;  $H_1$ , 6.2 (1.97 H, doublet  $|J_{1,2}| = 2.9 \text{ Hz}$ ), 6.95 (1.95 H); simultaneous irradiation at the resonance frequency of phosphorus and  $H_2$  collapses the olefinic resonances to two singlets.