

Figure 1. The pmr spectrum (60 MHz) of the N-CH<sub>2</sub> ( $\delta$  3.42) protons of dibenzylmethylamine (0.08 M in CH<sub>2</sub>CHCl) at various temperatures.

If nitrogen inversion (eq 1) is slow on the pmr time scale, the two methylene protons of a given benzyl group of dibenzylmethylamine are in a dissymmetric environment and should be nonequivalent exhibiting a typical AB spectrum. This situation should prevail even in the event of rapid C-N bond rotation. However, rapid nitrogen inversion on the pmr time scale *plus* rapid C-N bond rotation will render the two benzylic hydrogens equivalent.

Examination of the proton magnetic resonances (60 MHz) due to the N-CH<sub>3</sub> ( $\delta$  2.08) and N-CH<sub>2</sub> ( $\delta$  3.42) groups of dibenzylmethylamine (0.08 M in CH<sub>2</sub>CHCl) at  $-100^\circ$  revealed two sharp singlet resonances. At temperatures below  $-100^\circ$ , the N-CH<sub>3</sub> resonance exhibited broadening due to viscosity effects and/or quadrupole-induced <sup>14</sup>N relaxation<sup>7</sup> while the N-CH<sub>2</sub> peak broadened and separated in typical fashion into what is clearly an AB spectrum ( $J_{AB} \cong 12$  Hz;  $\Delta\nu_{AB} \cong 17$  Hz) consistent with *slow nitrogen inversion on the pmr time scale* (Figure 1). The first-order rate constant ( $k$  or  $k_{-1}$ ; eq 1) was calculated to be  $76 \text{ sec}^{-1}$  at  $-146^\circ$  using an analytic expression for the rate at coalescence of the pertinent resonances.<sup>8</sup> The barrier ( $\Delta G^\ddagger$ ) to inversion in dibenzylmethylamine is  $6.0 \pm 0.5$  kcal/mol at  $-146^\circ$  assuming the transmission coefficient of the Eyring equation to be unity.<sup>9</sup> Although the spectral behavior reported here may also be affected by slow C-N bond rotation, the relatively low rotational barrier in trimethylamine (4.4 kcal/mol)<sup>10</sup> indicates that C-N bond rotation is still rapid on the pmr time scale at  $-146^\circ$ .

Thus it is evident that inversion barriers in simple, acyclic trialkylamines can be determined using conventional variable-temperature nmr techniques and we are continuing our investigations especially with respect to steric and solvent effects on the inversion barriers.

**Acknowledgment.** We thank Research Corporation (Cottrell Grant) and the National Science Foundation (COSIP Grant) for support of this work and the referees for useful suggestions.

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(8) S. Alexander, *J. Chem. Phys.*, **37**, 966 (1962).

(9) A total nmr line-shape analysis for dibenzylmethylamine and several other amines is in progress and the results will be reported in the full paper.

(10) D. R. Lide and D. E. Mann, *J. Chem. Phys.*, **28**, 572 (1958).

C. Hackett Bushweller, James W. O'Neill

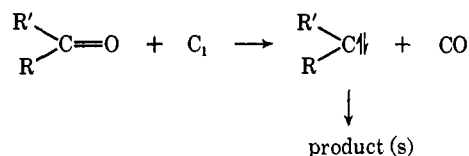
Department of Chemistry  
Worcester Polytechnic Institute  
Worcester, Massachusetts 01609

Received December 22, 1969

### Deoxygenation by Atomic Carbon. III. Dichlorocarbene and Methoxycarbene

Sir:

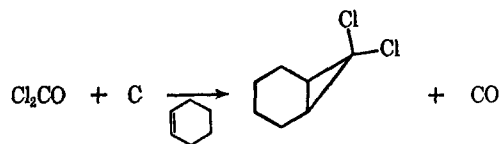
We have reported previously<sup>1</sup> that ketones and aldehydes react with excited state carbon atoms (<sup>1</sup>D and/or <sup>3</sup>S) during codeposition at a liquid nitrogen cooled surface to produce mono- and dialkylcarbenes and carbon monoxide. In the course of the ketone and aldehyde deoxygenation studies it was noted that prod-



uct formation always occurred in an intramolecular manner and that efforts to intercept the intermediate carbenes with cyclohexene were unsuccessful. This is apparently due to a low activation energy for intramolecular carbene stabilization.

We now wish to report that when carbenes having no intramolecular mode of stabilization are generated by deoxygenation in the presence of olefins, cyclopropanes are formed.

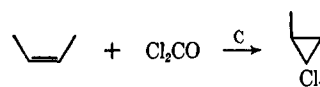
One example of this is the deoxygenation of phosgene in the presence of cyclohexene to produce 7,7-dichloronorcaradiene. When a gas-phase mixture of 75% phos-



gene and 25% cyclohexene was added to the reaction flask<sup>2</sup> and codeposited at the liquid nitrogen cooled surface with carbon vapor from a 16-V a.c. arc, 7,7-dichloronorcaradiene, determined by comparison with an authentic sample, is the major product formed in 25% yield.<sup>3</sup> No detectable quantity of tetrachloroethylene was found in the reaction.

This observation is consistent with the intermediacy of free dichlorocarbene from the deoxygenation of phosgene. To determine the stereochemistry of the addition of deoxygenative dichlorocarbene to olefins and thereby its multiplicity,<sup>4</sup> carbon vapor was cocondensed with mixtures of *cis*- and *trans*-2-butene and phosgene.

When a gas-phase mixture of 65% phosgene and 35% *cis*-2-butene was used as the reactive matrix, 1,1-dichloro-*cis*-2,3-dimethylcyclopropane was the major product (formed in 20% yield<sup>3</sup>) with no peak present in the gas chromatogram which corresponded to the *trans* isomer. When a mixture of 67% phosgene and 33%



(1) P. S. Skell and J. H. Plonka, *J. Amer. Chem. Soc.*, **92**, 836 (1970).

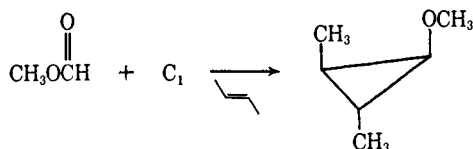
(2) P. S. Skell, L. Wescott, Jr., J. P. Goldstein, and R. R. Engel, *ibid.*, **87**, 2829 (1965), describes the reaction system.

(3) Based on C<sub>1</sub>; assuming 40% of the carbon vaporized is monatomic. See R. F. Harris, Ph.D. Thesis, Pennsylvania State University, 1968.

(4) P. S. Skell and R. C. Woodworth, *J. Amer. Chem. Soc.*, **78**, 4496 (1956).

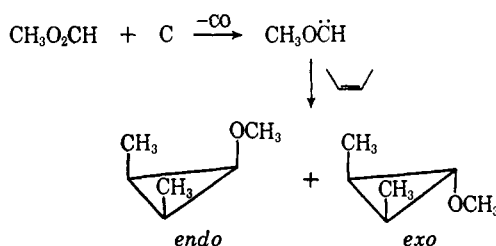
*trans*-2-butene was used as the reactive matrix, only the 1,1-dichloro-*trans*-2,3-dimethylcyclopropane was formed (20% yield<sup>3</sup>) free of the *cis* isomer. These results indicate that dichlorocarbene formed in the deoxygenation of phosgene is a singlet species. This observation is also consistent with spin conservation considerations presented previously<sup>1</sup> concerning the deoxygenation process.

When a mixture of 78% methyl formate and 22% *trans*-2-butene was used as a matrix for carbon vapor, deoxygenation took place with production of methoxycarbene, which gave only the *trans*-2,3-dimethylmethoxycyclopropane in 28% yield<sup>3</sup> (no more than



1% of the inverted isomer could have been formed). This result again implicates a singlet carbene intermediate.

The use of a reactive matrix containing 56% methyl formate and 44% *cis*-2-butene under deoxygenative conditions gave only the *exo*- and *endo-cis*-2,3-dimethylmethoxycyclopropanes<sup>5</sup> in 15% yield<sup>3</sup> with an *endo*:*exo* ratio of 6.2. This is in reasonable agreement with the



*endo*:*exo* value of 7.0 obtained from the addition of methoxycarbene from lithium chloromethyl methyl ether to *cis*-2-butene.<sup>6</sup> The correspondence of the *endo*:*exo* ratios for these two methoxycarbenes under greatly different conditions suggests that the same intermediate is involved in both reactions.

Recent work comparing the relative reactivity of dichlorocarbene produced from gas-phase pyrolysis of chloroform with dichlorocarbene from lithium trichloromethane<sup>7</sup> has shown that carbenes produced from  $\alpha$ -halolithiums are free. The correspondence of the above *endo*:*exo* ratios despite different media and temperatures of generation indicates that the methoxycarbene intermediate is also present in both these reactions.

**Acknowledgment.** We acknowledge the financial support of the Air Force Office of Scientific Research.

(5) The authors thank Dr. W. H. Atwell of Dow Corning, Midland, Mich., for providing authentic samples of the 2,3-dimethylmethoxycyclopropanes in question to facilitate the product identification.

(6) U. Schollkopf and J. Paust, *Chem. Ber.*, **98**, 2221 (1965).

(7) P. S. Skell and M. S. Cholod, *J. Amer. Chem. Soc.*, **91**, 6035 (1969).

(8) National Institutes of Health Predoctoral Fellow, 1967-1970.

P. S. Skell, J. H. Plonka<sup>8</sup>

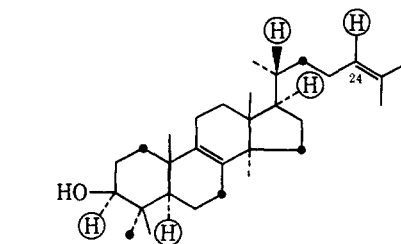
Department of Chemistry, Pennsylvania State University  
University Park, Pennsylvania 16802

Received November 29, 1969

## *trans* Reduction of $\Delta^{24}$ of Lanosterol in the Biosynthesis of Cholesterol by Rat Liver Enzymes

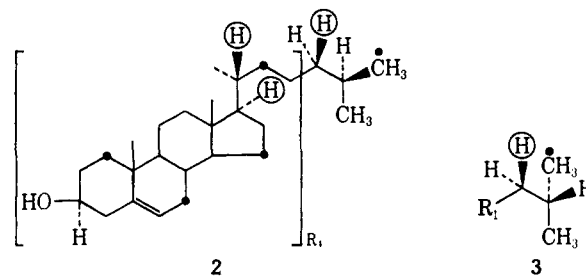
Sir:

An obligatory step in the sequence of the biosynthetic transformations of lanosterol (**1a**) to cholesterol<sup>1-3</sup> is the reduction of the C-24 double bond. We have proved, with the use of cholesterol biosynthesized from 4*R*-(2-<sup>14</sup>C,4-<sup>3</sup>H)-MVA in a rat liver enzyme preparation, that the hydrogenation of lanosterol (**1a**) is stereospecific at C-24 and proceeds by the addition of a 24-*pro-S* hydrogen.<sup>4</sup> The available evidence suggests that the addition of a hydrogen at C-25 is also stereospecific.<sup>5,6</sup> In addition, it has been shown that protonation takes place at C-24 and a "hydride ion" from TPNH adds at<sup>7</sup> C-25.



**1a**, (H) = 4-*pro-R*,H of MVA; (•) = C-2 of MVA

**b**, (H) = <sup>3</sup>H; (•) = <sup>14</sup>C



A *cis* reduction of  $\Delta^{24}$  would give cholesterol with the geometry indicated in **2**, while in a *trans* reduction the geometry would be as in **3**. The two methyls at the 25-*pro*-chiral carbon atom differ in that one originates from C-2 and the other from C-3' of MVA. Hence, knowledge of the configuration at C-25, taken together with the already proven addition of a 24-*pro-S* hydrogen, allows definition of the *overall* mechanism of reduction of the C-24 double bond of **1**. For the determination of the C-25 *pro*-chirality, it was necessary to differentiate between the 26- and 27-methyl groups. Consequently, cholesterol was incubated with *Mycobacterium smegmatis*,<sup>8</sup> and the nonsaponifiable residues from several experiments were pooled and purified by chromatography. The obtained **4a** was crystallized from ethyl acetate (mp 129-131°) (110 mg) and showed  $[\alpha]_D^{25} +87.1^\circ$

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