(2) K. Matsumoto, P. Stark, and R. G. Meister, *J. Med. Chem.*, in press.
(3) R. S. Marmor, *J. Org. Chem.*, **37**, 2901 (1972).
(4) P. Baeckstrom and G. Sundstrom, *Acta Chem. Scand.*, **24**, 716 (1970).
(5) J. F. Cannon et al., *Aust. J. Chem.*, **26**, 799 (1973).
(6) J. H. P. Tyman and A. A. Durrani, *Tetrahedron Lett.*, 2511 (1975).
(7) H. G. Krishnamurthy and J. S. Prasad, *Tetrahedron Lett.*, 2511 (1975).
(8) CIBA-GEIGY A. G., French Demande 2 212 317 (July 26, 1974); *Chem. Abstr.*, **82**, 139659h (1975).
(9) R. G. Agusto, F. A. Taylor, and H. L. Briggs, U.S. Patent 3 865 884 (Feb 11, 1975); *Chem. Abstr.*, **82**, 139674j (1975).
(10) Union Rhenische Braunkohlen Kraftstoffe A. G., Swiss Patent 517 680 (1970); E. Biller et al., *Chem. Ind. (London)*, 685 (1973).
(11) A. Brossi, A. Focella, and S. Teitel, German Offen. 2 002 815 (July 30, 1970); *Chem. Abstr.*, **73**, 66258d (1970).
(12) U. Lille and L. A. Bitter, Russian Patent 292 944 (Jan 15, 1971); *Chem. Abstr.*, **75**, 35407p (1971).
(13) H. Musso and D. Bormann, *Chem. Ber.*, **98**, 2774 (1965).
(14) This intermediate, as well as every other compound prepared in this work, has been isolated, purified, and fully characterized by spectra and analysis.
(15) G. W. Kenner and N. R. Williams, *J. Chem. Soc.*, 522 (1955).

Generation of the Trans Enolate of Chloroacetaldehyde via a β-Oxido Carbenoid

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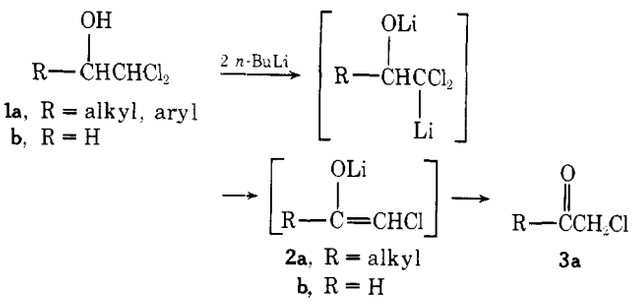
On treatment with 2 equiv of *n*-butyllithium, 1-substituted 2,2-dichloroethanols **1a** and related species undergo rearrangement via β-oxido carbenoids to afford ketones **3a** in high



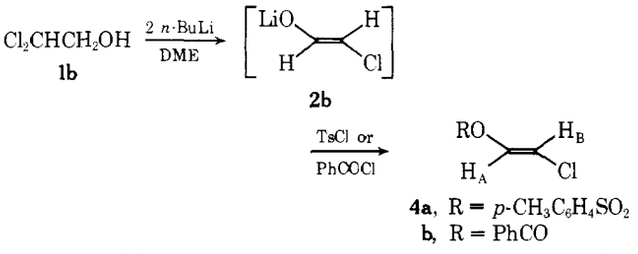
1a, R = alkyl, aryl
b, R = H

2a, R = alkyl
b, R = H

3a

yields.[1] Although the chemistry of β-oxido carbenoids has been intensively investigated by us[2] and others,[3] the stereochemistry of the double bond of the enolate anion **2** has not been elucidated. Investigation of the reaction of the parent compound, 2,2-dichloroethanol (**1b**), would give us not only information about the stereochemical outcome of this rearrangement, but also a way for the preparation of chloroacetaldehyde enolate (**2b**), a previously unknown enolate species.

We have found that 2 equiv of *n*-butyllithium effects rearrangement of 2,2-dichloroethanol (**1b**)[4] at −78 °C to give the lithium enolate of chloroacetaldehyde (**2b**). This enolate is subsequently allowed to react with *p*-toluenesulfonyl chloride and is isolated as the O-tosylated derivative **4a** in 86%



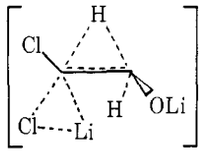
1b

2b

4a, R = *p*-$CH_3C_6H_4SO_2$
b, R = PhCO

yield. In addition, this rearrangement reaction gives exclusively the *E* isomer of the enol tosylate **4a** (vide infra). Although alcohols **1a** react rapidly (−50 °C, 30 min) with *n*-butyllithium,[2b] less than half of 2,2-dichloroethanol (**1b**) was consumed under the same conditions. At a higher temperature (−20 °C, 2 h) the yield of the enol tosylate **4a** was reduced to 58%, yet under the optimum conditions (−78 °C, 5 h), it reached the highest value of 86%. It is interesting that the enolate **2b** gives the O-tosylated derivative in high yield, and as a single isolable product, since the reaction of an enolate anion with arenesulfonyl chloride has long been known to afford mainly chlorinated products instead of sulfonylated products.[5]

In order to establish the stereochemistry of the enolate **2b**, the enolate **2b** was transformed to the corresponding enol benzoate **4b**, since a reliable stereochemical assignment by NMR spectroscopy is possible with enol ester derivatives.[6] The enolate **2b** generated in DME was treated with benzoyl chloride to give the expected enol benzoate **4b** in 56% yield. On NMR analysis the benzoate **4b** exhibited the same value of the coupling constant as the tosylate **4a**, i.e., J_{AB} = 11 Hz. A coupling constant between two vicinal protons attached to a disubstituted double bond is known to be closely related to the electronegativity of the substituents, and its magnitude is greatly reduced by both acyloxy and chloro groups.[6] Therefore, the value (J_{AB} = 11 Hz) of the enol benzoate **4b** should point out an *E* geometry of the double bond, and at the same time, the same geometry of the double bond of the lithium enolate **2b**.[7] With respect to the stereochemistry of the enolate **2b**, reactions at temperatures ranging from −100 to −20 °C uniformly gave the same result. An electronic repulsion in the transition state **6** is most likely the reason of the stereospecificity of this rearrangement.



6

Experimental Section

General. Melting points, which were determined in glass capillaries, and boiling points are uncorrected. Infrared spectra were obtained on a Hitachi EPI G3 spectrometer. NMR spectra were determined on a Varian Associates Model T-60 spectrometer and the chemical shifts (δ) are expressed in parts per million downfield from internal tetramethylsilane. Mass spectra were determined on a Hitachi RMU-7M spectrometer at Mass Spectral Laboratory, Tokyo Institute of Technology. Microanalyses were performed at Microanalytical Laboratory, Tokyo Institute of Technology.

(*E*)-2-Chloroethenyl 4-Toluenesulfonate (4a). 2,2-Dichloroethanol (114 mg, 1.00 mmol) in 5 ml of DME was treated with 1.55 M *n*-butyllithium in hexane (1.42 ml, 2.20 mmol) at −78 °C for 5 h. The resulting white suspension was treated with 197 mg of *p*-toluenesulfonyl chloride (1.00 mmol) dissolved in 2 ml of DME at −78 °C for 30 min and for 1 h at room temperature. The white reaction mixture was poured into 10 ml of water, and extracted with ether (10 ml × 3). The ethereal extract was dried ($MgSO_4$) and concentrated in vacuo to leave a yellow oil, which was homogeneous on TLC (R_f 0.45, benzene) and NMR analysis. Purification by preparative TLC gave the title tosylate **4a** (202 mg, 86%): bp 95–100 °C (bath temperature, 0.014 mm); ir (neat) 1600 (m), 1380 (s), 1195 (s), 1180 (s), 1070 (s), 890 cm^{-1} (m); NMR (CCl_4) δ 2.45 (s, 3 H, CH_3–), 6.00 (d, J = 11 Hz, 1 H, ClCH=C), 6.75 (d, J = 11 Hz, 1 H, OCH=C), 7.30 (unresolved d, J = 8 Hz, 2 H, aromatic protons ortho to methyl group), 7.70 (unresolved d, J = 8 Hz, 2 H, aromatic protons meta to methyl group); mass spectrum (70 eV) *m/e* (rel intensity) 232 and 234 ($M^{\cdot+}$), 155 (23), 91 (100), 65 (59), 63 (23), 51 (20), 49 (24), 39 (30).

Anal. Calcd for $C_9H_9O_3ClS$: C, 46.46; H, 3.90; S, 13.78. Found: C, 46.35; H, 3.95; S, 13.69.

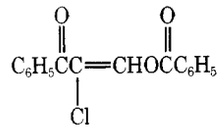
1-Benzoyloxy-2-chloro-(*E*)-ethene (4b). The DME (8 ml) solution of the lithium enolate **2b** which was prepared in the same manner as described above using 177 mg of 2,2-dichloroethanol (1.55 mmol) and 1.42 M *n*-butyllithium (2.18 ml, 3.10 mmol) was treated

at −78 °C with freshly distilled benzoyl chloride (218 mg, 1.55 mmol) in 2 ml of DME. After stirring for 30 min at −78 °C, the reaction mixture was allowed to warm to room temperature. The yellow mixture was subsequently poured into 10 ml of water, and extracted with ether (10 ml × 3). The extract was purified on preparative TLC to give two products, A and B.

A was the title compound **4b** (158 mg, 56%, R_f 0.5, benzene). Bulb-to-bulb distillation afforded an analytical sample which solidified on standing (mp 26–27 °): bp 65 °C (bath temperature, 0.015 mm); ir (neat) 1740 (s), 1640 (w), 1260 (s), 1130 cm^{-1} (s); NMR (CCl_4) δ 6.25 (d, J = 11 Hz, ClCH=C), 7.20–7.55 (m, 3 H, aromatic protons), 7.70 (d, J = 11 Hz, 1 H, OCH=C), 7.90–8.20 (m, 2 H, aromatic protons).

Anal. Calcd for $C_9H_7O_2Cl$: C, 59.20; H, 3.87. Found: C, 59.45; H, 3.97.

B was the doubly acylated product **7** (48 mg, 11%, R_f 0.25, benzene): mp 98.5–100 °C (hexane); ir (CCl_4) 1760 (s), 1730 (shoulder), 1675 (m), 1630 (m), 1600 (m), 1240 (vs), 1150 (vs), 1005 cm^{-1} (vs); NMR (CCl_4) δ 7.1–8.3 (m, 10 H), 8.45 (s, 1 H).



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Anal. Calcd for $C_{16}H_{11}O_3Cl$: C, 67.01; H, 3.87. Found: C, 66.72; H, 3.97

Registry No.—**2b**, 60537-99-7; **4a**, 60538-00-3; **4b**, 60538-01-4; **7**, 60538-02-5; 2,2-dichloroethanol, 598-38-9; *p*-toluenesulfonyl chloride, 98-59-9; benzoyl chloride, 98-88-4.

References and Notes

(1) Review: H. Normant, *J. Organomet. Chem.*, **100**, 189 (1975).
(2) (a) I. Kuwajima and Y. Kurata, *Chem. Lett.*, 291 (1972); (b) I. Kuwajima, H. Shinozaki, and S. Hayakawa, *ibid.*, 197 (1973); (c) I. Kuwajima and Y. Fukuda, *Tetrahedron Lett.*, 327 (1973).
(3) (a) J. Villieras, C. Bacquet, and J. F. Normant, *J. Organomet. Chem.*, **40**, C1 (1972); (b) G. Kobrich and J. Grosser, *Tetrahedron Lett.*, 4117 (1972); (c) H. Taguchi, H. Yamamoto, and H. Nozaki, *ibid.*, 4661 (1972); (d) H. Taguchi, H. Yamamoto, and H. Nozaki, *J. Am. Chem. Soc.*, **96**, 6510 (1974).
(4) C. E. Sroog and H. M. Woodburn, "Organic Syntheses", Collect. Vol. IV, Wiley, New York, N.Y., 1967, p 271.
(5) For instance: (a) H. Bohme and R. Marx, *Chem. Ber.*, **74**, 1664 (1941); (b) M. Burgnel and R. Truchet, *C. R. Acad. Sci.*, **190**, 753 (1930).
(6) (a) L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", 2d ed, Pergamon Press, Oxford, 1969, pp 184–185; (b) W. McFarlane in "Elucidation of Organic Structures by Physical and Chemical Method", Part I, K. W. Bentley and G. W. Kirby, Ed., Wiley-Interscience, New York, N.Y., 1972, pp 273–276.
(7) H. O. House, *Rec. Chem. Prog.*, **28**, 99 (1967).

Dehydroaporphines. Dichlorocarbene Addition to Dehydronuciferine

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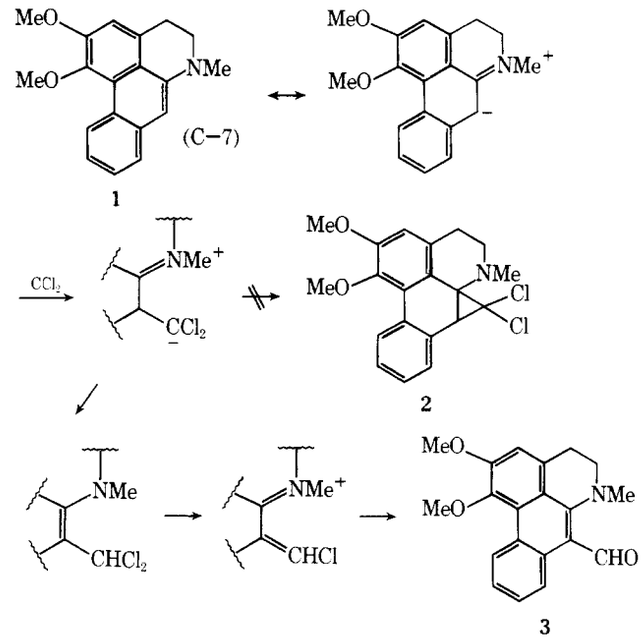
A recent protonation study of some representative dehydroaporphines has shown that protonation occurs readily at C-7, indicative of a certain degree of enamine-type character in dehydroaporphines.[1] This result suggested that the C-7 carbon of a dehydroaporphine might be sufficiently nucleophilic to allow the introduction of carbon substituents at this position, thus affording a route to a variety of hitherto unavailable but pharmacologically interesting 7-substituted aporphines. As part of a broad study of the scope and limitations of this idea, we now report the reaction of dichlorocarbene with dehydronuciferine (**1**), a typical dehydroaporphine.

It has been reported recently that dichlorocarbene adducts of olefins, including even phenanthrene, can be prepared conveniently and in high yield by the use of chloroform, aqueous sodium hydroxide, and a phase-transfer catalyst.[2] Under these conditions, dehydronuciferine (**1**) was cleanly converted into a single crystalline product, mp 161–163 °C. The composition and properties of this material showed that it was not the expected cyclopropane **2**, but rather dehydronuciferine-7-carboxaldehyde (**3**). In accord with this formulation, the infrared spectrum of **3** showed a conjugated carbonyl band at 6.24 μ. The NMR spectrum of **3** showed that the C-7 proton of dehydronuciferine (at δ 6.50) was replaced by a low-field aldehyde proton at δ 10.13; the N-methyl of **3** appeared at δ 3.30 as compared to δ 2.95 in dehydronuciferine, indicating a considerable deshielding effect of this methyl by the aldehyde group.



The formation of aldehyde **3** from dehydronuciferine can be rationalized by a mechanism analogous to that of the Reimer–Tiemann reaction, as illustrated below, the critical step being the attack of the electron-deficient CCl_2 by the nucleophilic C-7 carbon of the dehydroaporphine.

Reduction of aldehyde **3** with sodium cyanoborohydride at pH 3 afforded, in good yield, 7-methyldehydronuciferine (**5**), mp 99–100 °C. The uv spectrum of **5** was almost identical with that of dehydronuciferine (**1**), indicating the presence of the same chromophoric system; its NMR spectrum showed the presence of the new C-methyl at δ 2.68, the N-methyl being shifted upfield to δ 2.78 from its original value of 2.95 in **1**.

The reduction of **3** to **5** takes place through the intermediary formation of the unstable 7-hydroxymethyldehydronuciferine (**4**), which can be isolated when **3** is reduced under ordinary basic conditions by sodium borohydride. Treatment of alcohol **4** with sodium cyanoborohydride at pH 3 affords 7-methyldehydronuciferine (**5**), presumably via the stabilized iminium ion **6**. Evidence for the ready generation of cation **6** from alcohol **4** was obtained by the interception of cation **6** by hydrogen cyanide to give, in good yield, the crystalline 7-cyanomethyldehydronuciferine (**7**), mp 195–196 °C.

Attempts to effect the direct C-methylation of **1** to **5** by methyl iodide were unsuccessful, presumably because of insufficient nucleophilicity of the C-7 carbon of **1** toward the alkyl halide.

Experimental Section

Melting points are uncorrected. Chromatography was carried out using silica. NMR spectra ($CDCl_3$ containing tetramethylsilane as