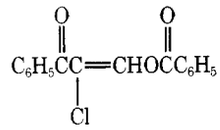
at −78 °C with freshly distilled benzoyl chloride (218 mg, 1.55 mmol) in 2 ml of DME. After stirring for 30 min at −78 °C, the reaction mixture was allowed to warm to room temperature. The yellow mixture was subsequently poured into 10 ml of water, and extracted with ether (10 ml × 3). The extract was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



7

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

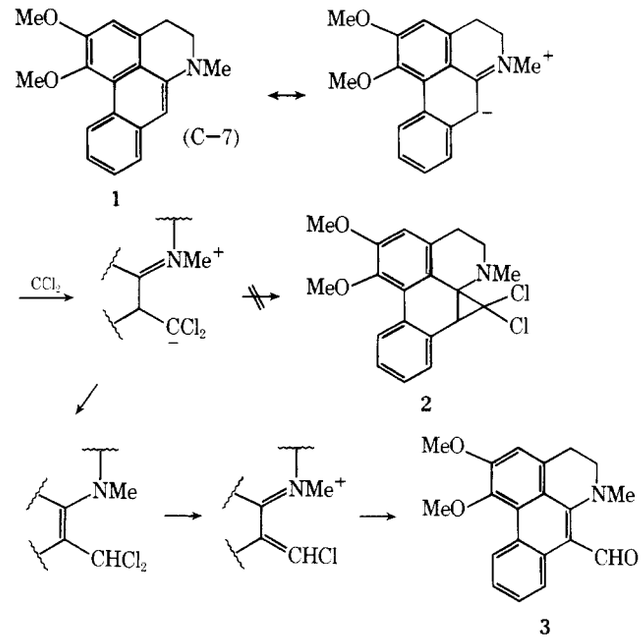
José M. Saá and Michael P. Cava*

Department of Chemistry, University of Pennsylvania, Philadelphia, Pennsylvania 19174

Received July 26, 1976

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.

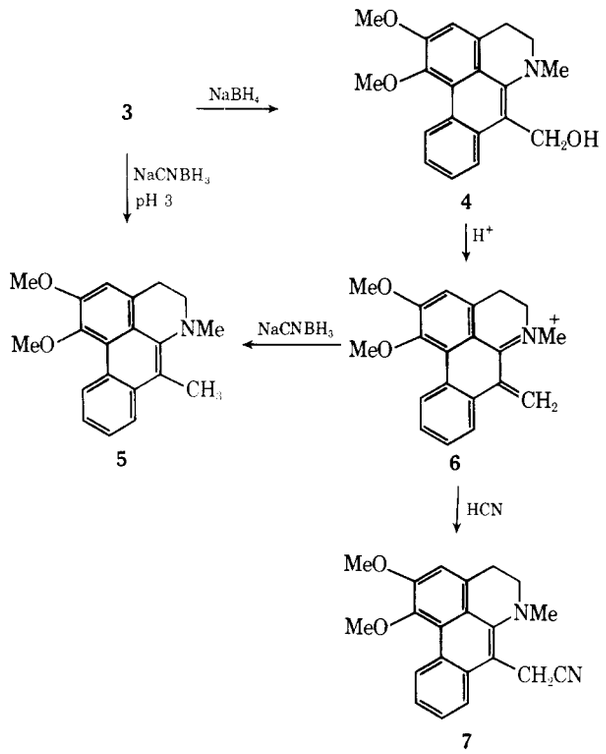
Reduction of aldehyde **3** with sodium cyanoborohydride at pH 3 afforded, in good yield, 7-methyldehydronuciferine (**5**), mp 99–100 °C. The uv spectrum of **5** was almost identical with that of dehydronuciferine (**1**), indicating the presence of the same chromophoric system; its NMR spectrum showed 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



internal standard), ultraviolet spectra (ethanol), infrared spectra (KBr), and mass spectra were determined using JEOL-JNH-PS-100 and Perkin-Elmer 202, 137, and 270 spectrometers, respectively. Microanalyses were performed by Midwest Microlab, Indianapolis, Ind.

Dehydronuciferine-7-carboxaldehyde (3). Aqueous sodium hydroxide (2 ml, 50%) was added to a solution of dehydronuciferine[3] (1, 0.360 g) in chloroform (10 ml) containing a few drops of 30% aqueous tetra-*n*-butylammonium hydroxide, and the mixture was stirred for 4 h (external bath at 55–65 °C). After washing with water, the dried organic phase was evaporated and the residue chromatographed (chloroform eluent) to give recovered 1 (0.144 g) and 0.190 g of aldehyde 3, which crystallized from acetone as dark brown prisms: mp 161–163 °C; ir 6.24 μ; uv λ_{max} 213 nm (ϵ 11 000), 261 (24 000), 280 (17 000), 315 sh (7200), 418 (8000); NMR δ 3.30 (s, 3 H, NMe), 3.74 (s, 3 H, OMe), 3.93 (s, 3 H, OMe), 3.03 (t, 2 H, J = 6.5 Hz), 3.52 (t, 2 H, J = 6.5 Hz), 6.88 (s, 1 H, C-3), 10.13 (s, 1 H, CHO), 7.27–9.31 (m, 4 H); mass spectrum m/e 321 (M^+, 100), 304 (92), 160.5 (1).

Anal. Calcd for $C_{20}H_{19}NO_3$: C, 74.76; H, 5.92; N, 4.33. Found: C, 74.86; H, 6.02; N, 4.29.

7-Hydroxymethyldehydronuciferine (4). Excess sodium borohydride was added to a solution of aldehyde 3 (0.050 g) in methanol (10 ml). Examination by TLC after a few minutes showed the absence of any aldehyde. Evaporation, addition of water, and chloroform extraction afforded the alcohol 4 (0.045 g) as a yellow oil which decomposed upon attempted chromatography over silica or alumina. Compound 4 was characterized spectroscopically as follows: uv λ_{max} 260, 325 nm; NMR δ 2.85 (s, 3 H, NMe), 3.21 (t, 2 H, J = 8.5 Hz), 3.28 (t, 2 H, J = 8.5 Hz), 3.86 (s, 3 H, OMe), 4.00 (s, 3 H, OMe), 7.08 (s, 1 H, C-3), 7.46–9.76 (m, 4 H); mass spectrum m/e 323 (M^+, 100), 308 (55), 306 (55), 292 (25), 290 (20), 161.5 (1).

7-Methyldehydronuciferine (5). A. A solution of alcohol 4 (0.040 g) in tetrahydrofuran (10 ml) was brought to pH 3–4 by the addition of a few drops of 5% hydrochloric acid, and excess sodium cyanoborohydride was added in portions, while maintaining the acidity of the solution. After 15 min, TLC showed no starting material to be present. Workup in the usual manner, followed by crystallization from methanol, gave compound 5 as yellow prisms (0.034 g): mp 99–100 °C; uv λ_{max} 254 nm (ϵ 100 000), 264 (100 000), 324 (25 000), 387 sh (4000); NMR δ 2.68 (s, 3 H, C-Me), 2.78 (s, 3 H, NMe), 3.21 (t, 2 H, J = 8.5 Hz), 3.28 (t, 2 H, J = 8.5 Hz), 3.88 (s, 3 H, OMe), 4.00 (s, 3 H, OMe), 7.06 (s, 1 H, C-3), 7.41–9.78 (m, 4 H); mass spectrum m/e 307 (M^+, 100), 292 (43), 153.5 (5).

Anal. Calcd. for $C_{20}H_{21}NO_2$: C, 78.17; H, 6.84; N, 4.56. Found: C, 78.00; H, 6.98; N, 4.48.

B. A solution of aldehyde 3 (0.050 g) in methanol (10 ml) was reduced at pH 3–4 with sodium cyanoborohydride as described above for alcohol 4. Workup afforded 5 in 84% yield.

7-Cyanomethyldehydronuciferine (7). Potassium cyanide (0.060 g) was added to a stirred solution of alcohol 4 (0.200 g) in a mixture of ethanol (5 ml) and 1% hydrochloric acid (15 ml). After stirring for 30 min at room temperature, the mixture was heated on the steam bath for 15 min. The usual workup, followed by filtration in chloroform through silica, gave crude nitrile 7. Crystallization from ethanol–chloroform gave 7 as prisms (0.160 g): mp 195–196 °C; ir 4.40 μ; uv λ_{max} 253 nm (sh) (ϵ 35 000), 262 (50 000), 323 (11 000), 370 (2400); NMR δ 2.98 (s, 3 H, NMe), 3.98 (s, 3 H, OMe), 4.01 (s, 3 H, OMe), 4.45 (s, 2 H, CH_2CN), 7.13 (s, 1 H, C-3), 7.50–9.75 (m, 4 H); mass spectrum m/e 332 (M^+, 100), 317 (57), 292 (49), 166.5 (1).

Anal. Calcd for $C_{21}H_{20}N_2O_2$: C, 75.90; H, 6.02; N, 8.43. Found: C, 76.03; H. 6.12; N, 8.42.

Acknowledgment. We thank the National Institutes of Health for a grant (CA-11445) in support of this work, and the Fundación Juan March for a supporting fellowship to one of us (J. M. Saá).

Registry No.—1, 7630-74-2; 3, 60538-11-6; 4, 60538-12-7; 5, 60538-13-8; 7, 60538-14-9.

References and Notes

(1) A. Venkateswarlu and M. P. Cava, *Tetrahedron*, **32**, 2079 (1976).
(2) G. C. Joshi, N. Singh, and L. M. Pande, *Tetrahedron Lett.*, 1461 (1972); *Synthesis*, 317 (1972).
(3) M. P. Cava, D. L. Edie, and J. M. Saá, *J. Org. Chem.*, **40**, 3601 (1975).

Gnididione, a New Furanosesquiterpene from *Gnidia latifolia*[1]

S. Morris Kupchan,* Yoshikazu Shizuri, Robert L. Baxter, and H. Richard Haynes

Department of Chemistry, University of Virginia, Charlottesville, Virginia 22901

Received June 30, 1976

In the course of a continuing search for tumor inhibitors from plant sources, we have isolated the potent antileukemic diterpenoid esters, gnidilatin 20-palmitate and gnidilatidin 20-palmitate, from *Gnidia latifolia* Gilg. (Thymelaeaceae).[2,3] Our isolation procedure also yielded a new sesquiterpene, gnididione (1). Gnididione is the first known guaiane-type sesquiterpenoid with a furan ring.

An ethanol extract of *G. latifolia* was partitioned between chloroform and water. The chloroform soluble material was chromatographed on SilicAR CC-7. Crystallization from methanol of the fraction which was eluted with 10% ethyl acetate in benzene gave gnididione (1).

Elemental analysis and mass spectrometry established a molecular formula of $C_{15}H_{16}O_3$ for 1. The ^{13}C NMR spectrum of 1 indicated the presence of two carbonyl groups [δ 206.3 (s) and 195.8 (s)], three double bonds [δ 154.0 (s), 153.6 (s), 142.2 (d), 137.9 (s), 126.5 (s), and 123.4 (s)], two methylene groups [δ 54.1 (t) and 40.7 (t)], two methine groups [δ 46.4 (d) and 32.8 (d)], and three methyl groups [δ 21.8 (q), 10.1 (q), and 9.8 (q)]. Furthermore, the ^1H NMR spectrum showed that one of the methyl groups was attached to a methine group [τ 8.88 (3 H, d, J = 7 Hz)]. The absorptions at 3.22, 6.33, and 6.69 μ in the ir spectrum indicated the presence of a furan ring, and the uv absorption at 338 nm showed that the carbonyl groups, double bond, and furan ring were conjugated. From the above data and from biogenetic considerations, gnididione (1) appeared to belong to the guaiane class of sesquiterpenes and to have either structure 1 or 2. The structure was confirmed by subsequent chemical transformations. Thus, reduction of 1 with lithium aluminum hydride, followed by dehydrogenation over palladium on charcoal, yielded artemazulene (4), which formed a crystalline trinitrobenzene complex. In order to avert possible intramolecular changes during dehydrogenation, the