**Preparation of 9,10-(Carbethoxymethano)-9-octadecenoate (2).**—Ethyl diazoacetate (3.4 g, 29.3 mmol) in the presence of 0.2 g of powdered copper bronze[12] was allowed to react with 5.9 g (20 mmol) of methyl stearolate to form the corresponding cyclopropenoid diester **2** as previously described.[8] Subsequently it was cooled to room temperature, filtered to remove the catalyst, and distilled *in vacuo*, bp[4] 174–176° (0.05 mm). The desired diester **2** was obtained in this way as a yellowish oil (3.9 g, 15.4 mmol, 77% yield).

**Preparation of the Fluorosulfonic Acid Decarbonylation Reagent.**—This reagent was prepared by mixing 2.5 ml of fluorosulfonic acid in 2.5 ml of methylene chloride at room temperature. The resulting 50% (v/v) solution contained 43.7 mmol of fluorosulfonic acid (17.5 *M*).

**Decarbonylation of 9,10-(Carbethoxymethano)-9-octadecenoate (2).**—Throughout the experiment a current of argon blanketed the reaction mixture. Decarbonylation was accomplished by slowly dropping 5 ml of the 17.5 *M* fluorosulfonic acid solution on 5.25 mmol of cyclopropenoid ester over a 0.5-hr interval at room temperature. After the solution had stood for an additional 0.5 hr, 20 ml of cold (−78°) methylene chloride was added and 5 g of type 4A or 5A molecular sieves.[13] The cold solution with the molecular sieves was allowed to stand for 1 hr under argon.

**Preparation of the Sodium Borohydride Reducing Solution.**—A three-necked round-bottomed flask equipped with a magnetic bar stirrer was placed in a Dry Ice–trichloroethylene bath maintained at −50°. Sodium borohydride (1 g) was charged in the flask followed by 25 ml of a stock solution of methanol saturated with sodium hydroxide. The reaction was blanketed by argon all the time and the solution was stirred and allowed to stand at −50°. This solution was designated as a 1.05 *M* sodium borohydride reducing reagent.

**Methyl Sterculate (7).**—Under a blanket of argon, the cyclopropenium cation solution was slowly dropped into the 1.05 *M* sodium borohydride reducing reagent. The mixture was stirred for 20 min at −50°. After stirring for an additional 10 min, the reaction mixture was allowed to warm to room temperature. During the reduction of the brown cyclopropenium cation solution, gas evolved and the solution was placed in a separatory funnel containing 10 ml of cold (−78°) petroleum ether (bp 55–60°) and 50 ml of saturated sodium bicarbonate. The ethereal layer was removed and further extraction was accomplished with two 50-ml portions of petroleum ether. The combined extracts were washed with water and dried over anhydrous sodium sulfate at room temperature for 2 hr. The dry petroleum ether solution was filtered and the solvent was evaporated under reduced pressure. The residual yellow oil in a small volume of petroleum ether was placed on top of a 1.2 × 100 cm column of 200–325 mesh silicic acid (Unisil)[14] prepared as a slurry in petroleum ether under a blanket of argon and water jet pump vacuum. A total of 750 ml of petroleum ether was passed through the column. Fractions of 50 ml were collected and the elutions were monitored by using silica gel G tlc and a solvent system consisting of petroleum ether–diethyl ether (95:5, v/v). All eluates which furnished a compound with the same $R_f$ value as a reference methyl sterculate were combined. Evaporation of the solvent under vacuum at room temperature yielded a colorless oil (1.03 g, 65%).

The synthetic methyl sterculate (*Anal.* Calcd for $C_{20}H_{36}O_2$: C, 77.82; H, 11.76. Found: C, 77.72; H, 11.61) gave a positive Halphen test. In infrared absorption spectra it showed peaks at 1750 (carbonyl), 1880 (cyclopropene), and 1020 $cm^{-1}$ (cyclopropene). In the last case, the vibration given by cyclopropenes normally at 1010 was shifted to 1020 $cm^{-1}$ due to the way the spectra were taken. Masson[15] also reported a value of 1020 $cm^{-1}$ for methyl sterculate when its infrared spectrum was taken in carbon tetrachloride. A check using pure methyl sterculate prepared from natural sources[16] verified this observation.

In nmr is showed signals at 9.23 (s, 2 H, cyclopropenyl $CH_2$), 9.10 (m, 3 H, distal terminal $CH_3$), 8.63–8.71 (m, 22 H, internal $CH_2$), 7.61–7.78 (diffuse m, 6 H, $\alpha$ to cyclopropenyl and $-CO_2-CH_3$), and 6.32 ppm (s, 3 H, methyl ester $CH_3$). Generally, the spectra were identical with those obtained with pure methyl sterculate obtained from *sterculia foetida*. Furthermore, the synthetic and natural materials gave single spots with the same $R_f$ value on thin layer plates and identical gas chromatographic curves.[17]

**Registry No.**—**2**, 30689-71-5; **7**, 3220-60-8.

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(12) Purchased from The British Drug House, Poole, England.
(13) Linde Division of Union Carbide Corp., Chicago, Ill.
(14) Clarkson Chemical Co., Inc., Williamsport, Pa.
(15) J. C. Masson, Ph.D. Thesis, University of Arizona, and University Microfilms, Ann Arbor, Mich., 59-3048 BB (1957).
(16) Pure methyl sterculate isolated from *sterculia foetida* seeds by the method of H. W. Kircher, *J. Amer. Oil Chem. Soc.*, **41**, 4 (1964).
(17) E. L. Schneider, S. P. Loke, and D. T. Hopkins, *ibid.*, **45**, 585 (1970).

## Absolute Configuration of the Phenyl-2-piperidylcarbinols

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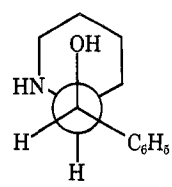
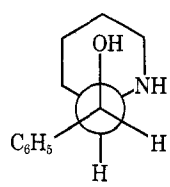
*Received March 1, 1971*

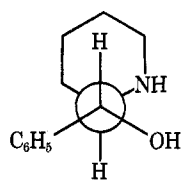
The Cotton effect associated with the $^1L_b \pi \rightarrow \pi^*$ transition[2] has been reported to be a reliable guide to the absolute configuration of both the ephedrine and the chloramphenicol stereoisomers.[3] This $^1L_b$ absorption band, as measured *via* circular dichroism (CD), is now used to assign the absolute configuration of the phenyl-2-piperidylcarbinols (**1** and **2**).



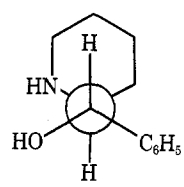
**1a**



**1b**



**2a**



**2b**

The diastereomeric carbinols (**1** and **2**) were prepared *via* the reduction of phenyl 2-pyridyl ketone with Brown catalyst,[4] which is a modification of the method of Crook and McElvain,[5] and separated *via* fractional crystallization. Diastereomers **1** and **2** were demonstrated to be erythro and threo, respectively, by acyl migration studies.[6] This conclusion is confirmed by

(1) To whom correspondence should be addressed.
(2) J. R. Platt, *J. Chem. Phys.*, **17**, 484 (1949).
(3) L. A. Mitscher, F. Kautz, and J. LaPidus, *Can. J. Chem.*, **47**, 1957 (1969).
(4) H. C. Brown and C. A. Brown, *J. Amer. Chem. Soc.*, **84**, 2827 (1962).
(5) K. E. Crook and S. M. McElvain, *ibid.*, **52**, 4006 (1930).
(6) A. Dudas and I. Weisz, *Chem. Ber.*, **94**, 412 (1961).

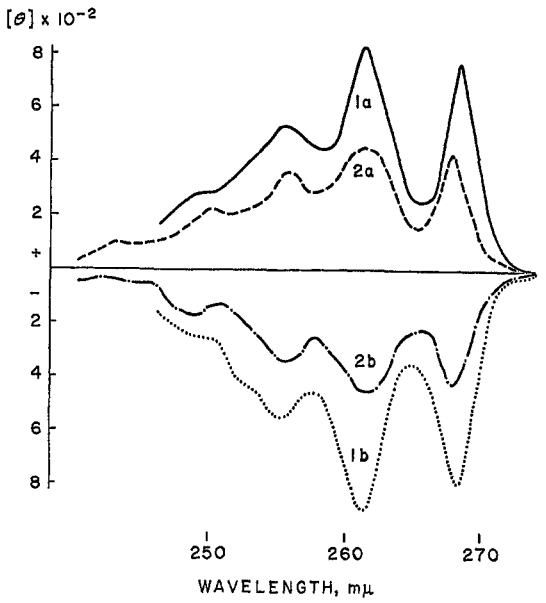



Figure 1.—Circular dichroism curves of the four isomeric phenyl-2-piperidylcarbinols.

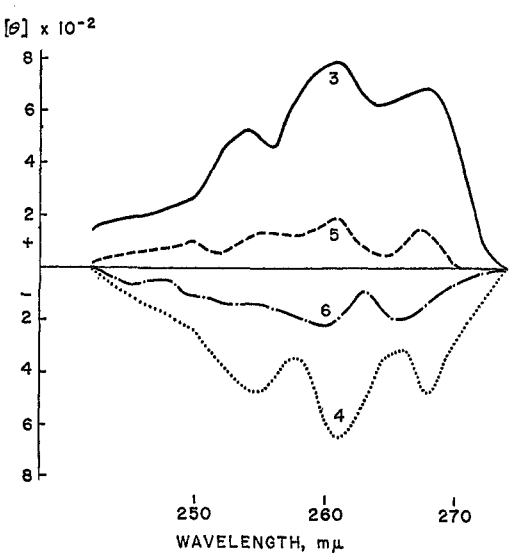



Figure 2.—Circular dichroism curves of the four isomeric ephedrines: (1*R*,2*S*)-ephedrine hydrochloride (**3**), (1*S*,2*R*)-ephedrine hydrochloride (**4**), (1*R*,2*R*)-pseudoephedrine hydrochloride (**5**), and (1*S*,2*S*)-pseudoephedrine hydrochloride (**6**).

noting that **1a** and **1b** give CD curves of larger amplitude than **2a** and **2b** (Figure 1), as would be expected,[3] and by noting that $J_1 = 3.3$ and $J_2 = 9.3$ cps, as would be expected.[7]

Resolution of **1** and **2** was accomplished with mandelic acid and di-*p*-toluoyltartaric acid, respectively. Comparison of the CD curves of the stereoisomers of phenyl-2-piperidylcarbinol (Figure 1) with the CD curves of the stereoisomers of ephedrine (Figure 2) allows us to assign the 1*R*,2*S* configuration to the erythro-(−) enantiomer (**1a**) which has the positive CD curve and the 1*S*,2*R* configuration to the erythro-(+) enantiomer (**1b**) which has the negative CD curve. Likewise, the 1*R*,2*R* configuration is assigned to the threo-(−) enantiomer (**2a**) which has the positive CD curve and the 1*S*,2*S* configuration to the threo-(+) enantiomer (**2b**) which has the negative CD curve.

## Experimental Section

**General.**—Melting points were determined in open capillaries on a Thomas–Hoover Uni-Melt apparatus and are uncorrected. The CD measurements were carried out using a Durrum–Jasco Model ORD/UV-5 instrument equipped with a CD attachment operating at ambient temperature.

**Phenyl-2-piperidylcarbinols (1 and 2).**—Brown catalyst was generated *in situ* in a Brown hydrogenator (Delmar)[8] from a 0.2 *M* ethanolic chloroplatinic acid solution (2 ml) and activated charcoal (2.0 g) according to the method of Brown.[4] To this was added phenyl 2-pyridyl ketone (Matheson Coleman and Bell) (9.15 g, 0.05 mol) dissolved in 50% ethanol–concentrated hydrochloric acid (20 ml) and the reaction was allowed to proceed until no further hydrogen uptake was observed. The reduction required 10 hr and 45.8 ml of sodium borohydride was consumed (theoretical 50.0 ml). The catalyst was removed *via* filtration and the solvent removed *in vacuo*, leaving a tacky oil which was fractionally crystallized according to the method of Crook and McElvain,[5] giving **1**, yield 1.5 g (16%), mp 140–142° (lit.[5] 141–142°), and **2**, yield 1.1 g (12%), mp 170–173° (lit.[5] 171–173°).

**Resolution of *erythro*-Phenyl-2-piperidylcarbinol (1).**—A solution of **1** (2.0 g) and (+)-mandelic acid (Aldrich) (1.2 g) in hot 95% ethanol (8 ml) was allowed to slowly cool to room temperature. The crystals which separated were removed *via* filtration and the mother liquor was set aside as solution A. The crystals were recrystallized twice from 95% ethanol (4 ml), mp 145–146°. A solution of these crystals in water (25 ml) was made basic with 10% potassium hyroxide, extracted with ether (four 20-ml portions), and dried ($MgSO_4$). The ether volume was reduced to about 20 ml and made acidic with gaseous hydrogen chloride. The resultant hydrochloride salt (**1b** HCl) was collected *via* filtration: yield 0.278 g (11.6%), mp 213.5–215°, $[\alpha]^{25}D$ +23.1° (water).

Solution A was taken to dryness and the free base was regenerated as described above. The resultant free base was combined with (−)-mandelic acid (Aldrich) (1.2 g) in hot 95% ethanol (4 ml). The solution was allowed to cool slowly to room temperature and the crystals were removed *via* filtration and recrystallized twice from 95% ethanol (4 ml), mp 144–146°. The free base was regenerated and converted to the hydrochloride salt (**1a** HCl) as described above: yield 0.464 g (22.3%), mp 213.5–215°, $[\alpha]^{25}D$ −22.0°.

**Resolution of *threo*-Phenyl-2-piperidylcarbinol (2).**—A solution of **2** (1.0 g) and (+)-di-*p*-toluoyltartaric acid (Aldrich) (1.3 g) in hot ethanol (2.0 ml) was allowed to come slowly to room temperature. The crystals which formed were removed *via* filtration and the mother liquor was set aside as solution B. The crystals were recrystallized five times from 50% butanol–ethanol, mp 185–186°. The free base was regenerated as above, the ether volume was reduced to about 20 ml, and the free base (**2a**) was precipitated (the hydrochloride salt could not be prepared): yield 0.118 g (11.8%), mp 149–151°, $[\alpha]^{25}D$ −15.9° (ethanol).

Solution B was taken to dryness and the free base was regenerated as above. The resultant solid and (−)-di-*p*-toluoyltartaric acid (Aldrich) (0.845 g) were dissolved in hot ethanol (2.0 ml). The crystals which formed upon cooling slowly to room temperature were removed *via* filtration and recrystallized five times from 50% butanol–ethanol, mp 185–186°. The free base was regenerated as above (**2b**): yield 0.132 g (13.2%), mp 149–151°, $[\alpha]^{25}D$ +16.2° (ethanol).

**Circular Dichroism Measurements.** (1*R*,2*S*)-**Phenyl-2-piperidylcarbinol (1a).**—CD measurements were made at $5.23 \times 10^{-5}$ *M* (ethanol): $[\theta]_{273}$ 0, $[\theta]_{268}$ 757, $[\theta]_{266}$ 252, $[\theta]_{261}$ 821, $[\theta]_{258}$ 442, $[\theta]_{255}$ 537, $[\theta]_{250}$ 284, $[\theta]_{248}$ 252, $[\theta]_{246}$ 158.

(1*S*,2*R*)-**Phenyl-2-piperidylcarbinol (1b).**—CD measurements were made at $5.23 \times 10^{-5}$ *M* (ethanol): $[\theta]_{274}$ 0, $[\theta]_{268}$ −789, $[\theta]_{265}$ −347, $[\theta]_{261}$ −884, $[\theta]_{257}$ −442, $[\theta]_{255}$ −537, $[\theta]_{250}$ −252, $[\theta]_{246}$ −158.

(1*R*,2*R*)-**Phenyl-2-piperidylcarbinol (2a).**—CD measurements were made at $6.55 \times 10^{-5}$ *M* (ethanol): $[\theta]_{274}$ 0, $[\theta]_{268}$ 434, $[\theta]_{265}$ 152, $[\theta]_{261}$ 455, $[\theta]_{257}$ 283, $[\theta]_{256}$ 354, $[\theta]_{251}$ 202, $[\theta]_{250}$ 222, $[\theta]_{245}$ 91, $[\theta]_{243}$ 101.

(7) A. A. Larsen, W. A. Gould, H. R. Roth, William T. Comer, R. H. Uloth, K. W. Dungan, and P. M. Lish, *J. Med. Chem.*, **10**, 462 (1967).

(8) H. C. Brown, K. Sivasankaran, and C. A. Brown, *J. Org. Chem.*, **28**, 214 (1963).

(1*S*,2*S*)-**Phenyl-2-piperidylcarbinol (2b).**—CD measurements were made at $6.55 \times 10^{-5}$ *M* (ethanol): $[\theta]_{274}$ 0, $[\theta]_{268}$ −414, $[\theta]_{265}$ −222, $[\theta]_{261}$ −455, $[\theta]_{258}$ −253, $[\theta]_{255}$ −333, $[\theta]_{251}$ −121, $[\theta]_{249}$ −162, $[\theta]_{242}$ −30, $[\theta]_{240}$ −40.

**Registry No.**—**1a,** 5583-31-3; **1a** HCl, 5583-32-4; **1b,** 5583-35-7; **1b** HCl, 5583-36-8; **2a,** 31002-84-3; **2b,** 30882-77-0.

## Anomalous Diborane Reductions of Benz[c]acridines[1]

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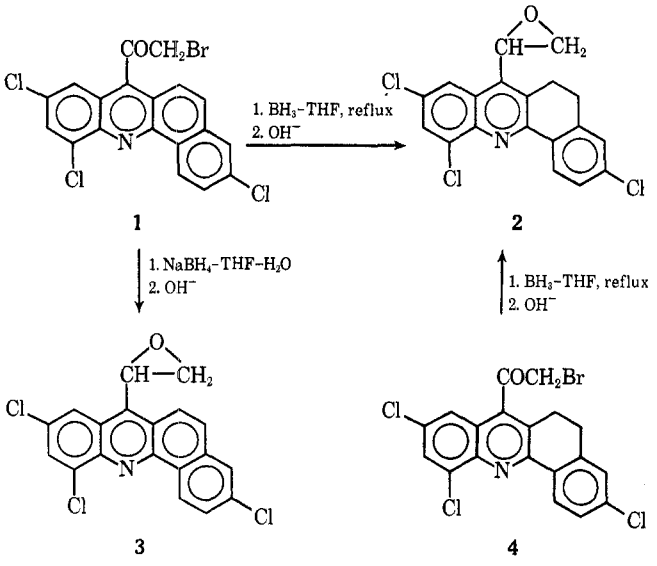
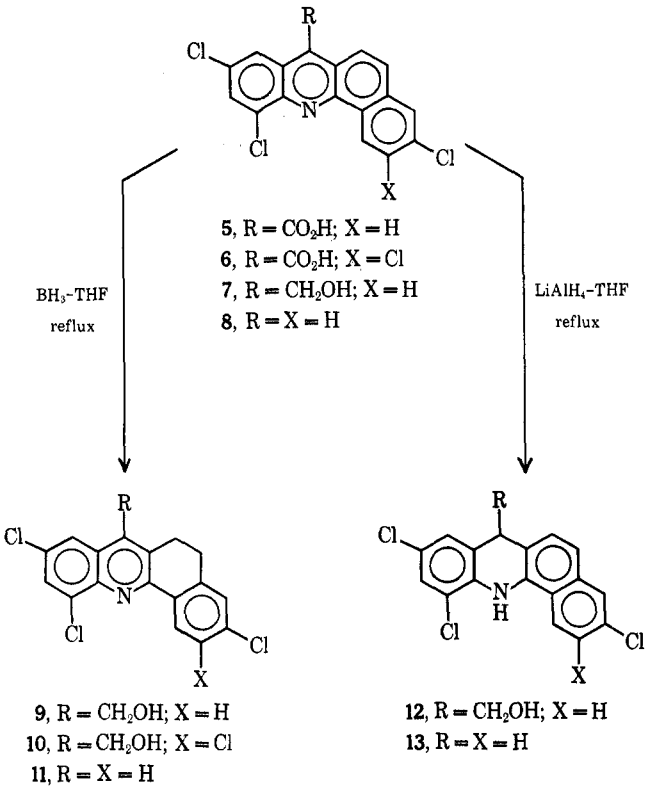
*Received April 13, 1971*

During the course of our work on the synthesis of benz[*c*]acridinemethanols as potential antimalarials,[2] we encountered an unusual diborane reduction of the benz[*c*]acridine ring system. Treatment of 7α-bromoacetyl-3,9,11-trichlorobenz[*c*]acridine (**1**) with diborane in refluxing tetrahydrofuran, followed by an alkaline work-up, unexpectedly yielded the 5,6-dihydro epoxide **2** instead of the desired aromatic product **3**. The identity of **2** was established beyond doubt by comparison with an authentic specimen prepared by reduction of the 5,6-dihydro bromomethyl ketone **4**.[2] Reduction of **1** with sodium borohydride in aqueous tetrahydrofuran at room temperature afforded the aromatic epoxide **3**.[2,3]




When diborane reduction in refluxing tetrahydrofuran was carried out with 3,9,11-trichlorobenz[*c*]acridine-7-carboxylic acid (**5**) or the 2,3,9,11-tetrachloro analog **6** (Scheme I), attack at the 5,6 double bond occurred again, with formation of alcohols **9** and **10**, respectively. Reduction of **5** with diborane at room temperature, on the other hand, afforded the aromatic alcohol **7** only, whereas reduction with lithium aluminum hydride in refluxing tetrahydrofuran yielded the 7,12-dihydro alcohol **12**.

SCHEME I




While it is well known that acridines can undergo reduction of the hetero ring upon treatment with metal hydrides[4] or diborane,[5] there appears to be no precedent in the literature for reduction of a carbocyclic aromatic ring by diborane. We considered the possibility that 5,6-dihydro compounds such as **2**, **9**, and **10** were perhaps being formed *via* reduction to the 7,12-dihydro compounds, which could then undergo rearrangement during work-up. This appeared feasible, at first, because alkaline conditions were used in the work-up of these compounds. However, inasmuch as reduction of **5** to **9** also proceeded with a neutral work-up, we were led to conclude that diborane is able to attack the double bond directly.[6]

Further evidence militating against the intermediacy of 7,12-dihydro compounds in the formation of 5,6-dihydro products was obtained by deliberate prolonged treatment of **12** with alkali. Two products were isolated, 7-methyl-3,9,11-trichlorobenz[*c*]acridine (**14**) and 3,9,11-trichlorobenz[*c*]acridine (**8**); however, no

(1) This investigation was supported in part by Research Contract DA-49-193-MD-3008 from the U. S. Army Medical Research and Development Command, Office of the Surgeon General. This is publication No. 871 from the Army Research Program on Malaria.

(2) A. Rosowsky, M. Chaykovsky, S. A. Yeager, R. A. St. Amand, M. Lin, and E. J. Modest, *J. Heterocycl. Chem.*, in press.

(3) It is of interest to note that reduction of 7α-bromoacetyl-2,3,9,11-tetrachlorobenz[*c*]acridine with sodium borohydride under these same conditions resulted in reduction of the hetero ring to give the 7,12-dihydro epoxide.[2]

(4) A. Campbell and E. N. Morgan, *J. Chem. Soc.*, 1711 (1958).

(5) W. J. Wechter, *J. Org. Chem.*, **28**, 2935 (1963).

(6) During the reduction of **5** to **9** with diborane, thin layer chromatography of samples of the reaction mixture on silica gel (2:2:1 benzene–cyclohexane–acetone) showed the formation of **9** with no evidence for the formation of the faster moving **12**. Apparently, partial hydrolysis of the boron intermediate can occur on the tlc plate. The ease of hydrolysis of the boron intermediates involved in 5,6 reduction by aqueous alkali is probably a consequence of the benzylic nature of the boron–carbon bond in these intermediates. The high reactivity of allylic boron derivatives has been reported; see H. C. Brown and H. Nambu, *J. Amer. Chem. Soc.*, **92**, 1761 (1970).