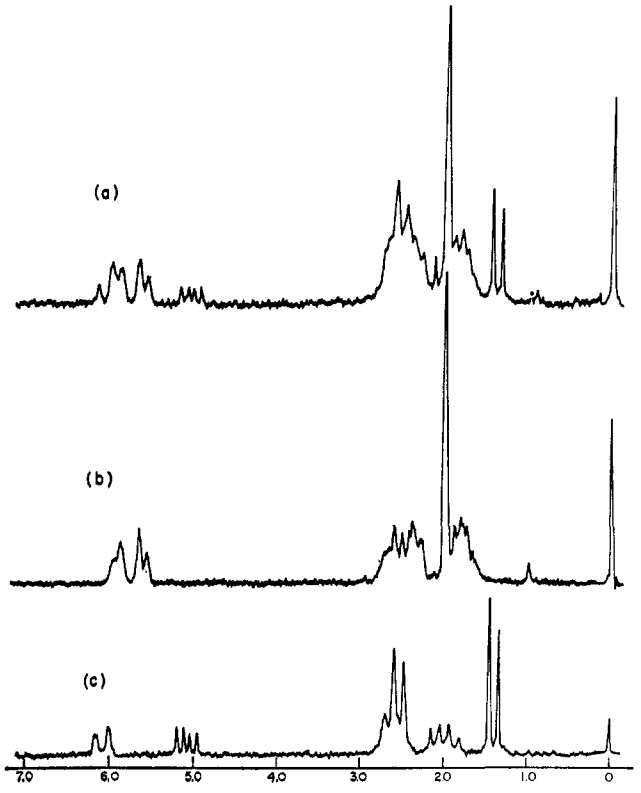


Figure 2. Nmr spectra of (a) a mixture of dihydroazepinones **15d** and **16d**; (b) pure dihydroazepinone **15d**; and (c) pure dihydroazepinone **16d**.

in these isomers, the doublet of the C_6 proton in **15d** (δ 5.62) and the quartet of the C_4 proton in **16d** (δ 5.07) (both protons are absent in the respective isomeric structures) are endowed with unique chemical shifts, and the areas of these multiplets can be quantitatively measured (planimeter). As a further check of the validity of this technique, the total area of these two absorptions was compared to the area of the two overlapping doublets in the δ 5.97–6.07 region attributable to the C_5 proton common to both molecules. The values invariably checked to within $\pm 2\%$.

This mixture of dihydroazepinones was separated by careful chromatography on Woelm neutral alumina (elution with hexane–benzene, 9:1). Dihydroazepinone **15d** displayed the following properties: mp 114–115° (from ethanol); $\nu_{max}^{CCl_4}$ 3200 (N–H), 1675 (amide carbonyl), and 1650 cm^{-1} (C=C); λ_{max}^{EtOH} 253 mμ (ϵ 6200); nmr, see Figure 2.

Anal. Calcd for $C_{10}H_{13}NO$: C, 73.59; H, 8.03; N, 8.58. Found: C, 73.43; H, 8.06; N, 8.46.

The isomeric dihydroazepinone was obtained as a fluffy white solid from ethanol, mp 157–158°; $\nu_{max}^{CCl_4}$ 3200 (N–H), 1675 (amide carbonyl), and 1610 cm^{-1} (C=C); λ_{max}^{EtOH} 253 mμ (ϵ 6200); nmr, see Figure 2.

Anal. Calcd for $C_{10}H_{13}NO$: C, 73.59; H, 8.03; N, 8.58. Found: C, 73.71; H, 7.93; N, 8.71.

Reaction of Sodio-1-methyl-2-naphthoxide with Chloramine. A 100-g (0.63 mole) sample of 1-methyl-2-naphthol[46] was heated under nitrogen to 120°, and 3.45 g (0.15 g-atom) of sodium was added in small pieces. After the sodium was completely consumed, the reaction mixture was heated to 150° and a cold (−70°) ethereal solution containing *ca.* 0.20 mole of chloramine was added in a thin stream at 120–150°. The excess naphthol was removed by distillation [bp 115–120° (1 mm)], and the cooled residue was treated with ether and water. The ether layer was washed with three 25-ml portions of 1 *M* sodium hydroxide and water, dried, and concentrated. The very dark resulting viscous oil (16.5 g) was twice chromatographed on Florisil (elution with hexane–ether, 9:1) to afford 2.0 g of a light brown oil. Molecular distillation afforded 1.1 g (4%) of 1-amino-1-methyl-2(1H)-naphthalenone (**20**) as a pale yellow oil.

Anal. Calcd for $C_{11}H_{11}NO$: C, 76.27; H, 6.40; N, 8.09. Found: C, 76.19; H, 6.56; N, 7.66.

The hydrochloride was prepared by the addition of a slight excess of ethereal hydrogen chloride to an ether solution of **20**. The resulting white crystals melted at 264° dec (from ethanol–ether); ν_{max}^{Nujol} 2900 (NH_3^+) and 1675 cm^{-1} (ketone carbonyl); λ_{max}^{EtOH} 237 (ϵ 23,000) and 311 mμ (ϵ 15,000).

Anal. Calcd for $C_{11}H_{12}ClNO \cdot H_2O$: C, 58.02; H, 6.20; N, 6.15. Found: C, 58.20; H, 6.19; N, 6.10.

Acknowledgment. We wish to thank Dr. J. C. Wollensak, Ethyl Corp., Detroit, Mich., for generous gifts of **8** and **9** and Dr. S. W. Tinsley, Union Carbide Corp., South Charleston, W. Va., for a sample of **13**.

(46) D. Lavil, *J. Chem. Soc.*, 2776 (1955).

The Total Synthesis of *dl*-Crinine[1]

H. W. Whitlock, Jr., and Gary L. Smith

Contribution from the Department of Chemistry, University of Wisconsin. Madison, Wisconsin 53706. *Received January 25, 1967*

Abstract: A stereospecific total synthesis of the alkaloid crinine is described.

Those amaryllidaceae alkaloids possessing the **5**-**10b** ethanophenanthridine skeleton have been the focus of a considerable amount of synthetic work recently.[2-4] Crinine (**1**), the subject of the present communication, has been recently synthesized by Muxfeldt and collaborators.[5] We wish now to report the total synthesis of *dl*-crinine by what we feel is both an economical and stereochemically rational route.

The key reaction in the proposed synthesis was the rearrangement of an N-vinylaziridine to a Δ^1-pyrroline. The desirability of working with rather large functionalized molecules led us to explore the heterolytic rearrangement of N-vinylaziridines possessing carbonyl groups on the 2 position of the vinyl residue as in eq

(1) Preliminary accounts of portions of this work have appeared: H. W. Whitlock and G. L. Smith, *Tetrahedron Letters*, 1389 (1965); G. L. Smith and H. W. Whitlock, *ibid.*, 2711 (1966).

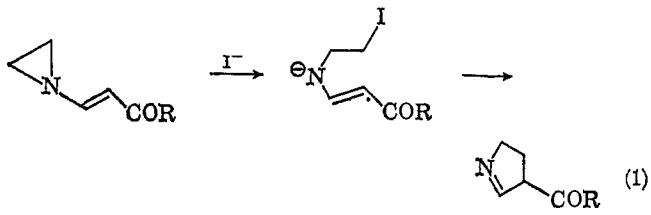
(2) J. B. Hendrickson, C. Foote, and N. Yoshimura, *Chem. Commun.*, 165 (1965).

(3) S. Uyeo, H. Irie, A. Yoshitake, and A. Ito, *Chem. Pharm. Bull.* (Tokyo), **13**, 427 (1965).

(4) H. Irie, S. Uyeo, and A. Yoshitake, *Chem. Commun.*, 635 (1966).

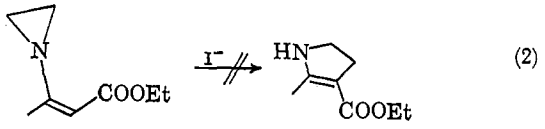
(5) H. Muxfeldt, R. S. Schneider, and J. B. Mooberry, *J. Am. Chem. Soc.*, **88**, 3670 (1966).

1. This reaction has, of course, ample analogy in the work of Heine and others on the iodide ion catalyzed rearrangement of N-acylaziridines.[6]



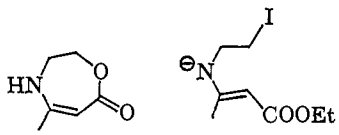
(1)

Several models of the desired rearrangement were investigated. The first to be studied was the rearrangement of ethyl β-aziridinocrotonate to ethyl 2-methyl-Δ²-pyrroline-3-carboxylate (eq 2). This reaction was not



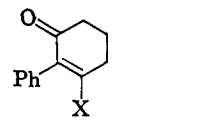
(2)

successfully carried out. We were able to isolate modest yields of ethyl β-aminocrotonate, ethyl β-(2-iodoethylamino)crotonate, and a basic substance tentatively formulated as the seven-membered ring lactone **2**. The principal problem here appeared to be protonation of the presumed intermediate ion **3** followed by dehydrohalogenation and general decomposition.

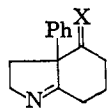


2 **3**

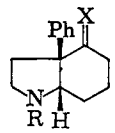
The second model to be studied was the rearrangement of 2-phenyl-3-(1-aziridino)-Δ²-cyclohexenone (**4c**) to 3a-phenyl-Δ[1,7a]-hexahydroindole (**5a**). Enamine **4c** was prepared by a sequence of reactions (**4a** → **4b** →



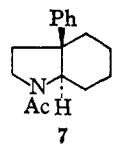
4a, X = OH
b, X = Cl
c, X = N(CH₂)₂
d, X = NH₂
e, X = NHCH₂CH₂I



5a, X = O
b, X = H₂



6a, R = H; X = O
b, R = Ac; X = O
c, R = Ac; X = 
d, R = Ac; X = H₂



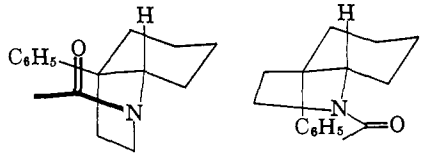
7

4c) starting from 2-phenyl-1,3-cyclohexanedione.[7] This somewhat indirect procedure was necessary, as attempted direct reaction of aziridine and **4a** led to polymerization of the amine; reaction of **4a** with pyrrolidine gave a mixture of the desired enamine and the ketoamide resulting from cleavage of the diketone. Enamine **4c** (λ_{max} 293 mμ) exhibited as expected a hypsochromic shift in its ultraviolet spectrum compared to that of the corresponding pyrrolidine enamine (λ_{max} 316 mμ). The rearrangement of **4c** was achieved by heating with sodium iodide. When carried out in refluxing dimethoxyethane, a mixture of the desired rearrangement product and **4d**, presumably arising from protonation and dehydrohalogenation of **4e**, was obtained. Rigorous drying of the solvent did not improve matters. The best procedure for affecting the rearrangement was ultimately found to be one wherein a mixture of **4c** and finely ground sodium iodide was placed in a flask and heated to 120° while nitrogen was bubbled slowly through the melt. Removal of the sublimate from an attached condenser gave a 37% yield of **5a**. The structure assigned to **5a** follows from (a) instrumental and analytical methods, and (b) structural correlation with the previously known **5b**. The mass spectrum and elemental analysis of **5a** indicated the expected formula $C_{14}H_{15}NO$. The infrared and ultraviolet spectra showed that the conjugated carbonyl had been replaced by a cyclohexanone carbonyl (5.85 μ) and that the chromophore of **4c** [λ_{max} 293 mμ (ε 15,000)] had been destroyed [λ_{max} 284 (424)]. The structural correlation of **5a** and **b** was achieved in the following manner. Catalytic hydrogenation of **5a** gave a single amino ketone **6a**, mp 64.5–66.5°. This was subjected to sequential acetylation, ethanedithiol ketalization, and Raney nickel desulfurization (**6a** → **6b** → **6c** → **6d**) to afford the acetamide **6d**, an oil homogeneous by vapor-phase chromatography. Barring epimerization during the desulfurization, the stereochemical purity of **6d** was guaranteed by the isolation and purification of the crystalline intermediates **6b** and **c**.

The amine **5b** was prepared by the procedure of Bachman and Fornefeld.[8] Catalytic hydrogenation of **5b** followed by acetylation of the resulting amine gave **6d** whose identity with the sample prepared from **5a** was established by infrared, mass spectral, and vpc retention time comparisons. On the other hand, reduction of **5b** with sodium borohydride or lithium aluminum hydride gave, after acetylation, a 6:4 mixture of **6d** and an isomer assigned the structure **7**. Spectral data leave no doubt that **6d** and **7** are isomers of the same over-all structure. Assignment of a *cis* ring fusion to the major product from catalytic hydrogenation of **5b** follows from two lines of reasoning. First, there is ample precedent[9] for the predominant formation of a *cis* ring fusion in the catalytic hydrogenation of angularly substituted Δ[1,7a]-tetrahydroindanes. The precedent is somewhat tenuous, however, since one is comparing an angular phenyl with what is normally an angular methyl substituent, and it is not immediately clear what, when confronted with a catalyst surface, the relative sizes of methyl and phenyl groups are. Second, the nmr spectra of **6d** and **7** can be interpreted simply in terms of the assigned stereochemistry. In the spectrum of **6d** the hydrogen at C-7a is strongly deshielded (δ 4.60), appearing as a multiplet shifted

(6) H. W. Heine, *J. Am. Chem. Soc.*, **85**, 2743 (1963).
(7) H. Born, R. Pappo, and J. Szmuszkovicz, *J. Chem. Soc.*, 1779 (1953).
(8) W. E. Bachman and E. J. Fornefeld, *J. Am. Chem. Soc.*, **73**, 51 (1951).
(9) A. F. St. Andre, H. B. McPhillamy, J. A. Nelson, A. C. Shabica, and C. R. Scholz, *ibid.*, **74**, 5506 (1952).

downfield from the general envelope of methylene absorptions, and there are *two* signals in a roughly 1:1 ratio for the methyls of the N-acetyl group. Heating



6d 7

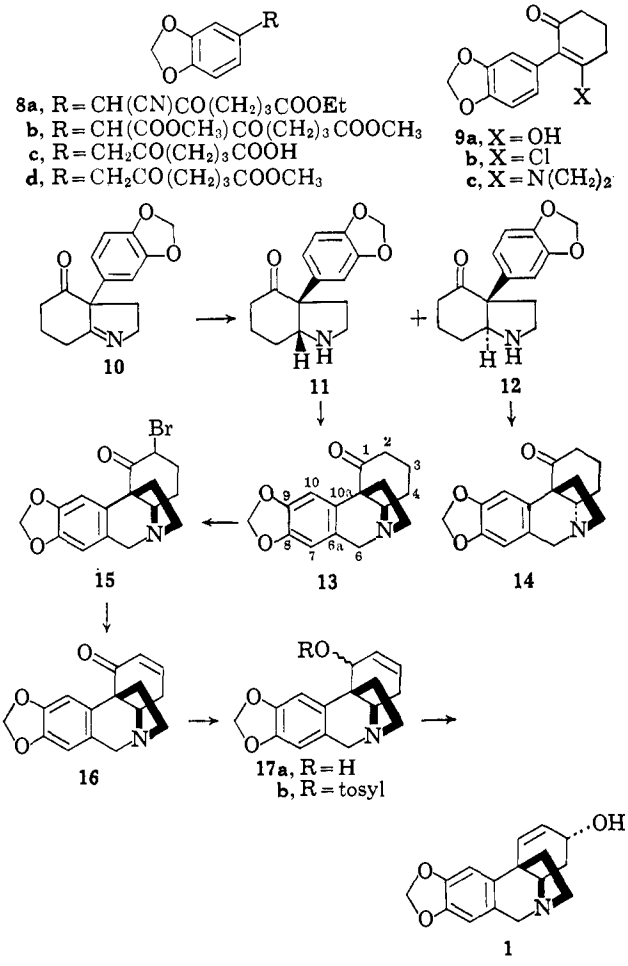
the sample to 100° led to collapse of these two signals to a single peak of intermediate chemical shift. The presence of two approximately equal energy conformers of the amide implies an equal congestion (or lack thereof) about both sides of the amide nitrogen. This condition is best satisfied by the conformation of **6d** shown, wherein the envelope conformation of the five-membered ring has C-7 as an "axial" substituent and the hydrogen at C-7a equatorial, being deshielded[10] by the amide carbonyl. The nmr spectrum of **7** is unexceptional; the C-7a hydrogen is shifted upfield (δ <3.75) into the region of general absorption of the skeletal hydrogens and only a single acetyl methyl is seen. Parenthetically one might add that further evidence for production of a *cis* ring fusion in the catalytic hydrogenation of **5a** and **b** is the fact that reduction of the 3,4-methylenedioxyphenyl analog of **5b** led ultimately to *dl*-crinane[11] whose stereochemistry (derived from a *cis* 6/5 ring fusion) has never been seriously in doubt.[12]

We feel that the above considerations establish two points: rearrangement of N-vinylaziridines to hexahydroindoles is a feasible reaction; and catalytic hydrogenation of functionalized 3a-aryl-α[1,7a]-hexahydroindoles produces predominantly if not exclusively the *cis*-octahydroindole.

dl-Crinine

The actual synthesis is as outlined (Scheme I). The preparation of 2-(3,4-methylenedioxyphenyl)-1,3-cyclohexanedione was patterned after the procedure for making 2-phenyl-1,3-cyclohexanedione. Ethoxide-catalyzed reaction of piperonyl cyanide with diethyl glutarate afforded ethyl 6-cyano-5-oxo-6-(3,4-methylenedioxyphenyl)hexanoate (**8a**). Since direct hydrolysis of **8a** to **c** by refluxing with hydrochloric acid led to extensive hydrolysis of the methylenedioxy moiety, a two-step procedure was used wherein **8a** was converted to **8b** by reaction with methanol and hydrogen chloride, and **8b** was hydrolyzed and decarboxylated to **8c** by refluxing with acetic and hydrochloric acids. Esterification[13] of **8c** produced **8d**[14] which was cyclized by heating with sodium methoxide in benzene[15] to **9a**. The conversion of **9a** to the enamine **9c** was as in the phenyl series (**9a** → **9b** → **9c**). Carrying out the isomerization of **9c** next as was done for the phenyl series afforded

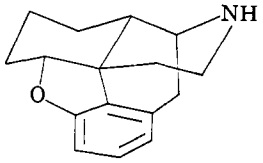
Scheme I

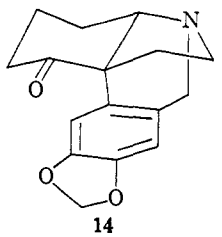


only poor yields of the hexahydroindole rearrangement product, presumably due to its decreased volatility. However, carrying out the rearrangement in diethylene glycol dimethyl ether at 145° for 2.5 hr gave a 55% yield of **10**, mp 119.5–121°. Catalytic hydrogenation of **10** using platinum oxide in acidic ethanol gave two isomeric $C_{15}H_{17}O_3N$ amines. The major product, isolated in 76% yield, was assigned the structure **11** which possesses a *cis* ring fusion, while the minor isomer, isolated in 5.5% yield, was assigned structure **12** possessing a *trans* ring fusion. Both amino ketones were characterized as their N-acetyl derivatives; assignment of the *cis* ring fusion to the isomer isolated in 76% yield follows from the considerations delineated above. Entry of the major isomer **11** into a Pictet–Spengler cyclization under carefully defined conditions afforded a high yield of 1-oxocrinane (**13**) which was shown to be *dl*-dehydrodihydrodesmethoxybuphanamine by direct comparison with a sample of this optically active degradation product of buphanamine.[16] Similar reaction of the minor product **12** afforded the isomeric tetracyclic ketone **14**. We were very pleased to prepare **14**, since it bears a very interesting relationship to the morphine alkaloids and, in fact, represents the stereochemistry once proposed for the amaryllidaceae alkaloids.[17] Space filling models of morphinane and **14** are almost identical, even to the spatial position of the nitrogens. It is unfortunate that the hydrogena-

(10) L. M. Jackman and R. H. Wiley, *J. Chem. Soc.*, 2886 (1960).
(11) W. C. Wildman, *J. Am. Chem. Soc.*, 80, 2567 (1958).
(12) W. C. Wildman, "The Alkaloids," Vol. VI, R. H. F. Manske, Ed., Academic Press Inc., New York, N. Y., 1960.
(13) R. O. Clinton and S. C. Laskowski, *J. Am. Chem. Soc.*, 70, 3135 (1948).
(14) The hydrolysis of 8d to 8c was very facile, presumably due to neighboring-group participation of the ketone hydrate.
(15) Precipitation of the sodium salt of **9a** was apparently an important feature in driving the reaction to completion, as use of methanol or ethers as solvents for this reaction led to very poor yields of the diketone.
(16) H. M. Fales and W. C. Wildman, *J. Org. Chem.*, 26, 881 (1961).
(17) N. Sugimoto and H. Kugitu, *Chem. Pharm. Bull.* (Tokyo), 5, 378 (1957).

tion of **10** was not subject to sufficient stereochemical control to allow the formation of **12** to become predominant, as structures related to **14** should have interesting physiological properties.





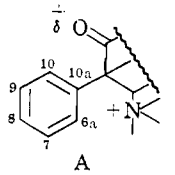
14

It is worth mentioning that, as in the case of ketones **6d** and **7d**, nmr spectrometry also afforded clear confirmation of the stereochemistry assigned to **13** and **14**. Each spectrum exhibited an AB quartet assignable to the benzyl methylene hydrogens at C-6 and a somewhat broadened singlet at δ 6.4 (**13**) and 6.5 (**14**) due to the aromatic hydrogen at C-7 weakly spin coupled to the benzylic hydrogens.[18] The sharp singlet assignable to the hydrogen at C-10, however, appeared at δ 7.7 in **13** but at δ 6.25 in **14**. This presumably represents another[10] example of the ability of a carbonyl group to strongly deshield a hydrogen which lies in the plane and to shield one which lies above the plane defined by the four atoms associated with the carbonyl group.

Conversion of **13** to *dl*-crinine proceeded by necessity in a classical manner. Numerous attempts were initially made at the direct introduction of a double bond conjugated with the carbonyl group of **13**. Direct dehydrogenation of **13** by reaction with 2,3-dichloro-5,6-dicyanoquinone (DDQ) afforded either starting material or decomposition products. Reaction of **13** with potassium triphenylmethyl afforded the enolate ion, as was evidenced by its reaction with acetic anhydride to produce the enol acetate, but reaction of the enolate ion and the enol acetate with DDQ afforded only recovered starting materials or decomposition products. Dehydrogenation of an enamine of **13** was precluded by our inability to prepare the morpholine enamine under a variety of conditions. These failures are readily understandable when one considers that the carbonyl group of **13** is relatively hindered, that **16** is probably more susceptible to continued oxidation (*via* enolization or elimination of the δ amino function) than is **13**, and that the bridgehead nitrogen represents what is probably a preferred but unfruitful site of electrophilic attack on reaction with quinones such as DDQ. Indeed, reaction of **13** with DDQ in benzene precipitated a red saltlike substance which regenerated **13** on trituration with base. In contrast with the impunity with which **13** greeted the above reagents, reaction of the hydrochloride of **13** with bromine in acetic acid gave in high yield a bromo ketone which could be directly dehydrobrominated in 77% yield by lithium chloride in refluxing dimethylformamide to afford the α,β-unsaturated ketone **16**.

It is interesting to consider the possible factors involved in the selective attack of bromine on the ketone instead of the relatively electron-rich methylenedioxydialkylbenzene moiety. Now **13** must exist almost entirely as the ammonium cation under the bromination reaction conditions. Two possibilities for explaining the observed results then arise: (1) the greater proximity of the positively charged nitrogen to the center of the aromatic ring (~3.6 A) than to the carbonyl oxygen (~4.6 A) results in a decrease of the susceptibility of the former toward electrophilic attack which is not matched by a reduced basicity (and hence reduced rate of enol formation) of the ketone carbonyl; (2) an inductive effect of the positively charged nitrogen and the electronegative oxygen on the proximal ring carbons leads to a substantial increase in the localization energy (L_R^+) for electrophilic attack on the ring.

Hückel molecular orbital (HMO) calculations were performed to test the latter hypothesis. The model chosen was that employing an inductive parameter,[19,20] wherein the nitrogen and oxygen, which are approximately equally placed with respect to the aromatic ring, effect the Coulomb integrals of the ring carbons (compound A) as follows. Case 1 which considers the



A

effect of both nitrogen and oxygen: $\alpha_7 = \alpha_8 = \alpha_9 = \alpha$; $\alpha_{10} = \alpha_{10a} = \alpha + 0.1\beta$; $\alpha_{6a} = \alpha + 0.2\beta$. Case 2 which considers the effect of nitrogen only: $\alpha_7 = \alpha_8 = \alpha_9 = \alpha_{10} = \alpha_{10a} = \alpha$; $\alpha_{6a} = \alpha + 0.2\beta$. Localization energies were also calculated employing the ω technique,[21] using the rapidly converging method of Ettinger[22] in writing the program. In order to compensate for the downward shift of the center of gravity of the eigenvalues that is seen when one employs the ω technique on cations, the center of gravity was assigned the value zero and the other values were adjusted accordingly. The resulting localization energies are presented in Table I. It is seen that the calculations more or less bear out the qualitative arguments above in that they predict a general increase in L_R^+ for attack at C-7 with increase of electronegativity of the ring carbons, and hence a decrease in the rate of electrophilic substitution reactions. Numerical arguments notwithstanding, however, the bromination of **13** represents a remarkably clean and selective reaction.

Table I. Localization Energies, in Units of $|\beta|$, for Attack on a Benzene Ring[a]

	HMO	ω
L_7^+, case 1	2.635	2.624
L_{10}^+, case 1	2.671	2.603
L_7^+, case 2	2.598	2.617
L_{10}^+, case 2	2.536	2.600
L^+, benzene	2.536	2.6106

[a] Numbering as in compound A. Case 1 and Case 2 as in text.

The conversion of **16** to *dl*-crinine (**1**) was designed on the basis of the following arguments. It is now well known from the work of Goering[23] that cyclohexenyl

(18) H. Rottendorf and S. Sternhell, *Tetrahedron Letters*, 1289 (1963).

(19) M. J. S. Dewar, *J. Am. Chem. Soc.*, 74, 3350 (1952).

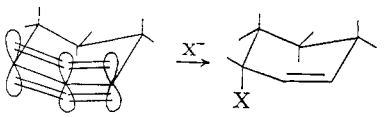
(20) A. Streitwieser, Jr., "Molecular Orbital Theory for Organic Chemists," John Wiley and Sons, Inc., New York, N. Y., 1961, pp 350–356.

(21) Reference 19, p 115.

(22) R. Ettinger, *Tetrahedron*, **20**, 1579 (1964).

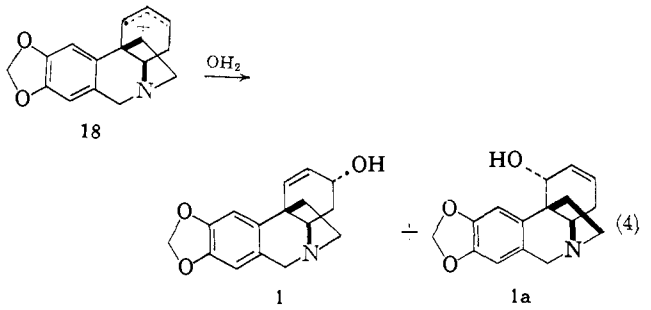
(23) H. L. Goering, *Rec. Chem. Progr.*, **21**, 109 (1960).

cations exhibit a pronounced tendency to pick up nucleophiles in a pseudo-axial manner (eq 3). Since



(3)

the uppermost six-membered ring of crinine is sterically unexceptional one can confidently predict that collapse of cation **18** will be as in eq 4 and that, of the two possi-



(4)

bilities, steric factors should clearly favor formation of **1** over **1a**. Thus generation of **18** under conditions so that it will be irreversibly captured by water should *stereospecifically* produce *dl*-crinine, if crinine indeed possesses structure **1**. In the event, this is exactly what happened. Reduction of **16** afforded an allylic alcohol which was allowed to react with butyllithium in tetrahydrofuran. The resulting solution of the lithium salt of **17a** was injected into a solution of an excess of *p*-toluenesulfonyl chloride in tetrahydrofuran and the resulting tosylate **17b** was solvolyzed in aqueous sodium bicarbonate. There was isolated a mixture of nonpolar materials (presumably elimination products) and a *single* alcohol **1** whose identity was established by direct comparison with both natural and synthetic crinine.

Experimental Section[24]

Ethyl β-(1-Aziridino)crotonate. A mixture of 80 g (0.55 mole) of ethyl β-chlorocrotonate, 108 g (1 mole) of triethylamine, and 92 g (2.14 moles) of ethylenimine in 600 ml of anhydrous ether was stirred at room temperature under a nitrogen atmosphere for 96 hr. The reaction mixture was filtered, and the filtrate was evaporated and distilled twice to afford 65 g (77% yield) of ethyl β-(1-aziridino)crotonate, bp 47–49° (0.5 mm); infrared: $\lambda_{max}^{CHCl_3}$ 5.89 (vs) and 6.16 μ (vs); ultraviolet: $\lambda_{max}^{Et_2O}$ 257 mμ (ε 1.2×10^4); nmr ($CDCl_3$): δ 5.07 (1 H, singlet), 4.0 (2 H, quartet, J = 7 cps), 2.21 (3 H, singlet), 1.88 (4 H, singlet), and 1.21 (3 H, triplet, J = 7 cps).

Anal. Calcd for $C_8H_{13}NO_2$: C, 61.91; H, 8.44; N, 8.03. Found: C, 61.89; H, 8.46; N, 9.06.

Rearrangement of Ethyl β-(1-Aziridino)crotonate. A mixture of 339 mg (2.95 mmoles) of the above enamine and 401 mg of anhydrous sodium iodide in 5 ml of anhydrous dimethoxyethane was heated at 180° in a sealed tube for 5 hr. Working-up afforded 350 mg of crude product which, on chromatography on preparative thin layer plates (alumina), afforded the following products: ethyl β-(1-aziridino)crotonate [27.5 mg, 8% recovery, R_f (benzene) 0.74]; ethyl β-aminocrotonate [17.4 mg, 6.2% yield, R_f (benzene) 0.52, identified by infrared comparison with an authentic sample]; ethyl acetoacetate (40 mg, 14.1% yield, R_f 0.61, identified by infrared comparison with an authentic sample); ethyl β-(2-iodoethylamine)crotonate [40 mg, 6% yield, R_f (benzene) 0.67, mp 52–55° (hexane); infrared: $\lambda_{max}^{CHCl_3}$ 6.02 (vs) and 6.19 μ (vs); ultraviolet: λ_{max}^{EtOH} 288 mμ; nmr ($CDCl_3$): δ 4.38 (1 H, singlet), 4.00 (2 H, quartet, J = 7 cps), 3.51 (2 H, triplet, J = 6 cps), 3.23 (2 H, triplet, J = 7 cps), 1.91 (3 H, singlet), and 1.20 (3 H, triplet, J = 7 cps); mass spectrum: *m/e* 156 (base, P–1), *m/e* 127 (50% of base). *Anal.* Calcd for $C_8H_{14}NO_2I$: C, 33.94; H, 4.98; N, 4.95. Found: C, 34.10; H, 4.90; N, 5.06]; rearrangement product **2** [11 mg, 4% yield, R_f (1% methanol in chloroform) 0.38, mp 130.5–132° (benzene); infrared: $\lambda_{max}^{CHCl_3}$ 6.00 (vs) and 6.20 μ (vs); ultraviolet: λ_{max}^{EtOH} 284 mμ (ε 2.56×10^4); nmr ($CDCl_3$): δ 4.46 (1 H, doublet, J = 2 cps), 4.32 (2 H, triplet, J = 4 cps), 3.58 (2 H, quartet, J = 4 cps), and 1.98 (3 H, singlet); mass spectrum: *m/e* 127 (parent ion). *Anal.* Calcd for $C_6H_9NO_2$: C, 56.68; H, 7.13; N, 11.02. Found: C, 56.79; H, 7.17; N, 10.89]; and the remainder of the reaction mixture could not be identified.

2-Phenyl-1,3-cyclohexanedione was prepared in 18% over-all yield from phenylacetonitrile by the general procedure of Born, Pappo, and Szmuszkovicz.[7]

2-Phenyl-3-chloro-Δ²-cyclohexenone (4c). A solution of 65 g (0.35 mole) of 2-phenyl-1,3-cyclohexanedione, 180 g (1.31 moles) of phosphorus trichloride, and 1.8 l. of chloroform was allowed to reflux for 3 hr. The solvent was removed by distillation, and the residue was added with vigorous stirring to 300 ml of ice water. After standing for 30 min, the reaction mixture was extracted with chloroform, and the combined chloroform extracts were washed three times with 100-ml portions of 5% sodium carbonate solution, washed with water, dried over anhydrous sodium sulfate, filtered, and evaporated. Recrystallization of the residue from hexane afforded 39 g (56% yield) of the enol chloride (**4c**), mp 92–93.5°; infrared: $\lambda_{max}^{CHCl_3}$ 5.92 μ (vs); ultraviolet: λ_{max}^{EtOH} 229 mμ (ε 1.4×10^4); nmr ($CDCl_3$): δ 7.10 (5 H, multiplet), 2.80 (2 H, triplet, J = 6 cps), 2.44 (2 H, triplet, J = 6 cps), and 2.0 (2 H, multiplet).

Anal. Calcd for $C_{12}H_{11}ClO$: C, 69.54; H, 5.36; Cl, 17.16. Found: C, 69.54; H, 5.41; Cl, 17.31.

N-(2-Phenyl-3-oxocyclohexenyl)aziridine (4b). A solution of 58.0 g (0.284 mole) of **4c**, 100.0 g (2.0 moles) of redistilled ethylenimine, 100 g of triethylamine (1.0 mole), and 1 l. of anhydrous ether was allowed to stir for 8 days at room temperature under a nitrogen atmosphere. The reaction mixture was then filtered and the filtrate evaporated. Recrystallization of the residue from hexane afforded 48.5 g (80% yield) of the enamine **4c**, mp 102–104°; infrared: $\lambda_{max}^{chloroform}$ 6.10 μ (vs); ultraviolet: λ_{max}^{EtOH} 293 mμ (ε 1.5×10^4); nmr: δ 7.19 (5 H, multiplet), 2.6–1.8 (6 H, complex multiplet), and 1.68 (4 H, singlet).

Anal. Calcd for $C_{14}H_{15}NO$: C, 78.84; H, 7.19; N, 6.57; mol wt, 213. Found: C, 78.93; H, 7.19; N, 6.58; mol wt, 213 (mass spectroscopy).

3a-Phenyl-4-oxo-Δ¹,⁷ᵃ-hexahydroindole (5a). A mixture of 1.0 g (4.7 mmoles) of enamine **4c** and 250 mg of dry sodium iodide was heated at 110° under a constant flow of nitrogn for 24 hr. The crystalline product which had sublimed into the cold trap was collected to afford 370 mg (37% yield) of hexahydroindole **5a**, mp 67–68.5°; infrared: $\lambda_{max}^{CCl_4}$ 5.85 (vs) and 6.09 μ (s); ultraviolet: $\lambda_{max}^{CCl_4}$ 284 mμ (ε 425); nmr: δ 7.10 (5 H, multiplet), 3.70 (2 H, multiplet), and 1.5–3.0 (8 H, multiplet).

Anal. Calcd for $C_{14}H_{15}NO$: C, 78.84; H, 7.19; N, 6.57. Found: C, 78.91; H, 7.14; N, 6.50.

Refluxing of a mixture of 250 mg (1.2 mmoles) of **4c** and 35 mg of sodium iodide in 15 ml of dimethoxyethane for 80 hr, gave, on chromatography on silica gel, 64 mg (26% yield) of **5a** together with a 14% yield of starting material and a 9% yield of 2-phenyl-3-amino-Δ²-cyclohexenone, identified by comparison of their infrared spectra with those of authentic samples.

***cis*-3a-Phenyl-4-oxooctahydroindole (6a).** A solution of 139 mg (0.65 mmole) of **5a** in 10 ml of concentrated hydrochloric acid was reduced by stirring with 50 mg of 30% palladium on charcoal under a hydrogen atmosphere for 30 min. The mixture was filtered; the catalyst was washed with ethanol, and the combined filtrates were evaporated. The residue was dissolved in 20 ml of water; solid sodium carbonate was added to it until basic, and the solution was extracted with chloroform. The chloroform extracts were dried over anhydrous sodium sulfate, filtered, and evaporated to afford 126 mg of residue. Crystallization of this from hexane–ethyl acetate afforded 50 mg (35% yield) of **6a**, mp 64.5–66.5°; infrared: $\lambda_{max}^{CCl_4}$ 5.84 μ (vs); nmr: δ 7.30 (5 H, singlet), 4.10 (1 H, multiplet), 3.10 (3 H, multiplet), and 1.5–2.5 (8 H, multiplet).

Anal. Calcd for $C_{14}H_{17}NO$: C, 78.10; H, 7.96; N, 6.51; mol wt, 215. Found: C, 78.10; H, 7.74; N, 6.42; mol wt, 215 (mass spectroscopy).

(24) Melting points were determined on a calibrated hot stage and are not corrected. Nmr spectra were determined in deuteriochloroform solution. Mass spectra were determined at 70 v ionizing potential on a CEC-103C instrument with a heated glass inlet held at 200°.

N-Acetyl-3a-phenyl-4-oxo-*cis*-octahydroindole (6b). Reaction of 171 mg of **6a** with acetic anhydride gave, after chromatography on alumina and recrystallization from hexane–ethyl acetate, 140 mg (69% yield) of **6b**, mp 104.5–106.5°; infrared: $\lambda_{max}^{CCl_4}$ 5.85 (s) and 6.11 μ (vs); nmr: δ 7.30 (5 H, singlet), 4.86 (1 H, multiplet), 3.42 (2 H, triplet, J = 6 cps), 1.6–3.0 (8 H, complex), and 2.06 (3 H, singlet).

Anal. Calcd for $C_{16}H_{19}NO_2$: C, 74.68; H, 7.44; N, 5.49; mol wt, 257. Found: C, 74.85; H, 7.32; N, 5.46; mol wt, 257 (mass spectroscopy).

N-Acetyl-3a-phenyl-4-oxo-*cis*-octahydroindole Ethanedithiol Ketal (6c). A mixture of 80 mg (0.24 mmole) of **6b**, 200 mg (2.1 mmoles) of ethanedithiol, and 0.2 ml of boron trifluoride etherate was heated at 35° for 12 hr. The reaction mixture was partitioned between chloroform and dilute sodium hydroxide solution, and the chloroform extracts were washed with water, dried over anhydrous sodium sulfate, and evaporated. Chromatography of the residue (alumina, 1:10 chloroform–benzene) afforded after recrystallization from hexane, 51 mg (49% yield) of **6c**, mp 107–110°; infrared: $\lambda_{max}^{CCl_4}$ 6.14 μ (vs); nmr: δ 7.75 (2 H, multiplet), 7.22 (3 H, multiplet), 5.00 (1 H, multiplet), 1.3–3.5 (14 H, broad), and 1.71 (3 H, singlet).

Anal. Calcd for $C_{18}H_{23}NOS_2$: C, 64.82; H, 6.95; N, 4.20; S, 19.23; mol wt, 333. Found: C, 65.00; H, 7.04; N, 4.11; S, 19.14; mol wt, 333 (mass spectroscopy).

N-Acetyl-3a-phenyl-*cis*-octahydroindole (6d). I. A mixture of 93 mg (0.28 mmole) of **6c** and 2 g of Raney nickel in 30 ml of absolute ethanol was heated under reflux with stirring for 1.5 hr. The mixture was filtered, and the filtrate was evaporated to afford 98 mg of residue. Distillation of this residue at 80° (0.05 mm) afforded 68 mg of **6d**, an oil; infrared: $\lambda_{max}^{CHCl_3}$ 6.16 μ; nmr: δ 7.30 (5 H, broad, phenyl hydrogens), 4.60 (1 H, broad, H at 7a), 1.0–4.0 (12 H, broad), and 1.18 and 1.68 (3 H, two singlets, collapsed to singlet at δ 1.90 at 100°, acetyl CH_3); mass spectrum: *m/e* 243 (parent, base), and *m/e* 215 (22% of base, P–C_2H_4).

Anal. Calcd for $C_{16}H_{21}NO$: C, 78.97; H, 8.70; N, 5.76. Found: C, 77.50; H, 8.39; N, 5.42.

II. Reduction of 155 mg of **5b** in 10 ml of ethanol containing 0.08 ml of concentrated hydrochloric acid and 50 mg of 30% palladium on charcoal gave, after acetylation and distillation of the crude acetylated product, 88 mg (50% yield) of **6d**. Comparison of mass spectral cracking patterns, infrared spectra (chloroform), and vpc retention times of the two samples showed them to be identical.

III. A 200-mg sample of **5b** was reduced at 0° in ethanol solution by sodium borohydride. Acetylation of the crude product gave a 7:3 mixture of *cis* and *trans* amides **6d** and **7** as determined by vpc. Both isomers were trapped from the vpc column and shown by repeated vpc to be free of the isomeric amide. The nmr spectrum ($CDCl_3$) of the *trans* isomer **7** showed absorptions at δ 7.32 (5 H, multiplet, phenyl H), 2.07 (3 H, singlet, methyl), and a broad envelope stretching from 3.75 to 1.20 (13 H). The mass spectra of **6d** and **7** were very similar but showed distinct differences in the intensity of various fragmentation peaks. Their infrared spectra were distinctly different in the fingerprint region.

Anal. of **7**. Calcd for $C_{16}H_{21}NO$: C, 78.86; H, 8.70. Found: C, 76.91; H, 8.67.

Piperonyl cyanide was prepared by the general procedure of Bills and Noller.[25]

Ethyl 6-Cyano-5-oxo-6-(3,4-methylenedioxyphenyl)hexanoate (8a). A mixture of 133 g (0.60 mole) of ethyl glutarate and 86.0 g (0.54 mole) of piperonyl cyanide was added dropwise over 0.5 hr to a stirred solution of 14 g (0.6 g-atom) of sodium in 250 ml of absolute ethanol. The reaction mixture was heated under reflux for 4 hr and then acidified by cautious addition of acetic acid. The reaction mixture was poured into a large volume of water, and the aqueous layer was extracted with chloroform. The combined chloroform extracts were washed with water, dried over anhydrous sodium sulfate, and evaporated. Distillation of the residue gave 162 g (70% yield) of **8a**, bp 215–220° (0.5 mm); infrared: $\lambda_{max}^{CHCl_3}$ 5.80 (s), 4.43 (w), and 4.50 μ (w).

Anal. Calcd for $C_{16}H_{17}NO_5$: C, 63.36; H, 5.65; N, 4.62. Found: C, 63.13; H, 5.45; N, 4.65.

In later runs the crude condensation product was used directly for conversion to methyl 5-oxo-6-(3,4-methylenedioxyphenyl) hexanoate.

Methyl 5-Oxo-6-(3,4-methylenedroxyphenyl)hexanoate (8d). A solution of 160 g of crude **8a** in 1.3 l. of hydrogen chloride saturated methanol was heated under reflux for 6 hr. The reaction mixture was concentrated to 600 ml, and 600 ml of water was added. The aqueous layer was extracted with chloroform, and the combined chloroform extracts were washed with water, dried over anhydrous sodium sulfate, and evaporated to afford a residue of 170 g of crude **8b**. This residue was dissolved in a mixture of 300 ml of 10% hydrochloric acid and 200 ml of water in 1 l. of acetic acid, and the resulting solution was heated under reflux for 15 hr. The solvent was removed *in vacuo*, and the residue was dissolved in chloroform. The chloroform solution was washed with water, dried over anhydrous sodium sulfate, and evaporated to afford a residue of 130 g of crude **8c**. This residue was esterified by the procedure of Clinton and Laskowski[13] to afford 49 g (35% yield from piperonyl cyanide) of **8d**, bp 182–185° (0.3 mm).

Anal. Calcd for $C_{14}H_{16}O_5$: C, 63.63; H, 6.10. Found: C, 63.67; H 6.28.

2-(3,4-Methylenedioxyphenyl)-1,3-cyclohexanedione (9a). A mixture of 200 g (0.76 mole) of methyl 5-oxo-6-(3,4-methylenedioxyphenyl)hexanoate (**8d**) and 40 g of solid sodium methoxide in 670 ml of dry benzene was heated under reflux with stirring under nitrogen for 24 hr. The reaction mixture was acidified by slow addition of 10% hydrochloric acid, diluted with water, and filtered. Recrystallization of the precipitate from ethanol–water gave 140 g (80% yield) of **9a**, mp 209–210°; ultraviolet: λ_{max}^{EtOH} 287 mμ (ϵ 7.6 × 10^3).

Anal. Calcd for $C_{13}H_{12}O_4$: C, 67.23; H, 5.21. Found: C, 67.09; H, 5.28.

2-(3,4-Methylenedioxyphenyl)-3-chloro-Δ^2-cyclohexenone (9b). A mixture of 60 g (0.26 mole) of **9a** and 100 ml of phosphorus trichloride in 2.5 l. of chloroform was heated under reflux with stirring for 3 hr. The chloroform was removed *in vacuo*, and the residue was poured on crushed ice. After stirring for 1 hr, the aqueous layer was extracted with chloroform, and the chloroform extracts were washed with 5% sodium carbonate solution and water, dried over anhydrous sodium sulfate, percolated through a bed of alumina, and evaporated. Recrystallization of the residue from benzene–hexane gave 41 g (63% yield) of **9b**, mp 111.5–11.25°; infrared: $\lambda_{max}^{CHCl_3}$ 5.95 μ (s); ultraviolet: λ_{max}^{EtOH} 237 mμ (ϵ 1.33 × 10^4) and 289 mμ (ϵ 3.4 × 10^3).

Anal. Calcd for $C_{13}H_{11}O_3Cl$: C, 62.28 ; H, 4.42; Cl, 14.15. Found: C, 62.20; H, 4.18; Cl, 14.08.

N-[2-(3,4-Methylenedioxyphenyl)-3-oxo-cyclohexenyl]aziridine (9c). A solution of 60 g (0.24 mole) of **9b**, 60 ml (1.46 moles) of triethylamine, and 130 g (1.29 moles) of ethylenimine in 750 ml of tetrahydrofuran was stirred under nitrogen room temperature for 3 days. After this time the reaction mixture was filtered; the filtrate was evaporated, and the residue was recrystallized from ethyl acetate to afford 50.0 g (80% yield) of **9c**, mp 120–121.5°; infrared: 6.11 μ (vs); ultraviolet: λ_{max}^{EtOH} 291 mμ (ϵ 1.32 × 10^4).

Anal. Calcd for $C_{15}H_{15}O_3N$: C, 70.02; H, 5.88; N, 5.44; mol wt, 257. Found: C, 70.08; H, 5.93; N, 5.41; mol wt, 257 (parent, base peak, mass spectroscopy).

3a-(3,4-Methylenedioxyphenyl)-4-oxo-$\Delta^{1,7a}$-hexahydroindole (10). A mixture of 15 g (0.058 mole) of enamine **9c**, 17 g of anhydrous sodium iodide, and 120 ml of dry diglyme was heated with stirring under nitrogen at 145° for 2.5 hr. The reaction mixture was cooled and added to 200 ml of water, and the aqueous layer was extracted with ether. The combined ether layers were washed with water, stirred at room temperature with Norit, filtered, dried over anhydrous sodium sulfate, and evaporated. Crystallization of the residue from hexane afforded, in addition to 0.5 g of recovered **9c**, 8 g (55% yield) of **10**, mp 119.5–121°; infrared: $\lambda_{max}^{CHCl_3}$ 5.85 (vs) and 6.05 μ (s); nmr: δ 6.58 (3 H, multiplet, aromatic H), 3.71 (2 H, multiplet, $=NCH_2$), 5.97 (2 H, singlet, OCH_2O), and 3.0–1.5 (broad, 8 H).

Anal. Calcd for $C_{15}H_{15}NO_3$: C, 70.02; H, 5.88; N, 5.44; mol wt, 257. Found: C, 70.08; H, 5.93; N, 5.46; mol wt, 257 (mass spectroscopy).

Carrying out the isomerization at 155° in a melt as was done for **4c** gave only a 16% yield of **10**.

***cis*- and *trans*-3a-(3,4-Methylenedioxyphenyl)-4-oxooctahydroindoles (11 and 12).** A solution of 2.8 g (10.9 mmoles) of **10** in 350 ml of ethanol was hydrogenated at atmospheric pressure, using 1.4 g of platinum oxide as catalyst. After consumption of 1 equiv of hydrogen by **10** had occurred, the reaction mixture was filtered, and the filtrate was evaporated. The residue was dissolved in water, and the aqueous solution was made basic with sodium carbonate and then extracted with chloroform. The combined chloroform extracts were washed with water, dried over anhydrous sodium sulfate, and evaporated. The residue was chromatographed

(25) J. L. Bills and C. R. Noller, *J. Am. Chem. Soc.*, **70**, 957 (1948).

on 1 kg of activity 5 Woelm alumina, using 1:1 benzene–hexane as eluting solvent. First to be eluted was 150 mg (5.5% yield) of 3a-(3,4-methylenedioxyphenyl)-4-oxo-*trans*-octahydroindole (**12**), mp 119.5–120.5°, on recrystallization from hexane–benzene; infrared: $\lambda_{max}^{CHCl_3}$ 5.85 μ (vs); nmr: δ 7.04 (3 H, complex), 5.95 (2 H, singlet), 3.80 (1 H, broad, disappears on addition of D_2O), and 3.0–1.3 (broad, 11 H).

Anal. Calcd for $C_{15}H_{17}O_3N$: C, 69.48; H, 6.61; N, 5.40; mol wt, 259. Found: C, 69.61; H, 6.66; N, 5.75; mol wt, 259. (mass spectroscopy).

Reaction of **12** with acetic anhydride gave the N-acetyl derivative, mp 202.5–203.5°; infrared: $\lambda_{max}^{CHCl_3}$ 5.84 (s) and 6.09 μ (s); nmr: δ 6.77 (3 H, singlet), 5.96 (2 H, singlet), 3.60 (3 H, multiplet), 2.12 (3 H, singlet), and 2.5–1.2 (8 H, broad).

Anal. Calcd for $C_{17}H_{19}O_4N$: C, 67.76; H, 6.36; N, 4.65; mol wt, 301. Found: C, 67.61; H, 6.56; N, 4.66.

Continued elution then afforded 2.14 g (76% yield) of the *cis*-ketoamine **11**, mp 100–101°, after recrystallization from hexane; infrared: $\lambda_{max}^{CHCl_3}$ 5.85 μ (vs); nmr: 6.75 (3 H, singlet), 5.93 (2 H, singlet), 3.95 (1 H, broad, disappeared on addition of D_2O), 3.00 (3 H, broad), and 2.5–1.4 (8 H, broad).

Anal. Calcd for $C_{15}H_{17}NO_3$: C, 69.48; H, 6.61; N, 5.40; mol wt, 259. Found: C, 69.61; H, 6.64; N, 5.39; mol wt, 259 (mass spectroscopy).

Acetylation afforded the N-acetyl derivative, mp 126.5–127.5°.

Anal. Calcd for $C_{17}H_{19}O_4N$: C, 67.76; H, 6.36; N, 4.65; mol wt, 301. Found: C, 67.76; H, 6.32; N, 4.69; mol wt, 301 (mass spectroscopy).

***dl*-1-Oxocrinane (13).** A solution of 1.44 g (5.6 mmoles) of **11** in a mixture of 6 ml of methanol and 15 ml of commercial formalin was allowed to stir at room temperature for 3 min. This solution was then poured into 450 ml of 6 *M* hydrochloric acid and allowed to stand for 2 hr at room temperature. The reaction mixture was then made basic with ammonium hydroxide and extracted with chloroform. The chloroform extracts were washed with water, dried over anhydrous sodium sulfate, and evaporated. Recrystallization of the residue from hexane gave 1.3 g (79% yield) of *dl*-1-oxocrinane, mp 123–125°; infrared: $\lambda_{max}^{CHCl_3}$ 5.89 μ (s); nmr: ($CDCl_3$) δ 7.71 (1 H, singlet), 6.41 (1 H, singlet), 5.88 (2 H, singlet), 4.00 (2 H, quartet, J = 16 cps, $\Delta\nu$ = 45 cps), and 3.45–1.5 (11 H, broad).

Anal. Calcd for $C_{16}H_{17}NO_3$: C, 70.83; H, 6.32; N, 5.16; mol wt, 271. Found: C, 70.76; H, 6.37; N, 5.28; mol wt, 271.

Comparison of its solution (chloroform) infrared spectrum and mass spectrum with those of dehydrodihydrodesmethoxybuphanamine showed them to be identical.

***dl*-4a-*epi*-1-Oxocrinane (14).** Reaction of the *trans* amine **12** with formaldehyde under the same conditions as for preparing 1-oxocrinane gave an 80% yield of **14**, mp 165.5–166.5°; infrared: $\lambda_{max}^{CHCl_3}$ 5.85 μ (vs); nmr ($CDCl_3$): δ 6.51 (1 H, singlet), 6.25 (1 H, singlet), 5.89 (2 H, singlet), 3.95 (quartet J = 18 cps, $\Delta\nu$ = 41 cps), and 3.4–1.2 (11 H, broad).

Anal. Calcd for $C_{16}H_{17}NO_3$: C, 70.83; H, 6.32; N 5.16; mol wt, 271. Found: C, 70.77; H, 6.26; N, 5.18; mol wt, 271 (mass spectroscopy).

Dehydrodesmethoxybuphanamine (16). The hydrochloride of **13** was prepared by passing hydrogen chloride through a solution of 600 mg (2.22 mmoles) of **13** in 120 ml of ether. The ether was evaporated, and the residue was dissolved in 30 ml of acetic acid. To the resulting solution was added a solution of 354 mg (2.2 mmoles) of bromine in 7 ml of acetic acid, and the resulting solution was allowed to stand in the dark at room temperature for 2 hr. The solvent was then evaporated *in vacuo*, and a mixture of the residue, 260 mg of anhydrous lithium chloride, and 40 ml of dimethylformamide was heated under reflux with stirring under nitrogen for 1.5 hr. The reaction mixture was cooled to 0° and added to a mixture of 200 ml of water and 5 ml of 6 *M* hydrochloric acid. The aqueous layer was extracted with chloroform (discarded), made basic with ammonium hydroxide, and again extracted with chloroform. The combined chloroform extracts from the basic mixture were dried over anhydrous sodium sulfate and evaporated. Chromatography of the residue on activity 3 Woelm alumina, using 7% ethyl acetate–benzene as solvent afforded after recrystallization from hexane 435 mg (73% yield) of **16**, mp 131–132°; infrared: $\lambda_{max}^{CHCl_3}$ 5.99 (vs); nmr: δ 8.02 (1 H, singlet), 6.83 (1 H, multiplet), 6.44 (1 H, singlet), 6.12 (1 H, multiplet), 5.89 (2 H, singlet), 4.07 (2 H, quartet, J = 17 cps, $\Delta\nu$ = 42 cps), and 3.8–2.0 (7 H, broad).

Anal. Calcd for $C_{16}H_{15}NO_3$: C, 71.36; H, 5.61; N, 5.20; mol wt, 269. Found: C, 71.11; H, 5.63; N, 5.30; mol wt, 269 (mass spectroscopy).

***epi*-Desmethoxybuphanamine (17a).** Reduction of 435 mg (1.62 mmoles) of **16** with lithium aluminum hydride in tetrahydrofuran gave, on chromatography of the crude product on activity 2 alumina, 260 mg (60% yield) of **17a**, mp 258–259.5° (ethyl acetate). Its insolubility precluded determination of its nmr spectrum. It had no carbonyl band in its infrared (KBr) spectrum.

Anal. Calcd for $C_{16}H_{17}NO_3$: C, 70.77; H, 6.28; N, 5.27; mol wt, 271. Found C, 70.83; H, 6.32; N, 5.16; mol wt, 271 (mass spectroscopy).

***dl*-Crinine.** I. A solution of 200 mg of **17a** in 75 ml of 10% hydrochloric acid was heated under reflux for 1 hr. The solution was then cooled to 5°, made basic with ammonium hydroxide, and extracted with chloroform. The combined chloroform extracts were dried over anhydrous sodium sulfate and evaporated to afford 190 mg of a residue. This residue was chromatographed on 200 g of activity 2 Woelm alumina to afford, in order of elution, the following products: (a) an oil, 31 mg, devoid of hydroxyl or carbonyl stretching frequencies in its infrared spectrum which was not investigated further; (b) starting material **17a**, 61 mg, identified by comparison of its infrared spectrum with that of an authentic sample; (c) a semisolid, 38 mg, which was not investigated further; (d) *dl*-crinine, 60 mg, mp 174–175° (lit.[5] mp 174–175°) whose infrared spectrum ($CHCl_3$) was, as far as could be told, identical with that of (−)-crinine.

II. To a solution of 60 mg (0.22 mmole) of **17a** in 7 ml of tetrahydrofuran was added a solution of 0.22 mmole of *n*-butyllithium in hexane. The reaction mixture was stirred at room temperature for 5 min and then injected over a period of 1 hr into a stirred solution of 150 mg (0.78 mmole) of toluenesulfonyl chloride in 1 ml of tetrahydrofuran at 0° under nitrogen. The reaction mixture was stirrred at room temperature an additional 2 hr. A 2% aqueous sodium bicarbonate (5 ml) was added to the reaction mixture, and the resulting solution was allowed to stir at room temperature for 14 hr. The mixture was then diluted with water, and the aqueous layer was extracted with chloroform. The chloroform extracts were washed with water, dried over anhydrous sodium sulfate, and evaporated. Chromatography of the residue on 40 g of activity 2 Woelm alumina afforded 25 mg (42% yield) of *dl*-crinine, mp 174–176°, after recrystallization from hexane–ethyl acetate. Its identity was established as in part I above.

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