Model Studies of the Synthesis of Echitamine and Related Indole Alkaloids[1]

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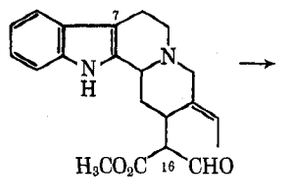
Cyclizations of 3-(1,2,3,4-tetrahydrocarbazol-1-yl)prop-1-yl tosylate (1) and its *N*-methyl derivative 2 have been examined as model reactions for the synthesis of indole alkaloids bearing a C-16 to C-7 bond. The action of potassium *tert*-butoxide or ethylmagnesium bromide cyclizes tosylate 1 to 6*H*-1,2,3,3a,4,5-hexahydropyrido[3,2,1-*jk*]carbazole (12) resulting from nucleophilic displacement by nitrogen. Formolysis of the *N*-methyl tosylate 2 gives the unstable 7*H*-2,3,3a,4,5-hexahydrocyclopenta[*d*]carbazole as the major product. Deuterium-labeling studies show that this reaction proceeds to the extent of about 70% by electrophilic attack at the β position of the indole ring. Formolysis of 2 thus proceeds *via* an intermediate which has four of the five rings common to the skeleton of deacetylakuammiline and related indole alkaloids bearing a C-7 to C-16 bond.

The echitamine structure[2] provided the first example of a group of indole alkaloids bearing a C-16–C-7 bond. A number of these alkaloids are now known[3] and their synthesis has proved to be a very difficult task. These compounds are almost certainly derived in nature by cyclization of a corynantheine derivative.[4]



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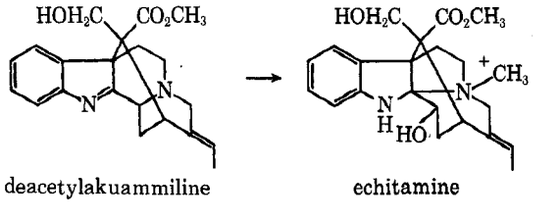
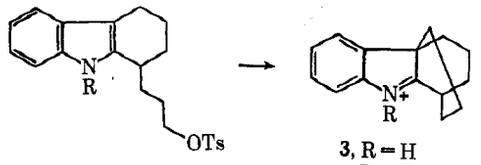


deacetylakuammiline echitamine

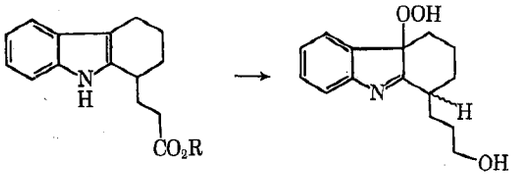
The great susceptibility of indoles to electrophilic attack at the β position suggests a carbonium ion reaction for the formation of another bond at the β position of a 2,3-disubstituted indole. However, a carbonium ion reaction would be an impossible model for the biosynthetic formation of the C-7 to C-16 linkage owing to the difficulty of generating a positive charge on C-16, which is attached to two carbonyl groups. Nevertheless, a carbonium ion reaction might be adapted to the *in vitro* synthesis of this group of compounds.

To test this possibility, we have examined the cyclization of the two tetrahydrocarbazole tosylates 1 and 2 which could lead to tetracyclic materials containing four of the five rings making up the skeleton of deacetylakuammiline-related indole alkaloids.



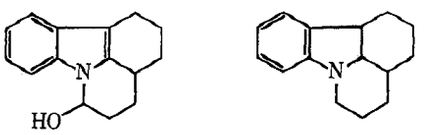
1, R = H
2, R = CH_3 3, R = H
4, R = CH_3

The synthesis of the alcohol from which tosylate 1 was prepared was attended by some unexpected difficulties. The obvious approach involves reduction of the well-known 3-(1,2,3,4-tetrahydrocarbazol-1-yl)propionic acid[5] (5) or its methyl ester 6. Lithium aluminum hydride reduction of the acid 5 afforded a mixture from which the hydroperoxyindolenine 7 was obtained. Since this reduction did not appear to be a very clean reaction in any case, some other reductions were examined.



5, R = H
6, R = CH_3 7

Lithium aluminum hydride reduction of the ester 6 gave the cyclic carbinol amine 8 in reasonable yield, whereas reduction of the acid 5 with diborane resulted in cyclization and reduction of the indole double bond to give the known 6*H*-1,2,3,3a,4,5,11b,11c-octahydropyrido[3,2,1-*jk*]carbazole[5] (9) in good yield.



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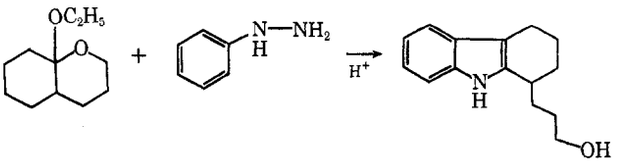
A thorough study of the reduction of 5 and 6 was not attempted, since another synthetic route appeared quite attractive. The synthesis of the desired 3-(1,2,3,4-tetrahydrocarbazol-1-yl)propan-1-ol (10) was achieved employing 9-ethoxy-1-oxadecalin[6] in a Fischer indole synthesis.



10

(1) The authors gratefully acknowledge financial support from the National Institutes of Health (Grant HE 90521) and a Public Health Service Career Program Award (1-K3-NB-28,105) from the National Institute of Neurological Disease and Blindness.

(2) J. A. Hamilton, T. A. Hamor, J. M. Robertson, and G. A. Sim, *J. Chem. Soc.*, 5061 (1962).

(3) J. E. Saxton, "The Alkaloids," R. H. F. Manske, Ed., Academic Press, New York, N. Y., 1968, p 501.

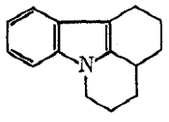
(4) A. I. Scott, *Accounts Chem. Res.*, **3**, 151 (1970).

(5) H. T. Openshaw and R. Robinson, *J. Chem. Soc.*, 941 (1937).

(6) H. Obara, *Nippon Kagaku Zasshi*, **82**, 60 (1961).

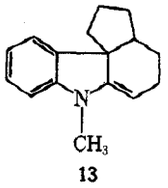
The synthesis of the analogous *N*-methyl compound, 3-(1,2,3,4-tetrahydro-9-methylcarbazol-1-yl)propan-1-ol (**11**), was completed by a lithium aluminum hydride reduction of the corresponding ester. Lithium aluminum hydride reduction proceeded smoothly and the *N*-methyl group obviated the difficulties encountered in the reduction of **5** and **6**. Carbinol **10** and its *N*-methyl derivative were obtained as oils but the corresponding tosylates, obtained by the action of pyridine and *p*-toluenesulfonyl chloride, were nicely crystalline.

Treatment of tosylate **1** with potassium *tert*-butoxide in *tert*-butyl alcohol gave a quantitative yield of the known tetracyclic indole derivative **12** identified from its spectroscopic properties and melting point.[5] The action of ethylmagnesium bromide on **1** afforded the same product **12** in 90% yield.



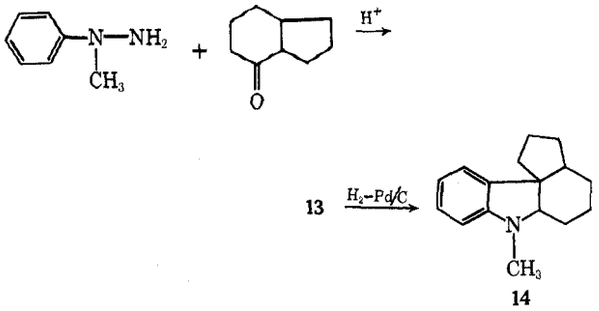
12

Since these reactions showed no sign of reaction at the β position of the indole ring, we turned our attention to the *N*-methyl tosylate **2**. Solvolysis of **2** in formic acid affords as a major product, in up to 65% yield, an unstable base whose ultraviolet spectrum indicates that it is an alkylidene indoline. The pmr spectrum which shows a triplet at δ 4.75 ascribed to a vinyl proton indicates that the material is not related to structure **4** in any event. The spectroscopic evidence and mechanistic considerations lead to structure **13** for the alkylidene indoline.



13

The material was characterized after catalytically reducing the enamine double bond to give the dihydro compound **14**. The structure was secured by independent synthesis involving a Fischer indole condensation employing perhydro-4-indanone and α-methylphenylhydrazine.

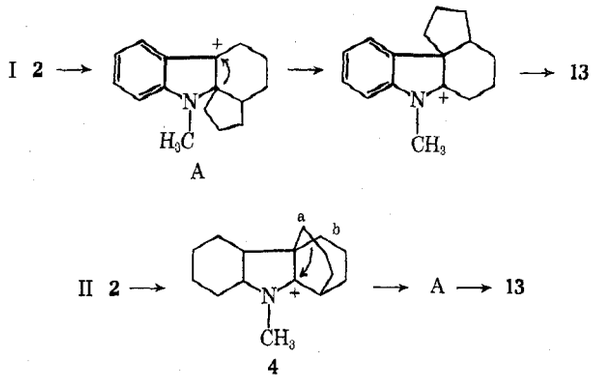


14

The material obtained from the Fischer indole synthesis and reduction was identical with the reduced solvolysis product.

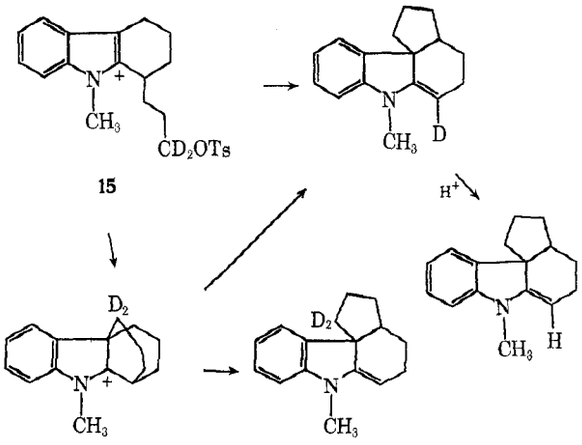
The results of the solvolysis of **2** pose an important mechanistic question. The simplest possible analysis indicates two pathways for the formation of **13** (Scheme I).

SCHEME I



Pathway I, involving initial bond formation at the α position of the indole ring, leads to **13** with only one rearrangement. Pathway II requires two rearrangements after initial bond formation at the β position. Deuterium labeling can be applied to make a straightforward distinction between the two pathways. Considering the possibilities using tosylate **2** labeled with deuterium at the carbinol carbon atom, pathway I would surely result in the loss of at least one deuterium and possibly show loss of both deuteriums by a subsequent exchange.

However, pathway II would involve the formation of **4** as an intermediate, redrawn above to emphasize its symmetry. In fact, carbons a and b are equivalent in structure **4** and assuming equal probability for migration, **13** would be formed as an equimolar mixture of doubly and singly deuterated species which would lead to undeuterated material by exchange. If pathway II was the only mechanism operative, then the product should contain 50% of doubly deuterated material with the remaining material consisting of singly deuterated and undeuterated material.



Solvolysis of the deuterated tosylate did give a mixture of doubly and singly deuterated material along with undeuterated material. For the purposes of the analysis, it was assumed that the deuterated tosylate **15** contained exactly two deuteriums. The material was not conveniently analyzed by mass spectrometry, but the pmr spectrum showed no signal for carbinol protons. Two solvolysis experiments were carried out. In one experiment the crude solvolysis product

was hydrogenated and separated by preparative tlc to give labeled **14**. To guard against any peculiar deuterium exchange associated with catalytic reduction, the crude solvolysis product from the second experiment was reduced with sodium borohydride and then separated as before. The reduced solvolysis products were analyzed by mass spectrometry. Labeled **14** from the first experiment showed 55% undeuterated material, 8% monodeuterated species, and 37% of dideuterated material. The second experiment gave material which was 51% undeuterated, 15% monodeuterated, and 34% dideuterated. The fact that different amounts of undeuterated and monodeuterated material were obtained in the two experiments is not surprising, since the undeuterated material is formed by an exchange reaction and the extent of deuterium loss would be affected by a number of variables. Importantly, the fraction of dideuterated material was very nearly the same in both experiments.

Within the simplified mechanistic scheme, the labeling results indicate that about 70% of the reaction leads to **13** through the symmetrical indolenine intermediate **4**. It may be that more of the reaction proceeds by initial attack at the β position to give an unsymmetrical intermediate related to **4**. However, the simplest explanation is that the remainder of the reaction takes place by initial attack at the α position of the indole ring. That the predominant course of the reaction involves electrophilic attack at the β position of the indole ring is completely consistent with the studies of Jackson and his colleagues on electrophilic substitution of substituted indoles.[7] The results indicate that a carbonium ion reaction may be applied to assembling indole alkaloids bearing a C-16–C-7 bond. Further studies in this direction are in progress.

Experimental Section[8]

3-(1,2,3,4-Tetrahydro-4a-hydroperoxycarbazolinin-1-yl)propan-1-ol.—To a suspension of lithium aluminum hydride (12.16 g, 0.32 mol) in dry tetrahydrofuran (500 ml) was added 38.8 g (0.16 mol) of 3-(1,2,3,4-tetrahydrocarbazol-1-yl)propionic acid, prepared as previously described.[5] The mixture was heated under reflux for 3 hr, after which the cooled reaction mixture was treated with water and sodium hydroxide.[9] The alumina was separated and the solvent was evaporated to yield a brownish oil (36 g). The oil was chromatographed on silica gel (500 g). Elution with 50% benzene–chloroform (1000 ml) afforded 21.6 g of material which deposited 3.5 g of crystalline material from benzene solution. Recrystallization from ethyl acetate gave pure hydroperoxyindolenine **7**: mp 134.5–135°; ir ν_{max}^{KBr} 1580 cm^{-1}; pmr (CD_3SOCD_3) δ 0.80–3.70 (complex multiplets, 13 H); 4.10–4.60 (complex multiplet, 1 H), 6.80–7.20 (complex multiplets, 4 H), 11.6 (s, 1 H); uv λ_{max} 255 nm (ϵ 5070); $\lambda_{max}^{EtOH-HCl}$ 284 nm (ϵ 7160); mass spectrum intense peak at m/e 245 (M − O·).

Anal. Calcd for $C_{15}H_{19}NO_3$: C, 68.94; H, 7.33; N, 5.36. Found: C, 68.98; H, 7.02; N, 5.28.

6*H*-1,2,3,3a,4,5-Hexahydropyrido[3,2,1-*jk*]carbazol-6-ol (8).—A mixture of methyl 3-(1,2,3,4-tetrahydrocarbazol-1-yl)propionate (3.00 g, 0.012 mol) prepared by Fischer–Spier esterification of the acid, lithium aluminum hydride (1.9 g, 0.05 mol), and dry ether (50 ml) was heated under reflux for 10 hr. The usual work-up afforded 2.6 g of pale yellow oil which was recrystallized from benzene–petroleum ether (bp 30–60°) to give the pure tetracyclic alcohol **8** (1.5 g, 56%): mp 134–136°; ir $\nu_{max}^{CHCl_3}$ 3500, 1600 cm^{-1}; pmr ($CDCl_3$) δ 0.8–3.0 (complex multiplets, 12 H), 5.0–5.6 (m, 1 H), 7.0–7.7 (m, 4 H); uv λ_{max} 222 nm (ϵ 29,035), 235 (18,300), 283 (8610); mass spectrum molecular ion at m/e 227.

Anal. Calcd for $C_{15}H_{17}NO$: C, 79.26; H, 7.54; N, 6.16. Found: C, 79.54; H, 7.42; N, 6.25.

6*H*-1,2,3,3a,4,5,11b,11c-Octahydropyrido[3,2,1-*jk*]carbazole (9).—A solution of 3-(1,2,3,4-tetrahydrocarbazol-1-yl)propionic acid (2.43 g, 0.01 mol) and diborane (0.83 g, 0.03 mol) in dry tetrahydrofuran (100 ml) was stirred at room temperature overnight. The reaction mixture was hydrolyzed with methanolic hydrochloric acid and processed to give the title compound (1.28 g, 59%); mp 75–77° after crystallization from petroleum ether (lit.[5] mp 81–82°); uv λ_{max} 255 nm (ϵ 10,550), 296 (2700); mass spectrum molecular ion at m/e 213.

Anal. Calcd for $C_{15}H_{19}N$: C, 84.46; H, 8.98; N, 6.57. Found: C, 84.69; H, 8.98; N, 6.60.

3-(1,2,3,4-Tetrahydrocarbazol-1-yl)propan-1-ol.—A solution of 9-ethoxy-1-oxadecalin (11.2 g, 0.065 mol), prepared by the procedure of Obara,[6] and phenylhydrazine (7.0 g, 0.065 mol) was heated at 100–120° for 2 hr. The reaction mixture was treated with 20% sulfuric acid (250 ml) and heated slowly to 80° and then at 100° for 10 min. The reaction mixture was diluted with water and extracted with chloroform to give a dark red oil (8.4 g) which was chromatographed on Florisil (600 g). Elution with 44% benzene–chloroform (2000 ml) afforded 5.7 g of the title compound as a pale yellow oil: ir $\nu_{max}^{CHCl_3}$ 3700–3200 cm^{-1}; uv λ_{max} 225 nm (ϵ 20,500), 283 (4900); pmr ($CDCl_3$) δ 0.8–2.2 (m, 8 H), 2.3–2.9 (broad, 3 H), 3.25 (s, 1 H), 3.45–3.7 (m, 2 H), 6.8–7.5 (m, 4 H), 8.35 (s, 1 H); mass spectrum molecular ion m/e 229. The material was used in the next step without further characterization.

3-(1,2,3,4-Tetrahydrocarbazol-1-yl)prop-1-yl Tosylate (1).—A solution of *p*-toluenesulfonyl chloride (1.9 g, 0.01 mol) in dry pyridine (10 ml) was added dropwise at 0° to a solution of the alcohol **10** (2.3 g, 0.01 mol) obtained above in pyridine (5 ml). The reaction mixture was refrigerated overnight and processed in the usual manner to afford the crude tosylate (3.0 g) as a light oil. The oil was chromatographed on Florisil (200 g); elution with 850 ml of 8% benzene–chloroform yielded 1.6 g (42%) of pure tosylate **1**: mp 84–86° from petroleum ether–benzene; ir $\nu_{max}^{CHCl_3}$ 3450, 1600, 1360, and 1175 cm^{-1}; pmr ($CDCl_3$) δ 1.20–2.2 (m, 8 H), 2.40 (s, 3 H), 2.50–3.00 (m, 3 H), 3.90–4.25 (undefined triplet, 2 H), 7.0–8.0 (m, 9 H); uv λ_{max} 226 nm (ϵ 43,170), 282 (6800).

Anal. Calcd for $C_{22}H_{25}NSO_3$: C, 68.91; H, 6.57; N, 3.65; S, 8.34. Found: C, 68.81; H, 6.45; N, 3.56; S, 8.52.

Ethyl 3-(1,2,3,4-Tetrahydro-9-methylcarbazol-1-yl)propionate.—A solution of ethyl 3-(2-oxocyclohexyl)propionate (5.0 g, 0.025 mol) and α-methylphenylhydrazine (3.05 g, 0.035 mol) was dissolved in 10 g of polyphosphoric acid. The mixture was gently warmed on the steam bath until the temperature began to rise rapidly. The mixture was cooled with cold water and then diluted with 100 g of ice–water. Extraction with methylene chloride afforded 5.25 g of crude product which was chromatographed on Florisil (600 g). Elution with 4 l. of petroleum ether gave 3.4 g (48%) of the ester **11** as an oil; pmr ($CDCl_3$) δ 1.17 (t, J = 7 Hz, 3 H), 1.5–3.0 (m, 11 H), 3.5 (s, 3 H), 4.1 (q, J = 7 Hz, 2 H), 7.2 (m, 4 H); uv, typical indole absorption.

3-(1,2,3,4-Tetrahydro-9-methylcarbazol-1-yl)propan-1-ol.—The ester (4.85 g, 0.017 mol) was heated under reflux for 2 hr with lithium aluminum hydride (0.76 g, 0.02 mol) in anhydrous ether. The usual isolation afforded 3.7 g (90%) of the crude alcohol as an oil which was used directly in the next step.

3-(1,2,3,4-Tetrahydro-9-methylcarbazol-1-yl)prop-1-yl Tosylate (2).—A sample (3.7 g) of the crude alcohol **11**, obtained above, was converted to the tosylate as described for tosylate **1**. The crude tosylate (4.5 g) was chromatographed on 500 g of Florisil. Elution with benzene (1800 ml) gave 2.33 g of the desired tosylate, which crystallized from benzene–hexane after 2 weeks in the refrigerator. Recrystallization from absolute ethanol gave pure **2** as white crystals: mp 63–65°; pmr ($CDCl_3$) δ 1.3–2.0 (com-

(7) A. H. Jackson and B. Naidoo, *Tetrahedron*, **25**, 4843 (1969), and previous papers in the series.

(8) All melting points and boiling points are uncorrected. Reactions involving strong bases or organometallic reagents were carried out under nitrogen. Infrared spectra were determined with a Beckman IR-5a infrared spectrophotometer. Ultraviolet spectra were determined in 95% ethanol with a Cary Model 15 spectrophotometer. Proton magnetic resonance spectra were determined at 60 MHz with a Varian Model A-60 spectrometer. The chemical shifts are recorded in δ values (parts per million) relative to tetramethylsilane internal standard. The mass spectra were obtained with a CEC Model 21-110 mass spectrometer equipped with a direct inlet system at an ionizing potential of 70 eV.

(9) L. J. Amundsen and L. S. Nelson, *J. Amer. Chem. Soc.*, **73**, 242 (1951).

plex multiplets, 8 H), 2.33 (s, 3 H), 2.5–3.0 (broad, 3 H), 3.52 (s, 3 H), 4.05 (t, J = 6 Hz, 2 H), 7.1–7.9 (m, 8 H); uv λ_{max} 226 nm (ϵ 44,643), 283 (6420).

Anal. Calcd for $C_{28}H_{27}NSO_3$: C, 69.50; H, 6.85; N, 3.52; S, 8.05. Found: C, 69.61; H, 7.07; N, 3.39; S, 8.22.

The deuterated material, 3-(1,2,3,4-tetrahydro-9-methylcarbazol-1-yl)propyl tosylate-*1,1-d*$_2$, was prepared as just described using lithium aluminum deuteride for the reduction of ethyl 3-(1,2,3,4-tetrahydro-9-methylcarbazol-1-yl)propionate.

6*H*-1,2,3,3a,4,5-Hexahydropyrido[3,2,1-*jk*]carbazole (12).—A solution of **1** (0.192 g) in 10 ml of 0.5 *M* potassium *tert*-butoxide in *tert*-butyl alcohol was heated under reflux for 10 hr. The alcohol was evaporated under reduced pressure and the residue was treated with dilute hydrochloric acid and extracted with ether. Evaporation of the ether afforded 0.106 g (100%) of the carbazole derivative **12**: mp 82–84° after crystallization from hexane (lit.[5] mp 87–88°); pmr δ 0.8–4.5 (complex multiplets, 13 H), 7.0–7.65 (m, 4 H); mass spectrum molecular ion at m/e 211.

Anal. Calcd for $C_{15}H_{17}N$: C, 85.26; H, 3.11; N, 6.63. Found: C, 84.93; H, 8.25; N, 6.43.

A similar result obtained upon treatment of tosylate with ethylmagnesium iodide in ether solution.

Formolysis of 3-(1,2,3,4-Tetrahydro-9-methylcarbazol-1-yl)-prop-1-yl Tosylate (2).—Tosylate **2** (0.200 g, 0.005 mol), 88% formic acid (10 ml), and benzene (3 ml) were heated under reflux overnight. The cooled reaction mixture was diluted with 10 ml of 10% hydrochloric acid and washed with ether. The aqueous portion was basified with 20% sodium hydroxide solution and extracted with ether to give 0.090 g of a yellow oil which was subjected to preparative tlc on silica gel with benzene. The compounds were observed; the major product, with an intermediate R_f, was collected (0.046 g, 41%) as a colorless oil which quickly changed to cherry red on exposure to air; ir $\bar{\nu}_{max}$ 1670, 1600 cm^{-1}; pmr δ 0.8–3.4 (comlex multiplets, 11 H), 2.92 (s, 3 H), 4.75 (t, J = 5 Hz, 1 H), 6.3–7.30 (m, 4 H); uv λ_{max} 248 nm (ϵ 60,200), 287 (2350); mass spectrum molecular ion m/e 225.

A sample of the product **13** (0.217 g, 0.964 mmol) obtained as just described was hydrogenated in ethanol (100 ml) over 10% palladium on carbon at atmospheric pressure. After hydrogen uptake ceased, the catalyst was filtered and the solvent was evaporated to yield 0.195 g of oil which was crystallized from ethanol to give pure **14**: mp 27–29°; ir $\bar{\nu}_{max}$ 1600 cm^{-1}; pmr δ 1.15–2.5 (complex multiplets, 13 H), 2.68 (s, 3 H), 3.0 (t, J = 2.5 Hz, 1 H), 6.4–7.3 (m, 4 H); uv λ_{max} 255 nm (ϵ 7700), 262 (8880), 267 (7100); mass spectrum molecular ion at m/e 227.

Anal. Calcd for $C_{16}H_{19}N$: C, 84.53; H, 9.31; N, 6.16. Found: C, 84.76; H, 9.21; N, 6.12.

The methiodide of **14**, mp 203–204° dec, from ethanol, was obtained by treating **14** with methyl iodide in benzene solution.

Anal. Calcd for $C_{17}H_{24}NI$: C, 55.28; H, 6.50; N, 3.80; I, 34.42. Found: C, 54.97; H, 6.68; N, 3.54; I, 34.46.

Perhydro-4-indanone.—Commercially available 4-indanol (20 g, 0.149 mol) in ethanol (200 ml) was hydrogenated over 5% Rh/C (1.5 g) at 60 psi for 15 hr. The catalyst was filtered and the solvent was evaporated to give 19.5 g of crude perhydro-4-indanol: pmr (CCl_4) δ 1.8–2.4 (complex multiplets, 14 H), 3.3–4.2 (m, 2 H).

The crude perhydro-4-indanol (19.5 g) was dissolved in acetone (200 ml) and stirred with 8 *N* chromic acid (50 ml) for 1 hr at 0°. The usual isolation and distillation afforded 14.0 g (68% based on 4-indanol) of perhydro-4-indanone, bp 100–104° (12 mm), ir $\nu_{max}^{CCl_4}$ 1710 cm^{-1}.

7*H*-2,3,3a,4,5,6,6a-Octahydrocyclopenta[*d*]carbazole (14).—A solution of perhydro-4-indanone (1.38 g, 0.01 mol) and α-methylphenylhydrazine (1.22 g, 0.01 mol) was heated at 120–125° for 2 hr. The crude phenylhydrazone was dissolved in acetic acid (3.0 g) and heated at 90° for 2 hr. The reaction mixture was diluted with water and washed with ether. The aqueous phase was then basified and extracted with ether to give 1.15 g (51%) of crude **13** as a red oil. The spectral properties of this material were virtually identical with those obtained from the solvolysis of **2**. The crude material was hydrogenated over Pd/C as previously described. The hydrogenation product was purified by preparative tlc on silica gel using benzene as eluent. The major product (0.596 g, 53%) was identical with the sample previously obtained.

Solvolysis of 3-(1,2,3,4-Tetrahydro-9-methylcarbazol-1-yl)propyl Tosylate-*1,1-d*$_2$.—Two samples of deuterated tosylate were solvolyzed in benzene–formic acid as previously described. In one experiment the crude product was hydrogenated over 10% Pd/C and separated by preparative tlc (silica gel–benzene). In the other experiment, the crude product was reduced with excess sodium borohydride in ethanol. The deuterated products were obtained in 40 and 65% yields, respectively, from the two experiments. The distributions of labeled material were computed from the 70 eV mass spectra. Under these conditions, the m − 1 peak for the parent compound was 9% of the parent peak. The calculations were carried out as described by Biemann.[10]

Registry No.—**1**, 32251-92-6; **2**, 32251-93-7; **7**, 32251-94-8; **8**, 32251-95-9; **9**, 32251-96-0; **10**, 32251-97-1; **11**, 32251-98-2; **12**, 32251-99-3; **13**, 32252-00-9; **14** methiodide, 32252-01-0; echitamine, 23106-72-1.

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Reduction of 6β-Methoxy-3α,5-cyclo-5α Steroids with Mixed Hydrides

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The reduction of 6β-methoxy-3α,5-cyclo-5α steroids with lithium aluminum hydride–aluminum chloride mixtures gives 3α,5-cyclo-5α steroids as the major product. The mechanism of the reaction is discussed. The reduction of cholesteryl tosylate with lithium aluminum hydride and mixed lithium aluminum hydride–aluminum chloride is also considered.

In the past few years considerable attention has been paid to the use of lithium aluminum hydride–aluminum chloride[1] as a reagent capable of reducing a large number of functions insensitive to lithium aluminum hydride; a well-known example is the reduction with mixed hydride of allylic and benzylic alcohols.[2]

In view of the unique electronic structure and the unusual properties of the cyclopropane ring, we decided to investigate the reactivity of several cyclopropylcarbinyl derivatives toward lithium aluminum hydride–aluminum chloride.

Preliminary work on 3α,5-cyclo-5α-cholestan-6β-ol showed that the reduction with mixed hydride gave 3α,5-cyclo-5α-cholestane, with a yield of 71%. This result seemed to support the similar behavior of the allylic alcohols and the 6β-hydroxy-3α,5-cyclo-5α

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