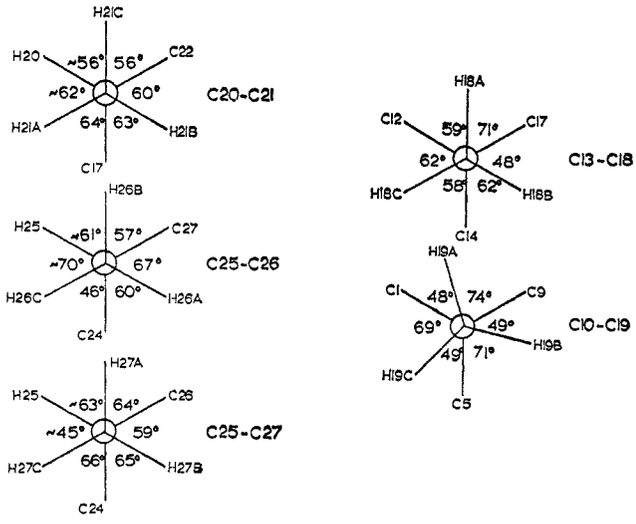

Figure 4.—Torsional angles for the five methyl groups in the molecule.

(see Figure 4), are due to the strained configuration at the C/D-ring junction. In the side chain, the three methyl groups have the expected staggered configurations, the only unexpected torsional angles being those involving H-25, the position of which, as has been pointed out previously, was not determined very precisely.

The side chain, with the exception of the C-21 and C-27 methyl groups, is planar to within 0.07 Å, and this plane lies at an angle of 120° to the plane through the steroid nucleus. The dihedral angle between the oxathiolane ring and the steroid nucleus is 82°.

Registry No.—Cholestan-4-one-3-spiro(2,5-oxathiolane), 17021-85-1.

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Di-5α-cholestan-3α-ylamine, a Diaxial Bis Steroidal Amine[1a]

JACK L. PINKUS[1b] AND THEODORE COHEN

Department of Chemistry, University of Pittsburgh, Pittsburgh, Pennsylvania 15213

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Ammonolysis of 5α-cholestan-3β-yl tosylate (**1**) in relatively small amounts of anhydrous ammonia leads to formation of the secondary diaxial amine **3** in addition to the major product, the primary axial amine **2**. The product amines have been characterized by pmr and mass spectrometry. As the minimum molar ratio of ammonia to **2** in a typical run is 75, it is clear that this highly hindered primary amine (**2**) is very much more effective at displacing tosylate anion from **1** than is ammonia. Attempts to prepare **3** from **1** and **2** in several solvents were not successful, while a low yield of **3** was obtained from a reaction conducted in the molten state. The uniqueness of the solvent liquid ammonia for this reaction is discussed.

Reaction of 5α-cholestan-3β-yl tosylate (**1**) with relatively small amounts of anhydrous ammonia has now been shown to furnish a new product, $C_{54}H_{95}N$, mp 165–166°, in addition to the major product,[2] 5α-cholestan-3α-ylamine (**2**). The new amine, which has been obtained in up to 16% yield, was assigned the structure of di-5α-cholestan-3α-ylamine (**3**) on the basis of its elemental analysis and molecular weight, the formation of an N-acetyl derivative lacking an N–H stretching vibration in the infrared spectrum, and on the basis of a pmr spectrum in deuteriochloroform. A signal at τ 7.22 with a half-band width (w) of ~7 cps (at 60 Mcps) for two equatorial 3β hydrogens clearly defines the stereochemistry.[3,4]

Compounds **2** and **3** showed molecular ions in their mass spectra at m/e 387 (Σ_{35} 1.19%) and m/e 757 (Σ_{35} 1.50%), respectively.[5] The two typical ions expected for a 3-amino- or 3-alkylamino-5α-cholestane are derived from carbons 1, 2, and 3 (less one hydrogen) and the amine function, and from carbons 3, 4, 5, 6, and 7 (less two hydrogens) and the amine function.[6] From

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(2) J. L. Pinkus, G. Pinkus, and T. Cohen, *J. Org. Chem.*, **27**, 4356 (1962).

(3) (a) N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry," Holden-Day, Inc., San Francisco, Calif., 1964, pp 77–85; (b) J. Tadanier and W. Cole, *J. Org. Chem.*, **27**, 4624 (1962); (c) R. U. Lemieux, R. K. Kullnig, H. J. Bernstein, and W. G. Schneider, *J. Amer. Chem. Soc.*, **80**, 6098 (1958), and **82**, 6427 (1960); (d) H. Feltkamp and N. C. Franklin, *Ann. Chem.*, **683**, 55 (1965); (e) H. Feltkamp, N. C. Franklin, K. D. Thomas, and W. Brügel, *ibid.*, **683**, 64 (1965); (f) H. Feltkamp, N. C. Franklin, W. Kraus, and W. Brügel, *ibid.*, **683**, 75 (1965); (g) H. Booth, N. C. Franklin, and G. C. Gidley, *Tetrahedron*, **21**, 1077 (1965).

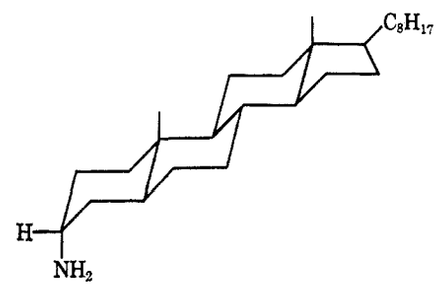
(4) Results with model amine and alcohol compounds are consistent with the stereochemical assignment. Equatorial hydrogens show w = 7–10 cps; examples are (solvent, τ, w in cps) *trans,trans*-2-decalylamine ($CDCl_3$, 6.78, ~8), *trans,trans*-10-methyl-2-decalylamine (neat, 6.87, ~8), 5α-cholestan-3α-ylamine (**2**) ($CDCl_3$, 6.87, ~8), *trans,trans*-2-decalyl acetate (neat, 5.00, ~7), and *trans,trans*-2-decalol ($CDCl_3$, 5.88, ~9). Axial hydrogens show w = 19–33 cps; examples are *trans,cis*-2-decalylamine ($CDCl_3$, 7.42, ~21), *trans,cis*-2-decalyl acetate (neat, 5.42, ~29), and *trans,cis*-2-decalol ($CDCl_3$, 6.47, ~19). Our w values for those of the above model compounds whose band widths have been measured elsewhere[3e,f] are about 20–30% less than the band-width values (W) reported since the latter values are based on an approach where band widths are measured at different band heights depending on conformation equilibria.

The pmr signal for the equatorial 3β hydrogens of **3** would be expected to occur as found at higher field than that observed for the model compounds with equatorial hydrogens, since alkylation of nitrogen results in increased shielding of the tertiary α hydrogen.[3g] Unfortunately, data are not available[3g] to make a quantitative prediction of the upfield shift expected in going from **2** to **3** (0.35 ppm observed).

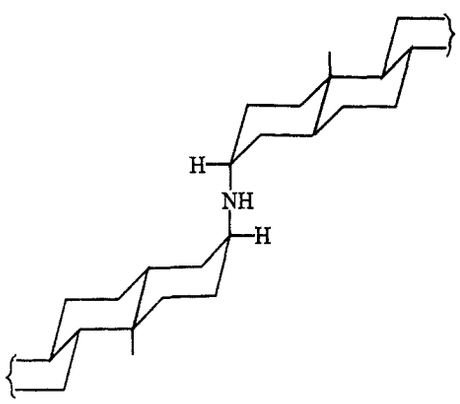
(5) These are nominal molecular weights, based on integral atomic mass units, and in the case of **3** is one atomic mass unit less than the actual molecular weight rounded off to the nearest integer.

(6) (a) L. Dolejš, V. Hanuš, V. Černý, and F. Šorm, *Collect. Czech. Chem. Commun.*, **28**, 1584 (1963); (b) W. Vetter, P. Longevialle, F. Khuong-Huu-Laine, Q. Khuong-Huu, and R. Goutarel, *Bull. Soc. Chim. Fr.*, 1324 (1963); (c) Z. Pelah, M. A. Kielczewski, J. M. Wilson, M. Ohashi, H. Budzikiewicz, and C. Djerassi, *J. Amer. Chem. Soc.*, **85**, 2470 (1963).

2, these ions are found at m/e 56 (Σ_{35} 5.73%) and m/e 82 (Σ_{35} 6.43%). The corresponding ions from **3** are m/e 426 (Σ_{35} 10.5%) and m/e 452 (Σ_{35} 2.09%).[7] These fragmentation patterns are not specific for the configuration at C-3.[6a,b]



2



3

The isolation of the secondary amine **3** in such substantial quantities is surprising as the axial primary amine **2**, in spite of its low concentration compared to that of ammonia, appears to compete with the latter effectively for the equatorial tosylate **1**. The minimum molar ratio of ammonia to **2** during a typical run is 75.[8] If the formation of **3** is assumed to involve displacement of a 3-β-*p*-toluenesulfonate group from **1** by a molecule of **2**, then the formation of the secondary amine **3** in 16% yield suggests that the primary amine **2** is at least 19 times [(75 × 16% yield of **3**)/64% yield of **2**] more nucleophilic than ammonia. This is unlikely in view of the hindered nature of axial amines and the crowded nature of the α side of **1** or the derived carbonium ion.[9]

The large competitive factor (19) may reflect a high local concentration of **2** in the vicinity of molecules of **1**. Since the formation of secondary amines in other cyclic systems was not observed previously,[2,10] it is proposed that **3** is formed by reaction in a nonpolar aggregate composed largely of the tosylate **1** and the primary amine **2**,[11] or by a heterogeneous reaction in which any undissolved tosylate **1** reacts with amine **2** which is adsorbed on its surface. The large, nonpolar, steroidal tosylate molecules would be expected to be less soluble and/or more prone to form aggregates in liquid ammonia than would the smaller molecules studied earlier.[2,10] Indeed, under one set of conditions the yield of **3** could be reduced from 10 to 1% by replacing some of the ammonia with the unassociated diluent ether. The use of smaller quantities of **1** in the same volumes of ammonia also effectively prevented the formation of **3**.

Three attempts were made to prepare the secondary amine in better yield by avoiding the competing substitution by ammonia. The first of these utilized sulfolane, a nonassociated solvent of high polarity[12] [dielectric constant (30°) 44[12a] compared to that for ammonia (25°) 16.9[13]] as a medium for the homogeneous reaction of the primary amine **2** and the tosylate **1**. The second involved the reaction of the latter compounds in the neat homogeneous melt,[14] while the third approach was to use methanol, an associated solvent of high polarity [dielectric constant (25°) 32.7][15] as a medium for the homogeneous reaction. Unfortunately, extensive elimination occurred in sulfolane[16] and in the melt, and only the reaction in the melt produced a detectable quantity of di-5α-cholestan-3α-ylamine (**3**). The yield was about 11% as determined by pmr analysis of the crude product, but only 5% could actually be isolated. No secondary amine was isolated from the reaction conducted in methanol. The primary amine was unable to compete with methanolysis and elimination.[17] Methanol, unlike ammonia, is apparently capable of solvating the reactant molecules individually; this is not surprising in view of the availability of the nonpolar methyl group on each solvent molecule.

Evidently, to obtain a high ratio of substitution to elimination in this type of system, it is necessary that the medium be very polar and that the concentration of good nucleophiles in the vicinity of the substrate be high. While the high polarity of sulfolane probably promotes the required SN1 reaction,[16,18] the second condition might not be met in this solvent, since its nonassociated nature presumably precludes aggregate formation of the reactants. Instead of reacting with the amine **2**, the unstable secondary carbonium ion from the tosylate can either lose a proton or undergo nucleophilic attack by the weakly basic solvent to form an unstable, axial displacement product which can, in turn,

(7) The percentage of the total ionization due to ions of this type increases with methylation of the amine function.[6a] The decrease observed in going from m/e 82 to m/e 452 may be a consequence of the large size (compared with methyl) or the secondary nature of the 5α-cholestan-3α-yl group.

(8) Moles of NH_3/(moles of **2** isolated + 0.5 × moles of **3** isolated); *e.g.*, 1.5/(0.019 + 0.001) = 75.

(9) (a) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, pp 288, 289; (b) J. Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, pp 173–175.

(10) T. Cohen, M. Malaiyandi, and J. L. Pinkus, *J. Org. Chem.*, **29**, 3393 (1964).

(11) For recent studies of aggregation in water, see E. S. Hand and T. Cohen, *J. Amer. Chem. Soc.*, **87**, 133 (1965); M. T. A. Behme and E. H. Cordes, *ibid.*, **87**, 260 (1965); M. T. A. Behme, J. G. Fullington, R. Noel, and E. H. Cordes, *ibid.*, **87**, 266 (1965).

(12) (a) R. L. Burwell, Jr., and C. H. Langford, *ibid.*, **81**, 3799 (1959); (b) E. M. Arnett and C. F. Douty, *ibid.*, **86**, 409 (1964).

(13) R. J. W. Le Fèvre and P. Russell, *Trans. Faraday Soc.*, **43**, 374 (1947).

(14) An additional rationale for this procedure was the consideration that the melt may behave as a colossal aggregate.

(15) P. S. Albright and L. J. Gosting, *J. Amer. Chem. Soc.*, **68**, 1061 (1946).

(16) The related solvent, dimethyl sulfoxide, provides an excellent medium for the solvolysis of **1** to a mixture of 5α-cholest-2-ene and 5α-cholest-3-ene; see H. R. Nace, *ibid.*, **81**, 5428 (1959).

(17) N. Pappos, J. A. Meschino, A. A. Fournier, and H. R. Nace, *ibid.*, **78**, 1907 (1956); H. R. Nace, *ibid.*, **74**, 5937 (1952).

(18) The attack of the hindered, axial amine on the hindered backside of the tosylate molecule by an SN2 reaction is extremely unlikely.

undergo elimination.[19] The polarity in the melt is probably too low to cause substantial SN1 reaction and an E2 reaction might be favored. Only in liquid ammonia are both requirements met, and the total substitution to elimination ratio is high (*ca.* 2).

Ammonolysis of equatorial steroidal tosylates might be of general synthetic value for obtaining diaxial bis steroidal amines. Apparently the polarity of the solvent is high enough to promote ionization while its ability to solvate large organic molecules is poor enough to cause high local concentrations (either in an aggregate or in a separate solid phase) of the tosylate and primary amine.

The presence of added primary amine in the ammonolysis reaction could be expected to increase the yield of secondary amine. When the ammonolysis was carried out under conditions favorable for secondary amine formation and in the presence of an equimolar quantity of primary amine, the yield of **3** increased to 26%.[20]

This study also points up the necessity, at least in the case of steroids, of using either dilute solutions or a cosolvent such as ether when primary amine, uncontaminated with secondary amine,[21] is desired from an ammonolysis reaction.[22,23]

Experimental Section[24]

Di-5α-cholestan-3α-ylamine (**3**).—A mixture of 7.00 g (12.9 mmol) of powdered 5α-cholestan-3β-yl tosylate (**1**)[25] and 95 ml of anhydrous ammonia in a steel bomb was maintained at 95–100° for 4 days. After the cooled bomb had been opened and the ammonia evaporated, the solid residue was triturated with 100 ml of anhydrous ether. Ethereal hydrogen chloride was added dropwise until precipitation of the amine hydrochloride was complete. The mixture was refrigerated for 2 hr, diluted with 50 ml of ether, and centrifuged at 1200 rpm for 6 min. The supernatent was decanted and the pasty residue was triturated with 50 ml of ether. The ether was removed by centrifugation, and the washing was repeated a second time. The residue was transferred to a medium-porosity sintered-glass funnel and residual ether removed in part by a mild aspirator vacuum. The residue was added to a solution of 15 ml of dioxane, 35 ml of ether, and 70 ml of 1 *N* sodium hydroxide solution, and the mixture was magnetically stirred for 20 min. The layers were separated and the aqueous solution was extracted with four 25-ml portions of ether. The combined ether extracts were washed several times with water, dried over anhydrous potassium carbonate, and evaporated under reduced pressure. The residual oil was dissolved in 25 ml of absolute ethanol at the boiling point. The cooled solution readily deposited crystals of secondary amine which were collected by filtration after cooling in an ice bath for 2 hr. The filtrate was evaporated under reduced pressure to furnish 2.78 g (55.6%) of 5α-cholestan-3α-ylamine (**2**), mp 86–87°. The melting points recorded for **2** are 87–88°,[2,26,27] 88–89°,[28] 104.0–104.5°,[2] 104.5–105.5°,[23] and 105–106°.[2]

The crude secondary amine was dissolved in 20 ml of ether at the boiling point and 20 ml of warm absolute ethanol was added gradually. Crystallization readily occurred. The cooled mixture was filtered, and the product was washed with absolute ethanol and dried in a vacuum desiccator with potassium hydroxide pellets: yield, 0.482 g (9.64%); mp 161–163°. Recrystallization from benzene–absolute ethanol furnished 0.435 g of flat plates, mp 164–165°. Additional recrystallizations from mixtures of anhydrous ethanol with petroleum ether (bp 60–80°), benzene, and ether furnished the analytical sample as glistening flat needles: mp 165–166°; $[\alpha]^{25}D$ +28° (*c* 2.0, chloroform) (reported for **2**, $[\alpha]^{chf}D$ +27°,[2,23,26] +28.6°;[26] reported for the N-acetyl derivative, $[\alpha]^{chf}D$ +36°,[2,26] +37°;[29] reported for 5α-cholestan-3β-ylamine, $[\alpha]^{chf}D$ +29°; reported for the N-acetyl derivative, $[\alpha]^{chf}D$ +12°[26]). As a first approximation, acetylation of **3** (a di-3α-ylamine) would lead to an increase in specific rotation, while acetylation of the isomeric di-3β-ylamine or 3α,3β-ylamine would lead to a decreased specific rotation. This expectation is borne out (see later section).

Anal. Calcd for $C_{54}H_{95}N$: C, 85.60; H, 12.60; N, 1.85; mol wt, 757.7. Found: C, 85.57; H, 12.50; N, 1.93; mol wt, 759 (osmometer).

When the ammonolysis is conducted in a similar manner with the same amount of **1** using a solvent mixture of 50 ml of ether and 45 ml of ammonia, or 80 ml of ether and 26 ml of ammonia, the yields of **3** dropped to 3.2 and 1.0%, respectively. The same trend is observed when lesser amounts of **1** (1.00 g, 1.84 mmol) are treated with 95 ml of ammonia only; no **3** was isolated. The use of greater amounts of **1** enhanced the yield of **3**. Treatment of 9.15 g (16.8 mmol) of **1** with 40 ml of ammonia only furnished **3** in 13.3% yield. Use of 15.7 g (29.0 mmol) of **1** and 41 ml (1.5 mol) of ammonia gave **3** (2.36 mmol) in 16.3% yield and **2** (18.6 mmol) in 64.0% yield. From these data the minimum molar ratio of ammonia to **2** was calculated in the discussion section.

The yields of **2** isolated in these studies varied from 48 to 82%. In some runs the isolated **2** was characterized by treating an anhydrous ether solution (4 ml/g of **2**) with acetic anhydride (50% excess) at room temperature to obtain the pure N-acetyl derivative[2] which immediately precipitated from the reaction mixture. Alternatively, a solution of **2** in petroleum ether (bp 64–66°) (15 ml/g of **2**) was treated with hydrogen chloride in ether solution to furnish the amine hydrochloride. The 5α-cholestan-3α-ylamine hydrochloride (**4**) was washed four times with the petroleum ether (12 ml/g of **2** used) employing centrifugation to separate **4**. The final residue was transferred to a medium-porosity sintered-glass funnel, washed with petroleum ether, and dried to furnish an amorphous solid, mp 323–325° uncor, with no decomposition (sealed evacuated Pyrex glass capillary, aluminum block melting point apparatus). The melt resolidifies quickly upon cooling. Recrystallization of **4** occurs readily at room temperature when 1 vol. of warm water is added to 9 vol. of a solution of **4** in 1-propanol–ethanol (5:4) at the boiling point: mp 330–331° uncor, with no decomposition (evacuated capillary); mp 261–263° uncor (open capillary), with decomposition to a red melt which did not resolidify upon cooling (lit.[28] open capillary mp 263° dec). The hydrochloride **4** was readily cut back to **2**, mp 102–103°, in the usual manner.

Acetylation of 3 was carried out in a 1:2 mixture of acetic anhydride and anhydrous pyridine (24 ml/g of **3**) during 24 hr at 95–100°. Work-up by various modifications of conventional procedures yielded crude N-acetyldi-5α-cholestan-3α-ylamine in up to 95% yield usually with mp ~159–162°. Several recrystallizations from ether–methanol and pentane–methanol furnished the analytical sample as needles: mp 163–164°; $[\alpha]^{20}D$ +70° (*c*

(19) D. S. Noyce and B. N. Bastian, *J. Amer. Chem. Soc.*, **82**, 1246 (1960); H. Weiner and R. A. Sneen, *ibid.*, **87**, 287, 292 (1965); G. R. Gray, F. C. Hartman, and R. Barker, *J. Org. Chem.*, **30**, 2020 (1965).

(20) This result suggests a practical approach to a bis steroidal amine synthesis involving an initial ammonolysis of a tosylate followed by the addition of a second batch of tosylate to the reaction mixture and continued heating.

(21) Two secondary amines were isolated, from the ammonolysis of cholest-5-en-3β-yl tosylate; see R. D. Haworth, L. H. C. Lunts, and J. McKenna, *J. Chem. Soc.*, 986 (1955).

(22) The standard 1-day ammonolysis reaction time previously employed[2] was later found to be a minimal period. Ammonolysis of *trans,cis*-2-decalyl tosylate for 4 days has been found by Dr. Edmond J. Jankowski in this laboratory to give an 80% yield of the pure *trans,trans*-2-decalylamine, compared to the 41% yield of the N-acetyl derivative previously reported.[2] Somewhat improved yields of **2** have also been recorded in this laboratory by Dr. M. Malaiyandi and Dr. L. Dennis McKeever.

(23) For an alternative efficacious synthesis of 5α-cholestan-3α-ylamine (**2**), see W. R. Hertler and E. J. Corey, *J. Org. Chem.*, **23**, 1221 (1958).

(24) Melting points were determined on a Kofler block utilizing polarized light and a stage-calibrated thermometer. The infrared spectra were taken on a Beckman IR-8 spectrophotometer. Pmr spectra were determined with a Varian A-60 spectrometer operated at 60 Mcps employing 6–10% w/v solutions or the neat compounds. Proton signals are reported in τ values relative to tetramethylsilane as an internal reference. Microanalyses were performed by Elek Microanalytical Laboratories, Torrance, Calif., and by Scandinavian Microanalytical Laboratory, Herlev, Denmark.

(25) (a) I. Malunowicz, J. Fajkoš, and F. Šorm, *Collect. Czech. Chem. Commun.*, **25**, 1359 (1960); (b) W. Stoll, *Z. Physiol. Chem.*, **207**, 147 (1932).

(26) C. W. Shoppee, D. E. Evans, H. C. Richards, and G. H. R. Summers, *J. Chem. Soc.*, 1649 (1956).

(27) A. K. Bose, J. F. Kistner, and L. Farber, *J. Org. Chem.*, **27**, 2925 (1962).

(28) L. Lábler, V. Cerný, and F. Šorm, *Collect. Czech. Chem. Commun.*, **19**, 1249 (1954).

(29) H. B. Henbest and W. R. Jackson, *J. Chem. Soc.*, 954 (1962).

2.0, chloroform). The infrared spectrum (Nujol solution film) showed absorption at 6.06 μ (amide carbonyl).

Anal. Calcd for $C_{56}H_{97}NO$: C, 84.04; H, 12.22; N, 1.75. Found: C, 84.05, 84.10; H, 12.06; 12.17; N, 1.71, 1.75.

The acetylation of **3** could not be carried out in the same way as that used for **2**. Addition of an excess of acetic anhydride to a 0.05 *M* solution of **3** in ether resulted in the immediate precipitation of **3** (63%). After 1 hr at room temperature, work-up of the reaction mixture afforded unchanged **3**. No amide carbonyl was detected in the infrared spectrum of any of the recovered **3**. However, acetylation readily occurred in a 0.07 *M* solution of **3** in acetic anhydride at 95–100° during 6 hr.

Reaction of 5α-Cholestan-3β-yl Tosylate (1) with 5α-Cholestan-3α-ylamine (2). A. Attempted Reaction in Sulfolane.—A solution of 0.679 g (1.25 mmol) of **1** and 0.969 g (2.50 mmol) of **2** in 25 ml of pure sulfolane[30] was maintained at 95–100° under nitrogen in a stoppered flask for 96 hr. Work-up afforded an olefinic mixture (2- and 3-cholestenes) (72%) identified by characteristic infrared[31] and pmr spectra and the amine **2** (76% recovery), mp 88–90° (identified as the N-acetyl derivative). In the alcohol-isolation step which usually leads to immediate precipitation of **3**, only a low-melting (<70°) solid (48 mg) separated after 1 day at 2° (10% yield calculated as olefin). Infrared and pmr evidence suggests that this fraction is mainly olefin. However, the presence of some **3** cannot be discounted.

B. Reaction in the Melt.—A similar reaction was carried out without solvent. The crude secondary amine fraction contained ~72% **3** (11% yield) based on integration analysis of the characteristic 3β-hydrogen signal in the pmr spectrum. Consecutive recrystallizations from ether–methanol, pentane–absolute ethanol, and ether–methanol afford 0.040 g (5.3%) of **3**, mp 163–164° (identified by a mixture melting point and its infrared spectrum). Recovered **1** was 23% and recovered **2** was 70%.

C. Attempted Reaction in Methanol.—A solution of 1.357 g (2.50 mmol) of **1** and 1.938 g (5.00 mmol) of **2** in 135 ml of methanol (reagent grade, distilled) was maintained at 95–100° in a sealed glass vessel for 94.5 hr. After removal of the solvent under vacuum, the solid residue was worked up in the usual way. No secondary amine was isolated. The starting amine **2** was isolated in 94% recovery with the mp 89–90°. The methyl ether and olefin fraction weighed 0.915 g. The theoretical yields of cholestenes and 3-methoxycholestane are 0.927 and 1.007 g, respectively. The infrared spectrum of this fraction, initially an oil which later solidified, as a thin film indicated that the mixture consisted mainly of the methyl ether.

D. The reaction in anhydrous ammonia was carried out with relative amounts of tosylate **1** and anhydrous ammonia comparable to the aforementioned ammonolysis reaction which led to **3** in 16.3% yield. The volume of anhydrous ammonia was 17 ml of which *ca.* 5.5 ml would be in the gaseous state during reaction. A mixture of 5.000 g (9.211 mmol) of **1**, 3.571 g (9.211 mmol) of **2**, and the anhydrous ammonia in a steel bomb was maintained at 100° for 97.5 hr. The reaction mixture was worked up to afford the crude secondary amine **3** which was purified by recrystallization from ether–absolute ethanol followed by recrystallization from absolute ethanol–petroleum ether (sodium dried, distilled, bp 95–99°) to afford 0.9183 g (26.3%) of **3** as minute plates, mp 165–165.5°. Recrystallization from ether–95% ethanol did not alter the melting point. The apparent yield of **2**, taken as the increase in weight of **2** over that originally present, was 1.3365 g (37.4%), mp 104–105.[32]

Mass spectra were obtained with a LKB-9000 mass spectrometer (LKB Produkter, Stockholm, Sweden), using the direct probe with a glass sample holder. The ionizing voltage was maintained at 70 eV and the ionizing current at 70 μA, using a rhenium ribbon filament; the accelerating voltage was 3.5 kV, and the ion source temperature was 250°.

The mass spectrum of **2** (probe temperature 40°) shows the base peak at *m/e* 370 (100%, M − NH_3, Σ_{35} 6.83%; m* 354.0: calcd 353.8 for 387 → 370). The ionized olefin further fragments in a characteristic manner.[33] Nitrogen-containing ions are found at *m/e* 82 (94%), *m/e* 69 (83%, Σ_{35} 5.69%),[34] *m/e* 56 (84%), and *m/e* 43 (50%, $\cdot CH_2CH{=}^{+}NH_2$).[6]

The mass spectrum of **3** (probe temperature 200°) in the high half of the mass range shows peaks at *m/e* 757 (14.3%, M), *m/e* 386 [44%, (M − $C_{27}H_{47}\cdot$), Σ_{35} 4.65%],[35,36] *m/e* 452 (20%; m* 270.0: calcd[37] 269.9 for 757 → 452), *m/e* 439 (1.7%),[34] and *m/e* 426 (100%; m* 240.0: calcd 239.7 for 757 → 426). In the low half of the mass range the spectrum is similar to that of **2**. Some of the pertinent ions are *m/e* 370 (11%), *m/e* 355 (2.7%), *m/e* 316 (2.0%), *m/e* 257 (2.8%), *m/e* 82 (12%, Σ_{35} 1.20%), *m/e* 69 (24%, Σ_{35} 2.52%),[34] and *m/e* 56 (18%, Σ_{35} 1.92%).

Registry No.—**2**, 2206-20-4; **3**, 16980-58-8; **3** (N-acetyl), 16980-59-9.

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(30) Kindly furnished by Professor J. F. Coetzee.

(31) H. B. Henbest, G. D. Meakins, and G. W. Wood, *J. Chem. Soc.*, 800 (1954).

(32) The primary amine **2** has more recently been recrystallized, without any apparent difficulty (compare ref 2), from ethanol–water or methanol–water with a high melting point.[23] High-melting **2** has been obtained following the procedure of Hertler and Corey,[23] while the similar procedure of Bose, Kistner, and Farber[27] furnished low-melting **2** in an initial run, but high-melting **2** in two subsequent runs.

(33) S. Bergström, R. Ryhage, and E. Stenhagen, *Svensk Kem. Tidskr.*, **73**, 566 (1961); H. Audier, M. Fétizon, and W. Vetter, *Bull. Soc. Chim. Fr.*, 1971 (1963); H. Budzikiewicz, J. I. Brauman, and C. Djerassi, *Tetrahedron*, **21**, 1855 (1965); H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Structure Elucidation of Natural Products by Mass Spectrometry," Vol. II, Holden-Day, Inc., San Francisco, Calif., 1964, pp 94–101.

(34) This ion may be, at least in part, the ion radical due to the amino function or substituted amino function and carbon atoms 3, 4, 5, and 6; see R. Goutarel, "Les Alcaloides Stéroidiques des Apocynacées," Hermann, Paris, 1964, pp 52, 53.

(35) Carbon–nitrogen bond cleavage, with loss of 5α-cholestan-3-yl radical (or a hydrogen atom and a mixture of 5α-cholest-2-ene and 5α-cholest-3-ene), leads to this even electron ion. This type of ion is observed to a small extent in the fragmentation of N-ethylcyclopentylamine (loss of ethyl radical), is more prominent in the fragmentation of N-acetyl-N-ethylcyclopentylamine (consecutive loss of ketene, with hydrogen rearrangement to nitrogen, and ethyl radical),[6c] and becomes the base peak in the fragmentation of N-methylcyclopentylamine (ring carbon–nitrogen cleavage) where the stable ion *m/e* 30 is formed.[36]

(36) J. H. Beynon, "Mass Spectrometry and Its Applications to Organic Chemistry," Elsevier Publishing Co., Amsterdam, 1960, pp 390, 391.

(37) The calculated value is the same for the change 370 → 316. However, metastable peaks were not detected for this reaction in the spectra of **2** and the N-acetyl derivative of **2**.