grams (2 moles) of thiolacetic acid was added slowly with stirring to 336.6 g. (4 moles) of 2-methyl-2-pentene (95% mol. % minimum, Phillips Petroleum Co, Special Products Division, Bartlesville, Okla.). The reaction mixture was irradiated during the addition with light from a 100 watt bulb,[5] and irradiation and stirring were continued for 1 hr. after addition of the thiolacetic acid was complete. Distillation of the reaction mixture yielded 308.5 g. (96.2%) of 1-ethyl-2-methylpropyl thiolacetate, b.p. 70° (13 mm.), n_D^{25} 1.4603.

Anal. Calcd. for $C_8H_{16}OS$: C, 59.95; H, 10.06. Found: C, 60.46; H, 10.12.

1-Ethyl-2-methylpropanethiol. Three hundred five grams (1.92 moles) of 1-ethyl-2-methylpropyl thiolacetate was refluxed for 1 hr. in 2.5 l. of 10% aqueous-alcoholic (50% by volume) potassium hydroxide solution. The solution was neutralized with glacial acetic acid and the non-aqueous phase separated. The aqueous portion was extracted three times with pentane and the pentane extracts were dried over anhydrous magnesium sulfate. The combined non-aqueous phase and pentane extracts were distilled giving 203 g. (90.5%) 1-ethyl-2-methylpentanethiol, b.p. 135°, n_D^{25} 1.4467.

Anal. Calcd. for $C_6H_{14}S$: C, 60.95; H, 11.93. Found: C, 61.46; H, 11.75.

The 2,4-dinitrophenyl sulfide derivative of the pure thiol was prepared according to the method of Bost, Turner, and Morton.[6] The sulfide melted at 60–60.5° after crystallization from absolute alcohol.

Anal. Calcd. for $C_{12}H_{16}O_4N_2S$: N, 9.85. Found: N, 10.13.

4-Methyl-1-pentyl thiolacetate. Starting with 200 g. (2.38 moles) of 4-methyl-1-pentene (95% mol. % minimum, Phillips Petroleum Co., Special Products division, Bartlesville, Okla.) and 121.2 g. (1.59 moles) of thiolacetic acid, 238 g. (93.5%) of 4-methyl-1-pentyl thiolacetate, b.p. 89° (16 mm.), n_D^{25} 1.4575, was obtained by the procedure described above.

Anal. Calcd. for $C_8H_{16}OS$: C, 59.95; H, 10.06. Found: C, 60.55; H, 9.56.

Cyclohexyl thiolacetate. This compound was prepared in 92.5% yield by the method described above. The boiling point of this compound was 77° (5.8 mm.). Cunneen[7] reported b.p. 90° (14 mm.).

2-Phenyl-1-propyl thiolacetate. This compound was prepared in 90% yield by the method described above. The boiling point of this compound was 105–107° (1.8 mm.). Brown, Jones, and Pinder[8] reported b.p. 105° (4 mm.).

1-Ethyl-2-methylpropanesulfonyl chloride. Twenty grams (0.12 mole) of 1-ethyl-2-methylpropyl thiolacetate, suspended in water, was chlorinated at 0°, and the product processed according to the procedure of Douglass and Johnson.[3] Distillation through a 3-plate Vigreux column yielded 14.8 g. (62%) of 1-ethyl-2-methylpropanesulfonyl chloride, b.p. 70–75° (2 mm.), n_D^{25} 1.4651.

Anal. Calcd. for $C_6H_{13}O_2SCl$: C, 39.23; H, 7.13. Found: C, 39.03; H, 6.72.

Lithium aluminum hydride reduction of 2-methyl-3-pentanesulfonyl chloride. Nine grams (0.05 mole) of 1-ethyl-2-methylpropanesulfonyl chloride in 25 ml. of dry ether was added slowly with stirring to a slurry of 5.7 g. (0.15 mole) of lithium aluminum hydride in 200 ml. of dry ether. After stirring and heating on the steam bath for an additional 2 hr., the excess lithium aluminum hydride was destroyed by addition of 250 ml. of 10% sulfuric acid. The non-aqueous layer was separated and the aqueous layer was extracted three times with 50 ml. portions of ether. The ether extracts and the non-aqueous layer combined and the ether distilled. Steam distillation of the residue gave 2 g. (30%) of crude 2-methyl-3-pentanethiol. The 2,4-dinitrophenyl sulfide derivative, prepared according to the method of Bost, Turner, and Morton,[6] melted at 60–61° after crystallization from alcohol. The melting point of a mixture with a comparable derivative, prepared from the thiol resulting from hydrolysis of 2-methyl-3-pentyl thiolacetate, was not depressed.

Other alkanesulfonyl chlorides. In a manner similar to that described above 17.5 g. (77%) of *4-methyl-1-pentanesulfonyl chloride*, b.p. 84° (2.5 mm.), n_D^{25} 1.4550, was obtained from 20 g. of 4-methyl-1-pentyl thiolacetate.

Anal. Calcd. for $C_6H_{13}O_2SCl$: C, 39.23; H, 7.13. Found: C, 38.97, 38.79; H, 6.63, 6.74.

A 72% yield of cyclohexanesulfonyl chloride, b.p. 70° (0.5 mm.), n_D^{25} 1.4958, was obtained from cyclohexyl thiolacetate. Borsche and Lange[9] reported a b.p. of 127–128° (15 mm.), and an anilide melting at 87°. The anilide prepared from our sulfonyl chloride melted at 85–85.5° (uncorr.).

A 54% yield of *2-phenyl-1-propanesulfonyl chloride*, b.p. 126° (2 mm.), was obtained from 2-phenyl-1-propyl thiolacetate.

Anal. Calcd. for $C_9H_{11}O_2SCl$: C, 49.42; H, 5.07. Found: C, 50.05, 50.07; H, 4.91, 5.03.

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(5) In most cases visible light is sufficient to initiate the reaction; in some cases, however, peroxides and heating on a water bath or in a bomb are required to increase the yield. Ref. (2) (b) in text.

(6) R. W. Bost, J. O. Turner, and R. D. Morton, *J. Am. Chem. Soc.*, **54**, 1985 (1932).

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(8) R. Brown, W. E. Jones, and A. R. Pinder, *J. Chem. Soc.*, 2123 (1951).

(9) W. Borsche and W. Lange, *Ber.*, **38**, 2767 (1905).

Conversion of Steroidal Alkaloids, Tomatidine and Solasodine into Dihydrosapogenins

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The elegant work of White[1] on the deamination of aliphatic amines prompted us to apply his method to the deamination of the steroidal alkaloids, tomatidine (I) and solasodine (II).

Accordingly, I and II were converted to their respective *O,N*-diacetyl-22,*N*-dihydro and *O,N*-diacetyl-5,6,22,*N*-tetrahydro derivatives[2] (Ia), (IIa) and treated with nitrogen tetroxide to give the corresponding *N*-nitrosoamides, Ib and IIb. Upon subjecting these crude *N*-nitroso derivatives to thermal deamination and hydrolyzing the resulting diacetates with methanolic alkali, nitrogen free products were obtained. Chromatography on alumina yielded dihydroneotigogenin[3] (Ic) (from tomatidine) and dihydrotigogenin (IIc)(from solasodine) in moderate yields. The deaminated prod-

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(2) Y. Sato and H. G. Latham, Jr., *J. Am. Chem. Soc.*, **78**, 3150 (1956).

(3) The authors are indebted to Dr. Callow of the National Institute for Medical Research, London, for a generous gift of neotigogenin acetate.

ucts agreed[4] in physical properties with authentic specimens.

The dihydrosapogenins (Ic and IIc) were also obtained from the alcohols, *N*-acetyl-22,*N*-dihydrotomatidine (Id) and *N*-acetyl-5,6,22,*N*-tetrahydrosolasodine (IId). In this case the intermediate is apparently the 3-nitrite ester (Ie, IIe) of the respective nitroso derivatives, as shown by their infrared spectra ($\lambda_{max.}^{chlf.}$ No hydroxyl; 5.78, 6.09 and 6.66 μ).

A second component, presumed to be 16,22-epoxycholest-25-en-3β-ol[1, 5] (III) from infrared absorption data ($\lambda_{max.}^{chlf.}$ 6.05, 11.24 μ, $R_1R_2C = CH_2$) was not obtained in sufficient purity for positive identification.

The sapogenins have previously been converted into steroidal alkaloids[6] and their derivatives[2] but the reverse transformation of steroidal alkaloids into dihydrosapogenins specifically has not hitherto been reported.

EXPERIMENTAL[7]

N-Acetyl-N-nitroso-22,N-dihydrotomatidine acetate (Ib). *O,N*-Diacetyl-22,*N*-dihydrotomatidine (1.07 g.)[2] was dissolved in 15 ml. of carbon tetrachloride, cooled to 0°, and added dropwise, with swirling, to 15 ml. of a carbon tetrachloride solution of nitrogen tetroxide (*ca.* 1.5*M*) at 0° containing 1.5 g. of anhydrous sodium acetate. The anhydrous sodium acetate was previously added to the nitrogen tetroxide solution at −60° and then allowed to warm slowly to 0°. After allowing the reaction mixture to stand at 0° for 15 min., then at room temperature for 20 min., a slurry of ice and water was added to the solution. The organic phase was washed with water, dried over anhydrous magnesium sulfate, and evaporated to dryness. The crude oil (1.1 g.) $\lambda_{max.}^{chlf.}$ 5.79, 6.66 μ, was used for deamination without further purification.

Dihydroneotigogenin (Ic). The crude nitroso derivative (Ib) was dissolved in 60 ml. of heptane (b.p. 98.5°) and refluxed gently for 16 hr. The crude, slightly colored oil, recovered after removal of the solvent, was subjected to chromatography on neutral alumina. Elution with benzene-ether (1:1) yielded 520 mg. of oil and further elution with 0.5% methanol in ether gave 273 mg. of another oily fraction.

The above benzene-ether (1:1) eluate was hydrolyzed with 20 ml. of methanolic potassium hydroxide (5%) for 1 hr. After partial concentration and addition of water the precipitate was collected and again subjected to chromatography. The portion eluted with 0.5% methanol in ether gave 155 mg. of dihydroneotigogenin. Recrystallization from acetone-hexane yielded plates, m.p. 170–173°, identical in all respects with an authentic specimen.

Anal. Calcd. for $C_{27}H_{46}O_3$: C, 77.46; H, 11.08. Found: C, 77.35; H, 10.92.

The dibenzoate, prepared in the usual manner (benzoyl chloride-pyridine) crystallized from ether-methanol as rods, m.p. 114–116.5°, identical with respect to melting point, mixture melting point, and infrared spectrum with an authentic specimen. The compound seems to crystallize with one-half mole of methanol. For analysis the substance was dried at 110° for 8 hr. in high vacuum.

Anal. Calcd. for $C_{41}H_{54}O_5$: C, 78.55; H, 8.68. Found: C, 78.68; H, 8.73.

The early portion of the 0.5% methanol-ether eluate was an oil which failed to crystallize. When this was rechromatographed over alumina and eluted with 0.25% methanol-ether, a small amount of substance, m.p. 68–80°, $\lambda_{max.}^{chlf.}$ 6.06, 11.24 μ, was obtained. Its infrared spectrum somewhat resembled 16,22-epoxycholest-25-en-3β-ol,[5] (III). It gave a positive tetranitromethane test for double bonds.

N-Acetyl-N-nitroso-5,6,22,N-tetrahydrosolasodine acetate (IIb). The compound was prepared in the same manner as Ib. From 320 mg. of IIa, 310 mg. of crude oil was obtained. The infrared spectrum of the compound, $\lambda_{max.}^{chlf.}$ 5.79, 6.66 μ, was similar to that of Ib.

Dihydrotigogenin (IIc). The crude nitroso derivative (IIb) (295 mg.) was deaminated in heptane (b.p. 98.5°, 50 ml.) and hydrolyzed in the same way as Ib. The collected crude, dry product weighed 170 mg. One hundred forty milligrams of the above substance was chromatographed over alumina and the fraction (53 mg.) eluted with 0.5% methanol in ether proved to be dihydrotigogenin. Recrystallization from acetone yielded rods of m.p. 168–170.5°. It agreed in properties (melting point, mixture melting point, and infrared spectrum) with authentic dihydrotigogenin.

Anal. Calcd. for $C_{27}H_{46}O_3$: C, 77.46; H, 11.08. Found: C, 77.36; H, 11.17.

The dibenzoate, crystallized as plates from ether-methanol, m.p. 112–114.5°, was identical with respect to m.p., mixture m.p., and infrared spectrum with an authentic specimen.

Anal. Calcd. for $C_{41}H_{54}O_5$: C, 78.55; H, 8.68. Found: C, 78.31; H, 8.92.

The sample for analysis was dried for 8 hr. at 110° in high vacuum.

The early oily fraction eluted with 0.5% methanol-ether, as in the case of Ic, was rechromatographed on a silica gel column but again no significant progress (m.p. 75–90°) was achieved toward the isolation of the expected unsaturated derivative, III.

Dihydroneotigogenin from N-acetyl-22,N-dihydrotomatidine, (Id). To 15 ml. of a carbon tetrachloride solution of nitrogen tetroxide (ca. 1*M*), containing 500 mg. of anhydrous sodium acetate, at 0° was added, dropwise and with swirling, 200 mg. of *N*-acetyl-22,*N*-dihydrotomatidine in 11 ml. of chloroform while cooling the mixture in an ice-bath. After standing for 30 min. at 0°, it was brought to room temperature and allowed to stand for an additional 15 min. Water was added to the mixture and the separated organic phase was washed thoroughly with water. Upon removal of the solvent a partially crystalline slightly yellowish substance (220 mg.) was obtained. A recrystallized sample, m.p. 104–108°, exhibited absorption bands at 5.78, 6.09, and 6.66 μ in chloroform. This is presumably the 3-nitrite ester, Ie.

When the above crude ester was successively deaminated, hydrolyzed (first with base and then with methanol-hydrochloric acid), and chromatographed as previously described (Ic) dihydroneotigogenin (30 mg.), m.p. 164–167°, was again obtained.

Dihydrotigogenin from N-acetyl-5,6,22,N-tetrahydrosolasodine, (IId). The 3-nitrate ester (IIe) was prepared in the same manner as Ie. The compound failed to crystallize. The infrared spectrum was similar to Ie. When the compound was processed in the above manner, dihydrotigogenin was obtained.

(4) It was noticed that Ic and IIc and their benzoates have nearly indistinguishable infrared spectra in chloroform or carbon disulfide. Their spectra in Nujol mulls differ somewhat.

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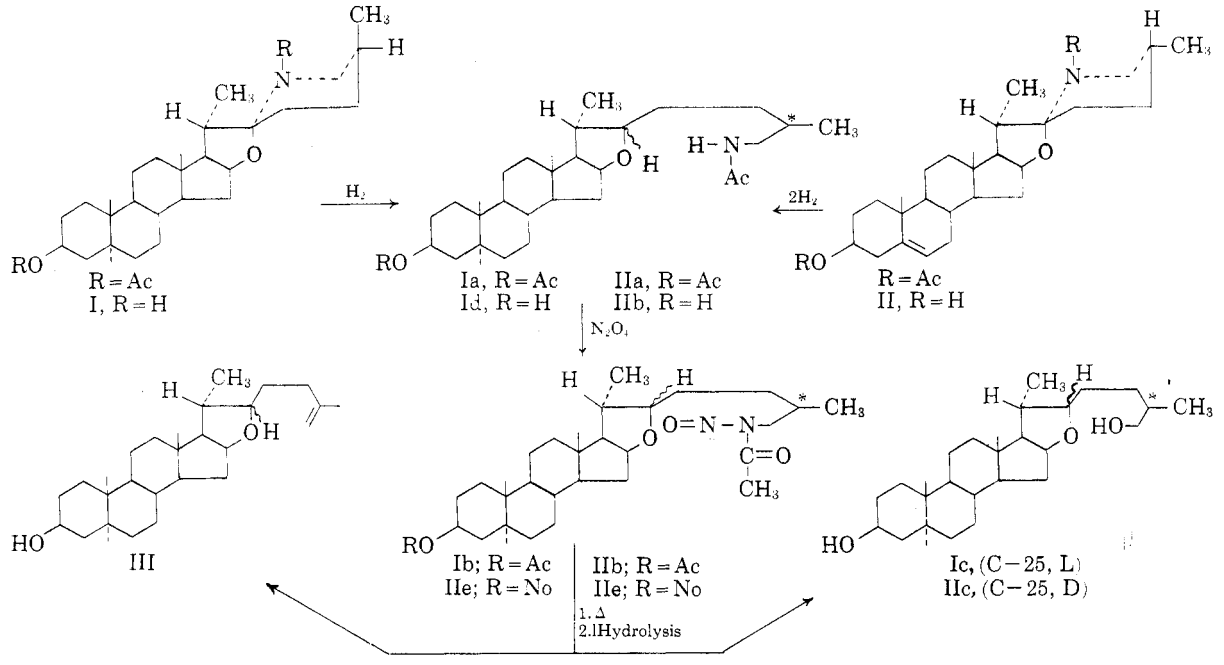
(7) All melting points were taken on the Kofler block and are uncorrected. We are indebted to Dr. W. C. Alford and his associates for the microanalyses and to Mr. H. K. Miller, all of this Institute, for the spectrophotometric measurements.



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A Convenient Method for Preparation of Quaternary Ammonium Salts

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Three laboratory procedures are generally available for the synthesis of quaternary ammonium salts.[1,2] These methods are: (*a*) neutralization of the free quaternary ammonium base with the acid of the desired anion, *viz.*, $R_4NOH + HX \rightarrow R_4NX + H_2O$, (*b*) metathetical reactions involving the formation of an insoluble compound and the quaternary ammonium salt, *viz.*, $R_4NY + AX \rightarrow AY + R_4NX$, and (*c*) alkylation of amines (the Hofmann reaction), *viz.*, $R_3N + RX \rightarrow R_4NX$.[2-4] The work reported here presents a fourth approach based upon the reaction of equivalent quantities of the free quaternary ammonium base and the ammonium salt of an anion.

The kinship of the quaternary ammonium bases to the alkali metal hydroxides is well known.[5,6] Accordingly, the quaternary ammonium hydroxides will tend to displace the more weakly basic ammonia from aqueous solutions of ammonium salts as per the equation: $R_4NOH + NH_4X \rightarrow R_4NX + H_2O + NH_3$. Because this latter reaction may be driven quantitatively to the right without destruction of the quaternary ammonium ion, a simple, direct means for the preparation of the quaternary ammonium salts of many of the less stable, less familiar acids is made possible. Though the ensuing examples utilize tetraalkylammonium bases, there should be no restrictions preventing the use of other quaternary ammonium bases under suitable experimental conditions.

EXPERIMENTAL

Aqueous solutions (2–3 wt. %) of tetramethyl- and tetraethylammonium hydroxide were prepared from the commercially available 10 wt. % solutions (Eastman Kodak "White Label" grade). The exact titers of the dilute solutions were obtained by titration with standard 0.1*N* acid to the phenolphthalein end-point. All ammonium salts used were of "Reagent" grade.

Tetramethylammonium thiocyanate. To 2.831 g. (0.03106 mole) of tetramethylammonium hydroxide in 125 ml. of water was added 2.364 g. (0.03106 mole) of ammonium thiocyanate. The solution was boiled down to a volume of 50 ml. three times, the water being replaced after each volume decrease. The mixture was then carefully heated to dryness and placed in an oven for 2 hr. at 100°. Yield: 100% (4.1 g.).

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