N-Methyl-exo-3-phenyl-5-norbornene-endo-2-amine. A mixture of 23.1 g. (0.125 mole) of *exo*-3-phenyl-5-norbornene-*endo*-2-amine and 50 g. of ethyl formate was refluxed for 1.5 hr.; after 1 hr. a precipiate which had formed dissolved again. The reaction mixture was concentrated *in vacuo* and the residual oil was dissolved in ether and added dropwise to a slurry of 7.0 g. of lithium aluminum hydride in 150 ml. of ether. After refluxing for 2 hr., 100 ml. of a mixture of ether--ethyl acetate (1:2) was added, followed by 35 ml. of water and 2 g. of anhydrous sodium sulfate. The suspension was filtered and the filtrate distilled to give 20.5 g. (82%) of an oil, b.p 92–102° (0.07 mm.), n_D^{25} 1.5487.

A *maleic acid salt* was prepared and on recrystallization from ethyl methyl ketone was obtained as white crystals, m.p. 186–186.5°.

Anal. Calcd. for $C_{14}H_{17}N \cdot C_4H_4O_4$: C, 68 55; H, 6.71. Found: C, 68.48; H, 6.82.

N,N-Dimethyl-exo-3-phenyl-5-norbornen-endo-2-amine. To 12 g. (0.25 mole) of 98% formic acid at 0° were added dropwise 9.4 g. (0.05 mole) of *exo*-6-phenylnorbornen-*endo*-5-amine and 15 g. of 37% aqueous formaldehyde. The reaction mixture was refluxed for 6 hr. and then 6 ml. of hydrochloric acid was added. The excess of formic acid and formaldehyde was removed *in vacuo,* the residue diluted with water, made basic with 40% sodium hydroxide, and extracted with ether; the ethereal extract was dried over magnesium sulfate, filtered, and distilled. Two fractions were obtained: (1) b.p. 123–127° (1.2–1.4 mm.) $n_D^{24.3}$ 1.5458, 5.7 g. (54%); and (2) b.p. 167–169° (1.6 mm.) $n_D^{24.3}$ 1.5659, 3.3 g. (31%). Fraction II showed a strong absorption at 6 μ in its infrared absorption spectrum which indicated the presence of an amide carbonyl band; the fractions were combined, dissolved in 60 ml. of anhydrous ether and added to a suspension of 2.0 g. of lithium aluminum hydride in 100 ml. of ether. After 2 hr. of reflux 30 ml. of an ethyl acetate–ether mixture (1:2) was added followed by 10 ml. of water. The suspension was filtered and the filtrate on distillation yielded 5.1 g. (52%) of an oil, b.p. 114–119° (1.1 mm.) $n_D^{22.5}$ 1.5472.

The *maleic acid salt* was prepared and recrystallized from an ethyl acetate–ether mixture. It was obtained as white crystals, m.p. 148.5–149.5°.

Anal. Calcd. for $C_{15}H_{19}N \cdot C_4H_4O_4$: C, 69.28; H, 7.04. Found: C, 69.24; H, 7.16.

N-Methyl-exo-3-cyclohexylnorbornane-endo-2-amine. A suspension of 1 g. of *N*-methyl-*exo*-3-phenyl-5-norbornen-*endo*-2-amine, 1 ml. of 12*N* hydrochloric acid, 20 ml. of absolute ethanol, and 0.1 g. of platinum oxide was shaken under 50 lbs. of hydrogen for 3.5 hr. After the suspension was filtered, the filtrate was concentrated and the residue dissolved in water, made basic with 10% sodium hydroxide, and extracted with ether. The ethereal extract was dried, filtered, and concentrated to yield an oil.

The *maleic acid salt* was prepared and was isolated as a white solid, m.p 139–141°.

Anal. Calcd. for $C_{18}H_{29}NO_4$: C, 66 96; H, 8.99; N, 4.34. Found: C, 66 92; H, 9 01; N, 4.23.

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Physical Constants of 6-Methylenedihydrodesoxymorphine

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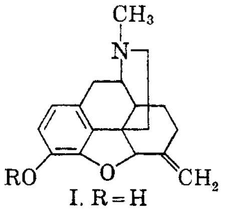
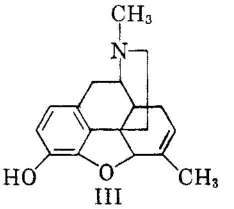
The synthesis of 6-methylenedihydrodesoxymorphine (I) has been described, and values have been reported for the melting point and specific rotation of the compound.[1] As the synthesis is based on the demethylation of 6-methylenedihydrodesoxycodeine (II) in the presence of an acidic catalyst. a possible by-product of the reaction is 6-methyl-Δ^6-desoxymorphine (III), resulting from the rearrangement of the exocyclic double bond of I to the more stable[2] endocyclic position.



I. R = H
II. R = CH_3



III

The results of investigations in our laboratories indicate that samples of I used in the above-mentioned determinations of melting point and specific rotation may have been contaminated with III. A sample of I prepared in our laboratories by the method described below showed a constant specific rotation, $[\alpha]_D^{25}$ −117°, and melting point, 208.5–210.5°, after three successive crystallizations from acetone. The value of specific rotation previously reported[1] for I is −140°, which is between −117°, the value for pure I, and −215°, the value reported for III.[3,4] It was observed during the work described here that a sample of III[5] and an impure sample of I had absorption maxima at 6.66 μ, 7.57 μ, and 12.3 μ, while the purified sample of I did not.

The identity of purified I was established by converting the material to the original compound II with diazomethane.

EXPERIMENTAL[6]

6-Methylenedihydrodesoxymorphine (I). A dry, 1 × 8-in. test tube was charged with 7 g. (0.061 mole) of pyridine hydrochloride (Eastman Practical Grade) and fitted with a rubber stopper bearing a tube for introducing nitrogen beneath the surface of the salt. The pyridine hydrochloride was dried by heating the test tube in an oil bath at 220–230° while nitrogen was passed through the molten salt. While the nitrogen was still flowing, the tube was cooled, and 2 g. (0.0674 mole) of II was added. The mixture was heated at a temperature of 190–195° for 16 min. in the presence of nitrogen and cooled slightly, after which 30 ml. of water contain-

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(1) M. S. Chadha and H. Rapoport, *J. Am. Chem. Scc.,* **79,** 5730 (1957).

(2) (a) H. C. Brown, J. H. Brewster, and H. Shechter, *J. Am. Chem. Soc.,* **76,** 467 (1954); (b) R. Fleck, *J. Org. Chem.,* **22,** 439 (1957); (c) H. C. Brown, *J. Org. Chem.,* **22,** 439 (1957).

(3) H. D. Brown, I. M. Rasmussen, G. B. Payne, and K. Pfister III, *J. Am. Chem. Soc.,* **75,** 6238 (1953).

(4) The specific rotation reported in reference (3) was determined on material which melted at 225–229°, whereas material crystallized once more melted at 235–237°.

(5) We are indebted to Dr. Karl Pfister III of Merck and Co. for a sample of authentic 6-methyl-Δ^6-desoxymorphine.

(6) All melting points are corrected.

ing about 0.02 g. of sodium hydrosulfite was added. The resulting solutions from ten such runs were combined, and adjusted to *p*H 12 with 50% sodium hydroxide. The mixture was extracted four times with 350-ml. portions of ether to remove nonphenolic materials (about 20–30% of the starting material was recovered). The aqueous phase was adjusted to *p*H 8.5 with ammonium chloride and extracted four times with 350-ml. portions of a 3:1 mixture of chloroform and isopropyl alcohol. Evaporation of the extract gave 8 g. of residue, which was fractionated by chromatography on 400 g. of Florisil to give 2.5 g. of crude product. Solvents used in the chromatographic separation were 2000 ml. of 75% (by volume) benzene–25% isopropyl alcohol, followed by 2200 ml. of 97% methanol–2% water–1% concentrated (28–30%) ammonium hydroxide. The crude products from four separations were combined and recrystallized twice from ethanol-water (the solid was dissolved in hot alcohol treated with Darco G-60 and water added until crystallization began) to give 5 g. of material, m.p. 198–201°. Three successive crystallizations from acetone gave a product with a constant specific rotation and melting point; yield, 2.8 g. (3.7% conversion, or about 5% after allowing for recovered starting material), m.p. 208.5–210.5°, $[\alpha]^{25}_{D}$ −117° (*c* 1.02, 95% USP ethanol).[7] Values previously reported[1] were $[\alpha]^{21}_{D}$ −140° (*c* 1.0), m.p. 196–198°.

6-Methylenedihydrodesoxycodeine (II). A sample of I was methylated with diazomethane in ether-methanol solution. The infrared absorption spectrum was identical to that of II prepared directly by the Wittig reaction,[1] $[\alpha]^{21}_{D}$ −124° (*c* 0.73, 95% USP ethanol), lit. $[\alpha]^{21}_{D}$ −123°.

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[7] The discrepancy in physical constants has been discovered independently by Prof. Henry Rapoport who reported in a private communication the values m.p. 207–209, $[\alpha]^{22}_{D}$ −115° (*c*, 0.9, ethanol).

Nitration of 1,1,1-Trichloro-2,2-bis(2-thienyl)-ethane[1]

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In the course of studying the physiological properties of compounds containing the nitro group, it was decided to prepare 1,1,1-trichloro-2,2-bis(5-nitro-2-thienyl)ethane (II) *via* the nitration of 1,1,1-trichloro-2,2-bis(2-thienyl)ethane (I). The nitration was carried out with a mixture of acetic acid, acetic anhydride, nitric acid, and 1,1,1-trichloro-2,2-bis(2-thienyl)ethane in a manner similar to that used for the nitration of thiophene.[2] When the temperature was carefully controlled and not allowed to rise above 10°, the expected product II was obtained as a white, crystalline material, m.p. 110–110.5°.

When the nitration temperature was allowed to rise to 20–30° a yellow oil was obtained. This oil crystalized readily when stirred with ethyl acetate and gave bright yellow crystals of III, m.p. 130–131°, which was subsequently identified as 1,1-dichloro-2,2-bis(5-nitro-2-thienyl)ethylene. Analysis of III indicated the composition $C_{10}H_4Cl_2N_2O_4S_2$. Attempts to convert II to III with alcoholic potassium hydroxide gave a tar; however, II was converted to III in excellent yield by heating an acetone solution of II with potassium permanganate. This procedure was used by Lorenz[3] to convert 1,1,1-trichloro-2,2-bis(4-nitrophenyl)ethane to 1,1-dichloro-2,2-bis(4-nitrophenyl)ethylene. 1,1,1-Trichloro-2,2-bis(2-thienyl)ethane (I) was not changed by refluxing in acetone with potassium permanganate for thirty-six hours.

Oxidation of III with chromic oxide in acetic acid gave a good yield of bis(5-nitro-2-thienyl)-ketone (IV), m.p. 152–154°. The 2,4-dinitrophenylhydrazone of IV melted at 222–223°.

The spectra of II and III showed strong bands in the region 1500 cm.$^{-1}$, 1335 cm.$^{-1}$ and 1495 cm.$^{-1}$, 1330 cm.$^{-1}$, respectively. These bands are indicative of the nitro groups. The ketone (IV) gave a carbonyl frequency of 1632 cm.$^{-1}$ and nitro frequencies of 1510 cm.$^{-1}$ and 1332 cm.$^{-1}$

EXPERIMENTAL

Nitration of 1,1,1-trichloro-2,2-bis(2-thienyl)ethane. Procedure A. A solution of 29.8 g. (0.1 mole) of 1,1,1-trichloro-2,2-bis(2-thienyl)ethane[4] in 75 ml. of acetic anhydride was cooled and added dropwise to a well stirred, cold solution of 11 ml. of nitric acid (90%) in 50 ml. of acetic acid. The temperature was kept below 10° during the addition. The reaction mixture was then stirred for 1 hr., poured over ice, and the oil washed several times with water. The gummy product was recrystallized from ethyl acetate and alcohol. Fourteen grams of white crystals of 1,1,1-trichloro-2,2-bis-(5-nitro-2-thienyl)ethane (II) were obtained, m.p. 110–110.5°.

Anal. Calcd. for $C_{10}H_5Cl_3N_2O_4S_2$: Cl, 27.44; N, 7.23. Found: Cl, 27.13; N, 7.25.

Procedure B. The same nitration was carried out except the temperature was maintained at 20–30° during the reaction and the reaction mass allowed to stand overnight. The product was isolated as above, and the yellow oil was stirred with a small amount of ethyl acetate. A yellow solid soon formed. This solid was dissolved in ethyl acetate, charcoaled, and cooled. The yellow crystals (24 g.) were removed and recrystallized twice from ethyl acetate to give 13 g. of 1,1-dichloro-2,2-bis(5-nitro-2-thienyl)ethane, (III), m.p. 130–131°.

Anal. Calcd. for $C_{10}H_4Cl_2N_2O_4S_2$: Cl, 20.10; N, 7.98. Found: Cl, 20.80; N, 7.64.

Conversion of 1,1,1-trichloro-2,2-bis(5-nitro-2-thienyl)-ethane (II) *to 1,1-dichloro-2,2-bis(5-nitro-2-thienyl)ethylene* (III). A mixture of 1.25 g. of II, 30 ml. of acetone, and 1 g. of potassium permanganate was refluxed for 1 hr., filtered, and the acetone allowed to evaporate. Recrystallization of the yellow solid from ethyl acetate gave 0.6 g. of III, m.p. 130–131°. The infrared spectra of this compound was identical with the yellow compound obtained by nitration of I *via* Procedure B.

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[1] This work was supported in part by a grant (CY-3908) from The National Cancer Institute, National Institutes of Health, Department of Health, Education and Welfare, Bethesda, Md.

[2] V. Meyer and O. Stadler, *Ber.*, **17**, 2648 (1884).

[3] W. Lorenz, *Chem. Ber.*, **81**, 422 (1948).

[4] E. D. Amstutz, *J. Am. Chem. Soc.*, **70**, 3136 (1948).