In a preliminary experiment, the mercaptan was added to the acrolein. From this reaction, in addition to the desired product, a fraction, b.p. 112° at 1 mm. ($n_D^{25.5}$ 1.4490) was obtained, which corresponded roughly in analysis to the addition product of one mole of the mercaptan to three moles of acrolein.

Anal. Calcd. for $C_{10}H_{13}F_3O_3S$: C, 44.5; H, 4.73; S, 11.8. Found: C, 43.56; H, 5.65; S, 10.26.

5-(β-Trifluoromethylmercaptoethyl)hydantoin. A mixture of 20.0 g. (0.127 mole) of β-trifluoromethylmercaptopropionaldehyde, 90.5 g. (0.79 mole) of finely powdered ammonium carbonate, 10.6 g. (0.40 mole) of sodium cyanide, 270 ml. of ethanol, and 270 ml. of water was stirred and heated to 50–55° for 16 hr. The mixture was concentrated to about 200 ml. at room temperature under reduced pressure, made slightly acid with concentrated hydrochloric acid, and heated to 90° for 5 min. to cyclize any of the hydantoic acid which might be present. After cooling the mixture to 0° overnight, the yellow crystals which deposited were removed by filtration. After drying, the compound was recrystallized from boiling chloroform to give 8.7 g., (30.0% yield) of 5-(β-trifluoromethylmercaptoethyl)hydantoin, m.p. 128–128.5°.

Anal. Calcd. for $C_6H_7F_3O_2N_2S$: C, 31.60; H, 3.09; F, 25.0. Found: C, 31.76; H, 3.19; F, 25.7.

S-Trifluoromethylhomocysteine. A solution of 17.0 g. (0.074 mole) of 5(β-trifluoromethylmercaptoethyl)hydantoin, 68.0 ml. of water, and 7.5 g. (0 19 mole) of sodium hydroxide were refluxed for 6 hr An additional 3.7 g (0.09 mole) of sodium hydroxide was then added and refluxing continued for 18 hr. The solution was cooled and neutralized with concentrated hydrochloric acid to a *p*H of 6. Cooling to 0° for 1 hr. produced a cream colored solid which was washed twice with water and twice with acetone, dried, and extracted with 560 ml. of boiling methanol. Cooling the methanol solution to 0° overnight gave 4.4 g. of *S*-trifluoromethylhomocysteine, m.p. 229° dec. Reduction of the volume of the methanol mother liquor and cooling produced an additional 4.5 g. of product. The total (8.9 g.) represented a 60% yield. Recrystallization from methanol gave an analytical sample, m.p. 230° with decomposition

Anal. Calcd. for $C_5H_8F_3O_2NS$: C, 29.60; H, 3.97; N, 6.94; F, 28.2. Found: C, 29.65; H, 3.95; N, 6.52; F, 26.6.

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16-Ketoyohimbane

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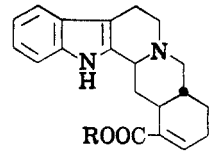
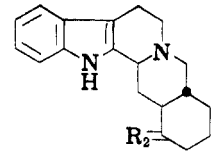
Because of its α,β-unsaturated ester grouping, apoyohimbine (I) should be convertible, by methods which transform a carboxyl group into an amino group, into 16-ketoyohimbane (III), a compound of interest in connection with stereochemical studies of the yohimbine alkaloids. An attempt to apply the Curtius reaction failed when apoyohimbine was recovered unchanged from treatment with hydrazine,[2] and apoyohimbic acid (II) was decomposed by thionyl chloride.

This transformation, however, was realized by means of the Schmidt reaction[3] on apoyohimbic acid, giving 16-ketoyohimbane in low yield. Evidence for the ketonic nature of the product was provided by the elementary analysis, a sharp carbonyl band in the infrared at 5.87 μ,[4] and the formation of an oxime.

The ketone could be reduced by the Huang-Minlon procedure to yohimbane[5,6] (IV), identical with the reduction product of 17-ketoyohimbane (yohimbone). Since the skeleton of yohimbine is in its most stable stereochemical configuration,[7–9] no isomerization takes place during this rather drastic reduction.



I. R = CH_3
II. R = H



III. R_2 = O
IV. R_2 = H_2

EXPERIMENTAL

16-Ketoyohimbane. Apoyohimbic acid hydrochloride[10] (6.7 g.) was dissolved in 30 ml. of concentrated sulfuric acid and stirred to drive off hydrogen chloride fumes. While stirring at room temperature, 40 ml. of a 0.6*N* chloroform solution of hydrazoic acid was added dropwise. Stirring was continued for 20 min., and 20 ml. more of the hydrazoic acid solution added. When gas evolution had ceased (about 30 min.), the mixture was poured into ice water, separated, and the aqueous layer filtered. The filtrate was made alkaline with ammonia, extracted with chloroform, and the extracts washed with saturated salt solution. Drying over sodium sulfate and evaporation left a tan solid which was recrystallized from ethanol. The yield was 1.1 g. (20%) of colorless needles; after two further recrystallizations from ethanol they melted at 283–285° (capillary inserted at 250°). Drying overnight at 100° *in vacuo* over P_2O_5 did not remove all the water of crystallization.

Anal. Calcd. for $C_{19}H_{22}N_2O \cdot {}^1/_2H_2O$: C, 75.21; H, 7.64; N, 9.23. Found: C, 74.88, 74.74; H, 8.03, 7.87; N, 9.00.

$[\alpha]_D^{21}$ −89° (*c*, 1.46 in pyridine).

An anhydrous sample could be prepared by two further recrystallizations from xylene, distilling half the xylene at each step to azeotrope the water. M.p. 274–276° dec.

(1) Taken in part from the B.A. thesis of Karl H. Muench, Princeton University, 1956.

(2) Compare the difficulty found in preparing the hydrazide and amide of yohimbine, by C. F. Huebner, R. Lucas, H. B. MacPhillamy, and H. A. Troxell, *J. Am. Chem. Soc.*, **77**, 469 (1955).

(3) H. Wolff, *Org. Reactions*, **III**, 1946.

(4) Yohimbone absorbs at the same frequency, somewhat shifted from the normal ketone position.

(5) J. Jost, *Helv. Chim. Acta*, **32**, 1297 (1949).

(6) B. Witkop and S. Goodwin, *J. Am. Chem. Soc.*, **75**, 3371 (1953).

(7) G. Stork, quoted in ref. 6.

(8) R. C. Cookson, *Chemistry & Industry*, **1953**, 337.

(9) M. M. Janot, R. Goutarel, A. Le Hir, M. Amin, and V. Prelog, *Bull. soc. chim. France*, 1085 (1952).

(10) G. Barger and E. Field, *J. Chem. Soc.*, **123**, 1038 (1923).

Anal. Calcd. for $C_{19}H_{22}N_2O$: C, 77.52, H, 7.53; N, 9.52. Found: C, 77.37 H, 7.62 N, 9.36.

The *oxime*, prepared by refluxing the ketone with hydroxylamine hydrochloride and pyridine in ethanol, was recrystallized from methanol, in which it is barely soluble. M.p. 316–319° dec.

Anal. Calcd. for $C_{19}H_{23}N_3O$: N, 13.6. Found: N, 13.9.

Yohimbane. 16-Ketoyohimbane (0.46 g.), 0.2 g of sodium hydroxide, and 3.0 ml. of 85% hydrazine hydrate were refluxed for 70 min. in 8.0 ml. of diethylene glycol. The condenser was removed, and water and hydrazine allowed to distill until the temperature reached 197°. The solution was refluxed at this temperature for 4 hr., diluted with water, and extracted with chloroform. The extracts were washed with water, dried over magnesium sulfate, and evaporated. Sublimation of the residue at 150° and 0.01 mm. gave 0.33 g (75%) of light yellow crystals. Recrystallization from ethanol yielded colorless needles, m.p. 204–206° alone, or mixed with an authentic sample of yohimbane.[6]

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Ozonization of Methylene Chloride and Chloroform[1]

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In studying the preparation of 3-ketobisnor-4-cholen-22-al by the selective ozonolysis of 4,22-stigmastadien-3-one[2] and 4,22-ergostadien-3-one[3] at −78° important new observations were made concerning the behavior of the solvents, methylene chloride and chloroform, towards ozone. This information should be useful to others who are planning to use ozonolysis as a preparative reaction for aldehydes.

As solvents for the above reaction acetic acid, formic acid, methanol, carbon tetrachloride, and ethyl acetate[4] were eliminated for various reasons and the choice was between methylene chloride and chloroform. Furthermore, since selective ozonolysis of the side-chain double bond was desired, it was important to know how much of the ozone was reacting with the solvent.

These solvents were studied by a method somewhat different from that employed by Greenwood,[5] and designed to show how much ozone dissolved in the solvent as well as the amount which reacted with it. The solvents were ozonized at a constant, known rate. The dissolved ozone which imparted an intense blue color was then swept out by a stream of nitrogen and the amount of ozone which had reacted with the solvent was determined by difference. These results are recorded graphically in Fig. 1.

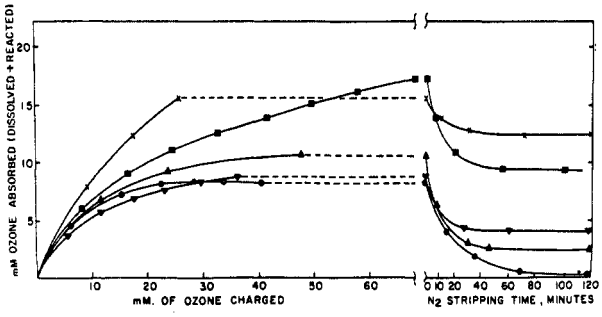

FIG. 1. OZONE ABSORBED BY SOLVENTS AND THE AMOUNT RECOVERABLE BY NITROGEN SPARGING. (⊙–Methylene chloride; △–methylene chloride + pyridine, ⊡–methylene chloride + diphenyl sulfoxide; x–methylene chloride + pyridine 1-oxide, ▽–chloroform.)

The curve obtained from the treatment of stabilized chloroform at −60° with ozone shows that this solvent underwent some attack by ozone. This attack was probably on the ethanol, which was present as the stabilizer, and could account for the acidity observed earlier in these laboratories[6] when chloroform was used as a solvent for ozonolysis of various steroidal olefins and enol acetates.

Ozone attack on methylene chloride at −78° was negligible, a saturated solution about 0.033*M* in ozone being formed from which all of the ozone could be recovered.

The inclusion of an organic base in the ozonolysis solvent for its acid-binding ability has been described[2,6,7] to be beneficial, resulting in higher yields.[8] Solutions of methylene chloride containing about 1% of the Lewis bases pyridine, diphenyl sulfoxide, and pyridine oxide were investigated in a similar manner. All of them consumed some ozone, the amount increasing in the order mentioned. Further investigation showed that the bases were not destroyed but probably only formed salt-like compounds (I) or complexes (II) with the ozone

(1) Included in part in a paper presented before the First International Ozone Conference, Chicago, Ill., Nov. 28–30, 1956.

(2) F. W. Heyl and M. E. Herr, *J. Am. Chem. Soc.*, **72**, 2617 (1950).

(3) D. A. Shepherd, R. A. Donia, J. A. Campbell, B. A. Johnson, R. P. Holysz, G. Slomp, J. E. Stafford, R. L. Pederson, and A. C. Ott, *J. Am. Chem. Soc.*, **77**, 1212 (1955).

(4) In ethyl acetate the yield of aldehyde was greatly lowered and large amounts of the corresponding acid were formed.

(5) F. L. Greenwood, *J. Org. Chem.*, **10**, 414 (1945).

(6) (a) F. W. Heyl, A. P. Centolella, and M. E. Herr, *J. Am. Chem. Soc.*, **69**, 1957 (1947); (b) F. W. Heyl and M. E. Herr, U.S. Patent 2,554,986 and U.S. Patent 2,601,287; (c) F. W. Heyl and A. P. Centolella, U.S. Patent 2,623,052.

(7) (a) W. Logemann and H. Dannenbaum, U.S. Patent 2,344,992; (b) W. L. Ruigh, U.S. Patent 2,413,000.

(8) The yield of 3-ketobisnor-4-chloenaldehyde from the ozonolysis of 4,22-ergostadien-3-one was 70% in chloroform. [A. F. Daglish, J. Green, and V. D. Poole, *J. Chem. Soc.*, 2627 (1954).] compared with 94.5%[3] in methylene chloride-pyridine.