Table II. Comparison of Infrared Spectra[a]

Assignment	$(M_2AsBH_2)_3$	$(M_2PBH_2)_3$	$(M_2PBD_2)_3$
B–H stretching	2530 (6.5)	2514 (2)	1889 (1.1)
	2449 (3.9)	2429 (0.6)	1794 (0.9)
C–F stretching	1190 (410)	1206 (170)	1205 (400)
	1154 (160)	1192 (167)	1192 (265)
	1123 (145)	1164 (100)	1164 (160)
BH_2 deformation?	1075 (5.3)	1152 w, sh	952 w
			852 w
BH_2 out-of-plane rock	960 (33)	995 (4)	755 (1.6)
CF_3 sym deformation	742 (20)	764 (0.8)	761 sh (1.2)
BH_2 in-plane rock	636 ? w	715 (17)	566 (9)
CF_3 asym deformation	(Too weak)	538 (3.6)	532 (2.0)
As–CF_3 stretching	332 (17)	. . .	. . .
P–CF_3 stretching	. . .	455 (6)	444 (6)
		436 (7)	431 (5)
		414 (5)	409 (0.7)
Uncertain		659 (10)	662 (12)
		621 (3)	602 (20)
		554 (1.5)	395 (2.2)

[a] M = CF_3; w = weak; sh = shoulder.

through formation of its acetyl chloride complex at −110°, and HCl was similarly removed as the $(CH_3)_2O$ complex, leaving a trace of SiF_4. The result was 2.06 HCl and 1.04 BF_3 (both ±5%) per calculated $(CF_3)_2AsBH_2$ unit. Thus the elementary analysis was complete, fully confirming the formula $[(CF_3)_2AsBH_2]_3$.

Infrared Spectra. The frequencies (cm^{-1}) of the infrared fundamental peaks observed for $[(CF_3)_2AsBH_2]_3$ in the vapor phase at 1.2 mm pressure (33°) are compared with the analogous peaks for $[(CF_3)_2PBH_2]_3$ and $[(CF_3)_2PBD_2]_3$ in Table II. The relative intensity appears in parentheses after each frequency.

Discussion. The 960-cm^{-1} peak for BH_2 out-of-plane rocking fits a previously recognized trend.[5] By comparison with the 812-cm^{-1} peak observed for $[(CH_3)_2PBH_2]_3$ and other pertinent data for such compounds, the 995-cm^{-1} peak suggests that the HBH angle in $[(CF_3)_2PBH_2]_3$ might be as much as 10° wider than the 119.3° reported for $[(CH_3)_2PBH_2]_3$.[6] Also, two different methods estimate the HBH angle as 2.5 to 2.8° narrower in $[(CF_3)_2AsBH_2]_3$ than in $[(CF_3)_2PBH_2]_3$. The latter comparison would agree with the expectation that As_{4d} would be less effective than P_{3d} for interaction with B–H bonding electrons, but in both cases such interactions, involving 12 electrons and 6 highly contracted d orbitals, would have important ring stabilizing effects.

(5) A. B. Burg, *Robert A. Welch Found. Conf.*, **6**, 142 (1962). In that lecture this mode was called "wagging." Also, the BD_2 in-plane rocking is reassigned to 566 cm^{-1} without affecting the argument.
(6) W. C. Hamilton, *Acta Cryst.*, **8**, 199 (1955).

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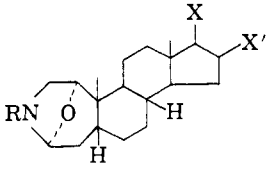
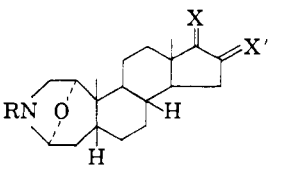
A Total Synthesis of Samandarone

Sir:

Salamander alkaloids were found in the toxic secretion of the alpine salamander by Zalesky in 1866.[1] Samandarine was isolated as a main component of these alkaloids, and its structure has been suggested by Schöpf and his colleagues to be Ia through chemical, optical, and X-ray crystallographic studies.[1-3] The characteristic skeleton of samandarine is common to four other alkaloids, *i.e.*, samandarone (IIa),[2] samandaridine,[4] O-acetylsamandarine,[5] and samandesone,[6] which differ from each other only in the D-ring substituent. We wish to record the total synthesis of samandarone, which will be a general intermediate for the preparation of structurally similar alkaloids.

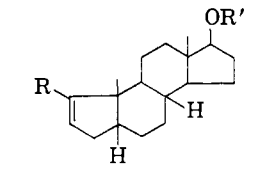


Ia, R = X = H; X′ = OH
b, R = $PhCH_2$; X = OH; X′ = H
c, R = X′ = H; X = OH

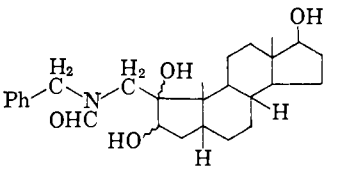


IIa, R = H; X = H_2; X′ = O
b, R = PhCO; X = H_2; X′ = O
c, R = $PhCH_2$; X = O; X′ = H_2
d, R = H; X = O; X′ = H_2
e, R = CHO; X = O; X′ = H_2
f, R = CHO; X = O; X′ = CHOH
g, R = CHO; X = O; X′ = CHO-*i*-Pr
h, R = CHO; X =  ; X′ = CHO-*i*-Pr
i, R = CHO; X = H_2; X′ = CHOAc

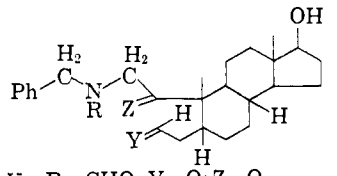
1-Formyl-A-nor-5β-androst-1-en-17β-ol (IIIa) was prepared from testosterone as described in a previous paper.[7] The benzylamino Schiff base of IIIa was reduced with sodium borohydride to give the unsaturated amine IIIb.[8] After protection of the amino group as the formamide IIIc (mp 130–132°),[9] the double bond was oxygenated with osmium tetroxide in diethyl ether–pyridine to afford the *cis*-glycol IV, which formed a crystalline acetonide (mp 248–250°). The glycol IV was cleaved by lead tetraacetate to give the seco-aldehyde Va (δ 9.60 (triplet, C*H*O), 8.33 (singlet, N–C*H*O), 7.30 (5 aromatic *H*), 4.39 and 4.07 (unresolved multiplet $N(CH_2)_2$, respectively), 2.42 (unresolved



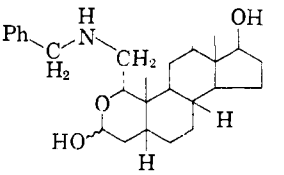
IIIa, R = CHO; R′ = H
b, R = $PhCH_2NHCH_2$; R′ = H
c, R = $PhCH_2N(CHO)CH_2$; R′ = CHO



IV



Va, R = CHO; Y = O; Z = O
b, R = CHO; Y =  ; Z = O
c, R = CHO; Y =  ; Z = 
d, R = H; Y =  : Z = 



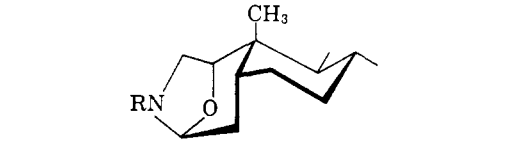
VI

(1) The review of these alkaloids is in C. Schöpf, *Experientia*, **17**, 285 (1961), and G. Habermehl, *Naturwissenschaften*, **53**, 123 (1966).
(2) E. Wölfel, C. Schöpf, G. Weitz, and G. Habermehl, *Chem. Ber.*, **94**, 2361 (1961).
(3) G. Habermehl, *ibid.*, **96**, 143 (1963).
(4) G. Habermehl, *ibid.*, **96**, 840 (1963).
(5) G. Habermehl, *Ann.*, **679**, 164 (1964).
(6) G. Habermehl, *Chem. Ber.*, **99**, 1439 (1966).
(7) S. Hara and K. Oka, *Tetrahedron Letters*, 1057 (1966).
(8) Infrared spectra for all reported compounds were taken with KBr tablets and are consistent with assigned structures.
(9) Satisfactory analytical data were obtained for crystalline compounds.

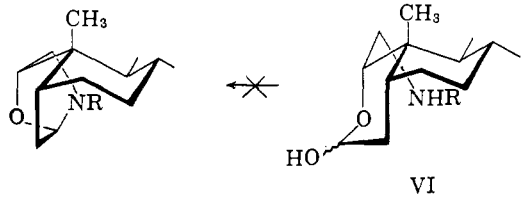
multiplet, CH_2CHO)),[10] in 50% over-all yield based on IIIa. The selective protection of the formyl group of Va as the ethylene acetal Vb was confirmed by the absorption band at 1721 cm^{-1} of the remaining keto group at C-1. Reduction of Vb with sodium borohydride gave the amide alcohol Vc (mp 170–172°) which showed a single spot on silica gel tlc, but the resonances of the 19 protons[10] of Vc (δ 0.86 and 0.85) clearly indicated the presence of two isomers, the 1α and 1β epimeric alcohols, in equal amounts. Saponification of the formamide Vc with 6% sodium hydroxide in aqueous ethanol led to the epimeric α-amino alcohols Vd, in 68% over-all yield based on Va.

Hydrolysis of the ethylene acetal Vd with 75% acetic acid at 100° afforded material showing two spots on a silica gel tlc (R_f 0.9 and 0.5, methanol–benzene saturated with aqueous ammonia, 1:5). Purification of the crude products by passing through a silica gel column gave two compounds in 45 and 38% yields. The former (Ib) was eluted and showed a single peak by vpc[11] (retention time 15.3 min, column temperature 245°), but the latter (VI) was not eluted. The infrared spectrum of Ib showed the characteristic absorption bands of the oxazolidine ring at 845 and 831 cm^{-1} [12,13] and bands due to ether between 1200 and 1100 cm^{-1}. These facts indicate that the intramolecular bicyclization between aldehyde and α-amino alcohol had been effected simultaneously with the removal of the protecting group. On the other hand, the second compound (VI) showed no oxazolidine absorption but C–O–C bands at 1159 and 1119 cm^{-1} probably due to the intramolecular hemiacetal and was not bicyclized.

Removal of the benzyl group from Ib was achieved by catalytic hydrogenation producing quantitatively Ic (mp 191–193°; retention time 4.1 min, column temperature 235°). The proton resonances[10] at δ 5.00 (unresolved multiplet, $HC(N)O$), 4.10 (triplet, C_1H), and 2.96 (unresolved multiplet, NCH_2), and the two intense infrared absorptions at 852 and 834 cm^{-1}, are very similar to those of the natural products.[12,14] Furthermore, since kinetic and thermodynamic factors demand that the orientation of the oxygen atom at C-1 of actually bicyclized compound be α, it is reasonable to presume that Ib and c have the identical pentacyclic nucleus of the natural products. On the contrary, the side chain at C-1 of the compound VI must be α oriented.



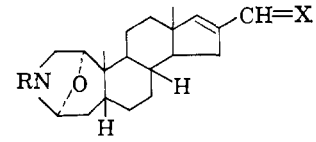
I

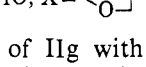


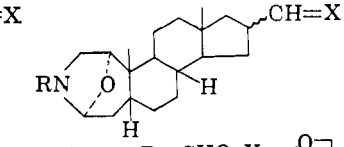
VI

For the transformation of the oxygen function at C-17 to C-16, without affecting the oxazolidine ring system, we applied the following reactions to Ib.

Oxidation of Ib with Jones reagent gave the 17-keto compound IIc (mp >330°), which was debenzylated to yield IId (mp 198–199°). The formamide IIe (mp 165–166°) prepared from IId was formylated at the 16 position with ethyl formate to give IIf (mp 216–218°; λ_{max}^{EtOH} 268 mμ (log ϵ 3.93); $\lambda_{max}^{0.01NKOH\text{-}EtOH}$ 307 mμ (log ϵ 4.30)), which was treated with isopropyl alcohol and *p*-toluenesulfonic acid to give the enol ether IIg (mp 218–220°).



VIIa, R = CHO; X = O
b, R = CHO; X = 



VIIIa, R = CHO; X = 
b, R = CHO; X = O

Reduction of IIg with sodium borohydride led to the 17-hydroxyl derivative IIh, which was treated with dilute hydrochloric acid to give an unsaturated aldehyde VIIa (mp 192–194°; λ_{max}^{EtOH} 240 mμ (log ϵ 4.14)). Catalytic hydrogenation of the ethylene acetal VIIb prepared from VIIa gave the dihydro derivative VIIIa, which was hydrolyzed to VIIIb (mp 200–201°; 2740 and 1727 cm^{-1} (CHO)) in 25% over-all yield based on Ib.

Enol acetylation of VIIIb (20 mg) was accomplished by heating in isopropenyl acetate containing sulfuric acid to give IIi, which was subjected to ozonolysis and then hydrolyzed to cleave the formamide group with hydrochloric acid. The crude product was treated with benzoyl chloride and, after chromatography, 3.5 mg of the N-benzoate IIb (mp 258–259°) was obtained. This material is identical with the samandarone N-benzoate[15] prepared from natural samandarone with respect to infrared, tlc, and mixture melting point test.

Finally, hydrolysis of IIb gave 1.5 mg of samandarone (IIa; mp 182–185°, natural, 185–187°), which is also identical with the natural product with respect to infrared, tlc, and vpc (retention time 11.8 min, column temperature 215°).

Thus the first total synthesis of the salamander alkaloids was complete. In view of the established conversion of samandarone to samandarine and samandaridine,[4] the total syntheses of samandarine and samandaridine were also complete.

Acknowledgments. We are grateful to Dr. C. Schöpf and Dr. G. Habermehl for supplying an authentic sample of samandarone. We wish to thank the Ministry of Education in Japan for financial support (Grant-in-Aid for Scientific Research), Dr. A. Tahara of the Institute of Physical and Chemical Research for measurement of nmr spectra, and Kowa Co. for a generous gift of testosterone.

(10) Nmr spectra were recorded on a Japan Electron Optics Laboratories JC-60 spectrometer using deuteriochloroform as the solvent and TMS as the internal standard.

(11) Shimadzu GC-1C gas chromatograph provided with a glass column (0.16 × 72 in.) was used; liquid phase, 1.5% SE-30; carrier gas, N_2, 30 cc/min.

(12) G. Habermehl, *Chem. Ber.*, **96**, 2029 (1963).

(13) R. Partch, *Tetrahedron Letters*, 1361 (1966).

(14) G. Habermehl and S. Göttlicher, *Chem. Ber.*, **98**, 1 (1965).

(15) C. Schöpf and W. Braun, *Ann.*, **514**, 69 (1934).

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