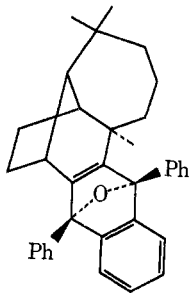
furnish an adduct which after the loss of carbon monoxide gave **9**, mp 261–262°, in 90% yield. The reaction of



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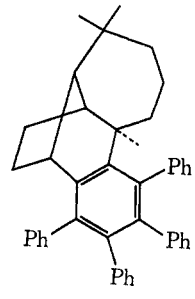
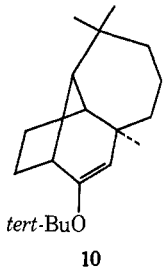
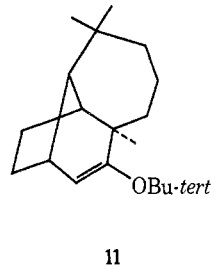


9

ω-bromolongifolene (**2**) with potassium *tert*-butoxide in the absence of any trapping agent furnished a high yield of a mixture containing ketones **4** and **5** and the *tert*-butyl enol ethers **10** and **11**. The formation of



10



11

these compounds is compatible with the formation of **3**. No dimeric products as reported[3] earlier were encountered in this reaction. Mechanistically, this base-induced rearrangement can be visualized as proceeding either *via* an alkylidene carbene[6] or an α-halogenoorganometallic intermediate.[2]

Experimental Section[7]

ω-Bromolongifolene[8] (2).—A solution of longifolene (**1**) (20.4 g, 0.1 mol) and *N*-bromosuccinimide (18 g, 0.1 mol) in dry benzene (150 ml) was refluxed for 4 hr in the presence of a catalytic amount of benzoyl peroxide (100 mg). The reaction mixture was poured into water and the organic layer was successively washed with dilute HCl (10%, three 50-ml portions, saturared $NaHCO_3$ (two 40-ml portions), and brine (two 25-ml portions) and dried. Removal of solvent and distillation gave ω-bromolongifolene: 20 g (72%); mp 40–41°; ir (neat) 3010, 1640, 790 cm^{-1} ($>C{=}C<^{H}$); nmr τ 9.04 (6 H, s, gem Me), 8.95 (3 H, s, Me), 4.37 (1 H, s, olefinic), 6.87 (1 H, broad, allylic bridgehead).

Diphenylisobenzofuran Adduct 7 of Acetylene 3.—A mixture of ω-bromologifolene (**3**) (2.8 g, 0.01 mol), potassium *tert*-butoxide (2.16, 0.2 mol), and diphenylisobenzofuran (**6**) (2.7 g, 0.1 mol) was refluxed in dry toluene for 8 hr. The reaction mixture was diluted with water and extracted with CH_2Cl_2 (two 50-ml portions). The organic phase was washed with brine and freed of solvent to give a solid residue, 4.5 g, mp 249–255°. Recrystallization from methanol gave colorless needles: mp 254–256°; ir spectrum 1655, 1603, 701, 690 (aromatic), 1210 cm^{-1} (ether). *Anal.* Calcd for $C_{35}H_{36}O$: C, 88.94; H, 7.68. Found: C, 88.73; H, 7.61.

Tetracyclone Adduct 9 of Acetylene 3.—A mixture of ω-bromolongifolene (2.80 g, 0.1 mol), tetracyclone (3.84, 0.1 mol), and potassium *tert*-butoxide (2.16 g, 0.2 mol) was refluxed in toluene until the color of tetracyclone was completely discharged (6 hr). The reaction mixture was poured into water and extracted with CH_2Cl_2 (two 60-ml portions). Removal of solvent gave a solid residue. Recrystallization from MeOH–C_6H_6 gave colorless crystals: mp 260–262° (90% yield); ir spectrum 695, 1480, 1601 and 3080 cm^{-1}. *Anal.* Calcd for $C_{43}H_{42}$: C, 92.42; H, 7.58. Found: C, 92.13; H, 7.51.

Rearrangement of 2 with Potassium *tert*-Butoxide.—A mixture of ω-bromolongifolene (5.6 g, 0.2 mol) and potassium *tert*-butoxide (7.3 g, 0.4 mol) in toluene was refluxed for 6 hr. The reaction mixture was poured into water and extracted with pentane (three 50-ml portions), washed with brine, dried, and freed of solvent to yield a pale yellow liquid, 4.13 g. A vpc analysis of the product showed the presence of at least seven components. The major components were in the ratio[10] of 1:5:1:2 and were identified as longihomocamphenilone[3,11] (**4**, mp 55–56°), longiisohomocamphenolone[3] (**5**, mp 51–52°), *tert*-butyl enol ether **10** [bp 140–150° (1 mm); ir spectrum 1645, 1170, 1195, 1240 cm^{-1} (enol ether). *Anal.* Calcd for $C_{19}H_{32}O$: C, 82.54; H, 11.66. Found: C, 82.21; H, 11.51], and the isomeric *tert*-butyl enol ether **11** [bp 140–145° (1 mm); ir spectrum 1650, 1170, 1190, 1240 cm^{-1} (enol ether). *Anal.* Calcd for $C_{19}H_{32}O$: C, 82.54; H, 11.66. Found: C, 82.31; H, 11.59]. The two *tert*-butyl enol ethers were characterized by converting them into the 2,4-dinitrophenylhydrazones of the corrsponding ketones **4**, mp 144°, and **5**, mp 164–165°, by reaction with Brady[12] reagent.

Registry No.—**2**, 1139-15-7; **4** 2,4-DNP, 1607-92-7; **5** 2,4-DNP, 1174-81-8; **7**, 31024-76-7; **9**, 31024-77-8; **10**, 31024-78-9; **11**, 31024-79-0.

(6) K. L. Erickson and J. Wolinsky, *J. Amer. Chem. Soc.*, **87**, 1142 (1965).

(7) Melting points and boiling points are uncorrected. All solvent extracts were dried over anhydrous Na_2SO_4. Ir spectra were recorded on a Perkin-Elmer Model 137 infracord as neat liquids or solids as KBr disks. Nmr spectra were recorded on a Varian A-60 spectrometer in $CDCl_3$ and chemical shifts are reported on a τ scale relative to tetramethylsilane (τ 10).

(8) The reported[9] preparation of **2** involved a two-step bromination–dehydrobromination of longifolene (**1**) and is less convenient.

(9) G. Dupont, R. Dulou, P. Naffa, and G. Ourisson, *Bull. Soc. Chim. Fr.*, 1075 (1954).

(10) The relative amount of the components varied in every reaction with time and the sample of the base used.

(11) P. Naffa and G. Ourisson, *Bull. Soc. Chim. Fr.*, 1115 (1954).

(12) O. L. Brady, *J. Chem. Soc.*, 756 (1931); J. Wolinsky, *J. Org. Chem.*, **26**, 705 (1961).

The Chemistry of Actinobolin. Oxidation of Actinobolamine

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Received January 8, 1971

Aromatization of cyclic portions of actinobolin[2,3] and of the products isolated after base-catalyzed[4,5] hydrolysis of the antibiotic made secure the molecular structures assigned to these compounds. Actinobolamine (**1a**),[5] the product formed by vigorous acid hydrolysis of actinobolin, resisted all attempts at achieving clean eliminative scission of the bond linking C-5 to nitrogen and subsequent aromatization of the substituted cyclohexenone. *N*-Acetylactinobolamine (**1b**) did, however, submit to nitric acid oxidation affording a readily isolable product displaying ir bands characteristic of lactone carbonyl. This observation

(1) (a) Support of this work by the National Institutes of Health through Research Grant AI-04720 is gratefully acknowledged. (b) This paper is based in part on the Ph.D. dissertation of D. B. Nelson, Arizona State University. (c) Presented at the 160th National Meeting of the American Chemical Society, Chicago, Ill., Sept 1970, ORGN 014.

(2) M. E. Munk, D. B. Nelson, F. J. Antosz, D. L. Herald, Jr., and T. H. Haskell, *J. Amer. Chem. Soc.*, **90**, 1087 (1968).

(3) F. J. Antosz, D. B. Nelson, D. L. Herald, Jr., and M. E. Munk, *ibid.*, **92**, 4933 (1970).

(4) D. B. Nelson, M. E. Munk, K. B. Gash, and D. L. Herald, Jr., *J. Org. Chem.*, **34**, 3800 (1969).

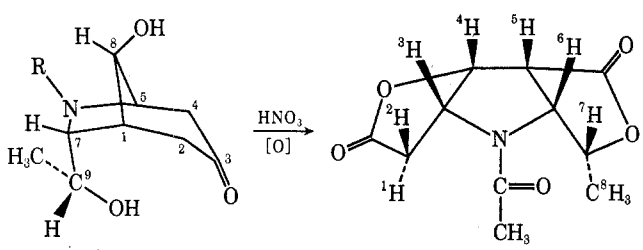
(5) D. B. Nelson and M. E. Munk, *ibid.*, **35**, 3832 (1970).

TABLE I
NMR ASSIGNMENTS FOR COMPOUND 2[a,b]

Assignment	Chemical shift[c] (no. of hydrogens)	Multiplicity	Spin decoupling[d] Signal irradiated	Spin decoupling[d] Multiplicity change to
H-8	1.01 (3)	d, $J_{8,7}$ = 6.5 Hz		
N-COCH$_3$	1.93 (3)	s		
H-1	2.67 (1)	d of d, $J_{1,2}$ = 18.5, $J_{1,3}$ = 1.5 Hz	H-3[e]	d, J = 18.5 Hz
H-2	3.07 (1)	d of d, $J_{2,1}$ = 18.5, $J_{2,3}$ = 7.0 Hz	H-3	d, J = 18.5 Hz
H-5	3.70 (1)	d of d, $J_{5,6}$ = 10, $J_{5,4}$ = 7.0 Hz		
H-3	4.73 (1)	Overlapping multiplets[f]		
H-7	4.83 (1)		H-8	d, J = 8.0 Hz
H-6	4.99 (1)	d of d, $J_{6,7}$ = 8.0, $J_{6,5}$ = 10.0 Hz	H-5	d, J = 8.0 Hz
H-4	5.21 (1)	d of d, $J_{4,3}$ = 5.5, $J_{4,5}$ = 7.0 Hz	H-5	d, J = 5.5 Hz

[a] In DMSO-d_6 at 100°. [b] Addition of D_2O to the nmr sample results in no loss of integral amplitude. [c] In δ units (ppm) downfield of external HMDS. [d] Frequency-sweep spin decoupling at 100 MHz and 100°. [e] Observation of the H-4 signal while irradiating H-3 indicated coupling of H-4 to H-3; however, decoupling of H-4 to a clean doublet, J = 7.0 Hz, was not achieved. [f] Irradiation of H-8 reduces H-7 to a doublet (J = 8.0 Hz) and reveals the H-3 signal as a seven-line pattern compatible with $J_{3,1}$ = 1.5, $J_{3,2}$ = 7.0, and $J_{3,4}$ = 5.5 Hz

suggested an alternate degradation of **1b**, retaining the pyrrolidine ring intact, and led to the studies reported here.



1a, R = H
b, R = CH_3CO

2

Elemental analysis and a mass spectral determination provided a molecular formula of $C_{11}H_{13}NO_5$ for the oxidation product. The infrared spectrum (KBr) displayed prominent bands characteristic of the γ-lactone carbonyl at 1788 and 1768 cm^{-1} together with a tertiary amide carbonyl band at 1640^{-1}. Bands associated with O–H or N–H stretching or indicative of unstrained carbonyl were not observed.

Several oxidative sequences are available to **1b**; however, the presence of two γ-lactone carbonyls in the isolated product and the change in molecular formula, *i.e.*, eq 1, suggest that the oxidation product is formed

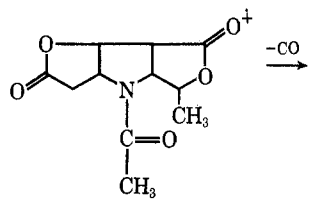
$$C_{11}N_{17}NO_4 \xrightarrow[-2H_2O]{+3O} C_{11}H_{13}NO_5 \qquad (1)$$

by oxidative cleavage of the σ bond linking C-2–C-3 to yield a dicarboxylic acid. Subsequent lactonization, which likely accounts for resistance to further oxidation, gives rise to the di-γ-lactone **2**.

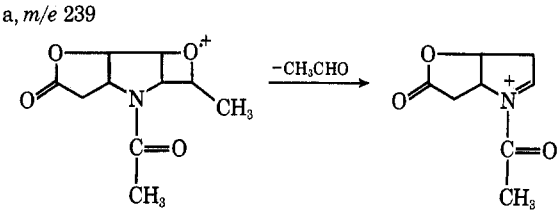
Of the diverse products possible on nitric acid oxidation of **1b** (by oxidation at C-8 and/or C-9 and subsequent σ-bond cleavage or oxidative cleavage about the C-3 ketone) only the di-γ-lactone structure **2** is consistent with the appearance of infrared bands at 1788 and 1768 cm^{-1}. Evidence to secure this structural assignment derives from the 100-MHz spectrum taken at 100°[6] (Table I).

In **1b**, carbon atoms 1, 5, 7, 8, and 9 possess the *R* configuration.[5] Retention of the *R* configuration at the corresponding centers of **2** requires the exo orientation for H-3, H-4, H-5, H-6, and H-7. Dreiding stereomodels indicate that the dihedral angles between each vicinal pair of hydrogens in the series H-3 through H-7 are comparable and small (approaching 0°). In view of the possible influence of the electronegative heteroatom and the electron-withdrawing carbonyl group,[7] the coupling constants observed, $J_{3,4}$ = 5.5, $J_{4,5}$ = 7.0, $J_{5,6}$ = 10.0, and $J_{6,7}$ = 8.0 Hz, while varied, do meet the requirements imposed by the retention in **2** of the stereochemistry assigned to **1b**.

The mass spectrum (see Experimental Section) displays few major peaks, all of which may be explained in terms of structure **2**. Transformation of the parent



a, *m/e* 239



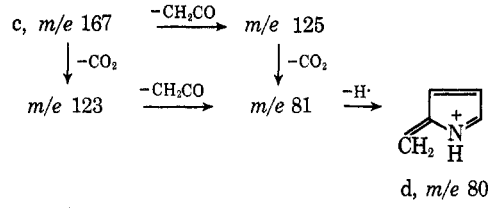
b, *m/e* 211 c, *m/e* 167

(6) Nmr spectra of **2** at room temperature appear to contain two duplicate sets of signals offset slightly from one another. At temperatures greater than 70° these patterns coalesce to a single set of signals. The temperature dependence of the nmr spectrum of **2** is explicable in terms of the presence of two slowly interconvertible rotational isomers which exist by virtue of the limited free rotation imposed by the double bond character of the amide carbon–nitrogen bond.

(7) N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry," Holden-Day, San Francisco, Calif., 1964, pp 49–54.

ion a (*m/e* 239) to the base ion c (*m/e* 167) can be pictured as proceeding *via* loss of carbon monoxide to b, followed by loss of acetaldehyde to give c. The presence of metastable ions at *m/e* 186.3 and 132.2 support this sequence. The high-resolution mass spectrum of **2** shows the *m/e* 167 peak to be *m/e* 167.0583 (calcd for $C_8H_9NO_3$, 167.0582); therefore, it does not arise *via* loss of carbon monoxide and carbon dioxide from the parent ion.

The pathways followed in the further decomposition of ion c are sequential variations of a common theme, *i.e.*, decay to the resonance stabilized ion d. The



d, *m/e* 80

m/e 125 ion also proceeds to d by the loss of 45 mass units in a sequence which must involve a one-hydrogen transfer prior to loss of a carboxyl radical. The sequences of decay to ion d are supported by the observation of the required metastable peaks.

Experimental Section[8]

Oxidation of *N*-Acetylactinobolamine.[9]—To a prewarmed 50-ml solution of 8 *N* nitric acid was added 2.339 g (10.3 mmol) of *N*-acetylactinobolamine. The exothermic nature of the reaction rapidly brought the solution to a condition of slow reflux which was maintained for a period of 10 min.[10] The reaction solution was poured into 250 ml of chilled water which was passed onto a column containing 550 ml of chilled Bio-Rad AG 21-K anion-exchange resin (hydroxide form). The column was eluted with 500 ml of water and 1500 ml of acetic acid–water (1:9). The eluents were freeze-dried. The bulk of the material appeared in the first 1000 ml of acetic acid eluent as a tan semisolid which on crystallization from ethyl alcohol gave 734 mg of crude **2**. Recrystallization from ethyl alcohol gave 490 mg of **2** as analytically pure material: mp 241° dec; $[\alpha]^{25}D$ +166° (*c* 6.1%, DMSO); homogenous to tlc (Bio-Sil A,[11a] ethyl acetate–ethyl alcohol, 2:1 v/v, and MN-cellulose,[11b] *n*-butyl alcohol–water–acetic acid, 4:1:5 v/v/v, upper phase). Column chromatography of the crystallization mother liquids (silicic acid[12] eluted with ethyl acetate containing increasing amounts of ethyl alcohol) followed by crystallization from ethyl alcohol gave an additional 155 mg of **2**, mp 241° dec, for a total yield of 645 mg of **2** (2.70 mmol, 26.2%). Pertinent ir and nmr are listed in the text; mass spectrum *m/e* (relative intensity 239 (4), 211 (5), 167 (100), 125 (14), 123 (3), 81 (8), 80 (10), metastable ions at 186.3, 132.2, 93.6, 90.5, 53.3, 52.5, 51.2, 79.0.

Anal. Calcd for $C_{11}H_{13}NO_5$: C, 55.23; H, 5.48; O, 33.44; mol wt, 239.0794. Found: C, 55.48; H, 5.71; O, 33.37; mol wt, 239.0807 (mass spectrum).

(8) Instruments used: Thomas-Hoover capillary melting point apparatus (melting points corrected); Perkin-Elmer Model 237B Infracord spectrometer; Rudolf Model 80 polarimeter; Varian Associates HA-100 spectrometer; Atlas CH-4B mass spectrometer (heated inlet, 19 μA, 70 eV); Atlas SM-1B high-resolution mass spectrometer. Fragmentation sequences and metastable peaks were matched with computer program CMSPKS, written by S. H. Brown of Stanford University. Microanalyses were performed by Midwest Microlab, Inc., Indianapolis, Ind.

(9) Performed with Mr. Chidambar L. Kulkarni.

(10) A preliminary thin layer (Bio-Sil A,[11a] ethyl acetate–ethyl alcohol, 2:1 v/v) chromatographic assay of the fate of *N*-acetylactinobolamine (**1b**) and **2** in refluxing nitric acid demonstrated the need for a short contact time.

(11) (a) Bio-Sil A, 10–30 μ with 5% binder, purchased from Bio-Rad Laboratories, Richmond, Calif.; (b) MN-cellulose powder 300G distributed by Brinkman Instruments, Great Neck, N. Y.

(12) Bio-Sil A, 100–200 mesh, purchased from Bio-Rad Laboratories.

Registry No.—**1b**, 31729-81-4; **2**, 31729-82-5.

Acknowledgments.—Special thanks are due to Dr. T. H. Haskell of Parke, Davis and Co., who performed the initial nitric acid oxidation of *N*-acetylactinobolamine, to Professor J. Kutney, University of British Columbia, and W. C. Jankowski, Varian Associates, for nmr spectra, and to Professor P. Brown, Arizona State University, for helpful discussions of the mass spectra. We are indebted to the National Science Foundation for funds to purchase the Atlas CH-4B (Grant GB 4939) and Atlas SM-1B (NSF Grant No. GP-6979).

Polarity Effects in the Solvolysis of Steroid Derivatives. The Synthesis and Acetolysis of 6α-Tosyloxy-3α- and -3β-chloro-5α-cholestane[1]

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Received March 16, 1971

Transmission of electrical effects from remote dipolar substituents to a reaction site has been long under investigation.[3] The phenomenon is usually regarded as a manifestation of either an inductive effect operative through the bonds or a field effect operative through space or solvent. In an elegant study of the dissociation constants of 4-substituted bicyclo[2.2.2]octane- and bicyclo[2.2.1]heptane-1-carboxylic acids, Wilcox and Leung[3] found that the ΔpK_a's were best correlated by the field effect model. Recently we reported studies on the influence of polar substituents upon the rate of solvolysis of esters of substituted cyclohexanols[4] and *trans*-1-decalols.[5] In all cases investigated we found that the solvolysis rates are most satisfactorily explained on the basis of a field effect. In this connection it became of interest to us to extend these studies to other conformationally rigid molecules. Because of its established conformational integrity, the steroid nucleus seemed well suited for our purpose. To this end we wish to report the synthesis and acetolysis of the *p*-toluenesulfonate esters of 3α-chloro-5α-chloestan-6α-ol (**4b**) and 3β-chloro-5α-cholestan-6α-ol (**2b**).

Synthetic Method.—Synthetic routes are summarized in Scheme I. Entry into the desired cholestan-6α-ol systems was accomplished smoothly *via* oxidative hydroboration of an appropriate cholesteryl derivative using a modification of the method reported by Shoppee, *et al.*[6] The expected least highly substituted alcohols were obtained in good yield. Stereochemically, the stanol products were exclusively equatorial (6α). This is presumably a result of steric hindrance by the

(1) This research was supported in part by Research Grant GP-6133X from the National Science Foundation.

(2) Postdoctoral Research Associate, 1966–1967. Lecturer in chemistry, 1967–1968.

(3) C. F. Wilcox and C. Leung, *J. Amer. Chem. Soc.*, **90**, 336 (1968), and references therein.

(4) D. S. Noyce, B. N. Bastian, P. T. S. Lau, R. S. Monson, and B. Weinstein, *J. Org. Chem.*, **34**, 1247 (1969).

(5) D. S. Noyce and B. E. Johnston, *ibid.*, **34**, 1252 (1969).

(6) C. W. Shoppee, R. Lack, and B. McLean, *J. Chem. Soc.*, 4996 (1964).