Figure 1.—Partial nmr spectra of (a) 4-[2-(1-aziridinyl)ethyl]-morpholine (IV), determined in $CDCl_3$; (b) crude 1,1′-(oxydiethylene)bisaziridine (I), free of mineral oil but contaminated with unconverted tosylate (peak at 2.45 ppm), determined in $CDCl_3$; (c) crude I, contaminated with mineral oil (peaks at 0.9 and 1.3 ppm) and an unidentified impurity peak (2.6 ppm), determined in CD_3COCD_3. Spectra b and c were obtained from the products of two reactions; in the former case mineral oil was removed from the sodium hydride dispersion prior to reaction with 1-(2-hydroxyethyl)aziridine.

2-[(2-Morpholinoethyl)amino]ethanethiol Dihydrochloride (VII). A. From IV as Derived from Bis-2-chloroethyl Ether.—4-[2-(1-Aziridinyl)ethyl]morpholine (IV, 6.1 g, 0.04 mole) was poured into a precooled solution of hydrogen sulfide (7 g) in 50 ml of methanol (−75°). The stirred reaction mixture was maintained at −60° for 20 min, then allowed to slowly warm to room temperature. Excess hydrogen sulfide and solvent were removed under reduced pressure leaving 6.8 g of a pale violet liquid. The crude free base was dissolved in 25 ml of water, and the solution was acidified with 6 *N* hydrochloric acid. After concentrating to dryness under reduced pressure, a quantitative yield of the solid dihydrochloride was obtained. This solid was recrystallized from methanol to provide 6.5 g (62%) of coarse, colorless needles, mp 186–188° (lit.[4] mp 185–188°).

B. From IV as Derived from 4-(2-Chloroethyl)morpholine Hydrochloride.—The reaction was carried out in the same manner as described under A above. The following amounts of reagents were employed: IV (10.0 g, 0.064 mole), hydrogen sulfide (8 g, in 50 ml of methanol). There was obtained 13.1 g (78%) of pure dihydrochloride, mp 185–187°. No depression was observed when a mixture melting point was taken with the dihydrochloride obtained from IV as derived from bis-2-chloroethyl ether. Infrared and nmr spectra of these two derivatives were identical.

Anal. Calcd for $C_8H_{20}Cl_2N_2OS$: C, 36.5; H, 7.6; Cl, 26.9; N, 10.6; S, 12.2. Found for VIIa: C, 36.5; H, 7.7; Cl, 26.7; N, 10.6; S, 12.1. Found for VIIb: C, 36.5; H, 7.9; Cl, 26.9; N, 10.6; S, 11.8.

Reaction of the Tosylate of 1-(2-Hydroxyethyl)aziridine with the Alkoxide of the Same Amino Alcohol.—1-(2-Hydroxyethyl)-aziridine (43.6 g, 0.50 mole) was added dropwise over 30 min to a suspension of sodium hydride (21.7 g, of a 58% mineral oil dispersion, 0.525 mole) in 1.5 l. of dry ether. [Prewashing of the sodium hydride–mineral oil dispersion with petroleum ether (bp 30–60°) was an effective means of removing the mineral oil, which interfered with subsequent nmr study of the crude reaction product.] The resulting white slurry was stirred at room temperature for 3 hr, then cooled to −10° (Dry Ice–methanol bath). A solution of *p*-toluenesulfonyl chloride (47.7 g, 0.25 mole) was added over 2 hr at −10°. The mixture was left overnight at room temperature. Sodium chloride and the sodium salt of *p*-toluenesulfonic acid, which had deposited quantitatively, were removed by filtration.

Small aliquots of the ethereal filtrate were evaporated under reduced pressure to provide samples of the crude liquid product (pronounced musty odor), which were used for nmr study. The spectra had to be obtained rapidly, since within minutes after solvent removal the liquid residues decomposed violently. Several runs were made using an excess of the alkoxide to ensure basicity of the reaction mixture. Results were always the same—product decomposition soon after solvent removal.

Registry No.—IV, 10580-47-9; V, 10220-23-2; VI 10562-13-7; VII, 10588-76-8; 1,1′-(oxydiethylene)bisaziridine, 10580-48-0.

Acknowledgment.—This work was supported in part by the U. S. Army Medical Research and Development Command under Contract No. DA-49-193-MD-2109. We wish to thank Professor Wilbert H. Urry of the University of Chicago, and Dr. John S. Driscoll of Monsanto Research Corp., for valuable consultation and assistance.

Amide Derivatives of 1,2,3,4,7,7-Hexachloro-3-hydroxy-5-sulfotricyclo[2.2.1.$0^{2,6}$]heptane Sultone

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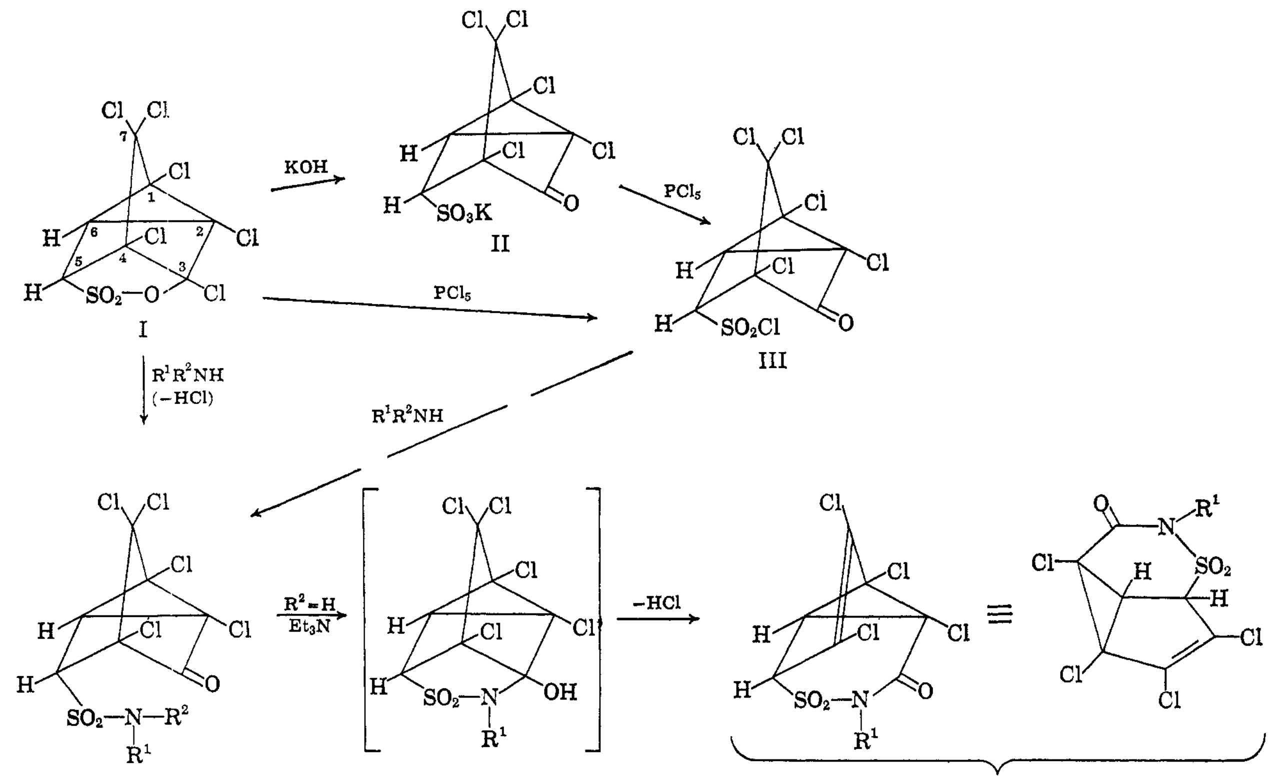
1,2,3,4,7,7-Hexachloro-3-hydroxy-5-sulfotricyclo[2.2.1.$0^{2,6}$]heptane sultone (I) is easily prepared by the homoallylic addition of sulfur trioxide to 1,2,3,4,7,7-

Scheme I



IVa, $R^1 = CH_3$; $R^2 = CH_3$
b, $R^1 = C_2H_5$; $R^2 = C_2H_5$
c, $R^1 = C_6H_5$; $R^2 = H$
d, $R^1 = 4\text{-}CH_3OC_6H_4$; $R^2 = H$

VIa, $R^1 = H$
b, $R^1 = C_2H_5$
c, $R^1 = n\text{-}C_4H_9$
d, $R^1 = C_6H_5$
e, $R^1 = 4\text{-}CH_3OC_6H_4$
f, $R^1 = 4\text{-}CH_3C_6H_4$

hexachlorobicyclo[2.2.1]-2,5-heptadiene.[1] The present report is concerned with the preparation of primary and secondary amido derivatives of I, either by the direct interaction of I with the corresponding amines, or by reaction of the amines with a novel sulfonyl chloride (III) derived from I.

Sultones as a class characteristically undergo ring cleavage upon treatment with ammonia, or with primary or secondary amines, forming the corresponding hydroxysulfonamides;[2] tertiary amines yield quaternary ammonium sulfonates. Sultone I, however, does not react with trimethylamine at 25°, or with triethylamine at 75°. It is therefore less reactive than 1,3-propane sultone. The behavior of sultone I with aliphatic secondary amines is analogous to its reaction with methanol.[1] The secondary amines give 3-ketosulfonamides of structure IV, apparently by the elimination of hydrogen chloride from the corresponding hypothetical intermediate *gem*-halohydrin.

The behavior of I with ammonia and with primary amines is more complicated. These form sulfocarboximides of structure VI, which involves not only cleavage of the sultone ring, but also of the carbon-to-carbon bond between positions 3 and 4, and the generation of olefinic unsaturation by the elimination of a second mole of hydrogen chloride. The first step in this sequence is thought to involve the formation of a type IV ketosulfonamide, a species actually isolated from reaction with aromatic amines, although not with the more basic ammonia or with aliphatic amines. The carbonyl carbon atom of type IV compounds should be highly electropositive, by analogy to another polycyclic ketone, the keto group of which is also situated between two $\gg$CCl moieties.[3] A weaker than normal carbon-to-carbon bond is also characteristic of this type of structure, rendering it susceptible to basic cleavage.[4] In the proposed hydroxy compound of type V such a bond cleavage presumably occurs in concert with the elimination of hydrogen chloride. Elimination probably occurs *trans*,[5] even though models show that the hydroxyl proton is in close proximity to the *cis* chlorine atom. Considerable reduction in ring strain would also be expected during the conversion of V to VI. (See Scheme I.)

The rate of reaction of aromatic amines with I increases with their basicity, a finding consistent with the considerations developed above. 4-Anisidine reacted at a reasonable rate to form IVd, which easily afforded VIe upon heating with more amine. Aniline and 4-toluidine, on the other hand, reacted sluggishly. 4-Chloroaniline was even less reactive, and 3,4-dichloroaniline remained virtually unchanged. In these cases,

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[1] E. D. Weil, *J. Org. Chem.*, **29**, 1110 (1964); unpublished research data, Allied Chemical Corp.

[2] E. E. Gilbert, "Sulfonation and Related Reactions," John Wiley and Sons, Inc., New York, N. Y., 1965, p 280 ff.

[3] B. S. Farah, E. E. Gilbert, P. Lombardo, and A. C. Pierce, *J. Chem. Eng. Data*, **11**, 409 (1966).

[4] K. V. Scherer, Jr., R. S. Lunt, III, and G. A. Ungefug, *Tetrahedron Letters*, **17**, 1199 (1965).

[5] J. Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p 190.

TABLE I

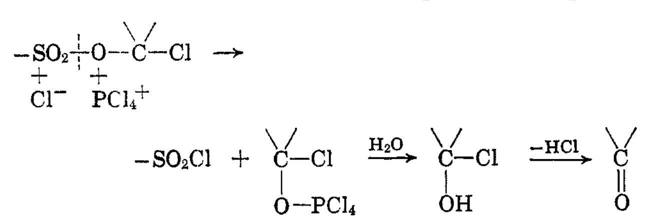
AMIDO DERIVATIVES OF I

					Nmr[a]			Calcd, %					Found, %				
Compd	R^1	R^2	Mp, °C	Yield, %	H_6, ppm	H_5, ppm	$J_{H_{56}}$, cps	C	H	Cl	S	N	C	H	Cl	S	N
IVa	CH_3	CH_3	205–210	95	3.32	4.27	2.5										
IVb	C_2H_5	C_2H_5	129–130	45	3.24	4.06	2.5	31.8	2.9	42.5	7.7	3.4	31.5	3.1	42.2	7.5	3.2
IVc	C_6H_5	H	177–185	*b*	3.63	4.43	2.5	35.8	1.8	40.7	7.3	3.2	35.6	2.0	40.0	7.6	3.3
IVd	4-$CH_3OC_6H_4$	H	198–200	55	3.85	4.60	2.5	36.1	2.2	38.2	6.9	3.0	36.7	2.4	37.8	...	2.7
VIa	H	...	228–231 dec	90	3.70	5.72	8.5	26.0	0.9	43.9	9.9	4.1	26.6	1.2	43.3	9.5	4.2
VIb	C_2H_5	...	134–141	73	3.12	4.95	9										
VIc	*n*-C_4H_9	...	108–110	79	3.18	5.04	9	34.9	2.9	37.5	8.5	3.7	35.2	3.0	37.2	8.5	4.0
VId	C_6H_5	...	185–187	*b*	3.68	5.80	9	39.0	1.8	...	...	3.5	38.5	1.9	...	...	3.2
VIe	4-$CH_3OC_6H_4$	...	234–235	63	4.17	6.42	8	39.0	2.1	...	...	3.3	39.1	2.1	...	...	3.1
VIf	4-$CH_3C_6H_4$	...	209–210	*b*	3.85	6.00	9	40.5	2.2	34.3	7.7	3.4	40.5	2.1	34.4	7.6	3.0

[a] Nmr chemical shifts are reported as obtained in $CDCl_3$ or $(CD_3)_2C{=}O$ in parts per million (ppm) downfield from tetramethylsilane as internal standard. [b] Small samples isolated by column chromatography.

the addition of triethylamine increased the rate of reaction to a satisfactory level. Ammonia and aliphatic amines, on the other hand, reacted rapidly forming only type VI products. Attempts to obtain type IV compounds by employing excess sultone were without success. The carboximide derived from ammonia (VIa) has the expected acid character, since it forms water-soluble ammonium and potassium salts. Acidification of the salts with strong acids regenerates VI.

The ketosulfonyl chloride III also gave products of types IV and VI. It can be prepared directly from I, or from the ketosulfonate (II) described by Weil,[1] by the treatment of either compound with phosphorus pentachloride. Since III is isomeric with I, it seemed possible that the phosphorus pentachloride was actually performing no useful function, and that I might be converted to III by simple heating. It was found, however, that pure I was unchanged by heating for 1 hr at 200–220°, while an 85% yield of III resulted even at 167° in the presence of phosphorus pentachloride. Pyrolysis of I at 250–280° gave a mixture of products not easily separable. No reaction occurred upon refluxing I with thionyl chloride for several hours. It was further noted that the phosphorus pentachloride was consumed during heating as judged by the gradual disappearance of sublimate. Following the proposals of Newman and Wood,[6] the following reaction sequence



is accordingly suggested. Failure of the carbon–oxygen bond to undergo cleavage to a $>CCl_2$ moiety, as ordinarily observed with phosphorus pentachloride,[6] is largely explained by the unusual bond strength resulting from the highly electropositive nature of the carbon atom. Earlier work at this laboratory[7] has shown that such cleavages require drastic conditions.

Experimental Section

Melting points were run on a Mel-Temp apparatus and are uncorrected. Nmr spectra were observed on a Varian spectrometer, Model A-60. Infrared spectra were observed on a Perkin-Elmer Infracord.

1,2,3,4,7,7-Hexachloro-3-hydroxy-5-sulfotricyclo$[2.2.1.0^{2,6}]$-heptane Sultone (I).—1,2,3,4,7,7-Hexachlorobicyclo[2.2.1]-2,5-heptadiene (Aldrich Chemical Co., 445 g, 1.5 moles) was added with stirring at 10 to 15° to stabilized sulfur trioxide (Sulfan, 240 g, 3.0 moles) dissolved in 500 ml of trichlorofluoromethane. The mixture was allowed to warm to room temperature over a 3-hr period with stirring, after which it was added to 2000 ml of ice water. The mixture was filtered after standing overnight and washed with water. The filter cake was dissolved in 2000 ml of carbon tetrachloride, washed with 200 ml of water, refluxed for 1 hr with 2 g of decolorizing carbon, filtered, and concentrated to 1200 ml. The crystals formed on cooling were filtered, yielding 340 g (62%) of I, mp 173–175° (lit.[1] mp 173.5–174°). Concentration of the filtrate gave an additional 57 g of I. Weil[1] employed oleum without a solvent. The H′ nmr spectra of this sultone gave a pair of doublets at 3.06 and 4.60 ppm with a coupling constant of 2.5 cps.

1,2,4,7,7-Pentachlorotricyclo$[2.2.1.0^{2,6}]$heptan-3-one-5-sulfonyl Chloride (III).—A mixture of sultone I (76 g, 0.2 mole) and phosphorus pentachloride (51 g, 0.25 mole) was refluxed (*ca.* 167°) for 10 hr. The reaction mixture was cooled and added with stirring to 200 ml of cold water. Filtration gave 65 g (85%) of crude III. It was purified by dissolving in carbon tetrachloride, refluxing for 30 min with decolorizing carbon, filtering, and cooling. The crystals so obtained were further purified by recrystallization from hexane–carbon tetrachloride (mp 115–120°). A similar procedure was employed for the preparation of III from II. The infrared spectrum of III showed a strong carbonyl absorption at 5.5 μ, while its H^1 nmr gave a pair of doublets at 2.97 and 4.45 ppm with a coupling constant of 2.5 cps, which are consistent with the assigned structure.

N-(Butyl)-8-oxo-1,2,3,4-tetrachloro-6-thia-7-azatricyclo-$[3.3.1.0^{2,9}]$non-3-ene 6,6-Dioxide (VIc).—To sultone I (19 g, 0.05 mole) dissolved in 100 ml of carbon tetrachloride was added *n*-butylamine (17 g, 0.164 mole), dissolved in 25 ml of carbon tetrachloride, over 20 min at 30–45°. After stirring for 1 hr the solid amine hydrochloride was removed by filtration. The filtrate was evaporated to dryness *in vacuo* to give a crude product which was purified by recrystallization from ethanol to give 15 g (yield 79%) of VIc.

Related compounds IVa–c and VIa–f (see Table I) were similarly prepared in good yields. Reaction times of 2 hr or less were employed except for the aromatic amido derivatives which required as much as 48 hr. Some of the aromatic amido derivatives were purified by column chromatography. The ammonia derivative VIa was purified by dissolution in water and precipitation by the addition of concentrated hydrochloric acid.

The infrared spectra were of substantial assistance in identifying the products, since the type IV materials gave a carbonyl absorption at 5.5 μ while type VI absorbed at 5.8 μ. The primary amine derivatives of type IV showed an NH absorption at 3.0 μ. The type VI compounds showed a C=C absorption at 6.25 μ. All compounds gave a weak absorption at 3.2 μ, believed due to the cyclopropyl hydrogen.

The ultraviolet spectra of compound VIb showed weak absorption at 235 mμ, indicating a nonconjugated system.

The similarity of nmr spectra of the starting sultone I, the sulfonyl chloride III, and compounds of type IV indicate similar

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(6) M. S. Newman and L. L. Wood, Jr., *J. Am. Chem. Soc.*, **81**, 4300 (1959).

(7) B. S. Farah and E. E. Gilbert, *J. Org. Chem.*, **30**, 1241 (1965).

ring structures. The increase in J_{H_5,H_6} from 2.5 cps for type IV materials to 9 cps for type VI indicates a large change in environment for these protons.

Registry No.—I, 10562-19-3; III, 10562-21-7; IVa, 10562-22-8; IVb, 10562-23-9; IVc, 10562-24-0; IVd, 10562-25-1; VIa, 10562-20-6; VIb, 10562-26-2; VIc, 10562-27-3; VId, 10562-28-4; VIe, 10562-29-5; VIf, 10562-30-8.

Acknowledgment.—The author wishes to express his gratitude to Dr. E. E. Gilbert and Professor J. Meinwald for helpful discussions, to Dr. J. O. Peterson for obtaining and interpreting the nmr data, and to Mr. Stephen Horensky for performing much of the experimental work.

Synthesis of *cis,cis*-4,8-Dimethyl-*cis*-2-oxa-6-ketodecahydroazulene. A Precursor in an Attempted Synthesis of β-Vetivone

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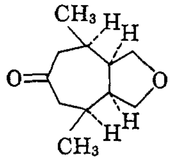
Received February 8, 1967

The synthesis of *cis,cis*-4,8-dimethyl-*cis*-2-oxa-6-ketodecahydroazulene (**1**) was undertaken to develop a stereospecific route to a seven-membered ring from the readily accessible unsaturated ether **2**. Through conversion of the tetrahydrofuran ring to the corresponding carbocyclic ring system, the intermediate **1** was envisioned as a precursor in a synthetic route to **3**.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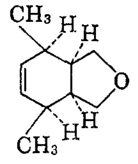
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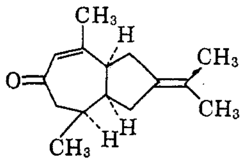
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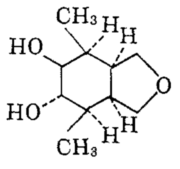
Structure **3** has been proposed for the sesquiterpene, β-vetivone.[2] The remarkably similar chemistry and physical properties of α- and β-vetivone led Naves and Perrotet to conclude that they differed only in the asymmetric center bearing the methyl group. However, a new structural formulation has been proposed for α-vetivone.[3]

The experimental facts do not rule out the structure of β-vetivone as being epimeric with **3** in having the methyl group and the ring-fusion hydrogens *cis*, that is, the structure originally assigned to α-vetivone.[2] It is possible that **1** may or may not be related to β-vetivone. The configuration of the methyl group in β-vetivone could be unambiguously established by a stereospecific conversion of **1** to **3** and a comparison of the latter compound to natural β-vetivone.

Results and Discussion

The reaction of **2** with performic acid has previously been reported by us as yielding the diol **4**.[4] The reaction of **4** with aqueous sodium periodate at 0° yielded the crude dialdehyde **5** in nearly a quantitative yield. The reduction of **5** to the diol **6** (R = H) was effected using sodium borohydride in methanol at 0°. This diol **6** (R = H) had previously been prepared by us *via* the sodium bismuthate oxidation of **4** and reduction of **5** to **6** (R = H) by use of lithium aluminum hydride.[4] The sodium periodate–sodium borohydride route is operationally simpler and also results in higher over-all yields.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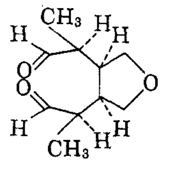
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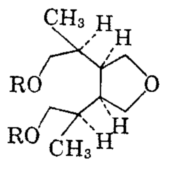
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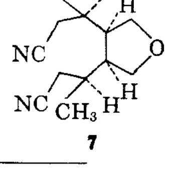
In order to obtain experimental data as to whether enolization of **5** under the oxidation conditions might effect the stereochemistry of the methyl groups, the sodium periodate oxidation was performed in deuterium oxide at 0°. Infrared analysis of the crude dialdehyde **5** showed no detectable incorporation of deuterium. The nmr [deuteriochloroform solution with values reported in parts per million (ppm) with TMS as an internal standard] exhibited a sharp doublet centered at 1.30 which can be assigned to the methyl groups ($J \sim 6$ cps with the adjacent hydrogen). A complex multiplet centered at 2.5 can be attributed to the tertiary hydrogens. A multiplet centered at 3.8 can be assigned to the hydrogens adjacent to the oxygen function, while a sharp doublet centered at 9.62 can be attributed to the protons of the aldehyde groups. Integration is in accord with the formulation of the structure as **5**. It seems reasonable to assume that no isomerization of the methyl groups occurred under the oxidation conditions utilized.

The formation of the ditosylate **6** (R = Ts) was readily effected by reaction of **6** (R = H) with excess *p*-toluenesulfonyl chloride in pyridine solution. The dinitrile **7** was obtained by reaction of the ditosylate with sodium cyanide using dimethyl sulfoxide as the reaction medium. The dinitrile **7** was quantitatively hydrolyzed to the diacid **8** by refluxing with aqueous sodium hydroxide followed by acidification. Pyrolysis of this diacid from a barium hydroxide–iron powder mixture[5] produced the ketone **1** in a 25% yield.

The structure of the ketone **1** was established by nmr spectroscopy. The spectrum (carbon tetrachloride solution with values reported in parts per million using TMS as an external standard) exhibited a doublet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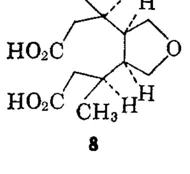
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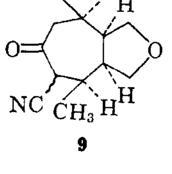
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(1) (a) National Defense Education Act Fellow, 1962–1965. (b) Abstracted in part from a thesis presented to the Graduate College of the University of Vermont, Sept 1965, in partial fulfillment of the requirements for the Ph.D. degree.

(2) (a) Y. R. Naves and E. Perrotet, *Helv. Chim. Acta*, **24**, 3 (1941). (b) For a summary of the experimental data, see J. L. Simonsen and D. H. R. Barton, "The Terpenes," Vol. III, Cambridge University Press, London, 1952, pp 224–232.

(3) K. Endo and P. de Mayo, *Chem. Commun.*, **2**, 89 (1967).

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