between 80° and 100° reduction of the carboxylic function took place, accompanied by the breaking of the N—N bond and the formation of β,β-disubstituted γ-amino alcohols. In the same solvent no reaction occurred when the temperature did not reach 70°. This behavior of primary hydrazides is different from that of secondary and tertiary ones, which leads to the corresponding hydrazines, and as far as we know, has not yet been described.

The prepared compounds, when subjected to broad pharmacological screening, showed some activity on the central nervous system. All compounds revealed convulsant properties, while some of them, at lower dosages, protected mice from electroshock seizures. The convulsant activity was particularly evident for 4,4-diethyl- 2-oxazolidinones, thus paralleling the observation made on the previously described 5,5-diethyl-tetrahydro-1,3-oxazine-2,4-dione.

## EXPERIMENTAL

*2-Oxazolidinones.* To a stirred suspension of 0.01 mole of hydrazide (II) in 30 ml. of water at 0° a solution of 0.03 mole of hydrochloric acid in 30 ml. of water was added. Some of the resulting hydrochlorides were soluble, others were sparingly soluble or insoluble. The solution or suspension of the hydrazide hydrochlorides was diazotized with a solution of 0.011 mole of sodium nitrite in 10 ml. of water at 0–5°. The oil which precipitated during the reaction was extracted with benzene and dried over sodium sulfate. The clear solution was gently refluxed for 0.5 hr. While heating a gas evolution was observed. After concentration *in vacuo* the residue was recrystallized from ligroin, ether–petroleum ether, or ethyl acetate–petroleum ether. The two oily compounds (Table I. No. 1 and 8) were distilled by Ronco's technique.[26]

*Reductions with lithium aluminum hydride. 1) γ-Amino-β,β-diphenylpropanol.* A mixture of 8.5 g. of α,α-diphenyl-β-hydroxypropionic acid hydrazide, 7 g. of lithium aluminum hydride, and 70 ml. of ethylmorpholine was heated for 4 hr. at 100°. The mixture was cautiously treated with water and extracted with ether. After evaporation of the ether the residue was recrystallized from isopropyl ether; yield, 5.1 g.; m.p. 103–105°. After a further recrystallization from diluted ethyl alcohol the m.p. reached 105–106°.

*Anal.* Calcd. for $C_{15}H_{17}NO$: C, 79.26; H, 7.54; N, 6.16. Found: C, 79.52; H, 7.64; N, 5.87.

*N,O-Diacetyl derivative* m.p. 134–136°.

*Anal.* Calcd. for $C_{19}H_{21}NO_3$: C, 73.28; H, 6.80; N, 4.50. Found: C, 73.10; H, 7.04; N, 4.83.

*Picrate,* m.p. 213–216°.

*Anal.* Calcd. for $C_{21}H_{20}N_4O_8$: N, 12.28. Found: N, 11.93.

*2) γ-Amino-β-phenyl-β-methylpropanol.* A mixture of 9.7 g. of α-phenyl-α-methyl-β-hydroxypropionic acid hydrazide, 9.5 g. of lithium aluminum hydride, 150 ml. of ethylmorpholine, and 150 ml. of tetrahydrofuran was refluxed for 24 hr. and worked up further as described in 1). The oily residue was distilled according to Ronco's technique[26]; yield, 4.4 g., b.p. 120–128° at 0.6 mm.

*Anal.* Calcd. for $C_{10}H_{15}NO$: C, 72.69; H, 9.15; N, 8.48. Found: C, 72.80; H, 9.30; N, 8.63. Acetylation equivalent: 98.8%.

*3) γ-Amino-β,β-diethylpropanol.* A mixture of 8.0 g. of α,α-diethyl-β-hydroxypropionic acid hydrazide, 9.5 g. of lithium aluminum hydride and 150 ml. of ethylmorpholine was heated at 100–110° for 24 hr. and worked up further as described in 1). The oily residue was distilled according to Ronco's technique[26]; yield 2.3 g. b.p. 85–87° at 0.6 mm.

*Anal.* Calcd. for $C_7H_{17}NO$: C, 64.07; H, 13.06; N, 10.68. Found: C, 64.08; H, 13.30; N, 10.52. Acetylation equivalent: 99.1%.

*Acknowledgment.* We are indebted to Prof. R. Fusco for the very useful discussion on this subject during the experimental work; and to Miss. Dr. G. Pelizza and Mr. A. Restelli for organic and microanalysis.

We thank Prof. Dr. G. Maffii and co-workers of the Pharmacological Department of Lepetit S.p.A. for the preliminary pharmacological results, which will be published elsewhere.

MILAN, ITALY

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(26) K. Ronco, B. Prijs, and H. Erlenmeyer, *Helv. Chim. Acta*, **39**, 2094 (1957).

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF ROCHESTER]

# Synthesis and Properties of Bicyclic Oxetanes[1]

A. ROSOWSKY[2] AND D. S. TARBELL

*Received September 13, 1960*

The bicyclic oxetanes 7-oxabicyclo[4.2.0]octane and 1-oxaspiro[3.5]nonane were prepared by internal nucleophilic displacement reactions of the appropriate glycol derivatives. The structure assigned to these compounds is supported by their physical properties, as well as by chemical reactions typical of simpler oxetanes, such as acid-catalyzed methanolysis and lithium aluminum hydride reduction, which occur predictably by attack on the least substituted carbon.

Among models once considered in connection with the antibiotic fumagillin[3] were structures containing an oxetane unit attached to a cyclohexane ring. The present paper will be concerned with two of these models, 7-oxabicyclo[4.2.0]-octane[4,5] (I) and 1-oxaspiro[3.5]nonane (II), the latter of which has not been reported previously.

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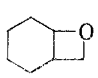
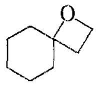
(1) This research was supported in part by Grant E-1138 of the U. S. Public Health Service.

(2) Abbott Laboratories Fellow, 1959–1960.

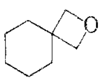
(3) D. S. Tarbell *et al.*, *J. Am. Chem. Soc.*, **82**, 1005 (1960).

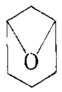
(4) (a) The synthesis of this compound was reported in a preliminary account to the 136th A. C. S. Meeting, Atlantic City, N. J., Sept. 1959, page 67P of the abstract; see also Ref. 5. (b) For the results of a similar study, published after the submission of this manuscript, see H. B. Henbest and B. B. Millward, *J. Chem. Soc.*, 3575 (1960).


I

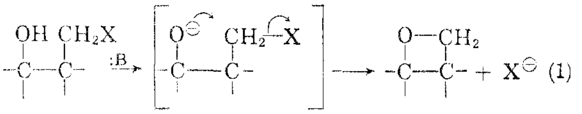

II

The literature dealing with bicyclic oxetanes has not been very extensive. Rupe and Klemm[4] claimed to have prepared I by acid-catalyzed intramolecular dehydration of 2-hydroxymethylcyclohexanol, but gave only scant chemical proof for their structure. In our hands several attempts to effect such cyclizations were unsuccessful. An oxetane closely related to II is 2-oxaspiro [3.5]nonane (III), which was recently reported by two groups of investigators.[6,7] The elusive bridged oxetane 6-oxabicyclo[3.1.1]heptane (IV) has thus far defied synthesis in at least four laboratories.


XV


XVI

*Synthesis of oxetanes.* The general method followed by us in the preparation of I and II can be represented by equation (1),



$$\mathrm{-\overset{OH}{\underset{|}{C}}-\overset{CH_2X}{\underset{|}{C}}-} \xrightarrow{:B} \left[\mathrm{-\overset{O^{\ominus}}{\underset{|}{C}}-\overset{CH_2-X}{\underset{|}{C}}-}\right] \longrightarrow \mathrm{-\overset{O-CH_2}{\underset{|}{C}-\underset{|}{C}}-} + X^{\ominus} \quad (1)$$

where: B is a base and X = —Cl or Bs (*p*-bromobenzenesulfonate). It has been stated[7,8] that chlorohydrins are precursors of choice in this type or internal nucleophilic displacement, and our experience is in accord with this view, as will be seen below.

The starting materials for the above cyclizations, accessible in a straightforward manner, were subjected to the reactions shown in Charts I and II.

The glycol III, previously shown to possess a *cis* configuration[11] was converted to monobrosylate IV and then to *cis*-2-chloromethylcyclohexanol (V) with lithium chloride in ethanol.[8] Cyclization to I could be accomplished in any of three ways: 1) treatment of IV with potassium *tert*-butoxide in *tert*-butyl alcohol at 0°,[9] 2) treatment of IV with sodium hydride in ether at reflux temperature, or 3) treatment of V with solid potassium hydroxide at elevated temperatures, with simultaneous removal of the product from the reaction zone.[6,8] Evidence of the 1,3-cleavage reaction observed in similar instances by other workers[9,10,12] was obtained by infrared spectroscopy for the reaction of IV with potassium hydroxide or sodium methoxide in methanol.

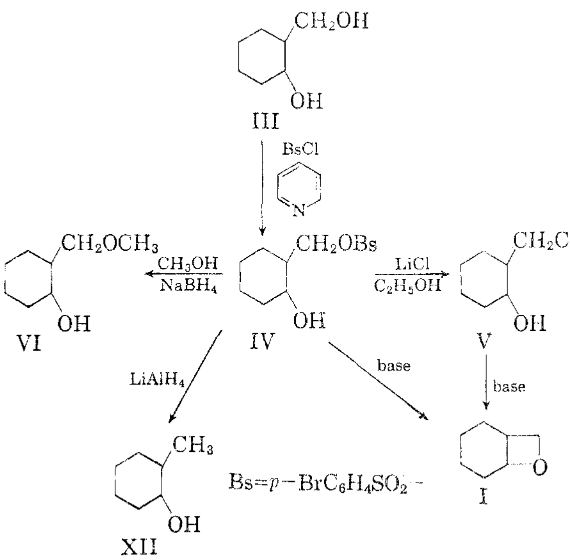


Chart I. Synthesis of 7-oxabicyclo[4.2.0]octane

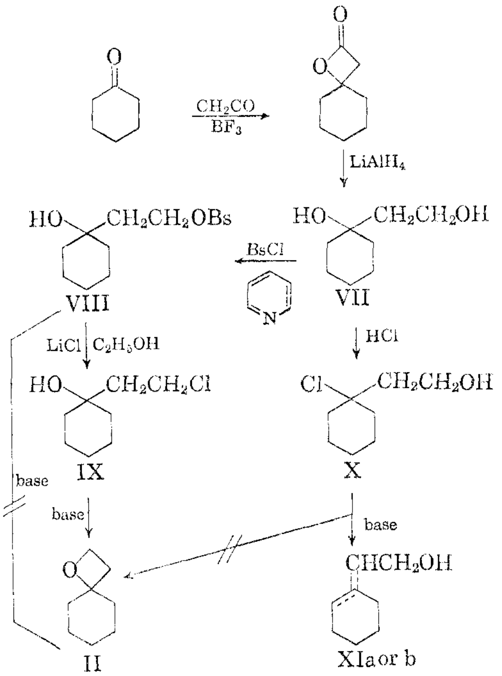


Chart II. Synthesis of 1-oxaspiro[3.5]nonane

For the preparation of II, cyclohexanone was treated with ketene in ether, using a catalytic amount of boron trifluoride etherate, as described by Nazarov and Kuznetsov.[13] The resulting $\beta$-lactone was not purified, but was reduced directly

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(5) H. Rupe and O. Klemm, *Helv. Chim. Acta*, **21**, 1538 (1938).

(6) S. Searles, Jr., E. F. Lutz, and M. Tamres, *J. Am. Chem. Soc.*, **82**, 2932 (1960).

(7) E. L. Wittbecker, H. K. Hall, Jr., and T. W. Campbell, *J. Am. Chem. Soc.*, **82**, 1218 (1960).

(8) M. F. Clarke and L. N. Owen, *J. Chem. Soc.*, 2103, 2108 (1950).

(9) R. B. Clayton and H. B. Henbest, *J. Chem. Soc.*, 1982 (1957).

(10) F. V. Brutcher, Jr., and H. J. Cenci, *Chem. & Ind.*, 1295 (1957).

(11) A. T. Blomquist and J. Wolinsky, *J. Am. Chem. Soc.*, **79**, 6025 (1957).

(12) S. Searles, Jr., R. G. Nickerson, and W. K. Witsiepe, *J. Org. Chem.*, **24**, 1839 (1959).

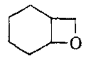
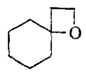
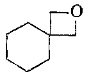
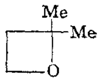
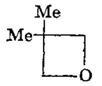
(13) I. N. Nazarov and N. V. Kuznetsov, *J. Gen. Chem., U.S.S.R.*, **29**, 754 (1959).

with lithium aluminum hydride to the glycol VII. The monobrosylate VIII of this glycol was converted to 1-(β-chloroethyl)cyclohexanol (IX) with lithium chloride in ethanol,[8] and this was in turn cyclized to II without prior purification by heating over potassium hydroxide as above.[6,8] When the related chlorohydrin X, prepared from VII by shaking with concentrated hydrochloric acid, was heated with potassium hydroxide, however, the product isolated appeared to be an unsaturated alcohol XIa or XIb, or a mixture of the two. The monobrosylate VIII, in contrast to IV, could *not* be cyclized with sodium hydride, polymerization occurring instead.

*Physical properties.* Oxetanes I and II are highly volatile compounds with a characteristic odor and a tendency to foam on distillation.[14] They are readily identified by intense absorption bands in the 10 μ region of the infrared, in accord with the findings of Searles, *et al.*[6,15] A bathochromic shift has been associated[6] with strain of the oxetane ring, and so the noticeable displacement of the 10 μ band of I and II relative to trimethylene oxide caused no surprise. The position of this band, along with other physical properties, is shown in Table I, three other oxetanes being included for comparison.

TABLE I

PHYSICAL PROPERTIES OF OXETANES

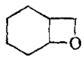
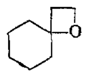
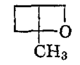
| Compound | B.P. | $n_D$ | Infrared, Main Peak |
|---|---|---|---|
|  | 44.5–45° (9–10 mm.) | 1.4625[a] | 10.4 μ |
|  | 78–79° (34–35 mm.) | 1.4520[a] | 10.4 μ |
|  | 64° (14 mm.)[c] | 1.4602[b] | 10.1 μ[b] |
|  | 70° (1 atm.)[d] | 1.3878[d] | 10.4 β[d] |
|  | 76–78° (1 atm.)[d] | 1.3956[e] | 10.2 μ[d] |

[a] $n_D^{25}$. [b] $n_D^{20}$, taken from Ref. 6. [c] Taken from Ref. 7. [d] $n_D^{25}$, taken from Ref. 15. [e] $n_D^{25}$, taken from Ref. 16.

Oxetanes I and II were further characterized by their NMR spectra, which are summarized in Table II. Trimethylene oxide itself has been reported to have a τ-value[17] of 5.4 for the α-$CH_2$ protons.[18a] The τ-values, splitting patterns, and relative areas were in harmony with the structures I and II. Also included for comparison is the compound 2-methyl-1-oxabicyclo[2.2.0]hexane, recently reported by Srinivasan.[18b]

TABLE II

NMR SPECTRA OF OXETANES

| Compound | Protons | τ-values[18] | Splitting |
|---|---|---|---|
|  | $—CH_2—O$ | 5.41, 5.1 | Quartet, quartet |
| | $—CH—O$ | 6.10 | Quartet |
| | $—CH—CH_2$ | 7.35 | Multiplet |
|  | $—CH_2—O$ | 5.68 | Triplet |
| | $—CH_2—CH_2$ | 7.80 | Triplet |
|  | $—CH_2—O$ | 5.09, 5.61 | Quartet, quartet |
| | $—CH—CH_2$ | 7.15 | Multiplet |

*Chemical reactivity.* In order to place I on a rough reactivity scale a number of its reactions were studied. These reactions, shown in Chart III, indicate that I probably possesses no unusual strain properties relative to simpler oxetanes previously studied.[19]

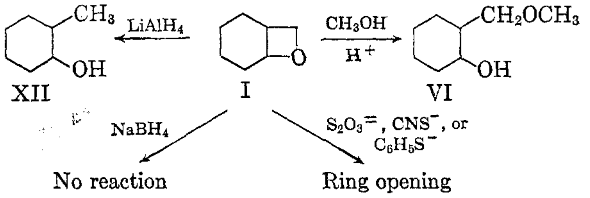


Chart III. Reactions of 7-oxybicyclo[4.20]octane

Methanolysis[19a,c] of I was facile when acid-catalyzed, but more difficult in base, although alkaline cleavage did occur in a sealed tube at 175°. The product could be converted to a six-membered cyclic ketone (1710 cm.$^{-1}$) on oxidation with chromic oxide in pyridine or acetone, which readily indicated the probable position of the hydroxyl group. Furthermore the product was shown, by mixed melting point determination on the *p*-nitrobenzoate, to be indentical with *cis*-2-methoxymethylcyclohexanol (VI) obtained earlier (IV → VI, see Chart I). Methanolysis therefore occurs by rupture of the $CH_2$—O bond in I. Vapor phase chromatography showed the acid-catalyzed reaction to be at least 90% selective.[30]

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[14] See ref. 28 for experimental precautions dictated by these physical properties.

[15] G. M. Barrow and S. Searles, Jr., *J. Am. Chem. Soc.*, **75**, 1175 (1953).

[16] L. F. Schmoyer and L. C. Case, *Nature*, **183**, 389 (1959).

[17] τ-values are based on an arbitrary assignment of τ = 10.0 for tetramethylsilane. See G. Van Dyke Tiers, *J. Phys. Chem.*, 62, 1151 (1958). The τ-value for trimethylene oxide was computed from the value given in reference 18a, in which chemical shifts are expressed in δ-units relative to water.

[18] (a) H. S. Gutowsky, R. L. Rutledge, M. Tamres, and S. Searles, Jr., *J. Am. Chem. Soc.*, **76**, 4242 (1954). (b) R. Srinivasan, *J. Am. Chem. Soc.*, **82**, 775 (1959).

[19] See for example (a) S. Searles, Jr., and C. F. Butler, *J. Am. Chem. Soc.*, **76**, 56 (1954); (b) S. Searles, Jr., K. A. Pollart, and E. F. Lutz, *J. Am. Chem. Soc.*, **79**, 948 (1957); (c) A. W. Adams, *et al.*, *J. Chem. Soc.*, 559 (1959).

Reductive cleavage with lithium aluminum hydride[19b] proceeded smoothly in refluxing ether, but not at 0°. The product was shown by mixed melting point determination on the *p*-nitrobenzoate, to be identical to *cis*-2-methylcyclohexanol (XII) prepared by another route (IV → XII with lithium aluminum hydride, see Chart I). The reaction appeared to be at least 90% selective, according to gas chromatographic analysis.[30] Sodium borohydride in boiling methanol likewise left the oxide ring intact. The reduction of I thus took place in predictable fashion, rupture occurring between oxygen and the least substituted carbon, as already noted by Searles.[19b] That oxetane I was unaffected by sodium borohydride points to the likelihood that I is not an intermediate in the reaction IV → VI (see Chart I). On the other hand, it is not possible at this time to exclude the possibility that I is an intermediate in the reaction IV → XII (see Chart I), since Goering and Serres[20] obtained the isomeric bicyclic ether 6-oxabicyclo [3.2.1] octane (XIV) by treating the monotosylated XIII of *cis*-3-hydroxymethylcyclohexanol with lithium aluminum hydride. If I were initially formed from IV it would of course be further reduced to XII in the presence of excess reagent.

XIII XIV

The attack of several other nucleophilic reagents on the oxide ring of I was examined. Thus, sodium thiosulfate reacts only to a small extent in the color reaction employed by Ross[21] and by Freeman, *et al.*[22] as a qualitative test for cyclic ethers of various sizes. In addition it was found that the more strongly nucleophilic thiophenoxide and isothiocyanate ions caused more extensive ring cleavage, although no detailed product analyses were made.

## EXPERIMENTAL[23]

*cis-2-Hydroxymethylcyclohexanol* (III) was prepared from methyl salicylate by catalytic hydrogenation over Raney nickel at 1800 p.s.i. and 125° in the presence of traces of alkali, followed by reduction with lithium aluminum hydride. Milder hydrogenating conditions gave more satisfactory results in our hands than did those described in the literature.[11,24] Alternately, cyclohexanone could be converted into IV by the route reported by Smissman and Mode.[25] The viscous glycol, b.p. 80–83° (0.12–0.15 mm.), crystallized slowly and yielded a bis-*p*-nitrobenzoate, m.p. 132.5–133° (lit.[25] m.p. 133.5–.34°).

*1-(β-Hydroxyethyl)-cyclohexanol* (VII).[13] Ketene was bubbled at a moderate rate for 6 hr. through a solution of 100 ml. of cyclohexanone and 1 ml. of boron trifluoride etherate in 200 ml. of dry ether at −10° to 0°. After washing with 5% sodium carbonate and rinsing with water, the ether solution was dried over magnesium sulfate and evaporated, yielding a crude product whose infrared spectrum showed a strong β-lactone peak at 5.52 $\mu$[26] and a moderate peak at 5.86 $\mu$ because of unchanged cyclohexanone. The β-lactone was not purified further, but was reduced directly with excess lithium aluminum hydride. After the usual workup and distillation, three fractions were obtained: a) 21.0 g. of cyclohexanol, b.p. 65–75° (0.2–0.3 mm.), $n_{\rm D}^{25}$ 1.4632, from reduction of unchanged cyclohexanone; b) 5.4 g. of an intermediate fraction, b.p. 75–90° (0.2–0.3 mm.), $n_{\rm D}^{25}$ 1.4645; and c) 80.1 g. of VII (58% based on initially used cyclohexanone, 74% after correction for recovered cyclohexanol), b.p. 90–105° (0.2–0.3 mm.), $n_{\rm D}^{25}$ 1.4835 (lit.[27] b.p. 112–114° (2 mm.), $n_{\rm D}^{26}$ 1.4850). Redistillation gave pure VII, b.p. 82–85° (0.03 mm.), $n_{\rm D}^{24}$ 1.4838.

*cis-2-Hydroxymethylcyclohexanol monobrosylate* (IV) was prepared in nearly quantitative yield by the conventional method (see for example Refs. 8–10 and 20). The product was an oil which crystallized slowly on standing in the refrigerator, care being exercised to remove all traces of pyridine. Darkening can be averted by avoiding unnecessary heating in workup. An analytical sample, m.p. 36–40° (softening at 33° was prepared by dissolving a small amount of the crude waxy product in ether, and adding sufficient petroleum ether (b.p. 30–60°) to cause crystallization upon cooling.

*Anal.* Calcd. for $C_{13}H_{17}O_4Br$: C, 44.70; H, 4.87. Found: C, 44.87; H, 5.05.

*1-(β-Hydroxyethyl)cyclohexanol monobrosylate* (VIII) was prepared in nearly quantitative yield by the conventional method.[8–10,20] The oily product tended to darken on standing and was utilized as soon as possible. Although some crystals could be formed in the cold they were low melting, and no analytical sample was made.

*cis-2-Chloromethycyclohexanol* (V) was prepared according to Clarke and Owen[8] by refluxing a solution of IV and lithium chloride in 95% ethanol, evaporating the solvent, and taking up the product in ether. The chlorohydrin was a liquid with a characteristic halogenic odor, and a tendency to darken which made itdesirable to use it quickly in the next step. Characterization was accomplished through the crystalline *p*-nitrobenzoate, m.p. 45–47°.

*Anal.* Calcd. for $C_{14}H_{16}O_4NCl$: C, 56.38; H, 5.38. Found: C, 56.18; H, 5.70.

*1-(β-Chloroethyl)cyclohexanol* (IX) was prepared in nearly quantitative yield from VIII with lithium chloride in refluxing 95% ethanol.[8] The chlorohydrin, possessing the typical halogenic odor, was used without distillation.

*1-(β-Hydroxyethyl)cyclohexyl chloride* (X) was prepared by stirring 10.6 g. (0.0736 mole) of glycol VII with 80 ml. of concd. hydrochloric acid for 8 hr. at room temperature, diluting with water, extracting with petroleum ether, rinsing with saturated sodium bicarbonate solution and water, drying over anhydrous magnesium sulfate, and evaporating, to obtain 10.6 g. of crude product. Distillation resulted in extensive elimination of hydrogen chloride, with recovery of only 6.8 g. of product, which turned yellow on standing. In subsequent runs the chlorohydrin was subjected to the next

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[20] H. L. Goering and C. Serres, Jr., *J. Am. Chem. Soc.*, **74**, 5908 (1952).

[21] W. C. J. Ross, *J. Chem. Soc.*, 2257 (1950).

[22] G. G. Freeman, *et al.*, *J. Chem. Soc.*, 1105 (1959).

[23] All melting points and boiling points are uncorrected. Elemental microanalyses were performed by T. Montzka of this laboratory, as well as Microtech, W. Manser, and F. Pascher. N. M. R. spectra were taken on a 60 Mc Varian instrument by Y. Kawazoe. Infrared spectra were taken on a Model 21 Perkin-Elmer spectrophotometer.

[24] H. C. Ungnade and F. V. Morriss, *J. Am. Chem. Soc.*, **70**, 1898 (1948).

[25] E. S. Smissman and R. A. Mode, *J. Am. Chem. Soc.*, **79**, 3447 (1957).

[26] L. J. Bellamy, *Infrared Spectra of Complex Molecules*, Wiley, New York, 1958, page 188.

[27] D. Papa, H. F. Ginsberg, and F. J. Villiani, *J. Am. Chem. Soc.*, **76**, 4441 (1954).

reaction without prior purification. A small purified sample of X had $n_D^{24}$ 1.4868.

*7-Oxabicyclo[4.2.0]octane (I).* A. To a solution of 225 g. (0.64 mole) of monobrosylate IV in 500 ml. of dry ether in a three-necked flask equipped with a stirrer and reflux condenser were added in small portions 40 g. (0.83 mole) of 50% sodium hydride-mineral oil dispersion (Metal Hydrides, Inc., Beverly, Mass.). Addition was continued occasionally over a period of about 2 days with gentle refluxing. Further addition caused no visible hydrogen evolution. The dense white precipitate of sodium *p*-bromobenzenesulfonate and unchanged sodium hydride was filtered, and the clear yellow filtrate was extracted once with 100 ml. of water. After drying over anhydrous sodium sulfate and solvent removal through a Vigreux column *without suction* or excessive heat, the dark orange solution remaining was distilled.[28] After a small forerun of solvent the product was collected in a receiver, cooled in a Dry Ice/acetone bath. Redistillation yielded the analytical sample, b.p. 44.5–45.0° (9–10 mm.), $n_D^{25}$ 1.4625 (lit.[5] b.p. 54° (11 mm.)). The yield of crude oxetane I was 35.6 g., or 49%.

*Anal.* Calcd. for $C_7H_{12}O$: C, 75.00; H, 10.41. Found: C, 74.53; H, 10.53.

B. To a solution of 4 g. of potassium in 100 ml. of *tert*-butyl alcohol was added 12.2 g. (0.0350 mole) of IV. A dense yellow-white precipitate formed rapidly. The mixture was allowed to stand in the refrigerator for 12 hr., then warmed to room temperature and filtered under suction (cooling the suction flask to −10° to minimize evaporative losses.) The solid thus obtained was dissolved in water, and the aqueous solution was extracted with several portions of ether. The combined ether extracts were added to the yellow *tert*-butyl alcohol filtrate, and after filtering off an additional quantity of white solid the solution was distilled at atmospheric pressure until all the ether and alcohol were removed. The semisolid residue was triturated with ether, and the combined ether triturates were dried over anhydrous sodium sulfate and evaporated at atmospheric, pressure, yielding a pale yellow liquid that gave on distillation the desired oxetane I, b.p. 47–49° (15 mm.). The yield of crude product was 1.85 g., or 47%.

C. A mixture of 3.40 g. (0.0231 mole) of IX and 5 g. of powdered (not dried) potassium hydroxide was heated in an apparatus suitable for removing product from the reaction zone and trapping it in a receiver cooled at −70°. The oil bath temperature was gradually increased from 90° to 150° after 1 hr., and the volatile products were collected and examined. Two phases were present, one of which was water, conveniently removed with a little alumina (Woelm, neutral, activity I). Distillation yielded the desired oxetane I, whose infrared spectrum matched those of previously prepared samples. The yield obtained by this procedure, 1.7 g. or 66%, was superior to the others described above.

*cis-2-Methoxymethylcyclohexanol* (VI). A. To 11.5 g. (0.033 mole) of IV in 100 ml. of absolute methanol were added 3–4 g. of sodium borohydride by inverse addition. After several hours the reaction mixture was cooled and the precipitate of fine white crystals was filtered off. The filtrate was evaporated, and the residue triturated with several portions of ether. The combined ether triturates were dried over anhydrous sodium sulfate and evaporated, leaving a pale yellow liquid with a pleasing odor. Distillation afforded 1.65 g., or 35%, of colorless product, b.p. 92–95° (12 mm.).

*Anal.* Calcd. for $C_8H_{16}O_2$: C, 66.67; H, 11.11. Found: C, 66.25; H, 10.80.

A *p*-nitrobenzoate, m.p. 110.5–112.5°, was prepared.

*Anal.* Calcd. for $C_{15}H_{19}O_5N$: C, 61.48; H, 6.49. Found: C, 61.34; H, 6.66.

The 3,5-dinitrobenzoate, m.p. 87–88°, was prepared but not analyzed.

B. A solution of 5.0 g. (0.045 mole) of I in 25 ml. of absolute methanol containing 2 drops of 95% aqueous sulfuric acid was stirred at 35–40° for 30 hr. Most of the methanol was distilled off and a small amount of solid sodium bicarbonate added to neutralize the acid. Distillation through a Vigreux column yielded a small forerun of methanol followed by 3.8 g. of product (VI), b.p. 92–96° (12–13 mm.), and an additional 0.9 g., b.p. 40–44° (0.3–0.4 mm.). The total yield was 4.7 g., or 67%, $n_D^{25}$ 1.4624.

The *p*-nitrobenzoate, m.p. 110–112°, was undepressed when mixed with the authentic sample prepared above.

*cis-2-Methylcyclohexanol* (XII). A. A solution of 11.7 g. of IV in 50 ml. of dry ether was added dropwise to an ice cold stirred suspension of 1.5 g. of lithium aluminum hydride in 50 ml. of dry ether. After 48 hr. and the usual workup there was obtained a colorless liquid, which on distillation yielded 2.2 g., or 59%, of the desired product (XII), b.p. 67–69° (17 mm.).

That XII is the *cis* isomer was demonstrated by means of its infrared spectrum which contained all the bands characteristic for this isomer,[29] and of a derivative, the *p*-nitrobenzoate, m.p. 56.5–57° (lit.[29] m.p. 55–56°).

B. To a stirred ice cold suspension of 1.15 g. (0.03 mole) of lithium aluminum hydride in 50 ml. of dry ether was added dropwise a solution of 2.24 g. (0.02 mole) of I in 25 ml. of dry ether. After 56 hr. of refluxing, the product was isolated in the usual manner and distilled, yielding 1.2 g., or 53%, of pure XII, b.p. 67–68° (13 mm.).

The *p*-nitrobenzoate, m.p. 56–57° (lit.[29] m.p. 55–56°), was undepressed when mixed with the authentic derivative prepared earlier. The 3,5-dinitrobenzoate, m.p. 101–102° (lit.[29] m.p. 99–100°), was likewise prepared.

Gas chromatographic analysis of the crude reduction product showed the reaction to be at least 90% selective.[30]

*1-Oxaspiro[3.5]nonane* (II). A mixture of 6.70 g. (0.0411 mole) of crude IX and 2 g. of 50% sodium hydride–mineral oil dispersion were stirred magnetically in just enough ether to maintain fluidity. Gas evolution was noticeable. After 1–2 hr. the reaction mixture was warmed gently to remove the solvent. Distillation into a trap cooled in a Dry Ice/acetone bath yielded 2.60 g. of volatile material, b.p. 60–70° (22 mm.), $n_D^{25}$ 1.4520, the bath temperature being raised gradually to 130° during distillation. The brown residue was triturated with ether, and the ether solution, treated as above, yielded an additional 0.2 g. of product. Redistillation of the combined product fractions yielded the desired oxetane II, b.p. 78–79° (34–35 mm.), $n_D^{26}$ 1.4521. The total yield before redistillation was 2.8 g., or 55%. The analytical sample was prepared by a further distillation from metallic sodium.

*Anal.* Calcd. for $C_8H_{12}O$: C, 76.19; H, 11.11. Found: C, 76.44; H, 11.35.

When VIII was treated with sodium hydride in refluxing tetrahydrofuran (it was not possible to dissolve VIII in ether) cyclization did not occur, no volatile products aside from solvent being isolable. When an intimate mixture of VIII and sodium hydride–mineral oil dispersion was warmed

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[28] The high volatility of the oxetanes, in spite of their relatively high boiling points necessitated cautious workup. Solvent take-off on the rotary evaporator was avoided. During vacuum distillation the receivers were cooled at −70° in order to minimize evaporative losses. Precise boiling point determinations, especially on small samples, were rendered difficult both by the tendency of the oxetanes to distill evaporatively, without visible boiling, and by their tendency to froth at the boiling temperature. Gas chromatography revealed traces of diethyl ether in the product even after redistillation.

[29] E. Eliel and C. A. Lukach, *J. Am. Chem. Soc.*, **79**, 5986 (1957).

[30] A portion of this work was done by Miss Joanne Groves in the course of her undergraduate research, University of Rochester, 1960. Gas chromatographic analyses were done on a five foot silicone column at a temperature of about 75°.

gradually with stirring to about 110° in the usual apparatus for simultaneous product take-off, only polymerization took place, a trace of water and unidentified, unpleasant smelling liquid being recovered from the trap.

When chlorohydrin X was treated with potassium hydroxide under the conditions used previously,[6] only an unsaturated alcohol was isolated, b.p. 105–106° (20 mm.), $n_D^{24}$ 1.4807, which could have been either or both of the two possible isomers XIa or b. No further effort was made to clarify this point, however, since no oxetane was obtained.

ROCHESTER 20, N. Y.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

# 2,2′,4,4′,6,6′-Hexamethyl-4,4′-bi-4H-pyran[1,2]

KENNETH CONROW[2a] AND PHILLIP C. RADLICK

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The title compound results from the action of strong organic reducing agents on the 2,4,6-trimethylpyrylium cation. It is believed that this is the first example of a bipyran in which the rings are linked by a single bond and the first example of an alkyl-substituted, nonfunctional 4H-pyran.

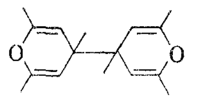
Hafner's elegant preparation of azulene derivatives involves the formation of the seven-membered ring by fusion of a five carbon chain from a pyrylium salt onto the five-membered ring of sodium cyclopentadienide.[3] It was hoped that substitution of the disodium salt of cyclooctatetraene[4] for the cyclopentadienide would not alter the sense of the reaction, so that there would be obtained hydrocarbons with fused seven- and eight-membered rings and extended conjugated double-bond systems.

The reaction between the disodium salt of cyclooctatetraene and 2,4,6-trimethylpyrylium perchlorate was modeled after Hafner's method for the preparation (*ca.* 80%) of the purple 4,6,8-trimethylazulene. The substance isolated (*ca.* 20%) was colorless and proved to have the molecular formula $C_{16}H_{22}O_2$. The possibility that the product arose from the interaction of one dianion of cyclooctatetraene ($C_8H_8=$), one trimethylpyrylium cation ($C_8H_{11}O^+$), and one hydronium ion ($H_3O^+$) (during work-up) was eliminated by the observation that other strong reducing agents, sodium diphenylketyl or the sodium anthracene complex, also act on the trimethylpyrylium ion to give the product (2 and 22% yield, respectively). Thus it is evident that the product arises from the trimethylpyrylium cation by a reductive dimerization process:

$$2C_8H_{11}O^+ + 2e^- = C_{16}H_{22}O_2$$

The best preparative method yet found for the substance (54% yield) involves the use of the potassium salt of cyclooctatetraene with trimethylpyrylium fluoroborate.

The accumulated evidence shows that the dimer has the structure, 2,2′,4,4′,6,6′-hexamethyl-4,4′-bi-4H-pyran (I).



I

The substance is very nonpolar; it is eluted from alumina before cyclooctatetraene and before anthracene. It exhibits only tail absorption in the quartz ultraviolet region. Thus there are no conjugated double bonds. A perbenzoic acid titration showed the presence of four double bonds. A C-methyl determination showed the presence of at least five methyl groups.

The most instructive single piece of evidence was the NMR spectrum which showed three sharp singlets at $\tau$ values of 5.73, 8.25, and 9.10 with areas in the approximate ratio 4:12:6, respectively. The singlet character of these resonance lines requires that no two carbons which bear hydrogen be linked directly to each other. The resonance occurs at the expected[5] shifts for vinyl hydrogens, allylic hydrogens and methyl hydrogens on saturated carbon, except that the vinyl hydrogens absorb at somewhat higher field than usual, probably because they are well shielded by adjacent methyl groups[6] and are vinylogous to the oxygen atom.[7]

During the early stages of the investigation of the structure of this dimer, two misleading results were obtained which considerably impeded our

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(2) Presented at the A.C.S. Southern California Regional Meeting, Dec. 3, 1960.

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(3) K. Hafner and H. Kaiser, *Ann.*, **618**, 140 (1958).

(4) (a) W. Reppe *et al.*, *Ann.*, **560**, 15 (1948); (b) See T. J. Katz, *J. Am. Chem. Soc.*, **82**, 3784, 3785 (1960); *J. Chem. Phys.*, **32**, 1873 (1960) for a description of recent evidence about the structure of this dianion and references to earlier investigations.

(5) G. V. D. Tiers, Minnesota Mining and Manufacturing Co. Handy Pocket Guide to Characteristic Nuclear Resonance Shielding Values, $\tau$, for Hydrogen Bonded to Carbon.

(6) N. F. Chamberlain, *Anal. Chem.*, **31**, 56 (1959); esp. Fig. 4 and p. 69.