at the boiling point and poured into a 3-l. beaker half full of crushed ice. After drying the precipitate was taken up in ether and the ether solution extracted three times with 5% sodium hydroxide solution. The sodium salt of the acid may precipitate but it can be dissolved by the addition of water. The combined alkaline extracts were acidified with 10% phosphoric acid to precipitate the azoxy acid. Additional amounts of the product can be obtained by extracting the filtrate from the oxidation with ether and isolating the acid as described. The total yield of crude product, 5'-nitroazoxybenzene-2'-carboxylic acid was 2.4 g. (59%), m.p. 165–175°. Satisfactory results were obtained using the crude acid in the decarboxylation reaction. Purification for analysis was effected by chromatography with a silicic acid column and 90% benzene-10% ether as the solvent. The pure acid melts at 191.5–193°.

Anal. Calcd. for $C_{13}H_9N_3O_5$: C, 54.36; H, 3.15; N, 14.63. Found: C, 54.30; H, 3.30; N, 14.43.

3'-Nitroazoxybenzene. To a solution of 0.2 g. of 5'-nitroazoxybenzene-2'-carboxylic acid in 20 ml. of pyridine there was added 0.5 g. of copper powder. The mixture was heated under reflux 14 hr., cooled, and the solution decanted from the copper. The solution was diluted with 100 ml. of ether and washed four times with 50-ml. portions of 10% hydrochloric acid, once with water, four times with 10% aqueous sodium hydroxide, and again with water. The solution was dried with anhydrous magnesium sulfate, filtered, and the ether evaporated. The residue was crystallized from hexane to yield 0.1 g. (59%) of yellow crystals, m.p. 91–91.5°. Meisenheimer[5] gives 86–88°.

Mixed m-nitroazoxybenzenes. Mixtures of the two isomers resulted when *m*-dinitrobenzene reacted with *N*-phenylhydroxylamine in the presence of alcoholic potassium hydroxide[5] and by the peracetic acid oxidation of *m*-nitroazobenzene.[4] The isomers in both instances were separated by chromatography with a silicic acid column saturated with nitromethane, using hexane saturated with nitromethane as the mobile solvent. Though quantitative data were not obtained, 3-nitroazoxybenzene was formed in the larger quantity.

Wallach transformation. A solution of 0.2 g. of 3-nitroazoxybenzene in 25 ml. of 82% sulfuric acid was heated near the boiling point for 15 min., at which time the solution gave no precipitate when a drop was added to 10% sodium hydroxide solution. The sulfuric acid solution was diluted and the resultant precipitate taken up in ether. The ether solution was extracted once with 2% sodium hydroxide and twice with 10% sodium hydroxide. The combined alkaline extracts were added to 25% phosphoric acid. The orange product melted at 159–161° and weighed 0.11 g. (65%).

When 3'-nitroazoxybenzene was treated similarly, the product melted at 161–162° and weighed 0.13 g. (77%). A mixture of the two products melted at 159–160.5°. They showed essentially the same infrared spectra. The substance is probably 4-hydroxy-3'-nitroazobenzene, which melts[14] at 159°, and would be an expected product of the rearrangement.

Acknowledgment. The authors wish to thank the National Science Foundation for financial support, in particular for a cooperative fellowship held by E. G. A. in 1960–1961.

STATE COLLEGE, MISS.

---

[14] A. W. Smith and C. E. Boord, *J. Am. Chem. Soc.* **44,** 1451 (1922).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, AMERICAN UNIVERSITY OF BEIRUT]

Pentaerythritol Derivatives. V.[1] Preparation of Diethers of Pentaerythritol by Reduction of Acetals and Ketals[2]

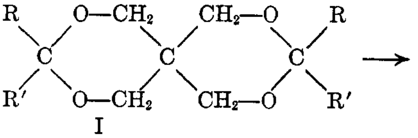
ABDUL-RAHMAN ABDUN-NUR AND COSTAS H. ISSIDORIDES[3]

Received July 5, 1961

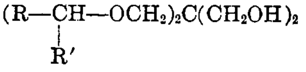
Diethers of pentaerythritol can be prepared in good yield from the corresponding cyclic diacetals and diketals by reduction with lithium aluminum hydride–boron fluoride etherate (or aluminum chloride). An improved method is described for the preparation of 2,6-dioxaspiro[3.3]heptane from pentaerythrityl dibromide.

Eliel and Rerick have described the reduction of acetals and ketals to ethers by lithium aluminum hydride–aluminum chloride (LAH–$AlCl_3$),[4] a method which was later extended to cyclic acetals, ketals and their hemithio analogs.[5]

As pentaerythritol forms cyclic diacetals and diketals readily, reduction by the "mixed hydride" offers a convenient route to the difficultly accessible diethers II.



I



$$(R\text{—}\underset{\displaystyle R'}{\underset{|}{C}}H\text{—}OCH_2)_2C(CH_2OH)_2$$

II

a. R = phenyl
   R' = H
b. R, R' = pentamethylene
c. R, R' = tetramethylene
d. R = methyl
   R' = H
e. R=R' = H

During this study we have used lithium aluminum hydride–aluminum chloride as well as lithium aluminum hydride–boron trifluoride etherate (LAH–BF_3) as reducing agents, and found the latter to

---

[1] For previous paper in this series see R. F. Nassar and C. H. Issidorides, *J. Org. Chem.*, **24,** 1832 (1959).

[2] Abstracted in part from the M.S. thesis of A. R. Abdun-Nur, American University of Beirut, June 1961.

[3] To whom requests for reprints should be addressed.

[4] E. L. Eliel and M. Rerick, *J. Org. Chem.*, **23,** 1088 (1958).

[5] E. L. Eliel and V. G. Badding, *J. Am. Chem. Soc.*, **81,** 6087 (1959).

TABLE I

DIETHERS OF PENTAERYTHRITOL

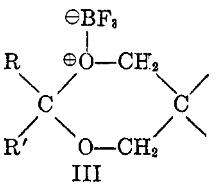
Ether	M.P.	B.P.	Yield, % LAH-$AlCl_3$	Yield, % LAH-BF_3	C, % Calcd.	C, % Found	H, % Calcd.	H, % Found	Acetal or Ketal
Dibenzyl (Ia)	72–74[a]		80	82	72.12	72.20	7.65	7.66	IIa[b]
Dicyclohexyl (Ib)	57.5–58.5[a]		85	91	67.96	68.14	10.74	10.71	IIb[c]
Dicyclopentyl (Ic)	63–64[d]		75	80	66.14	66.29	10.36	10.28	IIc[c]
Diethyl (Id)		114–116/ 5 mm.[e,f]	72	82					IId[g]

[a] Recrystallized from ethanol-water. [b] E. Bograchov, *J. Am. Chem. Soc.*, **72**, 2268 (1950). [c] V. M. Mićović and A. Stojiljković, *Tetrahedron*, **4**, 186 (1958). [d] Recrystallized from petroleum ether (b.p. 40–70°). [e] Lit. b.p. 115°/5 mm. [J. W. E. Glattfeld and J. M. Schneider, *J. Am. Chem. Soc.*, **60**, 415 (1938)]. [f] Diacetate, b.p. 142–143°/8 mm. Saponification equivalent calcd. for $C_{18}O_6H_{24}$, 138; found, 136.5. [g] J. A. Nieuwland, R. R. Vogt, and W. L. Foohey, *J. Am. Chem. Soc.*, **52**, 1018 (1930).

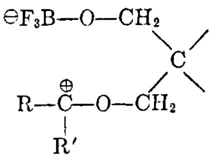
be preferable.[6] Reductions proceeded smoothly with either reagent, but the yields obtained with lithium aluminum hydride-boron trifluoride etherate were slightly better. Furthermore, boron trifluoride etherate was more convenient in handling and less troublesome during the final step of decomposition.

The general procedure for reduction with lithium aluminum hydride-boron trifluoride etherate is as follows. The "mixed hydride" is prepared in dry ether at 0° to −5° and the acetal or ketal is then added under anhydrous conditions either in the solid form or in solution (dry ether). After being stirred at 0° to −5° and then at reflux, the reaction mixture is decomposed, extracted with ether and worked up in the usual manner. The results are summarized in Table I, which includes microanalytical data for compounds IIa, IIb, and IIc. The diethyl ether of pentaerythritol (IId) is a known compound and was characterized as the diacetate.

It is noteworthy that the diformal Ie did not respond to the conditions used for the preparation of the dibenzyl (IIa), dicyclohexyl (IIb), dicyclopentyl (IIc), and diethyl (IId) ethers of pentaerythritol. Instead of the expected dimethyl ether (IIe), the starting material was recovered unchanged (80–85%).[7] Reduction of cyclic acetals and ketals by lithium aluminum hydride-boron trifluoride etherate may involve hydride displacement on the complex III possibly *via* the resonating oxocarbonium ion IV. On this basis, the sluggishness of the diformal (R=R′=H) is not surprising.[8]

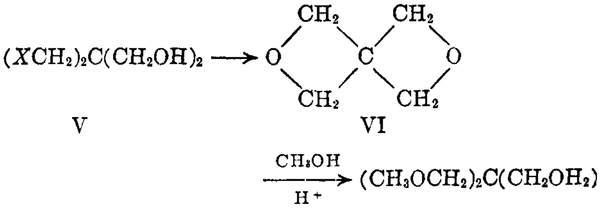


III



IV

Compound IIe was prepared from 2,6-dioxaspiro[3.3]heptane (VI) and methyl alcohol, by an extension of the method described previously for the preparation of pentaerythritol monomethyl ether.[9]



$(XCH_2)_2C(CH_2OH)_2 \longrightarrow$ VI $\xrightarrow[H^+]{CH_3OH} (CH_3OCH_2)_2C(CH_2OH_2)$

V VI IIe

This alternate route to diethers of pentaerythritol is seriously handicapped by the low yields reported in the literature for the preparation of VI (25%,[10] 17%,[11] 20%,[12] 32%[13]). The spirocyclic oxetane and other related intramolecular ethers of pentaerythritol are generally obtained by the action of alcoholic alkali on a pentaerythrityl halide. This dehydrohalogenation reaction, however, is very sensitive to experimental conditions, as evi-

---

[6] While this investigation was in progress, G. R. Pettit and T. R. Kasturi [*J. Org. Chem.*, **25**, 875 (1960)] reported the use of lithium aluminum hydride-boron trifluoride etherate for the direct reduction of esters to ethers.

[7] A cyclic formal in the carbohydrate series has been reduced recently by treatment of its boron trichloride complex with lithium aluminum hydride in ether-tetrahydrofuran [T. G. Bonner and N. M. Saville, *J. Chem. Soc.*, 2851 (1960)].

[8] Professor E. L. Eliel (private communication) has kindly pointed out to us that there is still some question as to whether the oxocarbonium ion is reduced directly or whether reduction proceeds *via* an alpha-halo-ether intermediate subsequent to the oxocarbonium ion. However, regardless of the outcome, it is reasonable that absence of stabilizing substituents on the ion would tend to hinder the reduction.

[9] C. H. Issidorides and A. I. Matar, *J. Am. Chem. Soc.*, **77**, 6382 (1955).

[10] (a) H. J. Backer and K. J. Keuning, *Rec. trav. chim.*, **53**, 812 (1934). (b) F. Govaert and M. Beyaert, *Proc. Acad. Sci. Amsterdam*, **42**, 641 (1939).

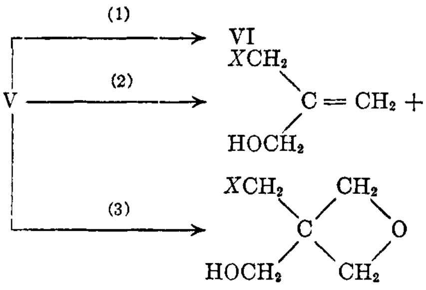
[11] S. Wawzonek and C. H. Issidorides, *J. Am. Chem. Soc.*, **75**, 2373 (1953).

[12] Kiyohisa Furukawa, Yasuo Wada, and Ryohei Oda, *Bull. Inst. Chem. Research, Kyoto Univ.*, **31**, 222 (1953); *Chem. Abstr.*, **48**, 7596h (1954).

[13] Henkel and Cie, G.m.b.H. (Rudolf Köhler and Helmuth Pietsch inventors), Ger. Patent **943,906** (June 1, 1956); *Chem. Abstr.*, **52**, 13314i (1958).

denced by the number of side products that have been isolated.[14]

Searles, Nickerson, and Witsiepe[15] have studied the alkaline decomposition of a series of 3-bromo-1-propanols of partial structure V, and have interpreted the effect of solvent, base concentration, and structural changes in the competition between the intermolecular Williamson reaction (path 1) and the 1,4-elimination of hydrogen halide (path 2).[16] In the present case, preferential one-sided intramolecular substitution is also possible (path 3).[17]



During this work we made several unsuccessful attempts to improve the yield of VI by modifying the isolation techniques described in the literature. From a study of the dehydrohalogenation reaction under different experimental conditions we found that the yield of the oxetane was decreased by the presence of water, by low reaction temperature, and by low concentration of the alcoholic alkali, especially when methanol was substituted for ethanol as the reaction medium. The desired compound was finally obtained by the simple expedient of slow addition of an ethanolic solution of pentaerythrityl dibromide (V. X = Br) to a distilling solution of excess potassium hydroxide in ethanol. This procedure practically eliminates formation of oily by products and gives 2,6-dioxaspiro[3.3]heptane, after chromatography and recrystallization, in 50–60% yield. The compound sublimes readily and shows characteristic oxetane infrared bands at 10.2 μ and 8.2 μ,[18] with an additional strong band at 10.7 μ.[19]

EXPERIMENTAL[20]

Reaction of acetals and ketals with lithium aluminum hydride-boron trifluoride etherate was carried out by a standard procedure illustrated by the following case. A 250-ml. three necked, round bottomed flask was equipped with an air-tight stirrer and a two-way addition tube provided with a condenser (protected by a calcium chloride tube) and a dropping funnel. An Erlenmeyer flask containing pentaerythritol dibenzal (Ia, 3.1 g.) was connected to the third neck of the flask by a section of rubber tubing. Boron trifluoride etherate (5.7 g.) was placed in the round bottomed flask and cooled in an ice-salt bath. A suspension of lithium aluminum hydride (0.4 g.) in 30 ml. of dry ether was then added through the dropping funnel in the course of 0.5 hr. to the cold, well stirred solution, followed by slow addition (10 min.) of the dibenzal. The mixture was stirrer for 1 hr. at −5° to 0° and for 2 hr. at reflux, cooled in an ice-salt bath and decomposed by slow addition of 10% sulfuric acid (100 ml.). The ether layer was separated and the aqueous layer extracted with ten 25-ml. portions of ether. The combined ether extracts were washed with two 30-ml. portions of 5% sodium bicarbonate and 30 ml. of water, dried over anhydrous sodium sulfate, filtered, and evaporated to dryness. Recrystallization of the crude product from ethanol-water gave IIa (2.6 g.; 82%) melting at 72–74°.

2,6-Dioxaspiro[3.3]heptane (VI). A 500-ml. round bottomed flask was connected by a Claisen head to a dropping funnel and a condenser set for downward distillation. Potassium hydroxide (40 g.; Merck, Darmstadt) was placed in the flask, followed immediately[21] by absolute ethanol (70 ml.). The mixture was heated gently by a heating mantle[22] and as soon as the alcohol began to distill, a solution of pentaerythrityl dibromide[17] (30 g.) in absolute ethanol (60 ml.) was added slowly to the distilling solution through the dropping funnel. The addition took 10 min., and during this period the rate of heating was regulated so that 30 ml. of alcohol was distilled. The mixture in the flask was cooled and extracted with ten 50-ml. portions of ether (removed each time by decantation). The combined ether extracts were dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure (30–35°/20 mm.) to a volume of 25 ml.[23] The oily residue was applied to an alumina column (200 g.) and eluted with petroleum ether (b.p. 30–50°; 720 ml.). The eluate, upon evaporation and recrystallization from petroleum ether (b.p. 40–70°), gave 5.7–7 g. (50–60%) of VI melting at 89–90° (lit.[24] m.p. 89°), λ^{CCl_4} 3.5 μ, 6.8 μ, 8.2 μ, 10.2 μ, 10.7 μ.

Pentaerythritol dimethyl ether (IIe). A solution of VI (6 g.), concentrated sulfuric acid (0.5 ml.) and methanol (50 ml.) was stirred for 2 days at room temperature, diluted with water (50 ml.), neutralized with solid sodium carbonate, and extracted with eight 25-ml. portions of ether. The combined ether extracts were dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to an oily residue, which solidified upon cooling. Recrystallization from petroleum ether (b.p. 40–70°) gave 5.9 g. (60%) of IIe melting at 33–35° (lit.[25] m.p. 32°; 34–35°).

Acetylation in the usual manner gave the diacetate boiling at 147–148°/15 mm. Saponification equivalent calcd. for $C_{11}O_6H_{20}$: 124; found: 125.

---

(14) E. Berlow, R. H. Barth, and J. E. Snow, *The Pentaerythritols*, Reinhold, New York, 1958, p. 126.

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

(16) For an example of this reaction in the pentaerythritol series, see ref. 9.

(17) C. H. Issidorides, R. C. Gulen, and N. S. Aprahamian, *J. Org. Chem.*, **21**, 997 (1956).

(18) G. M. Barrow and S. Searles, *J. Am. Chem. Soc.*, **75**, 1175 (1953).

(19) S. C. Sirkar, F. L. Voelz, and F. F. Cleveland, *J. Chem. Phys.*, **23**, 1684 (1955).

(20) Melting points and boiling points are uncorrected. Alumina used for chromatography was neutral, grade I "Woelm," to which 3% water was added. Infrared spectra were run on a Perkin-Elmer Model 137 Infracord double beam spectrophotometer. Microanalyses are by Pascher Mikroanalytisches Laboratorium, Bonn, Germany.

(21) The yield is decreased if the potassium hydroxide is allowed to absorb moisture.

(22) A heating mantle is recommended for effective control of the rate of distillation during the next step.

(23) Further concentration reduces the yield because of loss of the oxetane by sublimation.

(24) Ref. 14, p. 132.

(25) Ref. 14, p. 121.

Acknowledgment. We are grateful to the Research Corp. and to the Arts and Sciences Research Committee of the American University of Beirut for financial support, and to Professor E. L. Eliel for his helpful comments and criticism.

BEIRUT, LEBANON

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, WAYNE STATE UNIVERSITY]

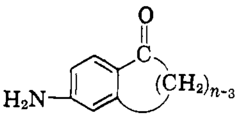
Synthesis of Some Functionally Substituted Benzocyclanones[1]

NORMAN L. ALLINGER AND EDWARD S. JONES

Received June 21, 1961

The synthesis of a group of indanones, tetralones, benzosuberones, and benzocyclooctanones is described. The compounds have various functional groups (amino, hydroxyl, carboxyl, fluoro, and derivatives) on the aromatic ring in the position *para* to the ketone group.

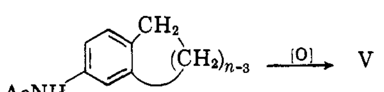
For studies concerning Hammett sigma constants a series of compounds VI was desired. The amines were selected as the first goal, since the amino group is easily convertible to various other groups that were required. This paper describes only the synthesis of these and related compounds; the theoretical studies will form the subject of a later paper.



VIa. $n=6$
b. $n=5$
c. $n=7$
d. $n=8$

A synthesis was desired which would be general and which could be extended to various homologs. Because of the more ready accessibility of starting materials, the $n = 6$ case was investigated first. There appeared to be two general synthetic routes which might be pursued. The first of these involved as a key step the introduction of the ketonic oxygen into the saturated side chain. The oxidation would be expected to occur at the desired methylene, rather than at the one *meta* to the amido group, since the intermediate radical or carbonium ion formed in the rate-determining step of the oxidation would be better stabilized.[2]

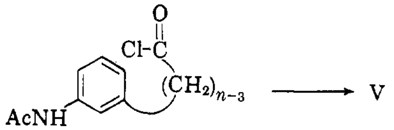
I



IV

A synthetic scheme based on this step is attractive in general since it can begin with hydrocarbons (I), which are accessible without undue difficulty, even for the medium rings.

An alternative synthetic scheme would place a Friedel-Crafts ring-closure step near the end of the synthesis. A disadvantage in this case is the poor yield anticipated in the cyclization step when a medium ring is closed.[3]



The first scheme appeared to offer the most promise and was undertaken initially. Compounds IVa and IVb are known, and their oxidation was studied. The reaction proceeded to give Va and Vb in yields of 57 and 74%, respectively. It was established (see below) that the oxidation took place at the *para* position as predicted. However, for the amide with $n = 7$, by the same procedure, no yield of the desired ketone could be obtained. Under the conditions which gave good results in the five- and six-membered rings, no oxidation occurred and the starting material was recovered. Under more strenuous conditions the starting material was not recovered, but none of the desired product could be isolated.

The alternative synthetic scheme, involving a Friedel-Crafts cyclization to yield the bicyclic amino ketones, was therefore undertaken. The method for synthesis of the benzosuberone derivative is outlined on the flow sheet. Nitration of γ-benzoylbutyric acid and reduction of the nitro group furnished the amino keto acid (XVIII). Acetylation of the amino group and hydrogenolysis of the ketonic oxygen gave the amido acid (XIX), which was cyclized to the amidobenzosuberone (Vc) both with polyphosphoric acid[4] and by treatment of the acid chloride with aluminum chloride in nitrobenzene.

This synthetic sequence was repeated beginning with β-benzoylpropionic acid, which led to the amino tetralone (VIa). The compound obtained in this way was identical with the sample prepared by the oxidation of IVa. This proves that the Friedel-

---

(1) This research was supported by the Office of Ordnance Research, U. S. Army, under Contracts No. DA-20-018-ORD-14652 and No. DA-20-018-ORD-22743.

(2) K. B. Wiberg and R. J. Evans, *Tetrahedron*, **8**, 313 (1960).

(3) R. Huisgen and W. Rapp, *Ber.*, **85**, 826 (1952).

(4) R. C. Gilmore, Jr., and W. J. Horton, *J. Am. Chem. Soc.*, **73**, 1411 (1951).