New Diols in the Furan and Pyran Series

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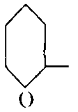
2,2-Bis(hydroxymethyl)tetrahydrofuran (I, R = H) and its tetrahydropyran analog (III, R = H) have been prepared by the reaction sequences indicated. In the synthesis of III (R = H), the intermediate 2,2-bis(hydroxymethyl)-3,4-dihydropyran (II, R = H) was also isolated and observed to isomerize to 1-hydroxymethyl-6,8-dioxabicyclo[3.2.1]-octane (IV, R = H) under the influence of acidic reagents or heat.

TABLE I

Physical Properties of the Diols

Compound	R—	M.P. (Uncorr.) or B.P. (Mm.)	Formula	Calculated C, %	Calculated H, %	Calculated N, %	Found C, %	Found H, %	Found N, %
I	H—[a,b]	51–53	$C_6H_{12}O_3$	54.52	9.16		54.14	9.17	
		110 (0.47)							
	p-$NO_2C_6H_4CO$—	179.5–180	$C_{20}H_{18}O_9N_2$	55.81	4.21	6.51	56.02	4.75	6.68
	$C_{17}H_{35}CO$—	67–68	$C_{42}H_{80}O_5$	75.85	12.13		75.84	12.04	
	CH_3—[c]	82 (15)	$C_8H_{16}O_3$	59.97	10.07		60.11	10.28	
		5							
		124 (0.06)	$C_{16}H_{28}O_5$	63.97	9.39		63.89	9.34	
II	H—	51–52	$C_7H_{12}O_3$	58.31	8.39		58.40	8.29	
	p-$NO_2C_6H_4CO$—	138–139	$C_{21}H_{18}O_9N_2$	57.01	4.10	6.33	57.03	4.16	6.39
III	H—[a]	44–45							
		97–100 (0.25)	$C_7H_{14}O_3$	57.51	9.65		57.45	9.48	
	p-$NO_2C_6H_4CO$—	127–128	$C_{21}H_{20}O_9N_2$	56.75	5.54	6.30	56.72	4.59	6.28
	$C_{17}H_{35}CO$—	45.5–46.5	$C_{43}H_{82}O_5$	76.05	12.17		76.35	12.17	
IV	H—[e]	101 (5)							
		114 (10)	$C_7H_{12}O_3$	58.31	8.39		58.48	8.31	
	p-$NO_2C_6H_4CO$—	94.5–95	$C_{14}H_{15}O_6N$	57.33	5.16	4.78	57.27	5.27	4.91
	$C_{17}H_{35}CO$—	36.5–37.5	$C_{25}H_{46}O_4$	73.12	11.29		73.17	11.00	

[a] Hygroscopic. [b] Hydroxyl; calcd.: 25.75; found: 24.63, 24.07. [c] n_D^{25} 1.4339. [d] n_D^{25} 1.4750. [e] n_D^{25} 1.4790.

EXPERIMENTAL[1]

Data for these compounds are included in Table I.

2,2-Bis(hydroxymethyl)tetrahydrofuran (I, R = H). To a stirred solution of tetrahydrofurfural (1 mol) in formalin (37%; 2.5 moles formaldehyde), aqueous sodium hydroxide (1.15 moles in 50 ml. water) was added dropwise over a period of about 10 min., while maintaining the temperature at about 50° by the aid of an ice bath. In another 15 min. the temperature started to decline and heat was applied (55–60°) for an additional 60–90 min. Exhaustive extraction with butanol and subsequent distillation of the butanol phase gave I (R = H), approximately 90% yield based on the tetrahydrofurfural, as a colorless oil which solidified on standing at room temperature. Alternatively, I (R = H) was also obtained by catalytic hydrogenation of A (see reaction scheme) which was formed *in situ* by reaction of equal moles of tetrahydrofurfural and formaldehyde under alkaline conditions.

2,2-Bis(hydroxymethyl)-3,4-dihydropyran (II, R = H). This diol was prepared in 83% yield from 2-formyl-3,4-dihydro(4H)pyran (acrolein dimer) and formaldehyde by a procedure similar to that of I (R = H), but wherein the final distillation step was conducted below 1 mm. pressure in order to minimize isomerization to IV (R = H).

2,2-Bis(hydroxymethyl)tetrahydropyran (III, R = H). Catalytic hydrogenation of II (R = H, 0.11 mole) in ethanol (150 ml.) over Raney (W-7) nickel (10 g.) at room temperature and 60 p.s.i.g., gave III (R = H), in quantitative yield on subsequent distillation. III (R = H) has also been obtained by catalytic hydrogenation of B (see reaction scheme) as formed *in situ* from equimolar proportions of acrolein dimer and formaldehyde under alkaline conditions. However, when so prepared, 2-hydroxymethyltetrahydropyran is invariably formed as a by-product in very significant amounts.

1-Hydroxymethyl-6,8-dioxabicyclo[3.2.1]octane (IV, R = H). Isomerization of II (R = H) was accomplished (a) by heating alone at 200° for 3 hr., (b) with boron trifluoride etherate in ether at reflux temperature for 2 hr., and (c) by distilling in the presence of 0.5% p-toluenesulfonic acid. The yield of IV (R = H) obtained on distillation was upward of 90% in all cases. Mineral acids and cation exchange resins of the sulfonic type also caused isomerization of II (R = H) to IV (R = H).

p-Nitrobenzoic esters[2] *of* I, II, III, IV (R = p-$NO_2C_6H_4$-CO—). The pale yellow derivatives, prepared by the pyridine method, were recrystallized from absolute ethanol.

Stearic esters of I, III, IV (R = $C_{17}H_{35}CO$—). These derivatives were obtained by heating I, II, III (R = H) with twice the molar amount of stearic acid at 200–230° for about 5 hr. and removing the formed water. Recrystallization from absolute ethanol produced the pure compounds. In the case of II (R = H), isomerization to IV (R = H) occurred during the heating period with stearic acid; the crude stearic ester of IV (R = $C_{17}H_{35}CO$—) was obtained by fractionation at 190–210° (0.35 mm.).

2,2-Bis(methoxymethyl)tetrahydrofuran (I, R = CH_3). This derivative was prepared using dimethyl sulfate.[3] The crude

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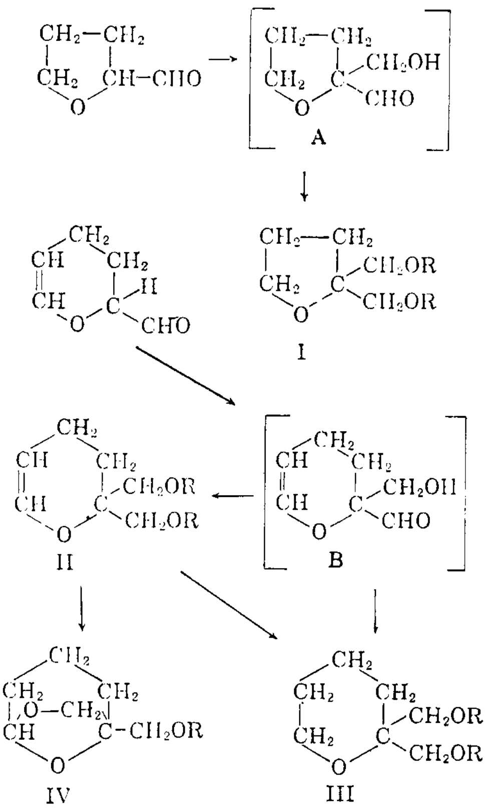
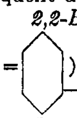
[1] Analyses by Micro-Tech Laboratories, Skokie, Ill.

[2] R. L. Shriner and R. C. Fuson, *The Systematic Identification of Organic Compounds*, 3rd ed., J. Wiley and Sons, Inc., New York, 1948, p. 164.

[3] W. R. Kirner, *J. Am. Chem. Soc.*, **52**, 3251 (1930).



product [b.p. 77–87° (15 mm.): 53% yield] was freed from monoether by heating with phthalic anhydride and subsequent distillation.

2,2-Bis(2-tetrahydropyranoxymethyl)tetrahydrofuran (I, R = ). Using a slight modification of the procedure of Woods and Kramer[4] and an excess of 2,3-dihydro(4H)pyran, a mixture of the mono- and bis-2-pyranoxymethyl derivatives was obtained. The pure "bis" compound was obtained by careful fractionation.

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[4] G. F. Woods and D. N. Kramer, *J. Am. Chem. Soc.*, 69, 2246 (1947).

3-Cyclohexene-1-acetamide

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As part of an investigation of the nucleophilic reactions of mono- and ditosyl derivatives of *cis*- and *trans*-1,4 - cyclohexanediols we condensed ethyl malonate with *trans*-1,4-ditosyloxycyclohexane in the presence of sodium ethoxide. A product was isolated in low yield whose elementary analysis corresponded to that calculated for 7,7-dicarbethoxynorbornane. Saponification and decarboxylation of the diester followed by conversion to the amide, however, gave a monocarboxamide whose properties differed from those of norbornane-7-carboxamide. The infrared spectrum of the condensation product supported the structure of an unsaturated dicarboxylic ester and the melting point of the monocarboxamide was in the range of those reported for the known cyclohexeneacetamides[1b] rather than that of the more compact and much higher melting norbornanecarboxamides.[2]

The behavior of certain tosyl esters in nucleophilic reactions has been recorded by earlier investigators. Although primary tosyl esters undergo nucleophilic displacement rather readily[3] and in good yields, the reactivity of the tosyl esters of secondary alcohols is greatly diminished.[4,5] The influence of steric factors upon the reactivity of certain alicyclic tosyl esters has been discussed[4] and Ingold[6] has pointed out the similarity in reactivity of the tosylates of secondary alcohols to that of tertiary alkyl halides.

These considerations indicated the structure of the diester to be ethyl 3-cyclohexene-1-malonate and that of the monocarboxylic acid amide derived from it to be 3-cyclohexene-1-acetamide.

The synthesis of 3-cyclohexene-1-acetic acid and its amide *via* the Diels-Alder condensation with unactivated dienophiles, such as vinylacetic acid, requires the use of high temperature and introduces the possibility of double bond migration. The reaction of butadiene with acrylic acid to form 3-cyclohexene-1-carboxylic acid, on the other hand, can be carried out at low temperatures without isomerization. When 3-cyclohexene-1-carbonyl chloride was subjected to the Arndt-Eistert reaction 3-cyclohexene-1-acetamide was obtained in good yield.

Elementary analysis, a comparison of the infrared spectra and mixed melting point deter-

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(1)(a) Present address: Shulton, Inc., Clifton, N. J.

(1)(b) Cyclohexeneacetamides: Δ^1-(m.p. 151°), O. Schnider and J. Hellerbach, *Helv. Chim. Acta*, **33**, 1437 (1950); Δ^2- (m.p. 147–148°), M. Mousseron and F. Winternitz, *Compt. rend.*, **217**, 428 (1943); α- (m.p. 146.5–147.5°), A. Ya. Berlin and L. V. Sokolova, *Zhur. Obshcheĭ Khim.*, **25**, 347 (1955).

(2) Norbornanecarboxamides: 1- (m.p. 235–236°), 2-*endo*- (m.p. 210.5–211.5°), W. R. Boehme, *J. Am. Chem. Soc.*, 81, 2762 (1959); 2-*exo*-(m.p. 192.5–193.5°), W. R. Boehme, E. Schipper, W. G. Scharpf, and J. Nichols, *J. Am. Chem. Soc.*, 80, 5488 (1958).

(3) W. Braker, E. J. Pribyl, and W. A. Lott, *J. Am. Chem. Soc.*, 69, 866 (1947).

(4) N. K. Matheson and S. J. Angyal, *J. Chem. Soc.*, 1133 (1952).

(5) L. N. Owen and P. A. Robins, *J. Chem. Soc.*, 320 (1949).

(6) C. K. Ingold, *Structure and Mechanism in Organic Chemistry*, Cornell University Press, Ithaca, 1953, p. 341.