The decrease in yield in the case of phloroglucinol is probably due to steric hindrance caused by the third hydroxyl group. The reactivity of pyrogallol is less than that of resorcinol since the third hydroxyl group deactivates the position *meta* to it for an electrophilic reagent. In the case of orcinol, the position *para* to a methyl group is deactivated for an electrophilic reagent. The activity of orcinol will therefore be less than that of resorcinol.

The substitution of the hydrogen atom on the α-carbon atom by methyl and ethyl groups lessens the activity of the β-keto ester in that order. Enolization of the β-keto ester takes place to a lesser extent when the hydrogen atoms are replaced by electron repelling groups. The ethyl-substituted ester is less reactive than the methyl substituted ester, due to a possible steric hindrance effect taking place. Conant and Thompson[14] have shown that the introduction of alkyl groups as substituents on the methylene group of ethyl acetoacetate decreases the degree of enolization.

The results given in Table I seem to bear out the above hypothesis.

After this investigation had been completed the authors noted a paper by Mastagli and Andric[15] who stated that they had used IRC-120 as a reagent in the von Pechmann reaction; but very low yields of coumarin were reported, due presumably to the low temperature at which the reaction was carried out, *viz.*, 90–100°.

EXPERIMENTAL

Preparation of cation exchange resin. The resin is crushed and washed free of smaller particles by decantation. It is allowed to soak for 10 min. in 10% hydrochloric acid and then washed with distilled water until the washings are neutral to litmus. The resin is then dried at 50° for 4 hr.

Preparation of hydroxycoumarins using exchange resin. The following is the general procedure used for the preparation of hydroxycoumarins:

Equimolecular quantities of phenol, β-keto ester, and a given quantity of resin (see table I) are heated with constant stirring in an oil bath at 150° under reflux until all reaction ceases. In many cases the coumarins separate out in the flask as a solid mass at the end of the reaction.

When *n*-hexane is used as the solvent, the reaction mixture is heated at 120°.

The effect of resin on the β-keto ester. In order to determine to what extent the resin hydrolyzes the β-keto ester, 26 g. of ethyl acetoacetate were heated under reflux, with varying amounts of resin, in an oil bath at 150°, a vigorous reaction occurring. After 1 hr. the acetone was distilled, and after washing and drying, the residual ethyl acetoacetate was weighed. The results are given in Table II.

TABLE II

HYDROLYSIS OF β-KETO ESTERS

Wt. Resin Used, g.	Wt. of Ester, g.	Wt. of Ester Hydrolyzed	% Ester Hydrolyzed
2.0	26.0	16.1	61.9
4.0	26.0	19.6	75.4
6.0	26.0	24.51	94.3
8.0	26.0	24.53	94.3

These results show that there is an optimum for the weight of resin used, beyond which there will be a decrease in yield of coumarin owing to the hydrolysis of the ester.

This was confirmed by a series of experiments with different phenols and β-keto esters in which varying amounts of resin were used.

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DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING
UNIVERSITY OF THE WITWATERSRAND
JOHANNESBURG, SOUTH AFRICA

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The Preparation of Tetrahydro-3,3,5,5-tetrakis(hydroxymethyl)pyran

THOMAS J. PROSSER

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Limited evidence found in the literature indicates that the base-catalyzed, exhaustive hydroxymethylation of ketones in which the carbonyl group is flanked by methylene groups gives rise to substituted tetrahydropyran-4-ols. Thus, the reaction of acetone and formaldehyde gives anhydroenneaheptitol (Ia),[1] whereas methyl ethyl ketone and diethyl ketone are reported to give tetrahydro-3,3,5-tris(hydroxymethyl)-5-methylpyran-4-ol (Ib) and tetrahydro-3,5-bis(hydroxymethyl)-3,5-dimethylpyran-4-ol (Ic), respectively.[2]

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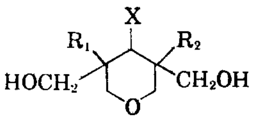

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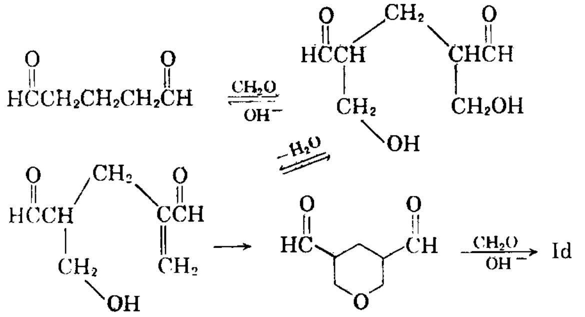
Ia. $R_1 = R_2 = CH_2OH$; X = OH
b. $R_1 = CH_2OH$; $R_2 = CH_3$; X = OH
c. $R_1 = R_2 = CH_3$; X = OH
d. $R_1 = R_2 = CH_2OH$; X = H

It has now been found that a similar reaction takes place in a 1,3-bis(methylene) system activated by terminal aldehyde groups rather than by a central ketone function. The exhaustive hydroxymethylation of glutaraldehyde gives the previously unreported tetrahydro-3,3,5,5-tetrakis(hydroxymethyl)-pyran (Id). A general reaction mechanism would seem to apply to all of the above cases. The following scheme is proposed for the glutaraldehyde-formaldehyde reaction and is analogous to that suggested for the formation of dipentaerythritol in the preparation of pentaerythritol from acetaldehyde and formaldehyde.[3]



The tetraacetate, dibenzylidene acetal, and diisopropylidene ketal derivatives of Id were prepared.

EXPERIMENTAL[4]

Tetrahydro-3,3,5,5-tetrakis(hydroxymethyl)pyran (Id). To 236 g. (3.30 moles) of 42% aqueous formaldehyde solution adjusted to pH 11.0 by addition of 50% sodium hydroxide solution was added 200 g. (0.50 mole) of 25% aqueous glutaraldehyde (Union Carbide Chemicals Co.) at 40–45° over a 1-hr. period. Thereafter, the temperature of the mixture was held at 50, 60, and 70° for 4, 3, and 2 hr., respectively. pH 11.0 was maintained throughout by intermittent addition of base. Theoretical base consumption was observed following the complete heating period. Deionization of the total crude reaction solution by passage through columns of Dowex 50 and Dowex 1 exchange resin, in that order, gave 60.6 g. of crystalline to semicrystalline product in the initial portions of effluent. Further rinsing gave an additional 10.3 g. of oily by-product considered to represent lower condensation products. The major portion of the latter material was absorbed by the exchange resin and not recovered. The main product contained 55.5% Id (32.6% yield) as determined by quantitative isolation of its dibenzylidene derivative. Preparation of an analytical sample of Id by water recrystallization gave a white crystalline solid; m.p. 176.5°.

Anal. Calcd. for $C_9H_{18}O_5$: C, 52.41; H, 8.80; OH, 32.99; mol. wt., 206.23. Found: C, 52.64, 52.51; H, 8.80, 8.96; OH (acetylation), 32.3, 31.9; mol. wt. (cryoscopic in ethanol), 206, 206.

Derivatives of tetrahydro-3,3,5,5-tetrakis(hydroxymethyl)-pyran (Id). (1) *Tetraacetate.* A mixture of 10 g. (0.049 mole) of Id, 40 g. (0.39 mole) of acetic anhydride, and 4 ml. of glacial acetic acid was heated under reflux for 1 hr., allowed to stand overnight, and then poured into 100 ml. of water. The crystalline white solid which separated amounted to 7.8 g. (43% yield), m.p. 91–95°, recrystallized from *n*-hexane, 94°.

Anal. Calcd. for $C_{17}H_{26}O_9$: C, 54.54; H, 7.00; mol. wt., 374.38; Sapon. No., 599.48. Found: C, 54.81, 55.00; H, 7.09, 7.17; mol. wt. (Rast), 386, 381; Sapon. No., 604.

(2) *Dibenzylidene acetal.* A mixture of 5.0 g. (0.024 mole) of impure Id, 25 ml. of water, 25 ml. of methanol, and 5 ml. of concd. hydrochloric acid was reacted with 10 ml. of benzaldehyde for 45 min. at steam bath temperature. There was obtained 8.14 g. (89% yield) of crude white solids which upon recrystallization from butyl acetate melted at 232–234°.

Anal. Calcd. for $C_{23}H_{26}O_5$: C, 72.22; H, 6.85; mol. wt., 382.43. Found: C, 72.37, 72.47; H, 7.01, 7.02; mol. wt. (Rast), 388, 403.

Tests with pure Id showed the dibenzylidene reaction to be quantitative and applicable to the determination of Id in mixtures, or compounds hydrolyzed under the reaction conditions.

(3) *Diisopropylidene ketal.* A mixture of 10 g. (0.048 mole) of Id, 150 ml. of acetone, 5 drops of concd. sulfuric acid, and 15 g. of 2,2-dimethoxypropane (Dow Chemical Co.) was heated under reflux overnight. Concentration of the reaction mixture gave 11.6 g. (91.4% yield) of white crystals. Recrystallization from acetone gave a melting point of 201–205°.

Anal. Calcd. for $C_{15}H_{26}O_5$: C, 62.91; H, 9.15. Found: C, 63.27, 63.25; H, 9.39, 9.29.

The Id content of the recrystallized product was determined by conversion to its dibenzylidene derivative: Calcd., 72.02; found, 71.2. Various samples of Id diisopropylidene ketal melted over a range of 153–206°, suggesting the presence of allotropic crystalline forms.

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HERCULES POWDER COMPANY
WILMINGTON, DEL.

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[4] All melting points are uncorrected.

Synthesis of Deuterated Biphenyls. II[1]

R. I. AKAWIE

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The synthesis of four deuterated isomers of biphenyl has been reported previously.[2] To complete the series studied by irradiation[3] and mass spectrometry[4] two new deuterium-substituted bi-

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