glycols was carried out by the periodate method[7] involving oxidation with excess periodate and determination of the residual periodate by addition of potassium iodide and titration with thiosulfate. This procedure also determines glyoxal and glycolaldehyde. In the ethylene experiments, where these compounds appeared to be present, a correction was made, based on the amount of 2,4-dinitrophenylhydrazone obtained. The latter compound was a reddish color, insoluble in most solvents, and melted above 300°. This description fits the glyoxal derivative, which is also obtained from glycolaldehyde. Infrared spectra of the residues obtained by evaporation of the water indicated the presence of glycolate and acetate salts. Oxalate, glyoxylic acid, formaldehyde, and formic acid were shown to be absent by chemical spot tests.[8] In one experiment the ethylene glycol was isolated by evaporating the aqueous solution to dryness, leaching the residue with propanol to reject inorganic salts, and evaporating the alcohol. The infrared spectrum of the liquid residue was identical with that of ethylene glycol.

The products of oxidation of 2-hexene were isolated by dilution of the system with water and extraction with ether, or by distillation of the solvent followed by partition between ether and water. From the ether was obtained a sweet-smelling liquid, whose infrared spectrum exhibited a strong alcoholic hydroxyl band at $2.88\ \mu$, and another band at $5.75\ \mu$, characteristic of the ester carbonyl group.

This data suggested that the liquid was a monoacetate ester of hexane-2,3-diol, and further evidence of its identity was sought. Monoacetate esters of this type are produced during the reaction of olefins with peroxyacetic acid,[9] and accordingly 2-hexene was oxidized by the procedure of Swern.[10] The product was purified on a vapor chromatography column, and its infrared spectrum was obtained. It was compatible with designation as a monoacetate ester of hexane 2,3-diol. A product from the thallium oxidation was chromatographed also, and the major product was found to behave identically on the chromatography column with the standard sample. Its infrared spectrum was also identical with that of the standard. In both chromatograms lesser amounts of a second component were observed, whose infrared spectra indicated it to be the diacetate ester. Approximate yields of the total ester product were obtained from the weight of product and the approximate purity as determined from the chromatograms.

A portion of the monoacetate prepared by the peroxidation procedure was hydrolyzed by refluxing 2 hr. in 10% sodium hydroxide solution, and the hexane-2,3-diol was isolated by extracting with ether, drying and evaporating the ether. An ester product from the thallium oxidation procedure was hydrolyzed in the same manner. The infrared spectrum of this hydrolysis product indicated it to be hexane-2,3-diol.

No attempt was made to ascertain whether the monoacetate was the 3-ester or the 2-ester of hexanediol. This point does not appear to have been studied in the peroxidation procedure either, and the question of the identity of the "standard" monoacetate is still open as well.

The carbonyl product obtained in the oxidation of 2-hexene in acetic acid was isolated from the distillate as the 2,4-dinitrophenylhydrazone, which was recrystallized from ethanol. It melted at 102–106°, compared to the literature values of 106° for the 2-hexanone derivative and 130° for the 3-hexanone derivative.

Acknowledgment. The author gratefully acknowledges the assistance of Mrs. Isabelle F. Dupzyk in much of the experimental work.

RESEARCH DEPARTMENT
DOW CHEMICAL COMPANY
PITTSBURG, CALIF.

---

[7] G. O. Curme, *Glycols*, Reinhold, New York, N. Y., 1952, p. 337.

[8] F. Feigl, *Spot Tests*, Vol. II, *Organic Applications*, Elsevier, 4th ed., 1954.

[9] D. Swern, *Org. Reactions*, 7, 378 (1953).

[10] D. Swern, G. W. Billen, T. W. Findley, and J. T. Scanlon, *J. Am. Chem. Soc.*, 67, 1786 (1945).

Use of Cation Exchange Resins in Organic Reactions.
I. The von Pechmann Reaction

E. V. O. JOHN AND S. S. ISRAELSTAM

Received March 16, 1960

It has generally been the practice to use large quantities of concentrated sulfuric acid as a condensing agent in the preparation of hydroxycoumarins by the von Pechmann reaction, i.e. the condensation of phenols with malic acid or with β-keto esters.[1,2] It has, however, been shown by Grieg-Gass[3] and Barris and Israelstam[4] that such large amounts of acid are unnecessary, since comparable yields of coumarins are obtained by using relatively small quantities of acid. The use of cation exchange resins as condensing agents was therefore investigated and it has now been shown that certain hydroxycoumarins are readily formed in good yield in this reaction using such resins.

In recent years anion exchange resins have been used in organic reactions with some success.[5–7] Apart from the use of cation exchange resins as hydrolytic agents, there have been very few applications of such resins in synthetic work.[7–9]

The cation exchange resins used in this work were Zeokarb 225 and Amberlite IR.120. These resins are resistant to high temperatures and can be used continuously at 100°, or at higher temperatures for short periods. The main advantages of cation exchange resins are that they may be recovered and used again and that they simplify the purification of the final product. Since β-keto esters were found to be hydrolyzed by cation exchange resins, it is necessary to limit the weight of resin used, generally between 20 and 40% by

---

[1] H. von Pechmann, *Ber.*, 17, 929 (1884).

[2] H. von Pechmann and C. Duisberg, *Ber.*, 16, 2119 (1883).

[3] A. Grieg-Gass, M.S. dissertation, University of the Witwatersrand, 1932.

[4] E. Barris and S. S. Israelstam, *Chem. & Ind.* (*London*), 1430 (1958).

[5] G. Durr, *Compt. rend.*, 242, 1630 (1956).

[6] C. J. Schmidle and R. C. Mansfield, *Ind. Eng. Chem.*, 44, 1388 (1952).

[7] N. B. Lorette, *J. Org. Chem.*, 22, 3346 (1957).

[8] S. Sussman, *Ind. Eng. Chem.*, 38, 1228 (1946).

[9] B. Loev and J. T. Massengale, *J. Org. Chem.*, 22, 8988 (1957).

TABLE I Yields of Coumarins Obtained

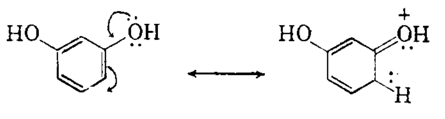
Coumarin R1	R2	R3	R4	R5	Phenol	β-Keto Ester	%[a] Resin Giving Max. Yield n-Hexane Without	%[a] Resin Giving Max. Yield n-Hexane With	Time of Reaction in Min. n-Hexane Without at 150°	Time of Reaction in Min. n-Hexane With at 120°	Maximum Yield n-Hexane Without	Maximum Yield n-Hexane With	Maximum Yield Lit.	M.P. Obtained	M.P. Lit.
			OH		Resorcinol	Ethyl acetoacetate	29.4	25.0	90	40	67.1	79.5	97.0[17]	185	185[17]
	OH		OH		Phloroglucinol	Ethyl acetoacetate	28.1	37.2	35	5	52.8	49.1	78.0[18]	284.5–5.0	282–4[18]
			OH	OH	Pyrogallol	Ethyl acetoacetate	18.7	26.7	45	20	37.8	50.8	32.0[19]	234–5	232–3[18]
	OH		CH_3		Orcinol	Ethyl acetoacetate	25.0	28.9	60	15	21.1	33.3	91.0[20]	253	250[21]
CH_3			OH		Resorcinol	Ethyl-α-methylacetoacetate	39.0	42.7	60	15	47.0	50.6	None	256	256[21]
CH_3	OH		OH		Phloroglucinol	Ethyl-α-methylacetoacetate	36.5	36.6	60	10	36.9	25.6	None	288–9	288[3]
CH_3			OH	OH	Pyrogallol	Ethyl-α-methylacetoacetate	39.2	30.2	60	10	24.0	36.0	31.0[19]	272–3	272–3[3]
CH_3	OH		CH_3		Orcinol	Ethyl-α-methylacetoacetate	60.0	50.6	60	20	11.5	8.3	None	249	249[3]
C_2H_5			OH		Resorcinol	Ethyl-α-ethylacetoacetate	32.5	32.5	30	30	52.0	49.8	54[16]	196–7	198[3]
C_2H_5	OH		OH		Phloroglucinol	Ethyl-α-ethylacetoacetate	20.0	34.8	15	5	17.8	18.4	46[16]	217	217[16]
C_2H_5			OH	OH	Pyrogallol	Ethyl-α-ethylacetoacetate	24.0	31.0	30	30	32.0	24.4	None	217–18	219–20[3]
C_2H_5	OH		CH_3		Orcinol	Ethyl-α-ethylacetoacetate	33.4	19.0	25	40	4.4	9.0	None	207	207[3]

[a] Per cent resin means per cent by weight of the total of phenol, β-keto ester and resin.

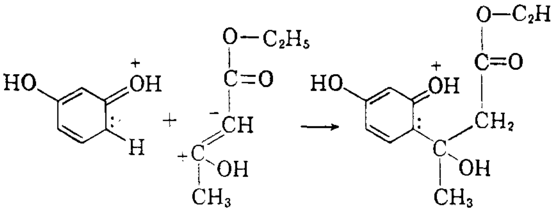
weight of the total reactants, in order to obtain the maximum yield of coumarins. (See Table I.) It is interesting to note that when a non-polar compound, such as n-hexane, was used as a solvent, the rate of reaction was increased quite substantially in many cases, the yields, too, being generally improved to some extent. This is probably due to the fact that there is an increased percentage of enol form of the β-keto ester in n-hexane,[10] *i.e.*, 63% as compared with the normal 7%.

Various mechanisms have been put forward to account for this reaction.[2,11–13] Since it has already been shown[6,4] that small quantities of acid are effective in bringing about the condensation, it would seem that the key factor in this reaction is the activity of the hydrogen ion. Bearing this point in mind the following mechanism is suggested:

Resorcinol as a result of resonance (1) has a center of high electron density at the position *ortho* to the hydroxyl group. Addition then takes place across the double bond in the enolic form of the β-keto ester as in (2)

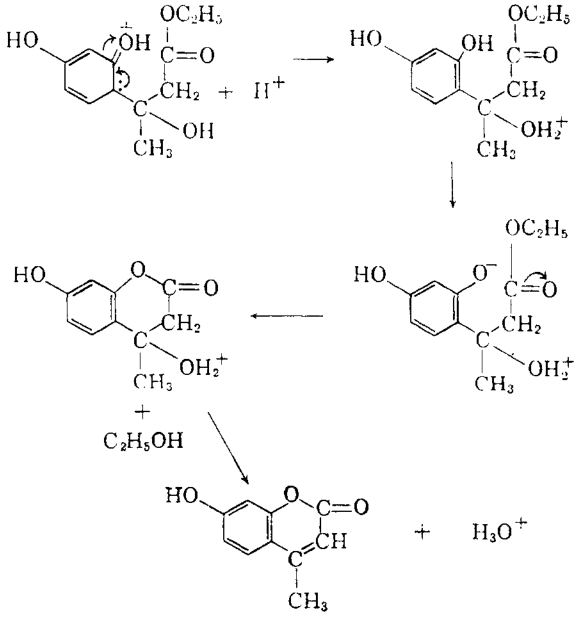


(1)



(2)

The hydrogen ions produced by the resin (or from any acid for that matter) would cause dehydration and produce an olefinic bond, at the same time ethyl alcohol would be eliminated with ring closure.



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.

Acknowledgment. One of the authors (E.V.O.J.) wishes to thank the S.A. Council for Scientific and Industrial Research for a grant and a research bursary.

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

---

(10) R. J. W. Le Fevre and H. Welsh, *J. Chem. Soc.*, 1909 (1949).

(11) S. Z. Ahmed and R. D. Desai, *Proc. Indian Acad. Sci.*, **6A**, 6 (1937).

(12) A. Robertson, R. B. Waters, and E. T. Jones, *J. Chem. Soc.*, 1681 (1932).

(13) R. N. Lacey, *J. Chem. Soc.*, 854 (1954).

(14) J. B. Conant and A. F. Thompson, *J. Am. Chem. Soc.*, **54**, 4039 (1932).

(15) P. Mastagli and N. Andric, *Compt. rend.* **246**, 3079 (1958).

(16) F. W. Cantor, F. H. Curd, and A. Robertson, *J. Chem. Soc.*, 1255 (1931).

(17) H. Appel, *J. Chem. Soc.*, 1031 (1935).

(18) Z. Horii, *J. Pharm. Soc., Japan*, **59**, 201 (1939).

(19) F. W. Cantor, A. R. Martin, and A. Robertson, *J. Chem. Soc.*, 1877 (1931).

(20) B. Krishnaswamy, K. R. Rao, and T. R. Seshadri, *Proc. Indian Acad. Sci.*, **19A**, 5 (1944).

(21) D. Chakravarti, *J. Indian Chem. Soc.*, **12**, 536 (1935).

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

THOMAS J. PROSSER

Received April 29, 1960

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]

---

(1) M. Apel and B. Tollens, *Ber.*, **27**, 1089 (1894), *Ann.*, **289**, 46 (1896); C. Mannich and W. Brose, *Ber.*, **55**, 3155 (1922).

(2) J. R. Roach, H. Wittcoff, and S. E. Miller, *J. Am. Chem. Soc.*, **69**, 2651 (1947).