

tained from the mother liquor. One recrystallization yielded pure calcium D-altronate-3.5H₂O, which was identified by analyses, and by its mutarotation in *N* hydrochloric acid (Table I).

*Anal.*¹⁶ Calcd. for (C₈H₁₁O₇)₂Ca·3.5H₂O: Ca, 8.13; H₂O, 12.78. Found: Ca, 8.13; H₂O, 12.63.

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(16) Through the kindness of Dr. W. T. Haskins of this Laboratory.

Summary

1. Sedoheptulose, the ketoheptose occurring in *Sedum spectabile*, Bor., has been degraded to D-altronic acid; this reaction confirms its formulation by Ettel as D-altroheptulose.

2. Sedoheptulose is suggested as a valuable starting point for the preparation of the rare sugars D-altrose and D-ribose, and their derivatives.

WASHINGTON, D. C.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF ST. JOHN'S UNIVERSITY AND OF NEW YORK UNIVERSITY]

Condensations of Ketones with Phenols¹

BY MARTIN E. MCGREAL, VICTOR NIEDERL AND JOSEPH B. NIEDERL

The systematic investigation as to the condensations of carbonyl compounds with phenols by J. B. Niederl and co-workers² has been extended to the field of saturated ketones.

The purpose of this investigation was to establish whether the behavior of phenol and that of the ortho alkylated phenols with ketones are similar, regardless of the type of saturated ketone and of the reaction conditions employed (mole ratio, type of catalyzer, concentration, temperature and solvent). Representative ketones of the three main types, *i. e.*, saturated aliphatic, alicyclic and aromatic ketones were selected. Thus, of the saturated aliphatic ketones, methyl ethyl (I, II), methyl *n*-propyl (III) and methyl isobutyl ketone (IV, V); of the alicyclic types, cyclohexanone (VI, VII), 3- and 4-methylcyclohexanone (VIII, IX) and cyclopentanone (X), and of the aromatic series, acetophenone (XI, XII) and methyl *p*-tolyl ketone (XIII) were chosen for this investigation.

It was found that the condensation products were invariably the crystalline diphenylmethane type of compounds, regardless of the reaction conditions or of the mole ratios of reactants. Such findings, at first glance, would suggest a direct elimination of one molecule of water from one molecule of the ketone and two molecules of the phenol. However, mole for mole addition has been observed in the case of acetophenone,³

(1) Several parts are taken from the theses of Thomas Murphy and of Daniel Marino presented to the Graduate School of St. John's University in partial fulfillment of the requirements for the degree of Master of Science, June, 1938.

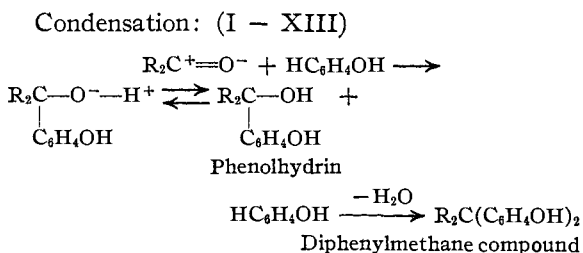
(2) J. B. Niederl, *THIS JOURNAL*, **50**, 2230 (1928); **51**, 2426 (1929); *Z. angew. Chem.*, **44**, 467 (1931); *Monatsh.*, **60**, 150 (1932); J. B. Niederl and co-workers, *ibid.*, **51**, 1038 (1929); *THIS JOURNAL*, **58**, 657 (1936); **59**, 1113 (1937).

(3) Zincke, *Ann.*, **363**, 275 (1908).

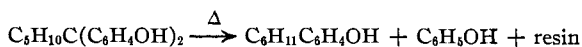
alloxan,⁴ and *d*-fructose.⁵ This would indicate that the first step in the condensation is an addition of the phenol to the carbonyl group, comparable to the addition of hydrocyanic acid, with the subsequent formation of a phenol-hydrin type of compound.⁶ In the next step one molecule of water is lost intermolecularly, *i. e.*, between one molecule of phenol-hydrin and one molecule of phenol with the subsequent formation of the crystalline diphenylmethane type of compounds. Thus, in this latter step, the ketones differ from the aldehydes, which lost water intramolecularly.

All the diphenolic condensation products obtained in the condensation of the alicyclic ketones (VI-X incl.) were subjected to pyrolysis and through disproportionation yielded in all cases the respective crystalline, alicyclic monophenol (VIA, VIIA, VIIIA, IXA and XA).

Schematically the reaction in both the condensation and the disproportionation may be presented as



Disproportionation: (VI - X)



(4) Boehringer, German Patent 107,720 (1900); **115**, 817 (1901).

(5) E. Fischer, *Ber.*, **27**, 1355 (1894); C. Counciler, *ibid.*, **28**, 24 (1895).

(6) J. B. Niederl and R. Maurmeyer, Rochester Meeting, Am. Chem. Soc., Sept., 1937.

TABLE I

COMPOUNDS, FORMULAS, PROPERTIES AND ANALYSES

All the analyses were performed microanalytically according to J. B. Niederl and V. Niederl, "Micromethods of Quantitative Organic Elementary Analysis," John Wiley and Sons, New York, N. Y., 1938. The molecular weight determinations were carried out cryoscopically according to the directions of K. Rast, in *ibid.*, pp. 171-174.

Condensation products	No.	Formula or derivative	M. p., °C.	Formula	Analyses						
					Carbon, %		Hydrogen, %		Calcd.	Found	
					Calcd.	Found	Calcd.	Found			
Aliphatic Ketones											
β, β -bis-(4-Hydroxyphenyl)-butane	I	$\text{CH}_3\text{C}(\text{C}_6\text{H}_4\text{OH})_2\text{C}_2\text{H}_5$	125	$\text{C}_{16}\text{H}_{18}\text{O}_2$	79.29	79.47	7.49	7.20			
	Ia	Tetranitro-	168	$\text{C}_{16}\text{H}_{14}\text{O}_{10}\text{N}_4$	45.49	49.92	3.34	3.24	N, 13.27		13.40
β, β -bis-(3-Methyl-4-hydroxyphenyl)-butane	II	$\text{CH}_3\text{C}(\text{C}_6\text{H}_3(\text{CH}_3)\text{OH})_2\text{C}_2\text{H}_5$	146	$\text{C}_{18}\text{H}_{22}\text{O}_2$	79.94	79.73	8.21	8.01			
	IIa	Di-acetate	71	$\text{C}_{22}\text{H}_{26}\text{O}_4$	74.53	74.63	7.40	7.34			
β, β -bis-(4-Hydroxyphenyl)-pentane	III	$\text{CH}_3\text{C}(\text{C}_6\text{H}_4\text{OH})_2\text{C}_3\text{H}_7$	149	$\text{C}_{17}\text{H}_{20}\text{O}_2$	79.63	79.85	7.87	8.07			
β, β -bis-(4-Hydroxyphenyl)- δ -methyl-pentane	IV	$\text{CH}_3(\text{C}_6\text{H}_4\text{OH})_2\text{CH}_2\text{CH}(\text{CH}_3)_2$	150	$\text{C}_{18}\text{H}_{22}\text{O}_2$	79.94	79.81	8.21	7.91			
	IVa	Tetranitro-	154	$\text{C}_{18}\text{H}_{18}\text{O}_{10}\text{N}_4$					N, 12.44		12.33
β, β -bis-(3-Methyl-4-hydroxyphenyl)- δ -methylpentane	V	$\text{CH}_3\text{C}(\text{C}_6\text{H}_3(\text{CH}_3)\text{OH})_2\text{CH}_2\text{CH}(\text{CH}_3)_2$	129	$\text{C}_{20}\text{H}_{26}\text{O}_2$	80.53	80.30	8.72	8.56			
Alicyclic Ketones											
1,1-bis-(4'-Hydroxyphenyl)-cyclohexane	VI	$\text{C}_6\text{H}_{10}(\text{C}_6\text{H}_4\text{OH})_2$	184	$\text{C}_{18}\text{H}_{20}\text{O}_2$	80.59	80.55	7.46	7.53			
	VIa	Di-acetate	124	$\text{C}_{22}\text{H}_{24}\text{O}_4$	75.00	74.84	6.78	6.90	M. w., 354		344
	VIb	Di-phenylurethan	148	$\text{C}_{32}\text{H}_{30}\text{O}_4\text{N}_2$					N, 5.53		5.55
4'-Hydroxyphenylcyclohexane	VIA	$\text{C}_6\text{H}_{11}\text{C}_6\text{H}_4\text{OH}$	132	$\text{C}_{12}\text{H}_{16}\text{O}$	82.28	82.18	8.57	8.34			
	VIAa	Acetate	145	$\text{C}_{14}\text{H}_{18}\text{O}_3$	71.79	71.82	7.69	7.83	N. e., 234		232
1,1-bis-(3'-Methyl-4'-hydroxyphenyl)-cyclohexane	VII	$\text{C}_6\text{H}_{10}(\text{C}_6\text{H}_3(\text{CH}_3)\text{OH})_2$	186	$\text{C}_{20}\text{H}_{24}\text{O}_2$	81.10	80.89	8.11	8.10			
	VIIa	Di-acetate	232	$\text{C}_{24}\text{H}_{28}\text{O}_6$					N. e., 206		204
	VIIb	Di-phenylurethan	142	$\text{C}_{34}\text{H}_{36}\text{O}_4\text{N}_2$					N, 5.22		5.17
1-(3'-Methyl-4'-hydroxyphenyl)-cyclohexane	VIIA	$\text{C}_6\text{H}_{11}(\text{C}_6\text{H}_3(\text{CH}_3)\text{OH})$	126	$\text{C}_{13}\text{H}_{18}\text{O}$	82.10	81.92	9.47	9.33			
	VIIAa	Acetate	134	$\text{C}_{15}\text{H}_{20}\text{O}_3$					N. e., 248		252
1,1-bis-(4'-Hydroxyphenyl)-3-methylcyclohexane	VIII	$\text{C}_6\text{H}_9(\text{CH}_3)(\text{C}_6\text{H}_4\text{OH})_2$	167	$\text{C}_{19}\text{H}_{22}\text{O}_3$	80.85	80.96	7.80	7.72			
1-(4'-Hydroxyphenyl)-3-methyl-cyclohexane	VIIIA	$\text{C}_6\text{H}_{10}(\text{CH}_3)\text{C}_6\text{H}_4\text{OH}$	110	$\text{C}_{13}\text{H}_{18}\text{O}$	82.10	82.23	9.47	9.22			
	VIIIAa	Acetate	127	$\text{C}_{15}\text{H}_{20}\text{O}_3$					N. e., 248		247
1,1-bis-(4'-Hydroxyphenyl)-4-methyl-cyclohexane	IX	$\text{C}_6\text{H}_9(\text{CH}_3)(\text{C}_6\text{H}_4\text{OH})_2$	180	$\text{C}_{19}\text{H}_{22}\text{O}_2$	80.85	80.62	7.80	7.59			
1-(4'-Hydroxyphenyl)-4-methyl-cyclohexane	IXA	$\text{C}_6\text{H}_{10}(\text{CH}_3)\text{C}_6\text{H}_4\text{OH}$	118	$\text{C}_{13}\text{H}_{18}\text{O}$	82.10	82.02	9.47	9.25			
	IXAa	Acetate	136	$\text{C}_{15}\text{H}_{20}\text{O}_3$					N. e., 248		245
1,1-bis-(4-Hydroxyphenyl)-cyclopentane	X	$\text{C}_6\text{H}_8(\text{C}_6\text{H}_4\text{OH})_2$	156	$\text{C}_{17}\text{H}_{18}\text{O}_2$	80.31	79.63	7.09	6.98	M. w., 254		248
(4'-Hydroxyphenyl)-cyclopentane	XA	$\text{C}_6\text{H}_9(\text{C}_6\text{H}_4\text{OH})$	90	$\text{C}_{11}\text{H}_{14}\text{O}$	81.98	81.82	8.07	7.98			
	XAa	Acetate	115	$\text{C}_{13}\text{H}_{16}\text{O}_3$					N. e., 220		224
Aromatic Ketones											
α -Phenyl- α, α -bis-(4-hydroxyphenyl)-ethane	XI	$\text{C}_6\text{H}_5\text{C}(\text{CH}_3)(\text{C}_6\text{H}_4\text{OH})_2$	175	$\text{C}_{30}\text{H}_{18}\text{O}_2$	82.72	82.66	6.25	6.09			
	XIa	Di-acetate	180	$\text{C}_{24}\text{H}_{22}\text{O}_4$	77.02	76.78	5.88	6.16			
α -Phenyl- α, α -bis-(3-methyl-4-hydroxyphenyl)-ethane	XII	$\text{C}_6\text{H}_5\text{C}(\text{CH}_3)(\text{C}_6\text{H}_3(\text{CH}_3)\text{OH})_2$	141	$\text{C}_{22}\text{H}_{20}\text{O}_2$	83.01	83.06	6.85	6.74			
	XIIa	Di-acetate	118	$\text{C}_{26}\text{H}_{24}\text{O}_4$	77.61	77.32	6.50	6.19			
α - <i>p</i> -Tolyl- α, α -bis-(4-Hydroxyphenyl)-ethane	XIII	$(\text{CH}_3)\text{C}_6\text{H}_4\text{C}(\text{CH}_3)(\text{C}_6\text{H}_4\text{OH})_2$	133	$\text{C}_{22}\text{H}_{22}\text{O}_2$	82.89	82.68	6.57	6.82			
	XIIIa	Di-acetate	151	$\text{C}_{26}\text{H}_{26}\text{O}_4$	77.32	77.52	6.18	6.14			

Experimental

Condensation Method

A. Aliphatic and Aromatic Ketones (I-V, XI-XIII).—One-half mole of the ketone and one mole of the phenol were placed in a one-liter round-bottomed flask which contained 50 cc. of glacial acetic acid. Dry hydrogen chloride gas was passed through the contents of the flask vigorously for three hours. The solution changed in color from yellow to a deep red. The flask was disconnected from the generator and tightly stoppered so as to keep the reactants in an atmosphere of hydrogen chloride. On standing, the contents of the flask became extremely viscous and finally crystallized. The period of standing ranged from one to four weeks; the yields from 10-25%.

The product formed was purified by being washed first with diisobutylene, and then reworked with toluene. Petroleum ether was used in some cases in place of diisobutylene. Recrystallization was carried out from a mixture of ether and toluene in the case of the mixed alkyl aryl ketone-phenol condensates. The alkyl ketone-phenol condensates were recrystallized from water.

B. Cyclic Ketones (VI-X).—One mol of the phenol, and one-half mol of the cyclic ketone were placed in a 2-liter 2-necked round-bottomed flask and 200 cc. of glacial acetic acid added. The reaction flask was provided with a reflux condenser and a gas inlet tube extending to the bottom of the vessel. A vigorous stream of dry hydrogen chloride gas was passed through the system for four hours, during which time the reaction mixture was heated to refluxing. After this the flask was removed, tightly stoppered and left standing at room temperature. The phenol-cyclohexanone (VI) and *o*-cresol-cyclohexanone (VII) condensation products were left standing for twenty-four hours and the phenol-cyclopentanone (X) condensation product for a week. During this time the reaction mixture crystallized in all cases. One liter of water was added to the reaction flask, and the crystals were collected on a Büchner funnel and washed with distilled water. The compounds were recrystallized from benzene or, in smaller quantities, from water. They were soluble in Claisen solution and in dilute alkalis. The yield of the above products ranged from 60% in case of the phenol-cyclopentanone (X) to 80% for the phenolcyclohexanone (VI) and *o*-cresol-cyclohexanone (VII). The phenol 3- and 4-methylcyclohexanone condensation products (VIII, IX) were prepared as above, except that they were refluxed for eight hours and left standing for three days. They also crystallized in the reaction vessel and were purified as stated above. The yield was approximately 70% in the case of the 4-methylcyclohexanone (IX) and 50% in the case of the 3-methylcyclohexanone (VIII).

Pyrolysis.—Thirty grams of any one of the above compounds (VI-X) was placed in a 125-cc. distilling flask, and, after heating for about thirty minutes below the boiling point of the substance, was subjected to slow distillation at atmospheric pressure. In each instance about 10 g. of the phenol or *o*-cresol, respectively, was obtained, and about 10 g. of the new monophenolic compound. The rest remained as a charred residue in the distilling flask. The phenol was identified by melting point and mixed melting point with a pure sample. The *o*-cresol was identified by its boiling point and by preparing the *o*-cresoxy-

acetic acid and making a mixed melting point with a standard sample, which showed no depression. The new phenol was fractionally redistilled and in all cases crystallized in the receiver (VIA, VIIA, VIIIA, IXA, XA).

Diacetates.—The diacetates were formed by the method of Shriner and Fuson.⁷ Three grams of the crystalline condensation product (II, VI, VII, XI-XIII) was mixed with 1.5 g. of powdered fused sodium acetate and 15 cc. of acetic anhydride. The mixture was heated on the steam-bath, with occasional shaking, for two hours. At the end of this time the warm solution was poured, with vigorous stirring, into 100 cc. of ice water. The mixture was allowed to stand, with occasional stirring, until the excess of acetic anhydride had been hydrolyzed. The crystals were removed by filtration, washed thoroughly with water, and purified by recrystallization from alcohol (IIa, VIa, VIIa, XIa, XIIa, XIIIa).

Aryloxyacetic Acids.—These compounds were prepared according to Shriner and Fuson⁷ (p. 148). One gram of the phenol (VIA-XA) was dissolved in 5 cc. of a 33% sodium hydroxide solution and 3 g. of chloroacetic acid added. The mixture was shaken thoroughly and heated on a water-bath at 100° for one hour. The solution was then diluted with 15 cc. of water, acidified with dilute hydrochloric acid to congo red and extracted with 50 cc. of ether. The ether was washed with an equal volume of water and then shaken out with 25 cc. of a 5% sodium carbonate solution. The solution was acidified with dilute hydrochloric acid and the product which precipitated out was filtered and dried on porous tile. It was recrystallized from diisobutylene (VIAa, VIIa, VIIAa, VIIIAa, IXAa, XAa).

Nitro Derivatives.—These derivatives were prepared by treating the diphenols (I, IV) with concd. nitric acid with the application of heat until complete solution was effected. The reaction mixture was allowed to stand until crystallization of the nitro derivative was complete. The compounds were recrystallized from alcohol (Ia, IVa).

Diphenylurethan.—This compound was prepared by treating the diphenol (VII) with an excess of phenyl isocyanate in a sealed test-tube on a steam-bath until the contents became crystalline. The diphenylurethan was recrystallized from diisobutylene (VIb).

Summary

1. The condensation of aliphatic, alicyclic and aromatic ketones with phenol and with *o*-cresol yielded crystalline products of the diphenylmethane type of compounds.

2. Alicyclic diphenols upon pyrolysis underwent disproportionation to the respective alicyclic monophenols.

3. The reactions, both the condensation and the disproportionation, were presented schematically and show an intermolecular effect with the resulting loss of a molecule of water between two molecules of the phenol and one molecule of the ketone.

(7) Shriner and Fuson, "The Systematic Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1935, p. 142.

4. This type of condensation is being extended to meta and para alkylated phenols and polyhydroxyphenols with ketones in order to check the

influence of the substituent group of the benzene ring in its different positions.

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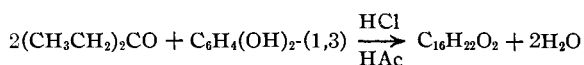
Simultaneous Multiple Alkylation of Phenols. The Synthesis of a Phenolic Coumarane Involving the Condensation of Diethyl Ketone with Resorcinol

BY JOSEPH B. NIEDERL AND VICTOR NIEDERL

Theoretical

In continuation of the studies of the condensations of carbonyl compounds with phenols, the condensation of diethyl ketone with resorcinol was investigated. In this condensation a new phenomenon was encountered, namely, the simultaneous di-alkylation of a phenol, regardless of the mole ratio of the reactants employed.

The empirical formula of the crystalline and non-polymeric condensation product obtained in quantitative yields by condensing diethyl ketone with resorcinol in glacial acetic acid solution in the presence of dry hydrogen chloride, corresponds to an addition of two molecules of diethyl ketone to the resorcinol followed by the elimination of two molecules of water as follows



This fact then adds to the already reported condensation systems of the mole ratios 1 : 1 (one mole phenol and one mole carbonyl compound),¹ 2 : 1 (two moles of phenol and one mole of carbonyl compound),² 2 : 3 (two moles of phenol and three moles of carbonyl compound),³ and now a condensation system involving a mole ratio of 1 : 2 (one mole of phenol and two moles of carbonyl compound). Thus it becomes apparent that the nature of the end-product is influenced not only by the type of carbonyl compound employed, but also by the type of phenol used in the condensations. This influence exerts itself particularly through the position of the second substituent in the benzene ring, *i. e.*, whether it is

ortho, meta or para to the hydroxyl group. The nature of the catalyst used in these condensations appears only to influence the yield but not the course of the reaction nor the type of condensation product obtained.⁴

Elucidation of the Structural Formula

Although the empirical formula of the crystalline condensation product suggests immediately a dipentenylresorcinol, structure proof work, however, revealed that there is only one free phenolic hydroxyl group present in the compound (formation of a monoacetate (IV) and a monophenyl urethan (V)) and that there is only one double bond in the compound, as evidenced by the formation of a tribromide (VI) from the free phenolic coumarane (III) (treatment of an aqueous solution of the phenol with excess bromine water) and a dibromide (VII) from the acetate (IV) (addition of an excess of bromine in carbon tetrachloride to a solution of the acetate in the same solvent). All this then suggests ring formation between one of the phenolic hydroxyl groups and one of the pentenyl radicals leading to the formation of a coumarane type of compound as has been observed in related condensation systems.⁵

Summarily, the reaction mechanism then would involve first the addition of the two molecules of diethyl ketone to resorcinol with the formation of an intermediate and under the given reaction conditions unstable phenol-dihydrin (I), which upon the loss of two molecules of water would give the dipentenylresorcinol (II). Then under the influence of dry hydrogen chloride, ring closure between one of the pentenyl groups and one of the phenolic hydroxyl groups appears to ensue with the formation of a phenolic coumarane (III), as follows

(1) E. Fischer, *Ber.*, **27**, 1355 (1894); Niederl and co-workers, *THIS JOURNAL*, **58**, 657 (1936); **59**, 1113 (1937).

(2) McGreal, Niederl and Niederl, *ibid.*, **61**, 345 (1939); Lunjak, *J. Russ. Phys.-Chem. Soc.*, **36**, 303 (1904); Dianin, *ibid.*, **23**, 492 (1891); Claus and Trauer, *Ber.*, **19**, 3009 (1886); Zincke and Grueters, *Ann.*, **343**, 85 (1905); Zincke, *ibid.*, **363**, 255 (1908).

(3) J. B. Niederl, *THIS JOURNAL*, **50**, 2230 (1928); *Monatsh.*, **60**, 150 (1932); Niederl and Casty, *THIS JOURNAL*, **51**, 1038 (1929).

(4) J. B. Niederl, *Ind. Eng. Chem.*, **30**, 1269 (1938).

(5) Niederl and Storch, *THIS JOURNAL*, **55**, 4549 (1933); Jordau, German Patent, 501,723 (1926).