crystallization needles were obtained which melted unsharply at 175°. Several recrystallizations from acetone gave a product which showed a strong positive Liebermann reaction and which melted at 183–184°, $[\alpha]^{25}D$ +27.0 (63 mg. in 5 cc. of absolute alcohol solution gave a reading of +0.68). When mixed with a specimen of 3-hydroxy-12-keto-9,11-cholenic acid a depression of the melting point was observed.

Anal. Calcd. for $C_{24}H_{38}O_3$: C, 76.96; H, 10.23. Found: C, 76.7; H, 10.5.

We wish to take this opportunity to express our thanks to the Rockefeller Foundation for a grant-in-aid which in part was used in support of this work.

Summary

1. A new route has been suggested to the preparation of sterol derivatives having a hydroxyl group C_{11}. Progress in this direction has been reported.

2. By the debromination followed by saponification of 3-acetoxy-11-bromo-12-ketocholanic acid, an unsaturated acid has been prepared which proved to be 3-hydroxy-12-keto-9,11-cholenic acid. This acid melts at 173° and possesses the characteristic absorption of the α,β-unsaturated keto derivatives.

3. The crude semicarbazone of the unsaturated keto-hydroxy acid, m. p. 221°, has been reduced according to the Wolf–Kishner method to 3-hydroxy-9,11-cholenic acid of m. p. 183–184°.

PRINCETON, NEW JERSEY RECEIVED OCTOBER 23, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF NEW YORK UNIVERSITY]

Steric Hindrance in Ketone–Phenol Condensations. The Condensation of Guaiacol with Cyclic Ketones

BY JOSEPH B. NIEDERL, VICTOR NIEDERL AND JOSEPH GRUMER[1]

In a previous publication[2] the effect of steric hindrance in ketone–phenol condensations has been investigated. It was established that, while the usual condensation product is an alkylidene-diphenol,[3] this is not formed when a reaction system is selected which would lead to the formation of a cycloalkylidene-diphenol in which there is a substituent group in *ortho* position to either one of the two reacting carbon atoms involved in the condensation. In these cases only equimolar condensation is possible, leading to the formation of cycloalkylenephenols or coumarans, respectively.

For a practical application of this hypothesis, a phenolic compound having an alkoxy group in *ortho* position to the free hydroxyl group was condensed with cyclic ketones. Condensation products analogous to the ones isolated in condensations involving an ortho alkylated phenol should be obtainable. As shown in the following, similar types of condensation products could actually be isolated.

Thus, the condensation of guaiacol with cyclohexanone itself and the *m*- and *p*-methylcyclohexanone isomers, yielded the expected alkylidene-diphenols (I, II, III), while the reaction of guaiacol with *o*-methylcyclohexanone resulted in the unsaturated cyclohexenyl-guaiacol (IV).

Of the four primary condensation products (I–IV) the following derivatives were prepared and verified by analysis: crystalline acetates (Ic, IIc, IIIc), benzoates (Id, IId, IIId) and phenylurethans (Ib, IIb, IIIb) of the three alkylidene-diphenols (I, II, III) and a crystalline aryloxyacetic acid (IVa) of the unsaturated monomolecular condensation product of guaiacol with *o*-methylcyclohexanone (IV).

Experimental

Condensation Method

1,1-*bis*-(3′-Methoxy-4′-hydroxyphenyl)-cyclohexane (I).—Molar quantities of guaiacol and half molar quantities of cyclohexanone were dissolved in 100 cc. of glacial acetic acid and the mixture placed in a 1-liter, triple-necked, round-bottomed flask which was provided with a reflux condenser, a thermometer and a gas inlet tube extending to the bottom of the vessel. A vigorous stream of dry hydrogen chloride gas was passed into the system for six hours at room temperature on two consecutive days, then the flask was stoppered and left standing at room temperature for four weeks. Crystals deposited which were filtered and recrystallized from benzene; m. p. 174°; yield, 31%.

Attempts to hydrolyze the ether groups in this compound by refluxing the compound with hydrobromic acid (48%)

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[1] The material presented in this paper is taken from the thesis presented by Joseph Grumer to the Graduate School of New York University in partial fulfilment of the requirements for the degree of Master of Science.

[2] J. B. Niederl and co-workers, THIS JOURNAL, **61**, 1785 (1939).

[3] M. E. McGreal and co-workers, *ibid.*, **61**, 345 (1939).

TABLE I

COMPOUNDS, FORMULAS AND ANALYSES

No.	Formula or deriv.	M. p., °C.	Empirical formula	Carbon, %		Hydrogen, %		Nitrogen, %	
				Calcd.	Found	Calcd.	Found	Calcd.	Found
	1,1-*bis*-(3′-Methoxy-4′-hydroxyphenyl)-cyclohexane								
I	$(C_6H_3(OH)OCH_3)_2C_6H_{10}$	174	$C_{20}H_{24}O_4$	73.40	73.38	7.34	6.93		
Ib	Phenylurethan	153	$C_{27}H_{29}O_5N$					3.13	3.08
Ic	Acetate	157	$C_{24}H_{28}O_6$	69.97	70.07	6.78	6.79		
Id	Benzoate	168	$C_{34}H_{32}O_6$	76.10	76.25	6.03	6.18		
	1,1-*bis*-(3′-Methoxy-4′-hydroxyphenyl)-4-methylcyclohexane								
II	$(C_6H_3(OH)OCH_3)_2C_6H_9(CH_3)$	165	$C_{21}H_{26}O_4$	73.68	73.60	7.62	7.90		
IIb	Phenylurethan	192	$C_{28}H_{31}O_5N$					3.04	3.05
IIc	Acetate	136	$C_{25}H_{30}O_6$	70.42	70.48	7.04	7.37		
IId	Benzoate	162	$C_{36}H_{34}O_6$	76.34	76.48	6.18	6.35		
	1,1-*bis*-(3′-Methoxy-4′-hydroxyphenyl)-3-methylcyclohexane								
III	$(C_6H_3(OH)OCH_3)_2C_6H_9(CH_3)$	149	$C_{21}H_{26}O_4$	73.68	73.68	7.62	7.72		
IIIb	Phenylurethan	187	$C_{28}H_{31}O_5N$					3.04	3.30
IIIc	Acetate	118	$C_{26}H_{30}O_6$	70.42	70.07	7.04	7.15		
IIId	Benzoate	171	$C_{35}H_{34}O_6$	76.34	76.56	6.18	6.38		
	1-(3′-Methoxy-4′-hydroxyphenyl)-2-methylcyclohexene-1								
IV	$C_6H_3(OH)(OCH_3)C_6H_8(CH_3)$		$C_{14}H_{18}O_2$	77.01	77.09	8.30	8.67	m. wt. 218	214
IVa	Aryloxyacetic acid	73	$C_{16}H_{20}O_4$	69.50	69.78	7.30	7.38	n. eq. 276	277

as well as with hydriodic acid (sp. gr. 1.7) proved unsuccessful. Guaiacol was obtained in the first and catechol in the second case. This would indicate that the diphenylmethane linkage is weaker than an aromatic ether linkage.

1,1-*bis*-(3′-Methoxy-4′-hydroxyphenyl)-4-methylcyclohexane (II).—Molar quantities of guaiacol and half molar quantities of *p*-methylcyclohexanone were condensed as described above and worked up in a similar manner; m. p. 165.5°; yield, 10%.

1,1-*bis*-(3′-Methoxy-4′-hydroxyphenyl)-3-methycyclohexane (III).—Molar quantities of guaiacol and half molar quantities of *m*-methylcyclohexanone were condensed as described above and worked up in a similar manner; m. p. 149°; yield 27%. In none of the above cases was the filtrate, which consisted chiefly of unreacted starting materials, investigated further.

1-(3′-Methoxy-4′-hydroxyphenyl)-2-methylcyclohexene-1 (IV).—Half molar quantities of guaiacol and *o*-methylcyclohexanone were dissolved in 50 cc. of glacial acetic acid and condensed as described above. There was no deposition of crystals. The mixture was treated on a water-bath with dry hydrogen chloride for another twelve hours. No crystallization occurred, even after standing for another two months. After this time, the reaction mixture was dissolved in 200 cc. of benzene, this solution washed several times with an equal volume of water and then extracted with 150 cc. of Claisen solution. The Claisen solution extract was acidified with dilute hydrochloric acid, the oil which separated was taken up in 100 cc. of benzene, washed with water and dried over calcium chloride. The benzene was distilled off and the residue was distilled at 14 mm. pressure. Three fractions were obtained. The lower boiling fraction (about 30%) consisted of unreacted guaiacol, the fraction boiling between 155–175° proved to be the above unsaturated phenol (IV) (approx. 20%) and the higher boiling fraction, 180°, its polymer (approx. 30%). The unsaturated phenol (IV) polymerizes slowly upon standing.

Aryloxyacetic Acid Derivative (IVa).—This derivative was prepared by dissolving the above compound (IV) in 30% sodium hydroxide solution to which sufficient methyl alcohol was added to effect solution. The calculated amount of chloroacetic acid was added, the reaction mixture gently refluxed for two hours, and worked up according to the directions given in Shriner and Fuson.[4] In testing for unsaturation, Baeyer's permanganate test was employed and found positive.[5]

Phenylurethans (Ib, IIb, IIIb).—One gram of substance was dissolved in 1 cc. of phenyl isocyanate in a test-tube which was sealed and placed in a beaker containing boiling water. The test-tube was opened when its content had solidified and the crystalline material was recrystallized from petroleum ether.

Acetates (Ic, IIc, IIIc).—One gram of the respective phenol was dissolved in 3 cc. of acetic anhydride and refluxed in an all-glass apparatus for four hours. The reaction mixture was poured into an excess of water and allowed to stand overnight, whereupon crystallization occurred. The acetates were recrystallized from 80% alcohol.

Benzoates (Id, IId, IIId).—One gram of the respective phenol was dissolved in 3 cc. of pyridine and 1.5 g. of benzoyl chloride added. The mixture was warmed over a low flame for a few minutes and then poured into 10 cc. of water and stirred thoroughly. After decanting the supernatant solution, the crystals were washed with 5 cc. of 5% sodium carbonate solution and recrystallized from alcohol.

Summary

Studies were made of the effect of substituent groups in cyclic ketones in their condensations with an ortho alkoxyphenol.

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(4) Shriuer and Fuson, "The Systematic Identification of Organic Compounds," J. Wiley and Sons, Inc., New York, N. Y., 1935, pp. 148–149.

(5) S. P. Mulliken, "A Method for the Identification of Pure Organic Compounds," J. Wiley and Sons, Inc., New York, N. Y., 1904, p. 79.

Cycloalkylidene-diphenols and a cycloalkylene-phenol were obtained and suitable derivatives thereof prepared. The results obtained further support the previously suggested steric hindrance hypothesis governing the condensation of cyclic ketones with ortho alkylated phenols.

WASHINGTON SQUARE COLLEGE
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[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF NEW YORK UNIVERSITY]

Steric Hindrance in Ketone–Naphthol Condensations. The Condensations of the Naphthols with Cyclohexanone

BY JOSEPH B. NIEDERL, VICTOR NIEDERL AND JESSE CHARNEY

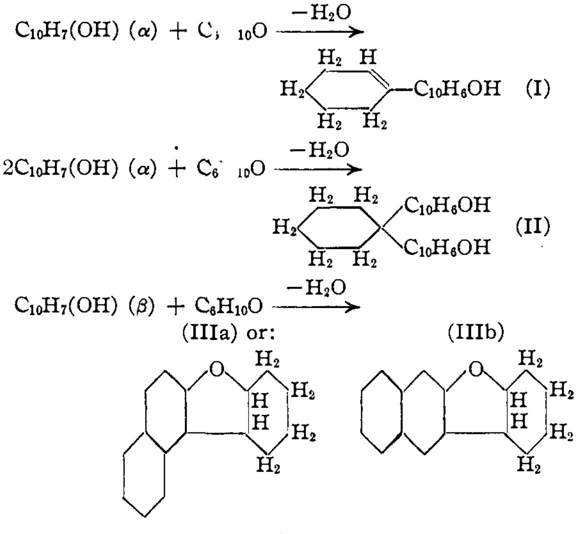
In a previous publication[1] it was asserted that in the condensation of ketones with phenols "the nature of the end product is influenced not only by the type of carbonyl compound employed, but also by the type of phenol used" and that "this influence exerts itself particularly through the position of the second substituent in the benzene ring, *i. e.*, whether it is *ortho*, *meta* or *para* to the hydroxyl group." This hypothesis was fully substantiated in a subsequent communication[2] in which condensations of various phenols with cyclohexanone derivatives were reported. In this it was shown that in cases where the alkyl radical in the final condensation product is adjacent to the carbon carrying the cyclohexenyl radical, steric hindrance effects inhibit the introduction of a second phenolic radical. Thus, instead of the normal di-phenols, unsaturated phenolic products are obtained. Further, it was indicated that when steric hindrance becomes too great, ortho alkylation takes place, leading to the formation of coumarans.

In continuation of these studies of steric hindrance in ketone–phenol condensations and in order to prove the generality of the above conclusion, these investigations were extended to the naphthols.

The results obtained were entirely in accordance with the foregoing postulation. Thus, when α-naphthol was condensed with cyclohexanone, not only was the normal di-naphthol, the 2,2-di-((4′-hydroxy)-naphthyl)-cyclohexane (II) obtained, but the cyclo-alkylene-naphthol, the 1-(4′-hydroxy)-naphthyl-cyclohexene-1 (I) was secured as well. To prove the unsaturated character of the latter, the acetate (Ia) was prepared and brominated, and the resulting crystalline dibromide (Ib) isolated. Titration of this dibromide (Ib) with 0.01 *N* sodium hydroxide solution gave a neutralization equivalent equal to one half the molecular weight of the compound, indicating the hydrolysis of at least one bromine atom and thus confirming the presence of bromine in the isocyclic side chain.

The condensation of β-naphthol with cyclohexanone was also studied. The condensation was slow, but positive, yielding no phenolic products, but, instead, the 2,3-tetramethylene-4,5[or 5,6]-benzocoumaran (IIIa or IIIb).

The formation of all three types of condensation product may be represented as



Experimental

1-(4′-Hydroxy)-naphthyl-cyclohexene-1 (I).—Half molar quantities of α-naphthol and cyclohexanone were placed in a 1-liter, triple-necked, round-bottomed flask which was provided with a reflux condenser, a thermometer and a gas inlet tube extending to the bottom of the vessel. The mixture was warmed until complete solution took place and then was cooled to below 30°. A vigorous stream of dry hydrogen chloride gas was passed into the system for six hours at room temperature, then the flask was stoppered and left standing for twelve hours, when com-

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[1] J. B. Niederl and co-workers, THIS JOURNAL, **61**, 348 (1939).

[2] J. B. Niederl and co-workers, *ibid.*, **61**, 1785 (1939).