REACTION OF 4-HYDROXY-3,5-DI-TERT-BUTYLBENZAL CHLORIDE WITH AMIDES

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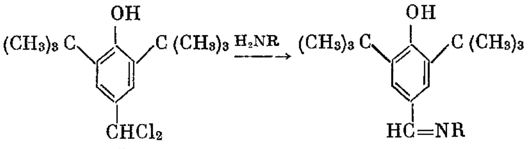
Due to its high reactivity, 4-hydroxy-3,5-di-tert-butylbenzal chloride can be used successfully for the preparation of highly diverse derivatives of sterically hindered phenols [1]. In the present paper we studied the reactions of benzal chloride (I) with a number of primary aliphatic and aromatic amines, some secondary amines, triethylamine, and pyridine.

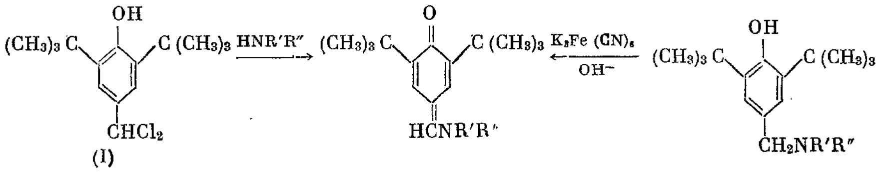
With primary amines the reaction takes place by simply mixing the reactants in an inert solvent (hexane, chloroform, CCl_4), and is ended in 2-3 h at room temperature. Independent of the nature of the primary amines, only the corresponding Schiff bases are formed in this reaction (Table 1). With aliphatic primary amines the yield of the Schiff base is 85-90%, while with aromatic amines it is 65-85%. In the IR spectra of the compounds obtained in this manner are present absorption bands in the regions 1655-1611 cm^{-1} (skeletal vibrations of $C=N$) and 3640-3650 cm^{-1} (unassociated hydroxyl of sterically hindered phenols)



R=Alk, Ar

4-Hydroxy-3,5-di-tert-butylbenzaldehyde is formed when the obtained azomethines are treated with mineral acid solutions.

With secondary amines the reaction also proceeds under mild conditions. The compounds formed in this case represent substituted methylenequinones (Table 2), in which connection some of them were obtained by us previously by the oxidation of the corresponding 4-aminomethyl-2,6-di-tert-butylphenols with alkaline potassium ferricyanide solution [2]



When (I) is reacted with morpholine the reaction does not stop at the stage of forming the methylenequinone. In this case the obtained methylenequinone forms a complex with excess morpholine, which is apparently formed via the hydrogen bond of the carbonyl group of the methylenequinone and the hydrogen of morpholine, since the basicity of morpholine, when compared with the other studied secondary amines, is considerably lower.

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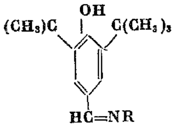
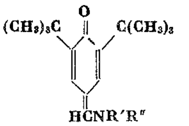
TABLE 1. 4-Hydroxy-3,5-di-tert-butylalkyl(aryl)imines



R	Mp, °C	$\nu_{C=N}$, cm^{-1} (CCl_4)	Yield, %	Empirical formula	Found, %			Calcd., %		
					C	H	N	C	H	N
CH_3	158—159	1655	91	$C_{16}H_{25}ON$	77,56 77,62	9,99 10,02	6,02 6,10	77,70	10,10	5,76
$CH(CH_3)_2$	177—178	1644	86	$C_{18}H_{29}ON$	77,09 79,02	10,40 10,31	5,21 5,16	78,50	10,52	5,10
n-C_4H_9	126—127	1635	89	$C_{19}H_{31}ON$	78,16 78,05	10,16 10,21	4,89 4,81	79,00	10,72	4,85
C_6H_{11}	96—97	1643	83	$C_{21}H_{33}ON$	79,91 80,01	11,12 11,07	4,69 4,71	80,00	10,50	4,45
C_6H_5	100—101	1632	73	$C_{21}H_{27}ON$	81,50 81,59	8,75 8,66	4,53 4,49	81,96	8,03	4,41
p-C_6H_4—OCH_3	117—118	1630	68	$C_{22}H_{29}O_2N$	77,90 77,81	8,56 8,51	4,12 4,21	77,63	8,46	4,83
p-C_6H_4—O—C_2H_5	131—132	1630	76	$C_{23}H_{31}O_2N$	78,20 78,29	8,78 8,65	3,96 4,04	78,35	8,35	4,54
p-C_6H_4—CH_3	113—114	1611	76	$C_{22}H_{29}O_2N$	81,80 81,72	9,00 9,15	4,34 4,51	81,28	8,80	4,62

TABLE 2. α-Aminoalkyl-2,6-di-tert-butylmethylenequinones



NR′R″	Mp, °C	$\nu_{C=O}$, cm^{-1}	Yield, %	Empirical formula	Found, %			Calcd., %		
					C	H	N	C	H	N
$N(CH_3)_2$	171—173	1619	84	$C_{17}H_{27}ON$	78,13 78,23	10,87 10,66		78,11	10,45	
$N(C_2H_5)_2$	134—135*	1615	87							
NC_5H_{10}	169—170†	1610	77							
$N(C_6H_{11})_2$	118—119	1610	79	$C_{27}H_{43}ON$	81,43 81,55	10,85 10,89	3,55 3,63	81,60	10,82	3,52
NC_4H_8O	164—165‡	1616	—	$C_{19}H_{29}ON$	75,34 75,43	9,82 9,75		75,25	9,63	
NC_4H_8O HNC_4H_8O	102—103	—	91	$C_{23}H_{38}O_3N$	71,20 71,56	9,69 9,78	7,29 7,35	70,81	9,75	7,18

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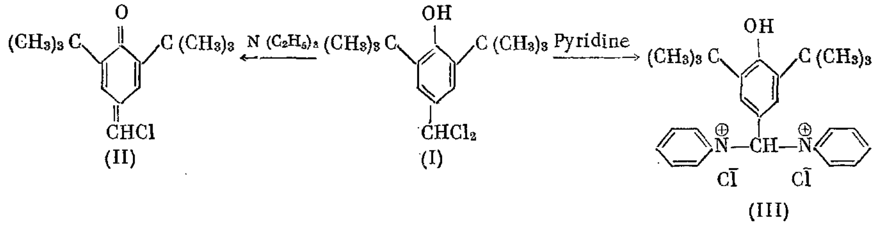
* From [2]: mp 133-134°.

†From [2]: mp 170-171°.

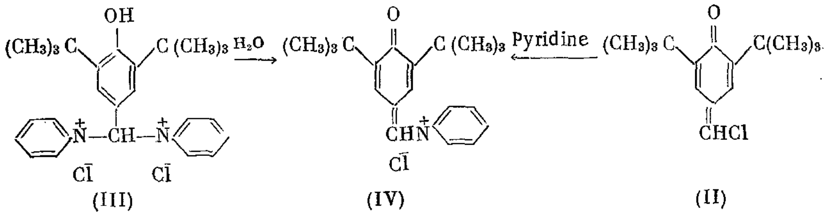
‡From [2]: mp 165-168°.

When this complex is heated (or in the presence of polar solvents) it decomposes with the liberation of morpholino-2,6-di-tert-butylmethylenequinone. In contrast to the Schiff bases, a band is present at 1600-1610 cm^{-1} in the IR spectra of the obtained methylenequinones, which is characteristic for the conjugated carbonyl group of aminomethylenequinones, and the absorption band (3640 cm^{-1}) of a sterically hindered phenolic hydroxyl is absent. Based on the data of the IR spectrum, in the complex of α-morpholino-2,6-di-tert-butylmethylenequinone are present both the frequency of a conjugated carbonyl group (1620 cm^{-1}) and the absorption frequency of a sterically hindered phenolic hydroxyl.

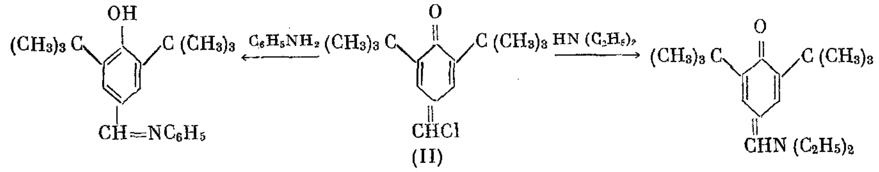
When benzal chloride (I) is reacted with triethylamine, ammonia, or $NaHCO_3$ there occurs cleavage of a molecule of hydrogen halide and α-chloro-2,6-di-tert-butylmethylenequinone (II) is obtained. This compound is stable in the pure state and is also reactive, just like (I). In the IR spectrum of methylenequinone (II) is present a doublet at 1610 and 1620 cm^{-1}, and an absorption frequency in the 3640 cm^{-1} region is absent. In addition, in the UV spectrum of methylenequinone (II) there is present characteristic absorption (λ_{max} 300 nm), which is also inherent to other methylenequinones [3]. The adduct with two molecules of pyridine (III) is initially formed in the reaction of benzal chloride (I) with pyridine. This adduct represents a saltlike compound that is soluble in water, in which connection all of the halogen is found as the anion (see Experimental Method). On the basis of the IR spectral data for adduct (III) it is possible to assume that this compound represents the bis-quaternary pyridine derivative of the sterically hindered phenol. The appearance in the IR spectrum of adduct (III) of a band in the 1610 cm^{-1} region is apparently associated with the presence of a positive nitrogen, the presence of which in the molecule leads to a sharp weakening of the O—H bond of the sterically hindered phenol



When adduct (III) is treated with water there occurs cleavage of pyridine hydrochloride and the pyridyl derivative of the methylenequinone (IV) is formed. The IR spectrum of the hydrochloride of α-pyridyl-2,6-di-tert-butylmethylenequinoid structure of this compound ($\nu_{C=O}$ 1610 and 1630 cm^{-1}). Methylenequinone (IV) is readily soluble in water, contains chloride ions, and was also obtained by the reaction of (II) with pyridine



It is interesting to mention that, as the result of the reaction of (III) with primary and secondary amines, the same as in the case of the reaction of (I) with amines, the same reaction products are formed. Thus, for example, as the result of the reaction of (II) with diethylamine we obtained α-diethylamino-2,6-di-tert-butylmethylenequinone, while when reaction was with aniline the corresponding Schiff base was obtained



(II) is quantitatively converted to (I) in the presence of hydrogen chloride. In connection with what has been said, it can be assumed that methylenequinone (II) is an intermediate compound in the reaction of benzal chloride (I) with amines.

The amines and imides of carboxylic acids do not react with (I) and (II) under analogous conditions.

EXPERIMENTAL METHOD

Reaction of 4-Hydroxy-3,5-di-tert-butylbenzal Chloride (I) with Primary Amines. To a solution of 0.04 mole of primary amine in 40 ml of CCl_4 was added a solution of 0.01 mole of (I) in 20 ml of CCl_4 at 20°. After 2 h the obtained precipitate of amine hydrochloride was separated, and from the solution, after evaporation of the solvent and recrystallization of the residue from hexane, were isolated the corresponding azomethines. The physical constants, yield, and elemental analysis data for the obtained compounds are given in Table 1.

Reaction of 4-Hydroxy-3,5-di-tert-butylbenzal Chloride (I) with Secondary Amines. To a solution of 0.04 mole of secondary amine in 15 ml of hexane at 20° was added 0.01 mole of (I) in 10 ml of hexane. After 1 h the obtained precipitate was separated, washed with water and dried. The physical constants, yield, and elemental analysis data for the obtained compounds are given in Table 2.

The recrystallization of the complex of α-morpholino-2,6-di-tert-butylmethylenequinone with morpholine from ethanol gave α-morpholino-2,6-di-tert-butylmethylenequinone.

α-Chloro-2,6-di-tert-butylmethylenequinone (II). To a solution of 0.1 mole of (I) in 20 ml of hexane at 0° was added 4 ml of $(C_2H_5)_3N$ in 30 ml of hexane. After 3 h the obtained precipitate of $(C_2H_5)_3N \cdot HCl$ was separated, and from the mother liquor by low-temperature crystallization was isolated 1.83 g (73% of theory) of (II), λ_{max} 300 nm (ε $3.4 \cdot 10^4$). Found: C 70.95, 70.88; H 8.17, 8.22; Cl 14.35, 14.22%; mol. wt. 265 (cryoscopically in benzene). $C_{15}H_{21}ClO$. Calculated: C 71.37; H 8.32; Cl 14.7%; mol. wt. 252.2.

A solution of 1.45 g of (I) in 30 ml of dichloroethane was treated with 1.68 g of $NaHCO_3$ in 20 ml of water. After 3 h the organic layer was separated and the solvent was vacuum-distilled. The residue was recrystallized from hexane. The yield of (II) was 90%, mp 56-57%. The obtained compound was identified by IR spectroscopy.

The reaction of (II) with methanol gives 4-hydroxy-3,5-di-tert-butylbenzaldehyde; yield 98%; mp 188-189°. From [4]: mp 188-189°. (I) is obtained in quantitative yield by the reaction of (II) with HCl in hexane solution, mp 97-98°. From [1]: mp 98°.

Dichloride of 4-(N,N-Dipyridylmethyl)-2,6-di-tert-butylphenol (III). To a solution of 6.6 ml of pyridine in 30 ml of dichloroethane was added 0.02 mole of (I) in 20 ml of dichloroethane. After 3 h the obtained crystals were separated to give (III) in 80% yield; mp 139-140°. Found: C 67.19, 67.25; H 6.58, 6.55; Cl 15.77, 15.86; N 6.48, 6.44%. $C_{25}H_{32}Cl_2ON_2$. Calculated: Cl 16.40, 16.10%.

Chloride of α-Pyridyl-2,6-di-tert-butylmethylenequinone (IV). To 7.15 g of (III) was added 50 ml of water. After 2 h the precipitate was filtered and recrystallized from dioxane. The yield of (IV) was 85%, mp 124-125°. Found: C 69.61, 69.54; H 8.10, 8.02; Cl 10.71, 10.24; N 4.10, 4.22%. $C_{26}H_{26}ClNO$. Calculated: C 69.20; H 7.50; Cl 10.25; N 4.03%. Mercurometric titration. Found: Cl 10.09, 10.20%.

To a solution of 2.5 g of (II) in 20 ml of dichloroethane was added 3.3 ml of pyridine in 30 ml of dichloroethane. After 3 h the solvent was vacuum-distilled, and the residue was recrystallized from dioxane. The yield of (IV) was 84%, mp 123-124°. The substance was identified by IR spectroscopy.

Reaction of (II) with Diethylamine. To a solution of 2.5 ml of $(C_2H_5)_2NH$ in 50 ml of CCl_4 was added 1.25 g of (II) in 20 ml of CCl_4. The yield of diethylamino-2,6-di-tert-butylmethylenequinone was 90%, mp 138-139°. The substances was identified by IR spectroscopy (see Table 2).

Reaction of (II) with Aniline. To a solution of 2 ml of aniline in 20 ml of CCl_4 was added 2.5 g of (II) in 20 ml of CCl_4. After 3 h the aniline hydrochloride was separated, and 4-hydroxy-3,5-di-tert-butylbenzaliminobenzene was isolated in 69% yield from the solution, mp 100-101°. The substance was identified by IR spectroscopy (see Table 1).

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CONCLUSIONS

A study was made of the reaction of 4-hydroxy-3,5-di-tert-butylbenzal chloride and α-chloro-2,6-di-tert-butylmethylenequionone with various amines.

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