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Figure 1

Figure 1: Figure 1

Abstract

Full Text

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Inhibitors of Free-Radical Reactions

The Self-Alkylation Reaction of 3,5-di-tert-butyl-4-hydroxybenzylamine

(Presented by Academician V. N. Kondrat’ ev, May 12, 1961)

As is known, the preparation of substituted tribenzylamines is associated with considerable difficulties, due chiefly to the fact that, when ordinary methods are used, difficultly separable mixtures of primary, secondary, and tertiary amines are formed. The directed synthesis of individual amines is laborious and requires several stages. In this connection, the development of such synthetic methods that would give individual products is an important problem.

In the present work we consider the self-alkylation reaction of 3,5-disubstituted 4-hydroxybenzylamines, as a result of which, under mild conditions and in quantitative yield, the corresponding tribenzylamines are formed.

Fig. 1. IR spectra of tri-(3,5-di-tert-butyl-4-hydroxy)benzylamine (**II**) and 2,6-di-tert-butyl-4-methylphenol (**I**)

(I) OH
aromatic ring with R substituents and CH_2NH_2 $\longrightarrow$ [OH
aromatic ring with R substituents and CH

Studying the properties of 3,5-di-tert-butyl-4-hydroxybenzylamine (**I**), we found that even upon crystallization from rectified alcohol, tri-(3,5-di-tert-butyl-4-hydroxy)benzylamine is formed (**II**, $R = C(CH_3)_3)^1$. This reaction also occurs when an alcoholic solution of the amine (**I**, $R = C(CH_3)_3$) is allowed to stand in a nitrogen atmosphere for 2–3 days at 20°. The process is accelerated by increasing the temperature and the moisture content of the alcohol.

To clarify the influence of the solvent and temperature on the nature of the reaction, a series of experiments was carried out (see Table 1). In all cases, one and the same product was obtained, with m.p. 231—231.5° (from nonane).

Fig. 2. NMR spectra of tri-(3,5-di-tert-butyl-4-hydroxy)benzylamine II (1), tribenzylamine (2), and 2,6-di-tert-butylphenol (3)

Figure 2: Fig. 2. NMR spectra of tri-(3,5-di-tert-butyl-4-hydroxy)benzylamine II (1), tribenzylamine (2), and 2,6-di-tert-butylphenol (3)

In order to establish the structure of the synthesized substance, its IR and NMR spectra were recorded, and its independent synthesis was carried out. The spectra of the tertiary amine formed (**II**, $R = C(CH_3)_3$) are given in comparison with the spectra of model compounds, which made it possible to interpret the results obtained. The model compounds used were tribenzylamine, 2,6-di-tert-butyl-4-methylphenol, and 2,6-di-tert-butylphenol.

The appearance of a new band in the region of 1010, 1030 cm^{-1} of the IR spectrum (Fig. 1) of tri-(3,5-di-tert-butyl-4-hydroxy)benzylamine (II, $R = C(CH_3)_3$) in comparison with the spectrum of 2,6-di-tert-butyl-4-methylphenol (I) is explained by the presence of the $C—N$ bond of a tertiary amine. From comparison of the NMR spectra (Fig. 2) of the reaction product II, 2,6-di-tert-butylphenol (3), and tribenzylamine (2), the presence of a signal of the protons of the CH_2 group in the first and third cases and its absence in the second is evident. The ratio of the intensities of the signals of the phenyl protons and the protons of the CH_2 groups ($1:1$) indicates their equal number. This fact confirms the presence of benzyl residues in the product.

It is interesting to note that the chemical shift of the hydroxyl-proton signal of 2,6-disubstituted phenols is approximately equal to the chemical shift of the proton signal of unsubstituted phenol extrapolated to infinite dilution in carbon tetrachloride ([2]). The displacement of the hydroxyl-proton signal into this region of the spectrum appears as the result of rupture of hydrogen bonds.

Apparently, the increase in the inhibiting activity of phenols upon introduction of substituents into the *o*-position may be explained by a decrease in the ability to form hydrogen bonds, or by its absence. On the basis of what has been said, the growth of inhibiting activity in the series 2,6-dimethyl-, 2,6-diisopropyl-, and 2,6-di-tert-butyl-4-methylphenols ([3]) and the absence of further growth for homologs with ortho substituents $C_6—C_8$ ([4]) are understandable.

Fig. 2. NMR spectra of tri-(3,5-di-tert-butyl-4-hydroxy)benzylamine II (1), tribenzylamine (2), and 2,6-di-tert-butylphenol (3)

Extension of the regularity found to other series of 0,0-disubstituted phenols will probably make it possible to confirm the supposition expressed.

The final confirmation of the correctness of the structure was the independent synthesis of tri-(3,5-di-tert-butyl-4-hydroxy)benzylamine

$$\underset{(I)}{HO{-}C_6H_2(+)_2}{-}CH_2NH_2 + 2\,\underset{(III)}{HO{-}C_6H_2(+)_2}{-}CH_2Br \longrightarrow \left[\underset{(II)}{HO{-}C_6H_2(+)_2}{-}CH_2\right]_3 N \leftarrow NH_3 + 3\,O{=}C_6H_2($$

When 3 g of 3,5-di-tert-butyl-4-hydroxybenzyl bromide (III) (^{5}) in 20 ml of dry benzene is added to a solution of 1.2 g of 3,5-di-tert-butyl-4-hydroxybenzylamine (I, $R = C(CH_3)_3$) in 45 ml of dry pyridine, a precipitate of pyridine hydrobromide separates. The mixture is left for 24 h at 20°. The precipitate is then separated, the solvents are removed in vacuo, and the residue is crystallized from nonane. Yield 1.1 g, mp 231-232°. 2,6-Di-tert-butyl-4-methylenequinone-2,5-one (IV) was obtained from the corresponding brominated benzyl (III) (^{6}). A stream of dry ammonia was passed through an ethereal solution of methylenequinone (IV) for 2 h. After removal of the ether, the residue is crystallized from no-

nonane. M.p. 231-232°. A mixed sample of the substituted tribenzylamine (II) gives no depression of the melting point with the product of the self-alkylation reaction.

On the basis of the study carried out, the compound formed as a result of the self-alkylation of benzylamine was assigned the structure tri-(3,5-di-tert-butyl-4-hydroxy)-benzylamine.

Found, %: C 80.28; 79.95; H 10.34; 10.37; N 1.93; 2.12
$C_{45}H_{69}O_3$. Calculated, %: C 80.42; H 10.34; N 2.08

An attempt to carry out the self-alkylation reactions by prolonged boiling in anhydrous organic solvents gave a negative result. For this purpose pyridine, higher alcohols, dioxane, and tetrahydrofuran were used. After removal of the solvent in a stream of nitrogen under vacuum, the starting amine (I) was regenerated. From Table 1 it is clear

Table 1

Effect of the moisture content of solvents and temperature on the formation of tri-(3,5-di-tert-butyl-4-hydroxy)-benzylamine*

Solvent	Water content, %	Reaction temp.	Reaction duration, min.	M.p., °C
Ethyl alcohol	4	75-80	60	218-224
»	4	30-40	120	220-224
»	4	20	3 days	228-230
»	10	15-80	20	226-230
»	20	75-80	20	224-228
Dioxane	2	75-80	30	228-231

Solvent	Water content, %	Reaction temp.	Reaction duration, min.	M.p., °C
»	20	75-80	20	227-230
Pyridine	5	75-80	25	229-231
»	20	75-80	20	228-231

* In all cases after crystallization from nonane the compound had m.p. 231-232°; the yield after crystallization was 83-90%.

that, in the process of self-alkylation, the moisture of the medium plays an important role.

It should be noted, however, that boiling the hydrobromide and hydrochloride of amine (I) in 75% alcohol for 3 hours does not lead to tri-(3,5-di-tert-butyl-4-hydroxy)-benzylamine.

Finally, attention is drawn to the fact that amine I, on standing, slowly loses ammonia, forming tri-(3,5-di-tert-butyl-4-hydroxy)-benzylamine. This process is also accelerated with increasing temperature. On heating I in a stream of nitrogen at 160-170°, tribenzylamine (II, $R = C(CH_3)_3$) is formed in quantitative yield. The transition of benzylamine (I, $R = C(CH_3)_3$), on melting, into a certain "substance of undetermined structure" is indicated by Müller et al. ([7]).

The mechanism of the process and its generality in the series of substituted *n*-hydroxy-, *n*-alkoxy-, and *n*-acyl-hydroxybenzylamines will be discussed in our further work.

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Note: Figure translations are in progress. See original paper for figures.