

LEUCKART REACTION OF CARBONYL DERIVATIVES

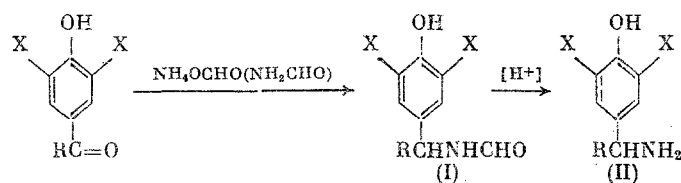
OF 2,6-DI-TERT-BUTYLPHENOL

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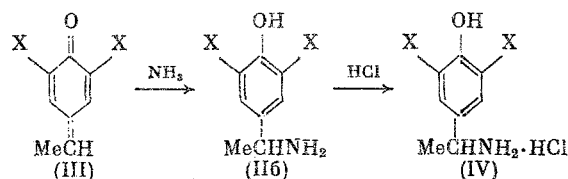
2,6-Di-tert-butyl-4-(α -amino)alkylphenols and their derivatives hold interest primarily as antiozonants and antioxidants. The methods available for the synthesis of such compounds [1] are time-consuming and involve multiple steps. We have studied the possibility of using the Leuckart reaction [2] for the preparation of sterically hindered aminophenols from 3,5-di-tert-butyl-4-hydroxybenzaldehyde, 3,5-di-tert-butyl-4-hydroxyacetophenone, and 3,5-di-tert-butyl-4-hydroxypropio-phenone.

Heating these carbonyl compounds in formamide or ammonium formate at 170-180°C gives 60-90% yields of formyl derivatives of amines (Ia-c) (Table 1), which on cooling the mixture readily separate out, and in acid hydrolysis in dioxane give the corresponding amines (IIa-c)

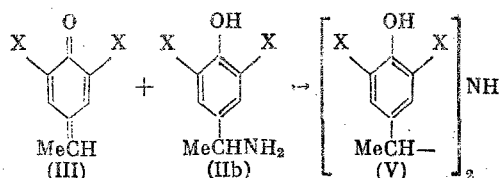


R = H (a), Me (b), Et (c), X = *t*-Bu.

Substituted phenylethylamine (IIb) was also obtained by the amination of the corresponding methylenequinone (III) in liquid ammonia. Aminophenol (IIb) was isolated as its hydrochloride salt (IV).



Since aminophenol (IIb) may, in turn, react with methylenequinone (III), di[1-(3,5-di-tert-butyl-4-hydroxyphenyl)ethyl]amine (V) is always found in the reaction mixture; the yield of (V) increases with increasing concentration of methylenequinone (III).



The formation of (V) by the deamination of (IIb) under the reaction conditions was excluded by a control experiment. The relatively high yield of (V) (about 20%) may be attributed to the formation of a sandwich compound consisting of two methylenequinone (III) molecules, which react with NH_3 to give (V).

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TABLE 1. N-[1-(3,5-Di-tert-butyl-4-hydroxyphenyl)-R]-N-formylamines (Ia)-(Ic)

R	Yield, %	mp, °C	Chemical formula	Found/Calculated, %		UV spectrum, λ_{max} nm (log ϵ)	IR spectrum (KBr pellet), ν , cm^{-1}		PMR spectrum, δ , ppm, CCl_4							
				C	H		C=O	NH	C(CH ₃) ₃	CH ₃	CH	OH	CH	HC=O	NH	CH ₂
H	90.0	125-126	C ₁₈ H ₂₃ NO ₂	72.94 72.96	9.50 9.57	301 (4.31)	1650	3300	1.35	-	CH ₂ 4.19	5.00	6.94	8.08	-	-
Me	90.0	86-88	C ₁₇ H ₂₇ NO ₂	73.94 73.60	9.82 9.81	281 (3.74)	1670	3450	1.30	1.38	4.80	5.12	6.88	7.70	-	-
Et	55.0	94-96	C ₁₉ H ₂₉ NO ₂	74.01 74.18	9.82 10.03	281 (3.59)	1650	3420	1.35	0.70	4.70	5.00	6.90	7.90	6.08	0.88

EXPERIMENTAL

N-(3,5-Di-tert-butyl-4-hydroxybenzyl)-N-formylamine (Ia). A sample of 10 ml (11.4 g, 0.25 mole) formamide was added to 1.0 g (4.3 mmoles) 3,5-di-tert-butyl-4-hydroxybenzaldehyde and heated for 0.5 h at 180°C. After cooling, water was added and the tar formed was separated and crystallized from benzene-hexane. The yield of (Ia) was 1 g (90%). The elemental analysis data and spectral characteristics are given in Table 1.

N-[1-(3,5-Di-tert-butyl-4-hydroxyphenyl)ethyl]-N-formylamine (Ib) and N-[1-(3,5-di-tert-butyl-4-hydroxyphenyl)propyl]-N-formylamine (Ic). These compounds were obtained by the method described above. The yields, elemental analysis data, and spectral characteristics are given in Table 1.

3,5-Di-tert-butyl-4-hydroxybenzylamine (IIa). A sample of 10 ml 35% hydrochloric acid and 10 ml water were added to 12.0 g (46 mmoles) N-(3,5-di-tert-butyl-4-hydroxybenzyl)-N-formylamine (Ia) in 30 ml dioxane and heated at reflux for 1 h. After cooling, the mixture was diluted with water and 10% aq. NH_4OH was added until the mixture was basic. The precipitate was separated, washed on the filter with water, and dried to give 7.2 g (67.3%) (IIa), mp 159-160°C [1].

1-(3,5-Di-tert-butyl-4-hydroxyphenyl)propylamine (IIb) and 1-(3,5-di-tert-butyl-4-hydroxyphenyl)propylamine (IIc). These compounds were obtained by the method described above. The yield of (IIb) was 69.0%, mp 127-128°C [1]. The yield of (IIc) was 61.3%, mp 80.5-81.5°C [1].

Hydrochloride Salt of 1-(3,5-Di-tert-butyl-4-hydroxyphenyl)ethylamine (IV). A solution of 0.12 g (0.5 mmole) α -methyl-2,6-di-tert-butylmethylenequinone in 25 ml ether was added dropwise with constant stirring to 40 g (2.22 moles) liquid NH_3 at -50°C. The solution was stirred for an additional 1.5-2 h at from -35° to -40°C. The greenish solution became colorless. The temperature was gradually raised to about 20°C and the solvent was evaporated in vacuum. A sample of 10 ml water acidified with hydrochloric acid was added to the white precipitate and the insoluble residue was separated. The addition of concentrated hydrochloric acid to the filtrate gave a precipitate of 0.11 g (75.5%) (IV) hydrochloride salt of 1-(3,5-di-tert-butyl-4-hydroxyphenyl)ethylamine.

CONCLUSIONS

1. 1-(3,5-Di-tert-butyl-4-hydroxyphenyl)ethylamine and its analogs were prepared in high yield by the Leuckart reaction from the corresponding ketones or aldehyde and ammonium formate or formamide.
2. The reaction of α -methyl-2,6-di-tert-butylmethylquinone with ammonia leads to 1-(3,5-di-tert-butyl-4-hydroxyphenyl)ethylamine.

LITERATURE CITED

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2. B. M. Bogoslovskii, in: *Reactions and Methods in the Study of Organic Compounds* [in Russian], Book 3, Goskhimizdat, Moscow (1954), p. 268.