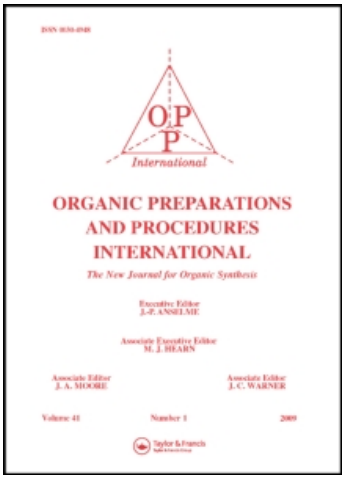


Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

N,N-DIALKYLAMINOPHENOLS

F. Minisoi[a]; R. Galli[a]; M. Perchinunno[a]
[a] Istituto di Chimica del Politecnico, Milano

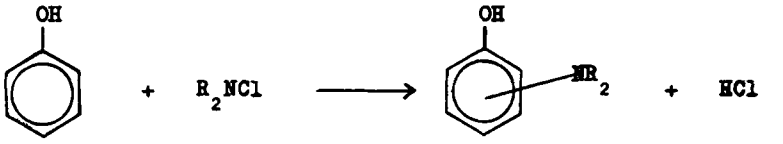
To cite this Article Minisoi, F. , Galli, R. and Perchinunno, M.(1969) 'N,N-DIALKYLAMINOPHENOLS', Organic Preparations and Procedures International, 1: 2, 87 — 90
To link to this Article: DOI: 10.1080/00304946909458357
URL: http://dx.doi.org/10.1080/00304946909458357

ORGANIC PREPARATIONS AND PROCEDURES 1(2), 87-90 (1969)

N,N-DIALKYLAMINOPHENOLS

F.Minisci,R.Galli and M.Perchinunno

Istituto di Chimica del Politecnico,Milano 20133



The synthetic interest of the homolytic aromatic amination by N-chloroamines has been recently emphasized[1].The reaction with aromatic substrata activated by electron-releasing substituents requires special experimental expedients in order to avoid competing electrophilic reactions, such as sulphonation (sulfuric acid is used as solvent) and chlorination by N-chloroamine. Theoretical implications connected with particular experimental conditions have been discussed elsewhere[1,2].

The present procedure describes the preparation of N,N-dialkylaminophenols from phenol and 2-chlorophenol.Different experimental conditions are required with the two phenols owing to the different degree of activation towards the electrophilic reactions. Availability of the reagents, simple experimental conditions, high selectivity and good yields contribute to the synthetic interest of these preparations.

Experimental

N-(hydroxyphenyl)-piperidine ortho and para.

To a mixture of 9.4 g of phenol, 14 g of ferrous sulfate heptahydrate, 15 ml of concentrated sulfuric acid and 6 ml of water is added dropwise with stirring 6 g of N-chloropiperidine (prepared according to Coleman[3]) dissolved in 15 ml of concentrated sulfuric acid.The temperature spontaneously rises from 5° to 40° during the addition, which is accomplished

shed in 10 minutes. Stirring is continued for additional 15 minutes at room temperature and then the reaction mixture is poured in 100 g of ice and 200 ml of water.The resulting diluted solution is extracted with ether to remove the excess of phenol, partially neutralized with 30% sodium hydroxide solution and then basified with sodium carbonate and extracted with ether.The ethereal solution is dried over anhydrous sodium sulfate, the solvent is removed and 7.7 g of crystalline basic product remains (87%). Crystallization from benzene yields 6.6 g of pure N-(p-hydroxyphenyl)-piperidine, m p 160-1°.

Anal. Calcd for $C_{11}H_{15}NO$: C,74.54; H, 8.59; N, 7.90. Found : C, 74.23; H, 8.76; N, 7.89.

Mol. wt. : 177 (mass spectrum) ; formula wt. : 177.

I.R. : 810 and 830 cm^{-1} (para-disubstituted benzene).

N.M.R. : Two couples of equivalent aromatic H at 6.75 δ (para-disubstituted benzene), 4 H centered at 2.95 δ (CH_2-N-CH_2) and 6 H centered at 1.55 δ (3 CH_2).

The mother liquor is removed and 1.1 g of solid crystalline product remains. Chromatography on silica gel and elution with benzene yields 0.7 g of N-(o-hydroxy-phenyl)-piperidine (m p 71-2°; lit.[4] m p 70-2°; I.R. : 758 cm^{-1},ortho-disubstituted benzene) and 0.3 g of N-(p-hydroxyphenyl)-piperidine (9% ortho and 91% para in the aggregate).

N-(3-chloro-4-hydroxyphenyl)-piperidine.

To a mixture of 12.9 g of 2-chlorophenol and 6 g of N-chloropiperidine in 30 ml of concentrated sulfuric acid is added with stirring 7 g of finely powdered ferrous sulfate heptahydrate.The temperature rises from 0° to 30°.The mixture is kept at room temperature for 30 minutes and then worked up as in the case of phenol.The yield of basic product amounts to 9.7 g (92%).Crystallization from petroleum ether leaves 0.4 g of tarry insoluble material and yields 4.3 g of crystalline solid m p 97°.

Anal. Calcd for $C_{11}H_{14}NOCl$: C, 62.42; H, 6.62; N, 6.62.

Found : C, 62.40; H, 6.56; N, 6.55.

Mol. wt. : 211 (mass spectrum); formula wt. : 211.

N.M.R. (acetone d_6): 3 aromatic H at 6.85 δ , 4 H centered at 2.95 δ (CH_2-N-CH_2) and 6 H centered at 1.55 δ (3 CH_2). The aromatic hydrogens are not sufficiently resolved to determine the position of the substituents.The product is assumed to be N-(3-chloro-4-hydroxyphenyl)-piperidine, by analogy with the behaviour of phenol and the general character of the reaction[1].

The mother liquor is removed and 5 g of semisolid product remains. Chromatography on silica gel and elution with benzene yields additional 3.2 g of N-(3-chloro-4-hydroxyphenyl)-piperidine and 1.3 g of a liquid isomer (mass spectrum identical to that of N-(3-chloro-4-hydroxyphenyl) piperidine).

N,N-dimethylaminophenol ortho and para.

N-chlorodimethylamine is prepared according to the following modified procedure of the general method[3]:

A solution of 16.5 g of dimethylamine hydrochloride in 80 ml of water is added dropwise with stirring at 0° to a mixture of 140 ml of 14% sodium hypochlorite aqueous solution and 200 ml of ether. The ethereal layer is separated and the aqueous layer is further extracted two times with 100 ml portions of ether. The combined ethereal extracts are washed with 5% sulfuric acid solution and then added dropwise with vigorous stirring and cooling (< 0°) to 19.6 g of concentrated sulfuric acid. The whithe crystalline N-chlorodimethylamine bisulfate is filtered with suction, washed with ether and directly used for the reaction after dissolution in concentrated sulfuric acid; 85-90% yield (iodometric titration). The sulfuric solution can be stored for months at 0°, whereas the solid bisulfate gradually deteriorates on standing.

To a mixture of 9.4 g of phenol, 14 g of ferrous sulfate heptahydrate, 15 ml of concentrated sulfuric acid and 6 ml of water is added dropwise with stirring 3.8 g of N-chlorodimethylamine dissolved in 16 ml

of concentrated sulfuric acid. The temperature spontaneously rises from 0° to 30°. The mixture is worked up as in the preceding cases. The yield of basic product amounts to 3.9 g (59%).Crystallization from benzene-ligroine yields 1.7 g of p-N,N-dimethylaminophenol, m p 77-8°, identical in all respects with an authentic sample. Thin layer chromatography of the semisolid residue, after removal of the mother liquor,indicates a mixture of ortho and para N,N-dimethylaminophenols. The mixture is transformed in the corresponding N,N-dimethylaminoanisoles with dimethyl sulfate and identified by preparative glc and comparison with authentic samples: only the ortho and para isomers are present.

REFERENCES

1. F.Minisci , Chimica e Industria , 49 , 705 (1967).
   F.Minisci and M.Cecere , Chimica e Industria , 49 , 1333 (1967).
2. F.Minisci,R.Galli,M.Cecere and V.Trabucchi , Chimica e Industria , 48, 1147 (1966).
   F.Minisci,R.Galli and M.Cecere , Chimica e Industria , 48 ,1324(1966).
3. G.H.Coleman, J.Am.Chem.Soc., 55 , 3001 (1933).
4. A.H.Sommers and S.E.Aaland, J.Am.Chem.Soc. , 75 , 5280 (1953).

(Received October 10, 1968)