and determination of their sodium content, after dilution with alcohol, by titration with standard acid using methyl red. This does not discriminate between sodium naphthalene and other suspended or dissolved alkaline sodium compounds in the solution but when pure solvent is used it gives a close approximation of the sodium naphthalene that has been formed.

B. In Dimethyl Ether.—The preparation of sodium naphthalene in dimethyl ether is carried out in much the same way as in dimethylglycol ether except for the changes occasioned by the low boiling point (−25°). The flask in which the reaction is to be carried out is cooled to about −50° in a bath of solid carbon dioxide and methanol, and the solvent is led in as a gas from a cylinder and condensed. The reaction is best carried out at a temperature of −30°. The nature of the solvent makes it difficult to make analyses in this case, but an approximate measure of the reacted sodium can be obtained easily by weighing the unreacted sodium recovered after the completion of the reaction.

Dimethylglycol Ether.—This reagent was prepared by the methylation of the monomethyl ether of ethylene glycol. It must be purified and thoroughly dried for use in alkali metal reactions. It is a colorless fluid with a characteristic ether-like odor boiling at 85°.

Dimethyl Ether.—This ether was sufficiently pure as obtained from the Ammonia Department of E. I. du Pont de Nemours & Company, Inc.

Summary

The reaction of aromatic hydrocarbons with sodium is so greatly facilitated by employing dimethyl ether or dimethylglycol ether as the solvent, in place of diethyl ether, that with the use of these special solvents even such hydrocarbons as naphthalene and diphenyl can be converted easily into sodium compounds.

NIAGARA FALLS, N. Y. RECEIVED SEPTEMBER 23, 1936

[CONTRIBUTION FROM THE BURROUGHS WELLCOME AND CO., U. S. A., EXPERIMENTAL RESEARCH LABORATORIES]

The Separation of Primary Aryl Amines from Secondary Alkylaryl Amines

BY CLAYTON W. FERRY AND JOHANNES S. BUCK

In the course of the preparation of a series of unsymmetrical alkylaryl ureas and thioureas[1,2] a number of secondary alkylaryl amines, substantially free from primary aryl amines, was required (small amounts of tertiary amines are unimportant, since they form no ureas). When alkoxy and certain N-alkyl groups are present in the secondary amine, the usual methods of preparation (*e. g.*, *via* the acyl derivatives, nitroso compounds, etc.) are not satisfactory[2] and it is necessary to alkylate the primary aryl amine directly and to remove unchanged primary amine from the product. A method for carrying out this removal, suggested by the work of Eibner and by several patents[3] and outlined by DeBeer, Buck, Ide and Hjort[2] is here described, whereby the primary amine is removed readily by shaking the crude secondary amine with benzaldehyde–sodium bisulfite compound and water. The primary amine combines with the reagent and is recoverable, while the secondary amine remains unattacked.

Experimental

Twenty grams each of primary aryl amine and secondary alkylaryl amine (the secondary amines mentioned in this report were all purified *via* the nitroso compound) were mixed and shaken mechanically with water and benzaldehyde–sodium bisulfite compound at room temperature. The mixture was then filtered from the solid with suction, the solid well washed with ether and the filtrate extracted with ether. The total ether was washed with brine, the ether evaporated and the residual amine tested for primary amine.

In the first series of experiments, designed to investigate the conditions of reaction, the above process was repeated until tests showed the absence of any appreciable amount of primary amine (< 0.5%). In the first treatment 50 cc. of water and one mol of bisulfite compound (calculated on the primary amine present) were used. In the second treatment 30 cc. of water and 0.5 mol of bisulfite compound and in the third and subsequent treatments, 30 cc. of water and 0.25 mol of bisulfite compound were used. In all cases the shaking was for two hours per treatment.

When this method was applied to mixtures of methyl aniline, *n*-butylaniline, ethyl-*m*-toluidine, ethyl-*p*-toluidine and ethyl-*o*-phenetidine, with the corresponding primary amine, over 80% of the secondary amine, containing less than 0.5% of the primary amine was obtained after the third treatment. Similar mixtures from ethyl-*p*-phenetidine and isopropyl-*p*-anisidine required, respectively, four and five treatments, about 54% of the secondary amine being recovered. A mixture from ethyl-*o*-toluidine was not purified to less than 10% of primary amine, even after five treatments.

The second series of experiments was carried out in order to simplify the process practically, and to reduce the losses in manipulation. It was found that, using the same mixture (20 g. primary amine, 20 g. secondary amine), efficient separation could be obtained by six hours of shaking

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[1] Buck, Hjort and DeBeer, *J. Pharmacol.*, **54**, 188 (1935).

[2] DeBeer, Buck, Ide and Hjort, *ibid.*, **57**, 19 (1936).

[3] German Patent 181,723, 132,621, 157,909; Eibner, *Ann.*, **316**, 89 (1901).

with two mols (calculated on the primary amine present) of bisulfite compound and 140 cc. of water. The yield also was much improved. Thus, with mixtures of methylaniline, *n*-butylaniline, ethyl-*m*-toluidine, ethyl-*p*-toluidine and ethyl-*p*-phenetidine with the corresponding primary amine, the content of primary amine was reduced to 0.5% or less. The recovery was, respectively, 80, 94, 92, 90 and 78% of the secondary amine taken. In practice, 50% of primary amine in a mixture is rarely encountered and the amount is usually much less, so that the separation would be correspondingly facilitated.

The major part of the primary amine may be recovered from the aqueous liquors from the extractions and from the solid filtered off, by adding to these 200 cc. of water containing 25 cc. of concd. sulfuric acid and steam-distilling the mixture. Benzaldehyde comes over and may be largely recovered. The acid liquid in the flask is then made alkaline with 30% sodium hydroxide solution and the steam distillation continued, the receiver being changed. The primary amine may be recovered by saturating the distillate with salt and extracting four times with ether. After drying, the ether is evaporated and the residual amine distilled. From the mixtures cited above there was recovered aniline, 92%; aniline 87%; *m*-toluidine, 88%; *p*-toluidine, 90%; and *p*-phenetidine, 75%, respectively.

The boiling points of the recovered secondary amines were the same as those of authentic specimens[4] (the yields throughout refer to distilled amines of the correct boiling point). As an additional check the recovered secondary amines from the first series of experiments were converted into the α-naphthyl ureas and these were compared with specimens prepared from authentic amines. The melting points of the ureas from the recovered amines were in general only two or three degrees lower than those of the corresponding purified ureas, except in the cases of ethyl-*o*-phenetidine and ethyl-*p*-phenetidine, where the melting points were, respectively, eight and five degrees lower. The yields, in all cases, were substantially the same from either recovered or authentic amine.

α-Naphthyl Ureas.—Three cc. of α-naphthyl isocyanate (20–25% excess) was added to 2 cc. of amine (weighed) in 15 cc. of hexane. The oil which separated soon crystallized, and was filtered off and well washed with petroleum ether and its melting point determined. The ureas (from authentic amines), recrystallized from alcohol, form small, glistening, granular crystals, readily soluble in hot alcohol and in hot benzene, that from ethyl-*o*-toluidine being considerably more soluble than the others. The α-naphthyl ureas, not previously described, are tabulated below.

α-ALKYL-α-ARYL-β-(α-NAPHTHYL) UREAS

α-Groups	Formula	M. p., °C.	Analyses, %N Calcd.	Found
Methyl, phenyl	$C_{18}H_{16}ON_2$	99	10.14	10.29
n-Butyl, phenyl	$C_{21}H_{22}ON_2$	99	8.80	9.03
Ethyl, *o*-tolyl	$C_{20}H_{20}ON_2$	85.5	9.21	9.27
Ethyl, *m*-tolyl	$C_{20}H_{20}ON_2$	95.5	9.21	9.39
Ethyl, *p*-tolyl	$C_{20}H_{20}ON_2$	103	9.21	9.51
Isopropyl, *p*-anisyl	$C_{21}H_{22}O_2N_2$	147	8.38	8.48
Ethyl, *o*-phenetyl	$C_{21}H_{22}O_2N_2$	136.5	8.38	8.43
Ethyl, *p*-phenetyl	$C_{21}H_{22}O_2N_2$	111	8.38	8.43

Benzaldehyde–sodium bisulfite compound was prepared in the usual manner and well washed with water. The product is satisfactory for ordinary purposes, but for the present work it was recrystallized from water, then washed with ether when dry.

Primary amines were tested for by a spot method, an adaptation of the method of Cumming, Hopper and Wheeler,[5] using both "R" salt and (better) "H" salt and comparing the colors produced with those given by known mixtures. The carbylamine reaction, also used, was carried out in the usual manner, with alcoholic potassium hydroxide and chloroform. Both tests readily showed the presence of 0.5% primary amine.

In attempting to purify ethyl-*o*-toluidine several bisulfite compounds were tried (from anisaldehyde, *m*-nitrobenzaldehyde, and salicylaldehyde) but without much improvement. The reaction of ethyl-*o*-toluidine with isocyanates is relatively sluggish, and this fact allows a fair separation from primary amine to be made. A specimen of ethyl-*o*-toluidine, containing 10% *o*-toluidine, in 4 volumes of petroleum ether was well cooled and phenyl isocyanate (1.5 times calcd. for the primary amine present) added in one lot. After two and one-half minutes strong ammonium hydroxide was added (twice the volume of the amine), the whole chilled and the crystalline material filtered off and washed with petroleum ether. The total petroleum ether, after washing with water and drying (potassium hydroxide) was evaporated and the residual amine distilled. There was obtained in 80% yield, ethyl-*o*-toluidine, b. p. 103–104.5° (16 mm.), containing about 1% *o*-toluidine.

The recovered secondary amines usually contain small amounts of benzaldehyde, which can be readily removed if necessary by dissolving the amine in acid. Estimated as acid-insoluble material, the benzaldehyde varied, with different amines, between 0.3 and 1.7%, but was usually close to the lower figure.

Attempts to extend the method to the separation of aliphatic amines were finally abandoned. In general the solubility of the amines in water, the instability of the azomethine compounds usually formed and the solubility of these compounds in organic solvents render a practical separation not feasible. The use of formaldehyde–sodium bisulfite compound helps matters somewhat, but the method still is not practical.

Summary

An expeditious method for separating mixtures of primary aryl amines with secondary alkylaryl amines is here described. The method depends on the preferential combination of benzaldehyde-sodium bisulfite compound with primary aryl amines, and is very generally applicable. An alternative method, involving the use of phenyl isocyanate, is suggested for mixtures of *o*-toluidine and ethyl-*o*-toluidine. Some α-naphthyl ureas derived from the secondary amines are described.

TUCKAHOE, N. Y. RECEIVED OCTOBER 10, 1936

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(4) Hjort, DeBeer, Buck and Ide, *J. Pharmacol.*, **55**, 152 (1935), and to be published later.

(5) Cumming, Hopper and Wheeler, "Systematic Organic Chemistry," 2d ed., D. Van Nostrand Co., New York, 1928, p. 501.