SOME CHEMISTRY OF 2,6-DIETHYLANILINE[1]

P. M. G. BAVIN[2] AND J. M. W. SCOTT[3]

ABSTRACT

Orientation in the nitration and bromination of amides derived from 2,6-diethylaniline has been shown to be dependent on the acidity of the reaction medium, as found previously for the 2,6-dimethyl homologues.

The acidity of the reaction medium is known to influence the orientation of substitution products of many amines (1, 2, 3, 4, 5, 6, 7) and their derivatives, particularly anilides and sulphonamides (8, 9, 10, 11). Derivatives of 2,6-dimethylaniline (*m*-2-xylidine) have proved to be of more than usual interest (9, 10), so that the opportunity has been taken to examine some of the chemistry of 2,6-diethylaniline.

2,6-Diethylaniline was recently prepared for the first time (12). It forms nicely crystalline salts with hydrochloric, hydrobromic, and perchloric acids which, as expected for the salts of weak bases (13), are partly hydrolyzed in water. With benzaldehyde it reacts smoothly to form a Schiff's base and readily forms amides with acetic anhydride, benzoyl chloride, and *p*-toluenesulphonyl chloride. The acetamide (X) is very resistant to acid hydrolysis so that the toluenesulphonamide (I) was preferred as an intermediate.

Nitration of (I) in the presence of nitrous acid (7, 10) gave an excellent yield of pure 4-nitro derivative (II), the structure of which was proved by conversion to the known 4-nitro-2,6-diethylphenol (IV) and 2,6-diethyl-1,4-benzoquinone (V). In sulphuric acid, nitration gave a rather lower yield of the 3-nitro derivative (VI), its structure being assumed by elimination. The acetamide (X) readily yielded a dinitro compound, almost certainly (VII), and considerable difficulty was encountered in obtaining the 3-nitro derivative (VIII).

Bromination of the acetamide (X) in sulphuric acid gave the 3-bromo derivative (IX), the structure of which is assumed by analogy with previous work on the dimethyl homologue (9). In acetic acid or chloroform, the 4-isomer (XII) was obtained. This compound, the structure of which is also assumed by analogy (9), has been shown to be formed by the rearrangement of the *N*-bromoacetamide (14). Bromination of the sulphonamide (I) in sulphuric acid, chloroform, or acetic acid gave products which were not obtained pure by repeated crystallization and whose infrared spectra showed them to be essentially identical. Removal of the tosyl group followed by acetylation gave almost pure (XII), showing that bromination had occurred predominantly in the 4 position.

Aniline, the toluidines, and related compounds are very much more reactive than their salts so that the small concentration of free amine present in sulphuric acid largely controls the orientation in nitration in this medium (1, 2, 3, 4, 5, 6, 7). Derivatives of 2,6-dialkylaniline (alkyl is methyl or ethyl) offer a more complex problem. The proximity of the ortho substituents twists the amide group out of the plane of the aromatic ring,* thereby greatly reducing mesomerism between the ring and the nitrogen (10, 15, 16).

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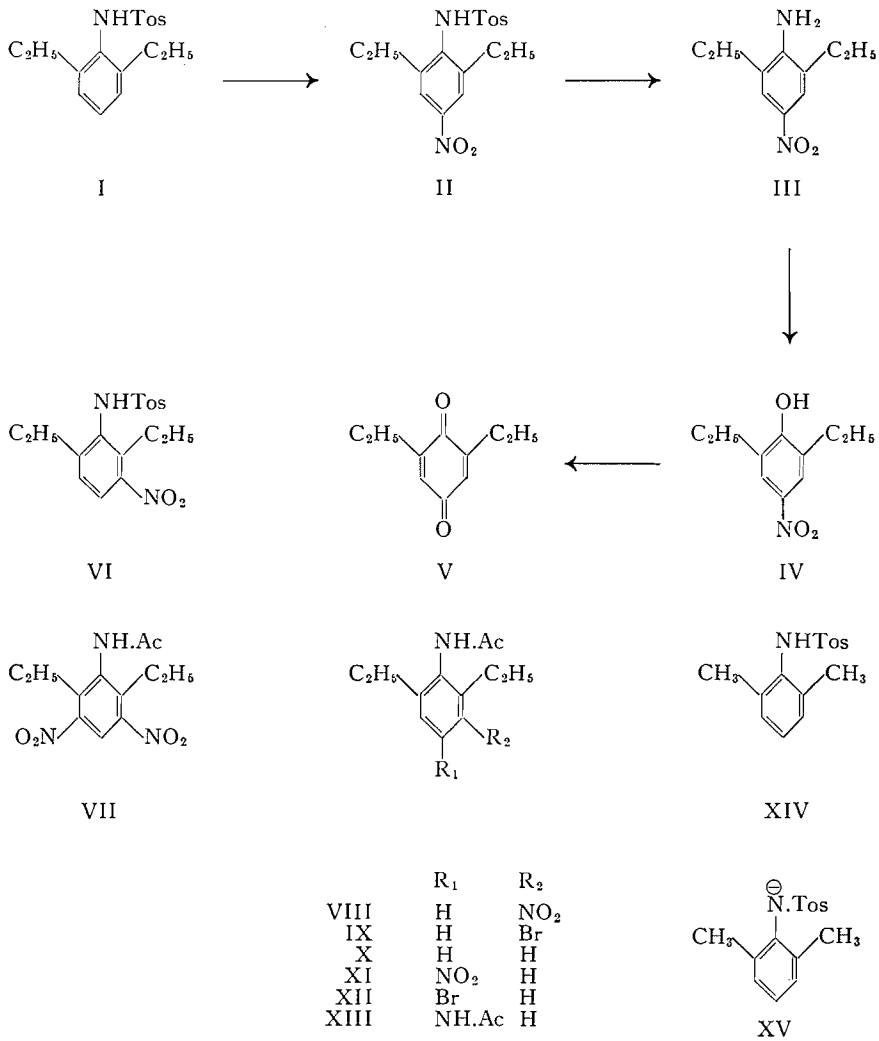
[2]*National Research Council of Canada Postdoctorate Fellow, University of Ottawa, 1954–56. Present address: the Ohio State University, Columbus 10, Ohio.*
[3]*National Research Council of Canada Postdoctorate Fellow, Division of Pure and Applied Chemistry.*

**Reducing mesomerism between the ring and the nitrogen will increase the basicity of the latter, but the compression caused by the ortho substituents may nullify or even out-balance this effect ((17), pp. 214–223).*



I II III IV V VI VII XIV XV

	R_1	R_2
VIII	H	NO_2
IX	H	Br
X	H	H
XI	NO_2	H
XII	Br	H
XIII	NH.Ac	H

This lowers the reactivity of the 4 position but leaves it more reactive than the 3 position (10). Since in sulphuric acid 3-derivatives are usually obtained, it appears that the protonated and unprotonated forms differ but little in reactivity at the 3 position.

The sulphonamides (I) and (XIV) and their *N*-nitroso derivatives are probably insufficiently reactive to undergo nitrosation (cf. (7)) so that (XV) has been suggested (10) as the reactive species in nitration in the presence of nitrous acid.

As expected, nitration of (I) and bromination of (X) are completely analogous to reactions of the dimethyl homologues (9, 10). That bromination of (I) in sulphuric acid gives rise to predominantly the 4-isomer may be due to the low basicity of the sulphonamide group and the greater selectivity of bromination compared with nitration (18).

It was hoped initially to confirm the structures of the bromination products by comparison of their infrared spectra with those of the corresponding nitro compounds. This hope was not realized, only approximate similarities being observed.

EXPERIMENTAL

2,6-Diethylaniline was supplied as a reddish liquid and used without purification.

Melting points are uncorrected. Most of the nitration products turned brown in light and were crystallized in covered flasks. Nitration conditions were essentially those used by Wepster for the dimethyl homologues (10).

2,6-Diethylaniline hydrochloride crystallized from dilute hydrochloric acid as colorless needles, m.p. 175–179° with decomposition. Calc. for $C_{10}H_{16}NCl$: C, 64.68; H, 8.69%. Found: C, 64.48; H, 8.44%. Crystalline salts were also formed with perchloric and hydrobromic acids but these were not characterized. The free amine separated as an oil when the salts were dissolved in warm water.

N-Benzal-2,6-diethylaniline.—On the gentle warming of a mixture of the amine (2 g.) with benzaldehyde (4 g.), water started to separate almost at once. Ethanol (2 ml.) was added and the mixture boiled under reflux for 10 minutes. The Schiff's base was obtained as a pale yellow solid by pouring the mixture into an excess of cold dilute sodium bisulphite solution. Two crystallizations from hexane afforded yellow prismatic needles (2.6 g.), m.p. 54–55°. Calc. for $C_{17}H_{19}N$: C, 86.03; H, 8.07; N, 5.90%. Found: C, 86.20; H, 8.08; N, 5.88%.

N-(2,6-Diethylphenyl)-benzamide was prepared by shaking the amine (2 g.) with benzoylchloride (3 ml.) and a solution of sodium hydroxide (5 g.) in water (10 ml.). The solid product was crystallized twice from toluene, affording slender needles (2.2 g.), m.p. 236–237°. Calc. for $C_{17}H_{19}NO$: C, 80.57; H, 7.56; N, 5.53%. Found: C, 80.73; H, 7.42; N, 5.66%.

N-(2,6-Diethylphenyl)-acetamide (X) was prepared by adding acetic anhydride (200 ml.) dropwise to the amine (100 g.) cooled in an ice bath. The reaction, which was rapid and exothermic, was completed on the steam bath. Addition of 10% sulphuric acid (500 ml.) and crushed ice precipitated the amide. Crystallization from ethanol (200 ml.) afforded white needles (110 g.), m.p. 139–140°, raised to 141–142° by two crystallizations from toluene. (Lit. m.p. 135–136°, (12).) Calc. for $C_{12}H_{17}NO$: C, 75.35; H, 8.96; N, 7.32%. Found: C, 75.56; H, 8.71; N, 7.46%.

N-(2,6-Diethylphenyl)-p-toluenesulphonamide (I).—The amine (150 g.) was dissolved in dry pyridine (500 ml.) and *p*-toluenesulphonyl chloride (210 g.) added slowly while the mixture was cooled with an ice–salt bath. Next morning, the mixture was poured onto crushed ice and the pyridine neutralized with dilute hydrochloric acid. Crystallization from methanol–acetone (Norite) afforded yellowish prisms (265 g.), m.p. 130–132°. An analytical sample was obtained as well-defined colorless prisms, m.p. 132–133°, after two crystallizations from benzene. Calc. for $C_{17}H_{21}NO_2S$: C, 67.31; H, 6.98; N, 4.62%. Found: C, 67.45; H, 6.98; N, 4.49%.

N-(4-Nitro-2,6-diethylphenyl)-p-toluenesulphonamide (II).—A mixture of the amide (I) (30 g.), acetic acid (100 ml.), fuming nitric acid (40 ml.), and sodium nitrite (2 g.) was boiled under reflux for 1 hour. Pouring onto ice precipitated a gum which soon crystallized. Successive crystallizations from methanol (Norite) and benzene–hexane afforded the nitroamide as pale yellow needles (22–25 g.), m.p. 140–141°. Calc. for $C_{17}H_{20}N_2O_4S$: N, 8.04%. Found: N, 8.18%.

4-Nitro-2,6-diethylaniline (III).—The nitroamide (II) (10 g.) was stirred overnight with sulphuric acid (30 ml.) containing water (4 ml.). Pouring onto ice precipitated the pale yellow amine sulphate, which was decomposed to the amine by neutralization with dilute ammonia solution. Two crystallizations from methanol gave long bright yellow needles of the amine, m.p. 137–138°. Calc. for $C_{10}H_{14}N_2O_2$: N, 14.42%. Found: N, 14.59%.

N-(4-Nitro-2,6-diethylphenyl)-acetamide (XI) was prepared by acetylating the amine (III). It crystallized from benzene–hexane as pale yellow needles, m.p. 195–196°. Calc. for $C_{12}H_{16}N_2O_3$: N, 11.96%. Found: N, 11.71%.

N,N-Diacetyl-2,6-diethyl-1,4-phenylenediamine (XIII).—The nitroamine (III) was reduced with hydrazine and palladized charcoal, giving the diamine as a colorless oil. Acetylation followed by two crystallizations from acetone–toluene afforded the bisamide as slender needles, m.p. 216–217°. Calc. for $C_{14}H_{20}N_2O_2$: N, 11.28%. Found: N, 11.30%.

4-Nitro-2,6-diethylphenol (IV).—To a cold (0–5°) solution of the nitroamine (III) (3 g.) in 50% sulphuric acid (40 ml.) was added sodium nitrite (2 g.). The mixture was left for 1 hour at room temperature and, after addition of urea to destroy excess nitrous acid, was maintained at 60° for 1 hour. During this time the phenol separated as a reddish solid. Attempted purification through the intensely yellow sodium salt was not successful but two crystallizations from methanol (Norite) afforded slightly reddish needles, m.p. 131–133° with decomposition. (Lit. m.p. 130–131° with decomposition (19).)

2,6-Diethyl-1,4-benzoquinone (V) was prepared by oxidizing the nitrophenol (IV) with lead tetraacetate, as described previously (19). It was obtained as bright yellow needles, m.p. 36–38°, by low temperature crystallization from pentane. (Lit. m.p. 35° (19); 39° (20).)

Attempts to oxidize the nitroamine (III) to the quinone, using chromic acid or lead tetraacetate, were not successful.

N-(3-Nitro-2,6-diethylphenyl)-p-toluenesulphonamide (VI).—A mixture of acetic acid (50 ml.), fuming nitric acid (4.5 ml., d. 1.5), and sulphuric acid (50 ml.) was added dropwise to a vigorously stirred suspension of the amide (I) (32 g.) in acetic acid (250 ml.) containing sulphuric acid (120 ml.). The addition required ½ hour during which time the temperature rose to 45°. After 6 hours the product was isolated by pouring the mixture onto crushed ice. Crystallization from aqueous ethanol (Norite) afforded buff prisms (17–26 g.), m.p. 149–151°. An analytical sample was obtained as pale yellow prisms after several crystallizations from benzene–hexane, m.p. 152–153°. Calc. for $C_{17}H_{20}N_2O_4S$: N, 8.04%. Found: N, 8.13%.

N-(3-Nitro-2,6-diethylphenyl)-acetamide (VIII).—Hydrolysis of the once-crystallized amide (VI) with 90% sulphuric acid gave the amine as a yellow oil. Acetylation followed by crystallization from methanol and then benzene–hexane afforded the acetamide as almost colorless needles, m.p. 153–154°. Calc. for $C_{12}H_{16}N_2O_3$: N, 11.96%. Found: N, 12.01%.

N-(3,5-Dinitro-2,6-diethylphenyl)-acetamide (VII) was commonly obtained when the acetamide (X) was nitrated in a mixture of acetic and sulphuric acids. It crystallized from toluene as pale yellow needles, m.p. 206–208° with some decomposition (capillary determination). On the hot stage, with a rapid rate of heating, the melting point was 211–212°. Calc. for $C_{12}H_{15}N_3O_5$: C, 51.24; H, 5.35; N, 14.94%. Found: C, 51.31; H, 5.31; N, 14.94%.

On a few occasions the mononitro compound (VIII) was obtained by nitrating (X) but reliable conditions for its preparation by this method were not found. Attempts to dinitrate the sulphonamide (I) were not successful, probably owing to hydrolysis.

N-(3-Bromo-2,6-diethylphenyl)-acetamide (IX) was prepared by shaking the acetamide (X) for several hours with a mixture of 98% sulphuric acid (400 ml.) and bromine (20 g.), during which time hydrogen bromide was steadily evolved. The product was isolated by pouring onto crushed ice, crystallization from benzene giving white needles (18 g.), m.p. 157–160°, raised to 161–162° by two crystallizations from methanol. Calc. for $C_{12}H_{16}NOBr$: C, 53.34; H, 5.18%. Found: C, 53.12; H, 5.95%.

N-(4-Bromo-2,6-diethylphenyl)-acetamide (XII) was obtained when the acetamide (X) was brominated in chloroform or acetic acid. It crystallized from methanol or benzene–hexane as long white needles, m.p. 181–182°. Addition of the 3-isomer (VII) depressed the melting point. Calc. for $C_{12}H_{16}NOBr$: C, 53.34; H, 5.97; N, 5.18; Br, 29.58%. Found: C, 53.30; H, 5.85; N, 5.13; Br, 30.25%.

Bromination of the sulphonamide (I) in chloroform (with or without addition of potassium carbonate), acetic acid, or sulphuric acid gave impure products having almost identical infrared spectra. Repeated crystallization from various solvents (methanol, acetone, ethyl acetate, benzene) gave white needles having melting points in the range 115–144°. Calc. for $C_{17}H_{20}NO_2SBr$: C, 53.41; H, 5.27%. Found: C, 53.58, 53.29; H, 5.25, 5.35%. Hydrolysis with 90% sulphuric acid gave, after acetylation, the 4-bromo-acetamide (XII), obtained after one crystallization from methanol.

INFRARED SPECTRA

The infrared spectra were obtained using potassium bromide disks and solutions in carbon disulphide or chloroform, and were calibrated against the spectrum of "Polystyrene".

The 1600–2000 cm.$^{-1}$ region, generally useful in orienting benzene derivatives (21, pp. 54–70), proved to be of little value as the acetamides showed strong carbonyl absorption at about 1650 cm.$^{-1}$. Comparison of the bands in the 700–1200 cm.$^{-1}$ region failed to reveal useful correlation with structure, and comparison of some of the spectra with those of the dimethyl homologues was also valueless.

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