NOTES

Trimethylamine Oxide Boron Fluoride

By Anton B. Burg and John H. Bickerton[1]

Direct evidence of the strong electron-donor character of trimethylamine oxide was found in the recent study of its reaction with sulfur dioxide.[2] The compound $(CH_3)_3NO{\cdot}SO_2$ is not measurably dissociated below the char-point (*ca.* 120°), and it is best interpreted as a case of strong attachment of the oxide to the sulfur atom. Since sulfur dioxide usually forms only rather weak bonds to electron donors, the external dative bonding power of the amine oxide appears especially strong.

We have now found that boron fluoride adds directly to anhydrous trimethylamine oxide to form the very stable compound $(CH_3)_3NOBF_3$, thus affording further evidence of the strong electron-donor character of this oxide.

Preparation of $(CH_3)_3NOBF_3$.—Hydrated trimethylamine oxide, prepared by the action of hydrogen peroxide upon trimethylamine and purified by recrystallization from alcohol, was pumped for some hours at 90–100° and then sublimed several times in high-vacuum to remove the last trace of water. The effectiveness of this procedure had been demonstrated earlier.[2] The anhydrous trimethylamine oxide was dissolved in dry chloroform, which appears to be almost unique among solvents in that it makes possible a convenient concentration of the anhydrous amine oxide, and yet does not damage it by irreversible reaction. Pure boron trifluoride[3] was then bubbled in. The resulting white precipitate was washed by fresh chloroform, collected upon a suction-filter stick and dried.

Analysis of $(CH_3)_3NOBF_3$.—The new compound was analyzed for boron as boric acid by titration (0.1 *N* NaOH, phenolphthalein) in the presence of mannite. The boric acid was first set free by digestion of the original compound with 10% calcium chloride solution at 100° (one-half hour); this procedure also eliminated fluoride interference, by precipitation of calcium fluoride. The resulting hydrochloric acid was neutralized to the methyl red end-point before mannite was added. This procedure was first tested and found quite satisfactory for recrystallized potassium fluoborate, and then used for analysis of the amine oxide boron fluoride, with results shown in Table I.

Table I

Titration of Boron from $(CH_3)_3NOBF_3$

Sample, mg.	Boron found, mg.	Boron calcd., mg.	% Error
57.8	4.37	4.38	−0.2
66.8	5.01	5.06	−1.0
102.0	9.61	9.72	−1.1

Properties of $(CH_3)_3NOBF_3$.—This substance is quite stable in the open air. It melts at 89°. At 100° it turns tan-colored, and gives off white fumes (probably BF_3), accompanied by a little sublimate. At 175° it becomes dark brown and begins to effervesce against the atmosphere at 200°. Charring is complete at 227°.

The compound is soluble in water, but less so than trimethylamine oxide. After evaporation of the water under reduced pressure at 60°, the original weight of solid material is regained, and there is no change in appearance. Evidently the hydrolysis of the boron fluoride is wholly prevented by attachment to the amine oxide, except at temperatures at which discoloration begins.

Other Addition Products.—Using dry chloroform as a solvent it was possible to make some preliminary studies of the addition of silicon tetrachloride and phosphorus trichloride to trimethylamine oxide. Either of these attaches itself rather firmly, but the formulas of the addition compounds have not yet been established to complete satisfaction. It appears that numerous electron-receptors, too weak to react with a tertiary amine, may form stable compounds by addition to the amine oxide. Further studies in this field will be undertaken.

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[1] This note represents a thesis presented by John Harvey Bickerton to the Graduate School of the University of Southern California in partial fulfillment of the requirements for the degree of Master of Arts, February, 1943.

[2] Burg, This Journal, **65**, 1633 (1943).

[3] Booth and Willson, *ibid.*, **57**, 2273 (1935).

New 2,5-Dimethylpyrrole Derivatives

By W. S. Bishop

In connection with a research project in these Laboratories a number of 2,5-dimethylpyrrole derivatives have been prepared. Previous investigators[1a,b] prepared such derivatives by refluxing the required diamine with acetonyl acetone in alcohol for several hours, pouring the reaction product into water, separating and then purifying by fractionation or crystallization. We have carried on these reactions very satisfactorily in benzene by azeotropic distillation whereby the water is continuously removed.

Procedure.—The general procedure can be illustrated by the preparation of 1,1′-ethylene-bis-2,5-dimethylpyrrole: 0.5 mole of ethylenediamine (68%), 0.25 mole of acetonylacetone and sufficient benzene (or toluene) are placed in a 500-cc. round-bottom flask which has a 24/40 standard-taper neck and a 10/30 S. T. joint as a side arm through which is inserted a S. T. J. thermometer. Bumping of the boiling mixture is prevented by the addition of a small piece of porous plate. The flask is connected to a Barrett water trap (having a stopcock at the bottom), and the trap to a water condenser. All-glass joints are preferred. The reaction flask is encased in a Glascol heating mantle, regulated by a variac.

The water collected in the trap indicates the rate and completeness of the reaction. At the end, by elevating the temperature of the mantle the benzene may be distilled. Finally, it may be found desirable to apply a vacuum, regulated by a screw clamp, to the top of the condenser to remove any excess acetonyl acetone and amine.

The dipyrrole is then poured into an open dish and powdered; m. p. 132–133°; color, light-brown; yield 96–100%. After two crystallizations from alcohol, the product is nearly colorless; m. p. 136.5°, yield 80%. A melting point of 125–126° has been reported by Paal.[2]

The ethylene dipyrrole may be reduced in a bomb over

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[1] (a) Barton, U. S. Patent 2,234,056; (b) Hazlewood, *et al.*, *J. Proc. Roy. Soc. N. S. Wales*, **71**, 92 (1937).

[2] Paal and Schneider, *Ber.*, **19**, 3157 (1886).

TABLE I

1,1'-(R)-BIS-(2,5-DIMETHYLPYRROLES)

Where (R) is:	M. p., °C.	B. p. °C.	B. p. Mm.	Crystallizing solvent	Color	Empirical formula	Nitrogen, % Found		Nitrogen, % Calcd.
m-Phenylene[1a]	264			Benzene	v.l.tan	$C_{18}H_{20}N_2$	10.49	10.71	10.61
Ethylene[1b]	136.5			Alcohol	v.l.tan	$C_{14}H_{20}N_2$	12.60	12.79	12.95
Hexamethylene	105.5–106.0			Alcohol	v.l.tan	$C_{18}H_{28}N_2$	10.09	10.46	10.29
Nonamethylene		211	2		Colorless	$C_{21}H_{34}N_2$	8.83	8.92	8.92
Decamethylene	68.5– 69.5			Alcohol	v.l.tan	$C_{22}H_{36}N_2$	8.20	8.44	8.55
(1,3-Butylene)		195	23		Yellow	$C_{16}H_{24}N_2$	11.36	11.39	11.48
Propylene	67.5– 68.0	160	8	Alcohol	l.yellow	$C_{15}H_{22}N_2$	12.18	12.21	12.17
(4,4'-Phenoxyphenyl)	178			Me cyclohexane	Brown	$C_{24}H_{24}ON_2$	7.61	7.64	7.65
β,β'-Diethyleneimine	80.0– 80.2			Alcohol	Yellow	$C_{16}H_{25}N_3$	15.99	16.03	16.16

TABLE II

MONO PYRROLES

1-R-2,5-Dimethylpyrroles

Where (R) is:	Empirical formula	M. p., °C.	B. p. °C.	B. p. Mm.	Crystallizing solvent	Color	Nitrogen, % Found		Nitrogen, % Calcd.
(*o*-Aminophenyl)[1a]	$C_{12}H_{14}N_2$	77.0			Alcohol	L.brown	14.75	14.96	15.05
(*p*-Aminophenyl)[1a]	$C_{12}H_{14}N_2$	97.5–98.0			Alcohol	L.brown	14.93	14.93	15.05
(*o*-Tolyl)[1b]	$C_{13}H_{15}N$		105	7.5		Colorless	7.55	7.69	7.57
Butyl	$C_{10}H_{17}N$		69	4		Colorless	9.01	9.46	9.28
Amyl	$C_{11}H_{19}N$		80	4		Colorless	8.15	8.15	8.49
Octyl	$C_{14}H_{25}N$		118	4		Colorless	6.63	6.65	6.79
(3-Diethylaminopropyl)	$C_{13}H_{24}N_2$		113	3		Colorless	13.09	13.45	13.46
(β-Hydroxyethyl)[4]	$C_8H_{13}ON$	52.0	106	4	Cyclohexane	Colorless			
(β-Phenylethyl)	$C_{14}H_{17}N$		142	7		Colorless	6.81	6.92	7.04
(3-Phenyl-*n*-propyl)	$C_{15}H_{19}N$		175	14		Colorless	6.43	6.56	6.58
(*p*-Ethylphenyl)	$C_{14}H_{17}N$	57.5–58.0			Alcohol	Colorless	6.90	7.07	7.04
(*p*-Isopropylphenyl)	$C_{15}H_{19}N$		109–110	4		Colorless	6.54	6.60	6.58
(*p*-Cyanomethylphenyl)	$C_{14}H_{14}N_2$	102–103			Alcohol	Gray	13.06	13.49	13.33
(4-Morpholylethyl[2])	$C_{12}H_{20}ON_2$		149	8		Colorless	13.21	13.23	13.46
(*p*-Acetylphenyl)	$C_{14}H_{15}ON$	110–110.5			Alcohol	L.brown	6.53	6.66	6.57
(*p*-Carboxyphenyl)[5]	$C_{13}H_{13}O_2N$	208–209			Cyclohexane	Green-gray	6.38	6.57	6.52
(2,5-Dichlorphenyl)[1b]	$C_{12}H_{11}NCl_2$		139	9		Colorless	5.70	5.88	5.84
Anilino[6]	$C_{12}H_{14}N_2$	115–115.5			Alcohol	Yellow			
(*p*-Phenylazophenyl)	$C_{18}H_{17}N_3$	76.0			Alcohol	Orange-red	15.01	15.05	15.27
(2-Benzothiazolyl)	$C_{13}H_{12}N_2S$	79.0–79.5			Hexane	L.brown	11.99	12.02	12.28

Raney nickel, but with considerable difficulty, several hours at 200° being required. After filtering off the catalyst, the alcohol is evaporated and 1,1'-ethylene-bis-2,5-dimethylpyrrolidine fractionated; $C_{14}H_{28}N_3$, colorless, b. p. 120° at 13 mm. Nitrogen content found was 12.10 and 12.24%; calcd. 12.50%.

As many of the reactions are violently exothermic, due precaution must be exercised when adding the amine to the acetonyl acetone. Often it is necessary to leave the trap out of the system, adding the amine slowly by pouring through the condenser. After the reaction has subsided the trap is connected and the water removed. Also, with low-boiling amines it is necessary to reflux for a sufficient period to complete the reaction before inserting the trap.

Even with mixtures containing 68% aqueous ethylenediamine, this method has proved very satisfactory. Also, this method has the advantage that the pyrrole, either liquid or solid, may be poured from the reaction flask and purified directly, or for practical purposes used without further purification. In these cases the yield is essentially 100%.

Negative results have been encountered in the preparation of dimethyl pyrroles by this method with urea,[1b] thiourea, phenyl thiourea, dicyandiamide, aminoguanidine bicarbonate, hydrazine,[3] melamine, benzene sulfonamide and 2-aminopyridine.

Seven new di-pyrroles and thirteen new mono-pyrroles with their properties and analytical data are listed in the following Tables I and II.

The following 1-R-2,5-dimethylpyrroles have also been prepared but not included in the table for lack of analytical data: R equals, allyl, b. p. 88° (22 mm.); octadecyl, m. p. 38–39°; *p*-hydroxyphenyl, m. p. 105–105.4; 3-hydroxybutyl, b. p. 128(7); and ω-hydroxydiethyleneimine, m. p. 42.5–43.0, b. p. 164°(6).

Appreciation is expressed to Mr. F. C. Koch of these Laboratories for the nitrogen analyses.

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(3) Blaise, *Compt. rend.*, **170**, 1324 (1920), believes the reaction product to be a dimer of dimethyl pyridazine.

(4) Knorr and Rabe, German Patent, 116, 335 *Frdl.*, **6**, 1215.

(5) See (1b) who reports a m. p. of 196–198° and pale pink color; Gilman and O'Donnell, THIS JOURNAL, **66**, 840, 1944; m. p. 196–197°.

(6) Knorr, *Ber.*, **22**, 170 (1889), reports m. p. 90–92°.

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The Preparation of 7-Benzoylamino-6-carbamylheptylic Acid

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It seemed possible that nordesthiobiotin (V, R = $(CH_2)_5COOH$)[1] might be synthesized by the

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(1) Dittmer and du Vigneaud, *Science*, **100**, 129 (1944).