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Organic Electrosyntheses

III.* Reduction of *N*-Nitrosamines

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A simple and general laboratory method for the preparation of 1,1-dialkylhydrazines have been worked out, and applied to 20 different symmetric, unsymmetric, and cyclic *N*-nitrosamines, which have been electrolytically reduced in acid medium. Polarographic half-wave potentials of starting materials and product hydrazines are given.

During the development of a polarographic method for the quantitative determination of hydrazine and hydroxylamine derivatives [1] some 1,1-dialkylhydrazines were needed. Some results on the electrolytic reduction of *N*-nitrosamines [2–13] and *N*-nitramines [14,15] had already been reported, and it was decided to work out a general and simple method for the laboratory preparation of 1,1-dialkylhydrazines by electrolytic reduction of the corresponding *N*-nitrosamines in acid medium, to demonstrate the applicability of the electrolytic method on a preparative scale.

For this purpose, 20 different symmetric, unsymmetric, and cyclic *N*-nitrosamines have been reduced at a mercury cathode at potentials above -0.9 V *vs.* Ag/AgCl on a 0.1 mol scale in a 1 : 1 mixture of 4 N hydrochloric acid and ethanol, with ice cooling in a conventional H-cell, and the results are given in Table 1. For each compound, the analytical (polarography [1]), isolated and current yields have been determined (based on at least 2 preparative electrolyses), and the melting or boiling range of the isolated material is stated; the half-wave potentials of the *N*-nitrosamines (cathodic, pH 0.4, 40 % ethanol) and the resulting hydrazines (anodic, pH 13) have also been included (conc. 5×10^{-4} M). The medium was chosen in order to give a reasonable solubility of the organic depolarisators, to give a good electrical conductivity, and to facilitate the work-up. At the same time, a harmless anode reaction is achieved: the elementary chlorine formed will react with the ethanol, giving mainly chloroacetaldehyde diethylacetal [16] and protons

* Part II, see Ref. 20.

Table 1. Results from electrolytic reduction of *N*-nitrosamines in 1 : 1 4 N hydrochloric acid-ethanol at −0.9 V *vs.* Ag/AgCl.

Amine moiety	Amount (g)	Yields (%) Anal.	Isol.	Curr.	M.p./b.p. (°C)	$-E_{\frac{1}{2}}$ *vs.* S.C.E. (V) >N−NO	>N−NH_2
Dimethylamine	10.1	76	70	85	68− 69[a]	0.93	0.38
Diethylamine	14.1	82	59	93	92−100_{760}	0.92	0.44
Diisopropylamine	15.4	90	69	94	133−137_{758}	0.88	0.40
Dibutylamine	17.9	92	77	100	180−188_{757}	0.77	0.44
Diisobutylamine	17.9	95	78	96	140−141[a]	0.82	0.45
Dicyclohexylamine	21.0	86	67	92	139−141[a]	0.74	0.36
Dibenzylamine	22.6	93	82	91	198−199[a]	0.64	0.36
Diallylamine	14.5	67	54	78	142−150_{762}	0.79	0.40
Methylcyclohexylamine	15.3	80	64	90	183−191_{765}	0.79	0.43
Methylbenzylamine	15.4	87	76	93	114−115[a]	0.81	0.41
Methylaniline	16.9	63	51	79	95−103_{11}	0.68	0.36
Ethylaniline	16.4	56	42	81	100−110_{11}	0.62	0.35
Phenylglycine	18.0	55	41	71	188−189[a]	0.64	0.33
Pyrrolidine	11.0	90	75	96	113−114[a]	0.81	0.46
Piperidine	15.6	87	77	99	147−148[a]	0.78	0.41
Hexamethylenimine	15.8	84	76	91	149−150[a]	0.87	0.43
Morpholine	12.1	82	72	92	138−139[a]	0.80	0.32
Tetrahydroquinoline	17.8	19	−	32	−	0.55	0.36
Tetrahydroisoquinoline	16.2	83	72	92	195−196[a]	0.62	0.38

[a] Hydrochloride.

to replace those consumed in the cathode compartment. Thus the preparative organic electrochemist's wish [17] of utilizing both electrode reactions of the cell for synthetic purposes was fulfilled. However, the chlorinated product is not very interesting in this connection, and was not isolated in the present work, but the process can be used in combination with many other organic electrolytic reductions.

To facilitate comparison, the same conditions have been used in all experiments, and no attempt was made to optimize the conditions (acidity, concentration, temperature, current density, *etc.*) for the individual compounds. The electrode reaction in acid medium is a simple 4-electron reduction of the protonated species, the only side reactions being hydrolysis of the starting material, giving the corresponding secondary amine as a by-product, and a little hydrogen evolution; this is substantiated by the generally very good current yields obtained with the pure aliphatic substrates. For the aromatic derivatives, the tendency of acid hydrolysis or rearrangement [11,18] is greater, and the yields correspondingly lower. This difficulty can be overcome by working at a higher pH, *e.g.* acetate buffer,[8] which, however, presents some practical problems when working on a larger scale (buffer capacity, conductivity, time factor), and has not been examined in the present investigation. With a purely aromatic compound, such as *N*-nitrosodiphenylamine, the method gave only traces of 1,1-diphenylhydrazine (not included in Table 1),

and the low yield with *N*-nitrosotetrahydroquinoline is explained by a known rearrangement in acid ethanol.[18]

The work-up procedure was very simple. The impure hydrazine hydrochlorides were obtained by evaporation of the catholyte, and the less hygroscopic ones could be recrystallized from abs. ethanol-ether. The others were isolated as the free bases by extraction and distillation after addition of excess potassium hydroxide to the oily residues. Attempts to obtain crystalline derivatives in these cases by evaporating the catholyte with an equivalent amount of sodium oxalate and extraction with methanol failed.

The possibility of using nitramines as starting materials was investigated with *N*-nitromorpholine under the same conditions. The analytical, isolated, and current yields (%) were found to be 62, 54, and 67, respectively, much less favourable than those for the *N*-nitrosomorpholine (Table 1). Thus the generally easier available *N*-nitrosamines seem to be preferable.

Some reductions [19] on a larger scale (0.4 – 0.5 mol) have also been performed in the earlier described cylindrical cell [20] with a few of the *N*-nitrosamines (dimethyl, diallyl, methyl-phenyl, and benzyl-methyl); the yields obtained were very close to those of Table 1, so that the reaction is suitable for scale-up, but the H-cell was simpler to work with in the elucidation of the scope of the procedure.

From the results of Table 1 it can be concluded that the present method offers a simple and efficient alternative (with possibilities for amelioration) to the common laboratory processes like zinc-dust reduction,[21] catalytic hydrogenation,[22] and hydride reduction,[23] especially for the preparation of non-aromatic 1,1-disubstituted hydrazines.

EXPERIMENTAL

Apparatus. The polarograph, potentiostat, and integrator were the same as earlier used.[20] The H-type cell has also been described.[24] Analytical GLC was performed on a Perkin-Elmer F11 instrument with a 1 % SE30 silicone oil column, NMR on a Varian Ass. A-60 spectrometer.

Materials. All the investigated *N*-nitrosamines were known and synthesized by nitrosations [25] in acid medium from commercially available secondary amines. The hydrazines were also known, and reference materials for the polarographic analysis were mostly obtained from electrolytic reductions on a 5 g scale in a smaller H-type cell. They were used in the form of doubly recrystallized hydrochlorides or oxalates, in some cases as the free bases estimated by GLC.

Reduction of N-nitrosamines. The cell was filled with a 1 : 1 mixture of 4 hydrochloric acid and 96 % ethanol (reference electrode Ag/AgCl in 4 N hydrochloric acid) and placed in a plastic container with crushed ice on a magnetic stirrer. The catholyte was prereduced at −1.2 V for 10 – 15 min, about 0.1 mol of *N*-nitrosamine (see Table 1) was added and reduced overnight at potentials less negative than −0.9 V. To avoid a considerable heat generation, the starting current was kept below 2 A (corresponding to a higher working electrode potential in the beginning of the electrolysis); in some cases, especially with the aromatic derivatives, this precaution was also necessary to minimize the hydrogen evolution that else would have caused lower current yields. The time of electrolysis was generally 15 – 20 h, with the less soluble depolarisators somewhat longer. The residual current was about 15 – 20 mA at the end.

The catholyte was diluted to 500 ml in a measuring flask, a 0.5 ml aliquot was withdrawn, diluted to 10.0 ml with water, 1.0 ml of the latter solution diluted to 25.0 ml with aqueous potassium hydroxide-sodium sulphite solution,[1] and polarographed (double determination); the yield of hydrazine was then calculated by means of a standard curve.

The main part of the catholyte was evaporated on a rotation evaporator, absolute ethanol was added and twice evaporated to remove traces of water. If solid, the residue was recrystallized from absolute ethanol or absolute ethanol-ether and dried *in vacuo*; if oily, the residue was treated with excess potassium hydroxide and ether, the ethereal solution dried over potassium hydroxide pellets, the solvent stripped off, and the residue fractionated on a small Vigreux column. Some of the hydrazines were a little difficult to handle, due to a strong foaming tendency. Melting and boiling point ranges (not corrected) are listed in Table 1.

The product from reduction of *N-nitroso-N-phenyl-glycine* [26] was shown by NMR and elementary analysis no longer to contain a free carboxyl group, but instead the hydrochloride of *N-amino-N-phenylglycine ethyl ester* was obtained; m.p. 193–194°C (abs. ethanol). Esterification thus must have taken place in the catholyte during electrolysis, evaporation, and recrystallization. NMR-data (CF_3COOH, δ in ppm): 1.31 (3H, triplet); 4.35 (2H, quartet); 4.51 (2H, singlet); 7.1–7.6 (5H, multiplet). (Found: C 51.95; H 6.47; Cl 15.42; N 11.90. Calculated for $C_{10}H_{15}ClN_2O_2$: C 52.08; H 6.54; Cl 15.37; N 12.14.)

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