Chemical and Electrochemical Synthesis of Some Substituted *N,N'*-Diacyl-*p*-phenylenediamines

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Some *N,N'*-diacyl-*p*-phenylenediamines substituted with halogens (**2a-c**) were prepared. Their polarographic reduction in *N,N*-dimethylformamide with Et_4NClO_4 was performed and discussed. The mechanism of the electrochemical reduction is stated. Large-scale electrolytic reductions of **2a-b** to **3a-b** were performed.

Chemische und elektrochemische Synthese einiger substituierter *N,N'*-Diacyl-*p*-phenylendiamine

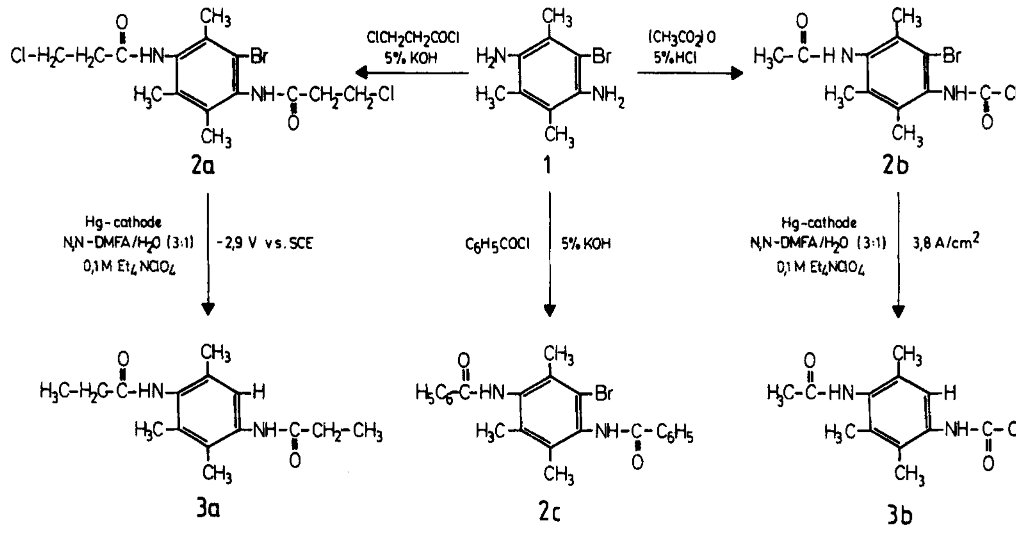
Einige mit Halogen substituierte *N,N'*-Diacyl-*p*-phenylendiamine (**2a-c**) wurden dargestellt. Ihre polarographische Reduktion in *N,N*-Dimethylformamid mit Et_4NClO_4 wurde geprüft und diskutiert. Ein Reduktionsmechanismus wird angegeben. Von **2a-b** ausgehend wurden die Verbindungen **3a-b** durch die präp. elektrochemische Reduktion synthetisiert.

In our previous work[1] we found that some substituted *N,N'*-diacyl-*p*-phenylenediamines have antifungal and antiaflatoxigenic activity. The present work reports the synthesis of some *N,N'*-diacyl-*p*-phenylenediamines by using chemical and electrochemical methods.

Compounds **2a-c** exhibit a polarographic activity in *N,N*-dimethylformamide and in a mixture of *N,N*-DMFA/H_2O (ratio 3:1) with 0.1 mol of tetraethylammonium perchlorate as the supporting electrolyte. We attempted to synthesize *N,N'*-diacyl-*p*-phenylenediamines (**3**) by means of preparative electrochemical treatment for reduction of the halogen atoms[2]. Compound **3a** was synthetized by electrochemical reduction at controlled potential of **2a** on the mercury cathode. The reduction of compound **2b** to **3b** was performed in an electrochemical procedure at constant current density on the mercury cathode predominantly with electrochemically generated tetraethylammonium amalgam[3]. Preparative electrochemical reduction of compound **2c** failed.

Experimental Part

Melting points: uncorrected.- IR-spectra: Perkin Elmer Infracord, Model 137, KBr.- UV-spectra: Perkin Elmer UV/VIS Model 124 spectrometer, EtOH.- Polarograms: Polariter PO4-Polarograph (Radiometer, Copenhagen). Saturated solutions of compounds **2a-c** were recorded in *N,N*-DMFA with 0.1 mol Et_4NClO_4 *vs.* SCE at 25°C.



Scheme

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Polarographic Investigation

In many cases the reduction of an organic halide at a mercury cathode involves initial addition of an electron to give a radical anion, which decomposes with fragmentation of the carbon-halogen atom to a σ-radical and halid anion. All three polarograms exhibit two polarographic waves (*Fig. 1*).

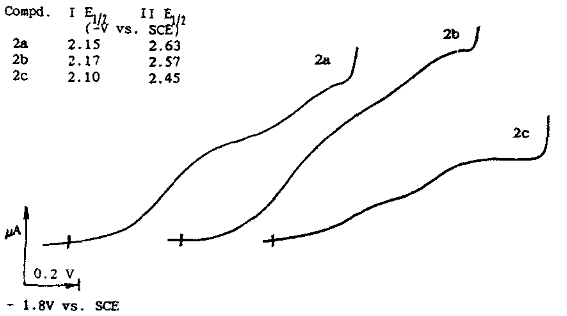

Fig. 1: Polarograms of saturated solutions of compounds **2a-c** in *N,N*-DMFA with 0.1 M Et_4NClO_4 at 25°C

In compound **2c** the ratio of polarographic waves hights is theoretically 1:1. The first wave corresponds to the one-electron reduction to its radical anion and the second wave results from the reduction of σ-radical to the carbanion according to the next step:

$$ArBr \xrightarrow{+e^-} ArBr^{\cdot -} \xrightarrow[-Br^-]{k} Ar^{\cdot} \xrightarrow{+e^-} Ar^- \xrightarrow{+H^+} Ar$$

A two-step electrochemical reduction mechanism of halogen atom(s) is valid for all three molecules **2a-c**. By comparison of their polarographic curves it can be concluded that, on the polarogram of molecule **2a** with one bromo and two chloro atoms the first polarographic wave corresponds to the reduction with three electrons and the second step is the reduction of the formed triradical with three electrons to the tricarbanion. The half-wave potentials of **2a** and **2b** exhibit a very small difference. It can be said that in molecule **2a** the bromo- and chloro-atoms are reduced at practically the same half-wave potentials. In molecules **2a-b** the hight of the second wave is smaller than that of the first wave. This could be explained by the relative stability of the radical anions formed in the first step and a smaller amount of radicals to be reduced with the next electron(s). It is not excluded that free radicals react in a concurrent reaction with the solvent hydrogen.

1-Bromo-2,5-bis(3-chloropropionylamino)-3,4,6-trimethylbenzene (**2a**)

1.5 g (6.55 mmol) of freshly prepared[4] 2-bromo-3,5,6-trimethyl-1,4-pehnylenediamine (**1**) was suspended in 30 ml 5% KOH, cooled in an ice bath with stirring on a magnetic stirrer, and 5 ml of 3-chloropropionyl chloride were added. After stirring for 2 h, the precipitate was filtered off and washed with water. The resulting solid was triturated twice with 50 ml ethanol and filtered off, yield 1.8 g (67%). After two recrystallizations from ethanol m.p. 315°C (decomp.).- $C_{15}H_{19}BrCl_2N_2O_2$ (410.2) Calcd. C 43.9 H 4.7 N 6.8 Br 19.5 Cl 17.3 Found C 44.0 H 5.0 N 6.8 Br 19.2 Cl 17.0.- IR: 3420; 3250 (NH); 3020-2920 (CH); 1658 (CO); 1530; 1300 (CN,NH); 705 (NH) cm^{-1}.- UV: λ max = 210 nm (very slightly soluble).- Polarographic half-wave potentials: $E_{1/2}$ = -2.15; -2.63 V *vs.* SCE.

1,4-Bis(acetylamino)-2-bromo-3,5,6-trimethylbenzene (**2b**)

A stirred solution of 1.5 g (6.55 mmol) of **1** in 50 ml 5% HCl was brought to slight turbidity by dropwise addition of 5% NaOH and the turbidity was then removed by a few drops of 5% HCl. The solution was cooled in an ice bath and under stirring 15 ml of acetic anhydride were added drop by drop, followed immediately by the addition of a solution of sodium acetate in water (20 g in 25 ml). After stirring for 2 h, the crude acetylated product **2b** was filtered off and washed with water and hot ethanol, yield 1.48 g (72%). After two recrystallizations from ethanol m.p. 300°C (decomp.).- $C_{13}H_{17}BrN_2O_2$ (313.2) Calcd. C 49.9 H 5.5 N 9.0 Br 25.5 Found C 49.9 H 5.7 N 8.9 Br 25.7.- IR: 3500; 3290 (NH); 3080-2920 (CH); 1660 (CO); 1530; 1280 (CN,NH); 725 (NH) cm^{-1}.- UV: λ max (lg ε) = 209 nm (4.88).- Polarographic half-wave potentials: $E_{1/2}$ = -2.17; -2.57 V *vs.* SCE.

1,4-Bis(benzoylamino)-2-bromo-3,5,6-trimethylbenzene (**2c**)

The reaction of 1.5 g (6.55 mmol) of **1** in 30 ml 5% KOH with 5 ml benzoyl chloride was performed as described for **2a**. The obtained solid was filtered, washed with water and hot ethanol, yield 2.0 g (70%). Recrystallized twice from ethanol m.p. 330°C (decomp.).- $C_{23}H_{21}BrN_2O_2$ (437.4) Calcd. C 63.2 H 4.8 N 6.4 Br 18.3 Found C 63.1 H 4.9 N 6.6 Br 18.0.- IR: 3400; 3290 (NH); 3080-2850 (CH); 1640 (CO); 1525; 1285 (CN,NH); 710 (NH); 1600; 1580; 1480; 710; 690 (benzene) cm^{-1}.- UV: λ max = 206; 224 nm (very slightly soluble).- Polarographic half-wave potentials: $E_{1/2}$ = -2.10; -2.45 V *vs.* SCE.

1,2,4-Trimethyl-3,6-bis(propionylamino)benzene (**3a**)

The prep. electrolysis was performed in a 250 ml jacketed cell with a ceramic diaphragm for separating the cathodic from the anodic compartment; the cathode was a mercury pool of 0.528 dm^2 area and the anode was a platinum spiral. A saturated calomel reference electrode was connected to the cathode compartment through a *Luggin* capillary. The catholyte (150 ml) and the anolyte (50 ml) were made up of *N,N*-DMFA/H_2O (3:1) with 0.1 mol Et_4NClO_4. The catholyte with 2.0 g (4.88 mmol) of **2a** was stirred, thermostated to 40°C, blowed out with N_2 and then the reduction was carried out at a controlled potential of -2.9 V *vs.* SCE. The electrolysis was completed and stopped when the current dropped from 0.60 to 0.01 A. The product was extracted from the catholyte with chloroform. The chloroform extract was dried (K_2CO_3), filtered, and destilled at reduced pressure to dryness. The product was triturated with ether and filtered off, yield 0.84 g (70%). Recrystallization from ethanol m.p. 322-325°C (decomp.).- $C_{15}H_{22}N_2O_2$ (262.4) Calcd. C 68.7 H 8.5 N 10.7 Found C 68.4 H 8.7 N 11.0.- IR: 3480; 3300 (NH); 3000-2900 (CH); 1660 (CO); 1540; 1280 (CN,NH); 737 (NH); 865 (CH aromatic) cm^{-1}.- UV: λ max (lg ε) = 209 (4.48), 235 nm (4.00).

1,4-Bis(acetylamino)-2,3,5-trimethylbenzene (**3b**)

The electrolysis was performed in the electrolytic cell on the mercury cathode, with the same catholyte (150 ml), anolyte (50 ml) and platinum anode and at 40°C as above. The catholyte with 2.0 g (6.40 mmol) of **2b** was electrolysed at constant current density of 2 A (3.8 A/cm^2). During the electrolysis the tetraethylammonium amalgam was generated. The electrolysis was stopped after 3 h. Next day, the reduced product was precipitated as a white powder, then filtered off and washed with water and ethanol, yield 1.3 g (80%). After recrystallization from ethanol m.p. 320-321°C (m.p. [5]: 310-310.5°C). Aromatic CH absorption is found in the IR-spectrum at 865 cm^{-1}.

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[Ph118]