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# Studies on the Oxidative S<sub>N</sub>H Amination of Aromatic Nitro Compounds

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Few examples of oxidative  $S_NH$  aminations (substitutions of aromatic H atoms by N-nucleophiles) [1] are described in literature. R. Huisgen obtained low yields of 2-piperidino nitrobenzene by reaction of lithium piperidide with nitrobenzene in ether [2]. F. W. Bergstrom studied the reaction of nitrobenzene with sodium and potassium diphenylamide in liquid ammonia and got about 50 % of 4-nitro triphenylamine [3]. S. S. Gandhi found that 4-nitro benzophenone reacts with potassium amide in liquid ammonia forming 3-amino-4-nitro benzophenone in moderate yield [4]. M. K. Stern obtained 4-nitro diphenylamine from aniline and nitrobenzene in presence of tetramethylammonium hydroxide [5].

We began our studies with an attempt to prepare 2,4-dinitro N,N-dimethylaniline from 1,3-dinitro-benzene and dimethylamine in dimethylformamide in presence of strong bases. In presence of potassium t-butoxide only about 5% of the desired product were found. Besides, 20 to 35% of 2,4-dinitrophenol (always formed if t-BuOK reacts with 1,3-dinitrobenzene [6–8]) were detected. Unexpectedly, we also found up to 20% 2,4-dinitro N-methylaniline. This product is formed by reaction of 2,4-dinitro N,N-dimethylaniline with t-BuOK under the conditions used. In independent experiments we showed that 2,4-dinitro N,N-dimethylaniline reacts with t-BuOK in DMF at 0°C forming about 3% 2,4-dinitro N-methylaniline and about 35% 2,4-dinitrophenol.

Because of the low conversions obtained in the reaction of 1,3-dinitrobenzene with dimethylamine in presence of t-BuOK, we further used the far more basic sodium hydride which forms the corresponding amide anion with dimethylamine in a preliminary reaction. Unexpectedly, we could not detect 2,4-dinitro N,N-dimethylaniline. Products were about 10 % of 3,3'-dinitro-diphenylamine, about 10 % of 3,3'-dinitro azoxybenzene and 3 to 10 % 3-nitro aniline. The formation of these compounds can be explained if sodium dimethylamide does not act as a nucleophile but as a reducing agent forming 3-nitro aniline and 3,3'-dinitro azoxybenzene from 1,3-dinitrobenzene. In a second step the 3-nitro-aniline reacts with excess 1,3-dinitrobenzene substituting one nitro group and giving 3,3'-dinitro diphenylamine. If this explanation is correct then 3,3'-dinitro diphenylamine must be formed in relatively good yields from 3-nitroaniline and 1,3dinitrobenzene in DMF and in the presence of sodium hydride. Actually, 2,4,3'-trinitro diphenylamine, the product of a S<sub>N</sub>H substitution (Formula Scheme 1), was formed in a yield of about 60% (Table 1). The only by-product identified was 3,3'-dinitro azoxybenzene, a reduction product of





1,3-dinitrobenzene, probably formed during the oxidation of the intermediate Jackson-Meisenheimer complex by excess 1,3-dinitrobenzene.

Other derivatives of aniline also attacked 1,3-dinitrobenzene in DMF after preliminary formation of the corresponding sodium anilides by reaction with sodium hydride. We obtained the corresponding derivatives of 2,4-dinitro diphenylamine in yields of about 50 % (Table 1). Instead of 1,3-dinitrobenzene 3-nitro chlorobenzene and 1-nitronaphthalene can also be used as aromatic nitro compounds. From 3-nitro chlorobenzene and aniline 2-chloro-4-nitro diphenylamine was formed in 30 to 70% yield; from 1-nitronaphthalene we obtained about 13 % 1-nitro-2-anilino and 45 % 1-nitro-4-anilino naphthalene. In the case of 3-nitro chlorobenzene the sodium anilide attacked not only the aromatic nucleus but also the nitro group forming 3-chloro azobenzene in a yield of 5-15 %. The reaction of anilines with aromatic nitro compounds forming the corresponding azobenzene derivatives is already known from the work of M. Martynoff [9].

Our results concerning the formation of diphenylamine derivatives by reaction of aromatic nitro compounds with sodium anilides in dimethyl formamide are comparable with those of F. W. Bergstrom [3] and of M. K. Stern [5]. The yields of about 50 % are of interest for synthetic chemistry. In most cases it is uncertain how the intermediate Jackson-Meisenheimer complexes are oxidized to the final products, but one must assume that the nitro compounds in the reaction mixtures act as oxidizing agents and are themselves reduced to azoxy or even azo compounds which could be identified only in a few cases. We avoided the use of molecular oxygen as oxidant because in earlier studies we had found that in presence of oxygen phenols are always formed from nitro aromatics and strong bases. Probably, oxygen reacts with the strong bases or the Jackson-Meisenheimer complexes forming the strong nucleophilic oxygen radical anion or the hydroperoxy anion.

starting compounds (mmol) <sup>a)</sup>			conversion <sup>b)</sup>	vield of final products (%) <sup>c)</sup>	
nitro compound	aniline derivative	NaH	%	Ă	B
1,3-DNB	3-NO <sub>2</sub>				<u></u>
(20)	(20)	(20)	89	61 E	4 F
(20)	(20)	(20)	89	68 E	4 F
1,3-DNB	Н				
(20)	(20)	(20)	9	42 G	traces F
(20)	(60)	(60)	72	75 G	7 F
1,3-DNB	2-Cl				
(20)	(60)	(60)	84	58 H	traces F
(20)	(60)	(60)	86	64 H	traces F
1,3-DNB	3-Cl				
(20)	(60)	(60)	94	44 I	traces F
(20)	(60)	(60)	94	43 I	traces F
1,3-DNB	4-Cl				
(20)	(60)	(60)	95	40 K	traces F
(20)	(60)	(60)	95	50 K	traces F
1-NH	Н				
(20)	(60)	(60)	100	13 L + 42 M	_
(20)	(60)	(60)	100	13 L + 47 M	-
3-NCB	Н				
(20)	(60)	(60)	48	77 N	7 O
(20)	(60)	(60)	57	61 N	5 O
(20)	(200)	(200)	89	32 N	19 O
(20)	(200)	(200)	86	29 N	15 O

Table 1 Reaction of aromatic nitro compounds with aniline derivatives in DMF in presence of NaH (in the preliminary stage formation of the corresponding sodium anilide from the aniline derivative and NaH in DMF). Temperature 0°C; DMF: 20 ml

<sup>a)</sup> 1,3-DNB: 1,3-dinitrobenzene; 1-NN: 1-nitronaphthalene; 3-NCB: 3-nitro chlorobenzene. Aniline derivatives: H: aniline; 3-NO<sub>2</sub> aniline; x-Cl: x-chloro aniline

b) related to the starting nitro compound

c) related to the starting nitro compound consumed

A: derivative of diphenylamine; B: azoxy or azo compound derived from the starting nitro compound; E: 2,4,3'-trinitro diphenylamine; F: 3,3'-dinitro azoxybenzene; G: 2,4-dinitro diphenylamine; H: 2,4-dinitro-2'-chloro diphenylamine; I: 2,4-dinitro-3'-chloro diphenylamine; K: 2,4-dinitro-4'-chloro diphenylamine; L: 1-nitro-2-anilino naphthalene; M: 1-nitro-4-anilino naphthalene; N: 2-chloro-4-nitro diphenylamine; O: 3-chloro azobenzene

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# Experimental

### Reaction of Dinitrobenzene with Dimethylamine

20 mmol dimethylamine and 20–60 mmol t-BuOK or NaH were given into 10 ml DMF at 0 °C. After 1 h stirring a solution of 1,3-dinitrobenzene in 10 ml DMF was added under vigorous stirring at temperatures between -20 and +20 °C. After 2 h the reaction mixture was poured on 100 g ice and the acidity was adjusted to pH = 5 by addition of hydrochloric acid. The mixture was extracted with methylene chloride; the organic phase was dried over Na<sub>2</sub>SO<sub>4</sub> and analyzed by thin-layer chromatography using Silufol plates (Fa. Kavalier, Votice) and toluene/acetone (90:10). On the basis of the results the conditions of the column chromatography were chosen. The residue remaining after the removal of the methylene chloride was weighed, the main part was dissolved in toluene/acetone (90:10) and given on a chromatographic column (diameter: 2.2 cm; length: 70 cm) filled with Kieselgel 60 (0.063–0.20 mm; Merck). As eluent a mixture of toluene/acetone (90:10) was used. The compounds were eluted in the order of their thin-layer  $R_f$ -values. The tarry compounds remained in the column. The eluted fractions were investigated by thin-layer chromatography. From the pure fractions the solvent was removed, the residues were recrystallized from ethanol and characterized by their melting points, n.m.r. spectra and elementary analyses. Quantitative analysis was performed by HPLC (benzophenone as internal standard; acetonitrile/H<sub>2</sub>O (62.5 : 37.5); Lichrospher 100-RP 18; UV detection (254 nm)). Most of the reaction products were prepared independently using methods known from literature: 2,4-dinitro-N,N-dimethylaniline [10]; 2,4-dinitro Nmethylaniline [11]; 3,3'-dinitro diphenylamine [12].

# Reaction of Aromatic Nitro Compounds with Aniline Derivatives

Into a 50 ml glass reactor, equipped with a heating/cooling jacket, a magnetic stirrer and a dropping funnel, 10 ml DMF and the aniline derivative were given at  $0^{\circ}C$  (amounts see Table 1). The sodium hydride was cautiously added in small portions. The mixture was stirred for 2 h, during which time

the anilide corresponding to the starting aniline was formed and gaseous hydrogen was evolved. Then a solution of the aromatic nitro compound in 10 ml DMF was added dropwise at 0 °C. After 2 h stirring at 0 °C the reaction mixture was poured on 100 g ice, and the resulting aqueous suspension was adjusted to pH = 5 by addition of hydrochloric acid. The further work-up took place as in the reaction of 1,3-dinitrobenzene with dimethylamine. Most of the reaction products were also synthesized independently using methods known from literature: 2,4,3'-trinitro diphenylamine [13]; 2,4-dinitro diphenylamine [14], 2,4-dinitro-3'-chloro diphenylamine [15]; 2,4-dinitro-4'-chloro diphenylamine [15].

#### Identification of the Reaction Products Isolated

In all cases when authentic samples had been synthesized the reaction products were identified by comparison of the melting point, the HPLC retention times, the TLC  $R_f$ -values and the <sup>13</sup>C-n.m.r. spectra with those of the authentic compounds. 3-Nitroaniline (F: 112 °C [16]), 3,3'-dinitro azoxybenzene (F: 142-144 °C [17]), 1-nitro-2-anilino naphthalene (F: 109–110 °C [18]), 1-nitro-4-anilino naphthalene (F: 152–153 °C [19]), 2-chloro-4-nitro diphenylamine (F: 113 °C [20]) and 3-chloro-azobenzene (F: 66 °C [21]) were identified by their melting points, their elementary analyses and their <sup>13</sup>C-n.m.r. spectra.

## <sup>13</sup>C-n.m.r. Spectra

The <sup>13</sup>C-n.m.r. spectra were taken with the Bruker apparatus HX 90R (20 MHz) or with the Jeol apparatus JNM-FX-200 (50.3 MHz) using deuterochloroform or acetone- $d_6$  as the solvents and hexamethyl disiloxane as the internal standard.

The expected chemical shifts were calculated from those of the corresponding mother compounds and the increments of the substituents [22]. The chemical shifts of the mother compounds were taken from literature: benzene [22]; diphenylamine [23]; dinitro aniline [24]; 1-nitro naphthalene [25]; 3chloro nitrobenzo [26]; azoxybenzene [27]; azobenzene [28]. In all cases the chemical shifts calculated corresponded to those found.

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