Journal of Fluorine Chemistry, 4 (1974) 19–23

2-FLUORO-3-NITROANILINE AND 2-FLUORO-1,3-PHENYLENEDIAMINE

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(Received April 26, 1973)

SUMMARY

2-Fluoro-3-nitroaniline (I), erroneously reported in the literature, has been synthesized by partial reduction of 2-fluoro-1,3-dinitrobenzene (II). Total reduction of (II) gives 2-fluoro-1,3-phenylenediamine (V). The NMR parameters of 1-fluoro-2,4-dinitrobenzene (IV), 2-fluoro-5-nitroaniline (III) and compounds (I), (II) and (V) are reported.

INTRODUCTION

In 1969, a synthesis of 2-fluoro-3-nitroaniline (I) by partial reduction of 2-fluoro-1,3-dinitrobenzene (II) was described[1]. The 2-fluoro-1,3-dinitrobenzene was prepared by two independent processes differing from the methods used previously[2–4].

One of the two preparations started from fluorobenzene. This was sulfonated, the sulfonic acid was—without isolation—nitrated and the dinitro compound was desulfonated, all in one reaction flask. The resulting fluorodinitrobenzene was described as a "yellow steam-volatile oil, b.p. 288–290 °C dec.". The same compound was reported to be obtained by halogen exchange and desulfonation of 4-chloro-3,5-dinitrobenzenesulfonic acid[1]. Stannous chloride reduction of the fluorodinitrobenzene obtained by these two procedures gave a fluoronitroaniline, m.p. 99–100 °C, claimed to be 2-fluoro-3-nitroaniline[1].

RESULTS AND DISCUSSION

In an attempt to synthesize 2-fluoro-3-nitroaniline, we prepared 2-fluoro-1,3-dinitrobenzene by halogen exchange from 2-chloro-1,3-dinitrobenzene[3]. A crystalline material, m.p. 60–62 °C, was obtained in agreement with the literature (m.p. 60–61 °C[4], 60–63 °C[2] and 62–63 °C[3]). Its partial reduction with stannous chloride or iron gave a fluoronitroaniline of melting point 115–116.5 °C, different from the one described previously (NMR spectra).

These findings increased our doubts about the correctness of the structure of the compound claimed as 2-fluoro-3-nitroaniline in the literature[1]. We therefore duplicated the experiments leading to the alleged compound and obtained a yellow oil, b.p. 287–288 °C (101–106 °C/0.02–0.025 mmHg), whose reduction with stannous chloride gave fluoronitroaniline, m.p. 99–101 °C (CCl_4). This melting point agrees with that of an isomer, 2-fluoro-5-nitroaniline (III), m.p. 100–101 °C (CCl_4), 102 °C (H_2O), obtainable by stannous chloride reduction from 1-fluoro-2,4-dinitrobenzene (IV)[5]. The discrepancies between the quoted publication and our findings can be interpreted as follows:

Instead of the usual and expected *para*-sulfonation of the benzene nucleus, the sulfonation of fluorobenzene took place *ortho* to fluorine*, and the two nitro groups in the subsequent nitration entered in the *para* and the other *ortho* position. Desulfonation gave 1-fluoro-2,4-dinitrobenzene (IV) instead of the anticipated 2-fluoro-1,3-dinitrobenzene (II). Partial reduction of 1-fluoro-2,4-dinitrobenzene with stannous chloride affects selectively the nitro group *ortho* to fluoride rather than the one in the *para* position[5]. It is not surprising that the authors of this report made an erroneous assumption concerning the orientation of the sulfonation reaction; what is strange, however, is that they did not note the discrepancies between the properties of their alleged compound (II) and authentic (II) as described previously[2–4].

In this communication, we report the synthesis of authentic 2-fluoro-3-nitroaniline (I) and of 2-fluoro-1,3-phenylenediamine (V). Both compounds were prepared by reduction of 2-fluoro-1,3-dinitrobenzene (II). Since stannous chloride reduction did not give satisfactory results, the reduction was worked out with iron using inverse addition of one equivalent of iron, *i.e.*, addition of iron to the nitro compound. When an excess of iron was used, 2-fluoro-1,3-phenylenediamine (V) was obtained. Better yields of this compound were achieved by catalytic hydrogenation.

The NMR parameters for compounds (I)–(V) are reported in Table 1. Proton spectra were obtained at 100 MHz and fluorine spectra were obtained at 94 MHz on a JEOL PFT-100 spectrometer. All of the analyses were carried out by a computer-assisted iterative least-squares line-matching procedure. Coupling constants should be accurate to ±0.2 Hz. The coupling constants found for (IV) in deuterochloroform are consistent with literature values in other solvents[7], and the chemical shifts reported in Table 1 for (III) and (IV) are also in good agreement with literatures values[8,9]. The small deviations are no doubt caused by small

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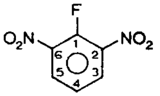
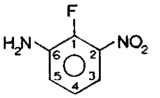
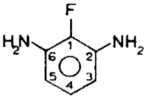
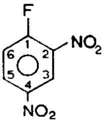
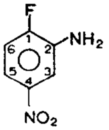
* Preferential electrophilic substitution *ortho* to fluorine is not uncommon. In fact, it is one of the supports of the hypothesis of p–π interaction of fluorine and the benzene nucleus (see ref. 6).

TABLE 1

PHYSICAL CONSTANTS OF SOME FLUORONITROBENZENES AND FLUOROANILINES

Compound	Formula	M.p. (b.p.)/°C	NMR spectral data[a]			
			Chemical shifts[b]/ppm		Coupling constants/Hz	
(II)		60–62[c] (297–299)	δ_3 = 8.41 δ_4 = 7.62	Φ = 37.0	$J(1,3)$ = 6.4 $J(1,4)$ = −1.7	$J(3,4)$ = 8.5
(I)		114–115.5[d] 115–116.5[e]	$\delta(NH_2)$ = 4.0 δ_3 = 7.35 (8.34) δ_4 = 7.03 (7.58) δ_5 = 7.03 (8.04)	Φ = 20.4 (−51.8)	$J(1,3)$ = 6.4 (7.0) $J(1,4)$ = −1.9 (−1.9) $J(1,5)$ = 7.8 (6.3)	$J(3,4)$ = 8.2 (8.6) $J(3,5)$ = 1.6 (1.7) $J(4,5)$ = 8.1 (8.4)
(V)		55–56	$\delta(NH_2)$ = 3.6 δ_3 = 6.21 (7.86) δ_4 = 6.74 (7.56)	Φ = 3.9 (−57.0)	$J(1,3)$ = 8.0 (7.2) $J(1,4)$ = −1.5 (−1.9)	$J(3,4)$ = 8.1 (8.3)
(IV)		(287–288)[f]	δ_3 = 9.01 δ_5 = 8.72 δ_6 = 7.78	Φ = 56.2	$J(1,3)$ = 6.5 $J(1,5)$ = 3.7 $J(1,6)$ = 9.9	$J(3,5)$ = 2.9 $J(3,6)$ = 0.0 $J(5,6)$ = 9.4
(III)		99–101[g]	$\delta(NH_2)$ = 4.1 δ_3 = 7.74 (8.70) δ_5 = 7.65 (8.55) δ_6 = 7.14 (7.59)	Φ = 37.0 (−36.3)	$J(1,3)$ = 7.5 (6.4) $J(1,5)$ = 4.1 (4.3) $J(1,6)$ = 10.1 (9.0)	$J(3,5)$ = 2.8 (2.7) $J(3,6)$ = 0.0 (0.0) $J(5,6)$ = 9.5 (9.4)

[a] Spectra were determined in deuterochloroform, and also trifluoroacetic acid in the case of compounds (I), (III) and (V). The parameters for trifluoroacetic acid are listed in parentheses. All concentrations were approximately 0.03 g per 0.5 cm^3.

[b] Proton shifts are downfield from TMS. Fluorine shifts are downfield from hexafluorobenzene ($CDCl_3$ runs) or upfield from trifluoroacetic acid (TFA runs).

[c] Literature values: 60–61 °C[4], 60–63 °C[2] and 62–63 °C[3].

[d] Melting point of the compound from $SnCl_2$ reduction.

[e] Melting point of the compound from Fe reduction.

[f] Literature value: m.p. 25.8 °C, b.p. 296 °C[11].

[g] Literature value: 102 °C[5].

variations in concentration. Interestingly, the spectra of compounds (I) and (III) approach first-order behavior when run in trifluoroacetic acid, for protonation of the amino group causes relatively large downfield shifts of the protons *ortho* and *para* to amino[10]. The chemical shift and coupling constant data confirm conclusively the correctness of the assigned structures for compounds (I)-(V).

EXPERIMENTAL

2-Fluoro-3-nitroaniline

(a) By reduction with stannous chloride

2-Fluoro-1,3-dinitrobenzene (II) prepared from 2-chloro-1,3-dinitrobenzene and potassium fluoride in DMSO[3] (1.8 g, 0.01 mol) was added to a solution consisting of 7 g (0.03 mol) of stannous chloride dihydrate in 16 cm^3 of 20% hydrochloric acid and 12 cm^3 of ethanol. The temperature rose spontaneously from 25 °C to 58 °C, all material dissolved and the solution turned yellow. After refluxing for 5 min, the dark-brown solution was cooled, made alkaline with 10 cm^3 of 50% sodium hydroxide, filtered and the filtrate extracted with ether. Evaporation of the extract gave 0.5 g (33%) of crude 2-fluoro-3-nitroaniline, m.p. 114–115.5 °C (CCl_4); mixed m.p. with compound (III), 76–80 °C.

(b) By reduction with iron

A mixture consisting of 9.3 g (0.05 mol) of 2-fluoro-1,3-dinitrobenzene, 50 cm^3 of water, 70 cm^3 of ethanol and 3 cm^3 of conc. hydrochloric acid was stirred and heated to reflux. Finely powdered iron (6 g, 0.011 mol) was added in small portions over a period of 40 min. Stirring and refluxing was continued for another 20 min. The pH value of the reaction mixture was 3 at the beginning and 5–6 at the end. The solution was decanted from iron oxides, the ethanol removed under reduced pressure, the residue extracted with 3 × 100 cm^3 portions of ether and the ethereal extract evaporated. The residue containing some water was dissolved in 50 cm^3 of chloroform, the small aqueous layer separated and the chloroform layer dried and evaporated to dryness *in vacuo*. The brown-black residue (6.4 g) was chromatographed over 170 g of silica gel. Elution with benzene (2300 cm^3) gave 4.4 g (56.4%) of golden-yellow crystals, m.p. 113.5–115 °C. Recrystallization from carbon tetrachloride afforded 3.1 g (40%) of pure 2-fluoro-3-nitroaniline, m.p. 115–116.5 °C.

2-Fluoro-1,3-phenylenediamine (V)

(a) By reduction with iron

A mixture consisting of 1.6 g (0.0086 mol) of 2-fluoro-1,3-dinitrobenzene, 10 cm^3 of water, 15 cm^3 of ethanol, 1 cm^3 of conc. hydrochloric acid and 3 g (0.054 mol) of finely powdered iron was stirred and refluxed for 1.75 h, and then stirred at room temperature for 15 h. The unreacted iron (0.4 g) and a sludge of iron oxides was filtered with suction, and the dark-brown filtrate was extracted with 3 × 20 cm^3 portions of ether. The extract was evaporated to dryness *in vacuo* at a temperature below 40 °C to give 0.6 g (55%) of a dark-brown oil which crystallized in a refrigerator. Recrystallization from 6 cm^3 of carbon tetrachloride gave 0.35 g (32%) of almost white felt-like needles of 2-fluoro-1,3-phenylenediamine, m.p. 55–56 °C.

(b) By catalytic hydrogenation

A solution consisting of 0.6 g (0.0032 mol) of 2-fluoro-1,3-dinitrobenzene in 20 cm^3 of absolute ethanol was hydrogenated over 0.25 g of 10% palladium on activated charcoal for 15 min (theoretical consumption of hydrogen). After filtering off the catalyst, the filtrate was evaporated to dryness *in vacuo* at a temperature below 40 °C. Cooling and seeding of the residual oil gave 0.3 g (43%) of solid, almost white, crystals which after crystallization from carbon tetrachloride afforded 0.2 g (49%) of pure 2-fluoro-1,3-phenylenediamine, m.p. 55–56 °C, identical with the product obtained by reduction with iron.

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