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Disubstitution on hexafluorobenzene with formanilides

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Abstract

Nucleophilic attack on hexafluorobenzene by sodium formanilides gave *N,N'*-diphenyl-2,3,5,6-tetrafluorophenylene-1,4-diamine as the main product at elevated temperature and *N,N'*-diformyl-*N,N'*-diphenyl-2,3,5,6-tetrafluorophenylene-1,4-diamine as the main compound at ambient temperature. Metallation of formanilide with lithium hydroxide instead of sodium hydride gave only 2,3,4,5,6-pentafluorodiphenylamine.

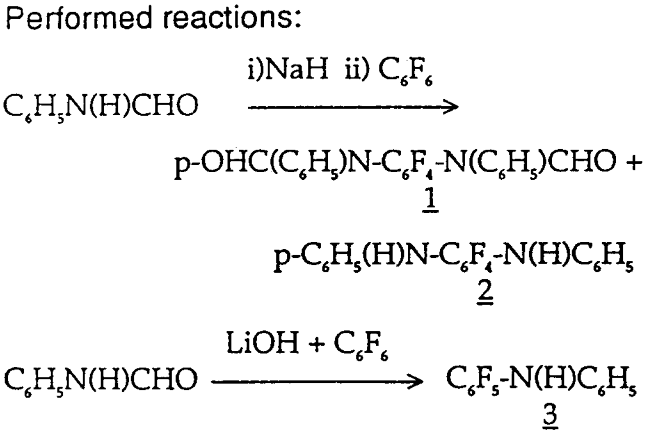
Keywords: Disubstitution; Fluorobenzene; Formanilides

1. Introduction

It has previously been shown that two-stage nucleophilic attack by anilides on hexafluorobenzene causes replacement of the fluorines in the para-position [1–4]. The disubstitution reactions with anilides gave only the para-substituted compound in low yield both at 90 °C [2] and at 190–200 °C [1]. The purpose of the present investigation was to test the hypothesis that formanilides as nucleophiles would give a better entry to 1,4-disubstitution on hexafluorobenzene with formation of the corresponding *N,N'*-diphenyl-2,3,5,6-tetrafluorophenylene-1,4-diamine after hydrolysis of the formamides.

2. Results and discussion

Since no reaction occurs between formanilide and hexafluorobenzene under normal conditions, metallation of the formanilide was necessary. Sodium hydride and lithium hydroxide were employed as metallation reagents. The main reaction products obtained with sodium hydride depended upon the solvent and reaction temperature. In THF or THF/DMSO at room temperature the main compound was *N,N'*-diformyl-*N,N'*-diphenyl-2,3,5,6-tetrafluorophenylene-1,4-diamine (**1**) together with *N,N'*-diphenyl-2,3,5,6-tetrafluorophenylene-1,4-diamine (**2**). At elevated temperature in THF/DMF, DMF or THF/DMSO **2** was formed with only traces of **1**, if **1** was present at all. With lithium hydroxide as the metallation reagent only 2,3,4,5,6-pentafluorodiphenylamine (**3**) was formed in a low yield.



Performed reactions:

$$C_6H_5N(H)CHO \xrightarrow{\text{i)NaH ii) } C_6F_6} \underset{1}{\text{p-}OHC(C_6H_5)N\text{-}C_6F_4\text{-}N(C_6H_5)CHO} + \underset{2}{\text{p-}C_6H_5(H)N\text{-}C_6F_4\text{-}N(H)C_6H_5}$$

$$C_6H_5N(H)CHO \xrightarrow{LiOH + C_6F_6} \underset{3}{C_6F_5\text{-}N(H)C_6H_5}$$

From these reactions with sodium formanilide no 2,3,4,5,6-pentafluorodiphenylformamide or amine was isolated. This finding indicates a faster reaction of sodium formanilide with 2,3,4,5,6-pentafluorodiphenylformamide than with hexafluorobenzene as only disubstituted compounds could be found in the reaction mixture.

Mass spectra of the formanilides concur with the normal pattern [M–CO] followed by [(M–CO)–CO] [5,6].

It has previously been shown that the chemical shifts of formanilides in $CDCl_3$ solution are concentration dependent. However, the shift differences seem to be small [7–9]. NMR analyses at different concentrations were not performed, as the ^1H NMR spectra of compound **1** gave the same chemical shifts at two arbitrarily chosen concentrations. The ^1H NMR spectrum of compound **1** in CD_2Cl_2 showed one strong –CHO singlet and a triplet. Based on previous findings [7,8] the –CHO singlet at the lowest field is interpreted to be due

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to the trans isomer, i.e. when the carbonyl and phenyl groups have a trans relationship to each other.

The ^{19}F NMR spectra of **1**, both in CD_2Cl_2 and THF-d_8, gave two multiplets of equal intensity, with a line-shape compatible with an asymmetrically para-disubstituted fluorobenzene, and two signals compatible with symmetrically para-disubstituted fluorobenzenes. This is interpreted as indicating the presence of the cis–trans, trans–trans and cis–cis isomers [6]. It is proposed that the trans–trans resonances lie to the low field of those of the cis–cis [6] isomer and that from the ^{19}F integration the ratio of trans–trans/cis–cis/cis–trans is 74:2:24 in CD_2Cl_2 at ambient temperature. The ^1H spectrum seems more complicated but is in reasonable agreement with the proposed structure and isomers. Compound **2** had a pale pink colour [1] when recrystallized. The colour darkened by leaving the compound dissolved, most probably as a result of oxidation. On standing, a sublimed sample [2] acquired a pale pink colour.

3. Experimental

NMR spectra were obtained with a Varian XL-300 (300 MHz proton frequency) spectrometer. ^1H chemical shifts are reported with reference to $SiMe_4$ and ^{19}F chemical shifts with respect to C_6F_6 with a reference line position at 163.0 ppm. Downfield shifts were positive. Mass spectroscopy data were obtained with a VG Micromass 7070F instrument with the data system VG 11-250J.

All reactions were performed under N_2. Reaction mixtures were hydrolysed, after adding ether (30 ml), by addition of 10% hydrogen chloride to give an acidic medium, extracted with ether, dried with anhydrous sodium sulphate, concentrated and chromatographed on silica (230–400 mesh) starting with light petroleum as the elution solvent. When no more could be eluted from the mixture, more and more ether was added to the eluent, ending with pure ether. Recrystallization, when necessary, was performed from a mixture of light petroleum (b.p. 40–60 °C) and ether.

3.1. Sodium formanilide in tetrahydrofuran

Sodium hydride (0.042 mole, 1.00 g in oil) was added slowly to a mixture of formanilide (0.042 mole, 5.09 g) in tetrahydrofuran (20 ml) on an ice/water bath. The mixture was stirred at ambient temperature over night to give a low viscosity, white mixture used in the following reactions.

3.1.1. In tetrahydrofuran/dimethylsulphoxide

I. Dimethylsulphoxide (20 ml) was added to the sodium anilide mixture placed on an ice/water bath and followed by the addition of hexafluorobenzene (0.02 mole, 3.72 g). A green mixture was formed. The ice/water bath was removed. A faint exothermic reaction took place after 20–30 min, and a clear, brown reaction mixture was formed. Work up next morning gave 2.14 g (28%) *N,N′*-diformyl-*N,N′*-diphenyl-2,3,5,6-tetrafluorophenylene-1,4-diamine (**1**) (nc), m.p. 229–229.5 °C, and 1.3 g (20%) *N,N′*-diphenyl-2,3,5,6-tetrafluorophenylene-1,4-diamine (**2**), m.p. 151–153 °C [1,2].

Found for **1**: *m/z*:(i.e. 70 eV) (% rel. int.): 390(3), 389(24), 388(100), 361(5), 360(22), 333(17), 332(86), 331(12), 312(7), 311(9), 310(3), 293(4), 292(17), 291(18), 267(3), 266(14), 265(3), 257(17), 255(15), 235(8), 220(10), 208(6), 166(12), 104(6), 77(87). High resolution: $C_{20}H_{12}F_4N_2O_2$ requires $M = 388.0835$. Found, 388.0855. NMR (CD_2Cl_2): δ (–CHO) 8.65 (s), 8, 42 (t). ^{19}F NMR (CD_2Cl_2): δ 19.65 (m), 15.93 (m) (amount 24%), 18.59 (small sideband at 18.64. In THF-d_8 only a singlet was present at 18.67) (amount 74%) and 16.96 (s) (amount 2%). IR in KBr: 1703 (s), 1593 (m), 1502 (s), 1492 (w), 1345 (m), 1271 (s), 1217 (s), 1003 (m), 973 (m), 875 (m), 768 (m), 709 (m), 696 (w), 643 (w), 599 (m), 522 (w).

II. Reaction mixture as in **I**. 1.5 h after addition of hexafluorobenzene the mixture was placed on a 95 °C bath for 2.5 h, cooled on an ice/water bath and hydrolysed with 40 ml 10% HCl. Work up gave 3.91 g (59%) *N,N′*-diphenyl-2,3,5,6-tetrafluorophenylene-1,4-diamine (**2**) [2].

3.1.2. In tetrahydrofuran/dimethylformamide

To the sodium formanilide mixture placed on an ice/water bath dimethyl-formamide (20 ml) and then hexafluorobenzene (0.02 mole, 3.72 g) were added whereupon the bath was removed. After 1 h the mixture was placed on a 95 °C bath for 4.5 h. Gas chromatography (GC) of the crude showed traces of *N,N′*-diformyl-*N,N′*-diphenyl-2,3,5,6-tetrafluorophenylene-1,4-diamine (**1**), together with *N,N′*-diphenyl-2,3,5,6-tetrafluorophenylene-1,4-diamine. Work up gave 1.87 g (28%) *N,N′*-diphenyl-2,3,5,6-tetrafluorophenylene-1,4-diamine (**2**) [2].

3.2. Sodium formanilide in dimethylformamide

Sodium formanilide was formed in dimethylformamide as described above for tetrahydrofuran. Next morning hexafluorobenzene (0.02 mole, 3.72 g) was added all at once to the sodium formanilide mixture placed on a tap-water bath. After 2 h the bath temperature was raised to 80 °C and held for 6 h. Work up gave 3.02 g (45%) *N,N′*-diphenyl-2,3,5,6-tetrafluorophenylene-1,4-diamine (**2**) [2].

3.3. Lithium hydroxide in tetrahydrofuran

Lithium hydroxide (1.5 g) was added during 30 min to a stirred mixture of formanilide (0.042 mole, 5.09 g) in tetrahydrofuran (20 ml) at ambient temperature. Next morning hexafluorobenzene (0.02 mole, 3.72 g) was added all at once. The yellow mixture was hydrolysed after being refluxed slowly for 24 h. GC analysis of the dried ether solution showed only two main compounds present, formanilide and 2,3,4,5,6-pentafluorodiphenylamine. After the solvent was stripped off, the mixture was chromatographed with light petroleum resulting in 1.0 g (19%) 2,3,4,5,6-pentafluorodiphenylamine (**3**) [1,2].

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