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Journal of Fluorine Chemistry 101 (2000) 65–67

JOURNAL OF FLUORINE CHEMISTRY

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Regioselective ortho-hydrodefluorination of pentafluorobenzoic acid by low-valent nickel complexes

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Received 14 June 1999; accepted 3 August 1999

Abstract

2,3,4,5-Tetrafluorobenzoic and 3,4,5-trifluorobenzoic acids were prepared in high yields by reaction of C_6F_5COOH with zinc in the presence of $NiCl_2$–2′-bipyridine (or 1,10-phenanthroline) complexes.

Keywords: Hydrodefluorination; Nickel complexes; Reductive defluorination

1. Introduction

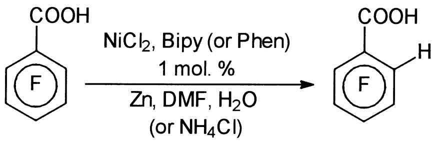
There are several methods of hydrodefluorination of pentafluorobenzoic acid **1**. Electrochemical reduction leads to the formation of 2,3,5,6-tetrafluorobenzoic acid **2** together with fluorine containing benzaldehydes and benzyl alcohols [1]. Action of sodium in liquid ammonia on acid **1** results in a complex mixture of fluorobenzoic acids $C_6H_nF_{5-n}COOH$ ($n = 0$–5) [2]. Reduction of **1** with zinc [2] or Zn(Cu) couple [3,4] proceeds more selectively and gives only acid **2**.

In contrast, the interaction of acid **1** with ytterbium(II) compounds yields mainly 2,3,4,5-tetrafluorobenzoic acid **3**. Indeed, a mixture of both acids **2** and **3** are obtained from C_6F_5COOH and ytterbium(II) iodide [5]. Regiospecific ortho-hydrodefluorination of **1** takes place under the action of *bis*(pentafluorophenyl)ytterbium or $Yb(Cp_2)$dme [6,7].

Recently we showed that hexa- and pentafluorobenzenes, octafluoronaphthalene and pentafluoropyridine react easily with zinc dust in the presence of $NiCl_2$–2,2′-bipyridine (Bipy) (or 1,10-phenanthroline (Phen)) to give the less fluorinated benzenes, naphthalenes and pyridines [8]. In the course of our systematic investigation, we studied the reactions of C_6F_5COX (X = OH, OC_2H_5, NH_2) with the above mentioned reductive system.

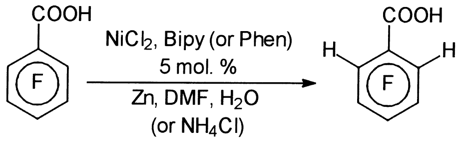
2. Results and discussion

Pentafluorobenzoic acid did not react with zinc dust or Zn–$NiCl_2$ (5 mol%) in aqueous DMF at 70°C (Table 1, entries 1,2). However, in the presence of in situ generated catalysts $NiCl_2$–Bipy (or phen) (1 mol%), 2,3,4,5-tetrafluorobenzoic acid was obtained in 83% yield (Table 1, entry 3).



1 **3**

Increased amount of catalyst (up to 5 mol%) and the reaction duration favoured the further removal of ortho-fluorine atoms (Table 1, entry 4). In this way, acid **4** was obtained in quantitative yield.



1 **4**

To study the reaction conditions, we investigated some factors which influenced the reaction routes. For instance, interaction of **1** with a reduced amount of zinc (2.3 eqv.) and $NiCl_2$–Bipy (1 mol%) resulted in ca. 10% conversion of the substrate within 2 h (Table 1, entry 5). Increasing the amount of catalyst to 5 mol% and the reaction duration to 4 h did not affect on the conversion of acid **1** (Table 1, entry 6).

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0022-1139/00/$ – see front matter
PII: S0022-1139(99)00181-5

Table 1
Reaction of C_6F_5COOH[a] with $NiCl_2$–Bipy (or Phen)–Zn in DMF

Entry	Catalyst		Proton source	Molecular ratio (**1** : Zn : H^+)	Temperature (°C)	Time (h)	Conversion of **1** (%)	Yield (g)	Product distribution (mol%)	
	Composition	Amount (mol%)							**3**	**4**
1	–	0	H_2O	1 : 10 : 56	70	24	∼0	2.1	–	–
2	$NiCl_2$	5	H_2O	1 : 10 : 56	70	24	∼2	2.0	–	–
3	$NiCl_2$–Bipy	1	H_2O	1 : 10 : 56	60	0.75	83	1.8	100	–
4	$NiCl_2$–Bipy	5	H_2O	1 : 10 : 56	60	6	100	1.5	–	100
5	$NiCl_2$–Phen	1	H_2O	1 : 2.3 : 56	70	1	9.5	1.7	100	–
6	$NiCl_2$–Phen	5	H_2O	1 : 2.3 : 56	70	4	9.7	1.5	100	–
7	$NiCl_2$–Phen	5	H_2O	1 : 2.3 : 56	50	4	63	1.68	95	5
8	$NiCl_2$–Phen	5	H_2O	1 : 3 : 56	50	6	83	1.7	77	23
9	$NiCl_2$–Phen	5	NH_4Cl	1 : 3 : 2	50	1	100	1.8	5	95
10	$NiCl_2$–Bipy	5	NH_4Cl	1 : 3 : 2	50	1	100	1.72	–	100
11	$NiCl_2$–Bipy	5	–	1 : 5 : 0	70	1.5	64	1.73	96	4
12	$NiCl_2$–Bipy	5	NH_4Cl	1 : 3 : 2	35	6	96	1.8	87	13

[a] The amount of **1** 2.12 g (10 mmol).

Surprisingly, lowering the temperature to 50°C increased the conversion of **1** to 63% under the same reaction conditions (Table 1, entry 7). The probable reason is in deactivation of the catalyst at high temperatures. The conversion of **1** increased to 83% when 3 equ. of zinc were used, but simultaneously the ratio **3** to **4** changed from 95 : 5–77 : 23 (Table 1, entry 8).

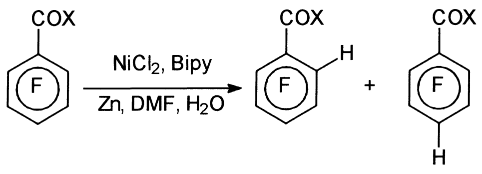
The replacement of water by ammonium chloride as proton donor led to acceleration of hydrodefluorination. Thus, reaction of acid **1** with $NiCl_2$–Bipy (or Phen)–Zn–NH_4Cl in DMF gave 3,4,5-trifluorobenzoic acid **4** in nearly quantitative yield at 50°C within 1 h (Table 1, entries 9, 10). At the lower temperature (35°C) we obtained the opposite result: acid **3** became the main product (Table 1, entry 11). A similar picture was observed at 70°C without ammonium chloride (Table 1, entry 12). In this case the starting acid or $NiCl_2\cdot 6H_2O$ could be the proton sources.

It should be noted that the catalytic activity of $NiCl_2$–Bipy does not differ from that of $NiCl_2$–Phen.

In contrast to acid **1**, the reactions of ethyl pentafluorobenzoate **5** or pentafluorobenzamide **6** with $NiCl_2$–Bipy (or Phen)–Zn proceed with less regioselectivity to give comparable amounts of 2,3,4,5- and 2,3,5,6-C_6HF_4COX ($X = OC_2H_5$, NH_2) (Table 2).

Table 2
Interaction of ethyl pentafluorobenzoate **5** and pentafluorobenzamide **6** with $NiCl_2$–Bipy–Zn

Entry	Substrate	Time (h)	Conversion (%)	Isomer distribution (mol%)	
				a	*b*
1	**5**	2	47	43	57
2	**6**	2	22	73	27
3	**6**	4	59	64	36



X= OC_2H_5 **(5)** **(5a)** **(5b)**

X= NH_2 **(6)** **(6a)** **(6b)**

Under similar conditions, the reactivity of C_6F_5COX increased in the order $X = NH_2 < OH < OC_2H_5$. Moreover, no derivatives of benzoic acid **4** were found when the conversions **5** or **6** did not exceed ca. 60%.

We assume that above mentioned transformations involve the generation of zero-valent nickel complexes and follow formation of a hydride complex **7**, which acted as the reactive intermediate.

$$NiCl_2 + nL + Zn = ZnCl_2 + Ni(0)L_n$$

$$n = 1,2;\ L = 2,2'\text{-bipyridine};\ 1,10\text{-phenanthroline}$$

$$Ni(0)L_n + HX = \underset{7}{HNi(II)XL_n}$$

The reaction pathway of the intermediate **7** is determined by the structure of the polyfluoroarene. The normal nucleophilic ortho- and para-hydrodefluorination takes place when polyfluoroarenes were C_6F_6, C_6F_5H, C_5F_5N, $C_{10}F_8$ [8] as well as ester **5** and amide **6**. Alternatively, the regioselective ortho-hydrodefluorination of acid **1** can be rationalized as an intramolecular process via the coordination of the carboxylic group with intermediate **7** (cf. [7]). The latter pathway seems to partially contribute also to ortho-hydrodefluorination of **5** and **6**, increasing the yield of the corresponding 2,3,4,5-C_6F_4HCOX derivatives (cf. hydrodefluorination with $LiAlH_4$ [9]).

3. Experimental

^{19}F NMR spectra were measured on a Bruker WP-200SY instrument at 188.3 MHz with respect to internal C_6F_6. HPLC analysis was carried out on a Milichrom-4 chromatograph equipped with a UV detector (at 230 and 254 nm). A Separon C-18 analytical column (2 mm i.d. × 6.2 cm) at 40°C was used with 40% methanol in 0.1% aqueous phosphoric acid and the flow rate was 200 μl/min.

3.1. Hydrodefluorination of pentafluorobenzoic acid and its derivatives (general procedure)

1. A three-necked flask (25 ml) equipped with the thermometer and magnetic stirrer was charged with $NiCl_2 \cdot 6H_2O$, Bipy (or Phen), zinc dust, DMF (10 ml) and H_2O (or NH_4Cl). The stirred reaction mixture was warmed and kept for within 30 min. Then a solution of acid **1** in DMF (5 ml) was added and the resulting suspension was kept under HPLC control. Then it was filtered, the solid residue was washed with DMF and washings were combined with the filtrate. The latter was diluted with water and extracted with diethyl ether (5 × 10 ml). The extract was washed with water, dried with $MgSO_4$ and ether was removed under reduced pressure. A solid residue was crystallised from hexane. Yields and composition of products are in Table 1.
2. Reactions of ester **5** or amide **6** (10 mmol) with $NiCl_2 \cdot 6H_2O$ (120 mg, 0.5 mmol), Bipy (80 mg, 0.5 mmol) and zinc dust (1.3 g, 20 mmol) were performed in a similar way (see Table 2).

The reaction products **3**, **4**, **5a**, **5b**, **6a** and **6b** were identified by ^{19}F NMR spectrometry.

References

[1] F.G. Drakesmith, J. Chem. Soc., Perkin Trans. 1 (1972) 184.
[2] S.S. Laev, V.D. Shteingarbs, Tetrahedron Lett. 38 (1997) 3765.
[3] V.I. Krasnov, V.E. Platonov, Zh. Org. Khim. 29 (1993) 1078.
[4] V.E. Platonov, V.I. Krasnov, Zh. Org. Khim. 30 (1994) 1271.
[5] G.B. Deacon, P.I. MacKinnon, T.D. Tuong, Aust. J. Chem. 36 (1983) 43.
[6] G.B. Deacon, P.I. MacKinnon, Tetrahedron Lett. 25 (1984) 783.
[7] G.B. Deacon, C.M. Forsyth, J. Sun, Tetrahedron Lett. 35 (1994) 1095.
[8] N.Yu. Adonin, V.F. Starichenko, Mendeleev Commun., in press.
[9] G.M. Brooke, J. Fluorine Chem. 86 (1997) 1.