DIRECT FLUOROALKYLATION OF AROMATIC COMPOUNDS CATALYZED BY TETRAKIS(TRIPHENYLPHOSPHINE)NICKEL

QI-LIN ZHOU AND YAO-ZENG HUANG

Shanghai Institute of Organic Chemistry, Academia Sinica
345 Lingling Lu, Shanghai (China)

SUMMARY

In the presence of tetrakis(triphenylphosphine)nickel, fluoroalkylation reactions of benzene, furan, thiophene and pyrrole take place regioselectively, giving moderate to good yields of the corresponding fluoroalkyl derivatives.

INTRODUCTION

Several methods have been reported for direct fluoroalkylation of aromatic compounds. Among them there are thermolytic [1-4], photolytic [5-9], and copper promoted [10-12] methods, and the use of $R_FI(Ph)(X)$ [14,15] and perfluoroperacid anhydride [16-18]. However no report has appeared in the literature for direct fluoroalkylation of aromatic and heteroaromatic compounds catalysed by metal derivatives.

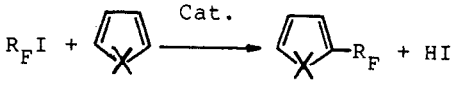
0022-1139/89/$3.50

In the studies of nickel group metal catalyzed aminovinylation of perfluoroalkyl iodide [19,20], we found that tetrakis (triphenylphosphine)nickel was able to efficiently catalyze the direct fluoroalkylation of aromatic compounds with polyfluoroalkyl iodide. In the previous article we reported the direct fluoroalkylation of aniline and its derivatives [21]. Here we would like to report the direct fluoroalkylation of aromatic compounds.

RESULTS AND DISCUSSION

In the presence of catalytic amounts of tetrakis(triphenylphosphine)nickel (5-10%), polyfluoroalkyl iodide reacted with benzene, furan, thiophene, or pyrrole at 60-80 °C to form polyfluoro-benzene, furan, thiophene or pyrrole respectively. The reaction was regioselective and α-polyfluoro-derivatives were found to be the sole products in the case of heteroaromatic compounds. The results are shown in the Table.

$$R_FI + C_6H_6 \xrightarrow{\text{Cat.}} C_6H_5R_F + HI$$



$R_F = Cl(CF_2)_n$, n = 4, 6, 8

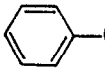
X = O, S, NH

For fluoroalkylation of benzene, benzene itself was used as solvent while for heteroaromatic compounds, the reaction could not be carried out in the solvents themselves. The best solvent was found to be dioxane.

In order to carry the reaction to completion, addition of NaH was required so as to absorb HI. In the case of fluoroalkylation of pyrrole, NaH was unnecessary, but excess amounts of pyrrole should be used.

TABLE

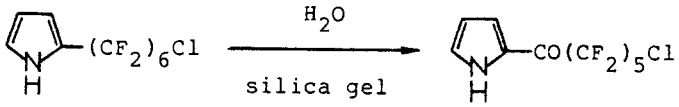
Direct Fluoroalkylation of Aromatic Compounds

	ArH	R_FI	Temp./Time (°C/h)	I	B.P. (°C/mmHg)	Yield(%)*
a)		$Cl(CF_2)_4I$	80/6		52/15	96
b)		$Cl(CF_2)_6I$	80/6		61/15	91
c)		$Cl(CF_2)_4I$	60/3		143/760	95
d)		$Cl(CF_2)_6I$	60/5		69-70/20	93
e)		$Cl(CF_2)_8I$	60/8		63-65/8	90
f)		$Cl(CF_2)_6I$	80/4		60-62/10	37
g)		$Cl(CF_2)_6I$	80/3		68-70/5	50

* Based on polyfluoroalkyl iodide.

From the data of the Table, we can see the reactivities of benzene and furan are the best, and those of thiophene and pyrrole are less good. It is ascribable to that the thiophene could destroy the catalyst while pyrrole, under the reaction conditions, partially polymerized.

It is noteworthy that the direct fluoroalkylation of heteroaromatic compounds gave solely the 2-fluoroalkyl products regioselectively. When 2-polyfluoroalkylpyrrole **Ig** passed through silica gel, hydrolysis took place, giving 2-polyfluoroacylpyrrole **IIg**. Under the same condition, hydrolysis of **Ia-If** did not occur. The mechanism of hydrolysis is similar to that of parapolyfluoroalkyl aniline [21].



Ig **IIg**

EXPERIMENTAL

$Ni(PPh_3)_4$ catalyst was prepared according to the literature [22], polyfluoroalkyl iodide and aromatic compounds were redistilled before use, dioxane was treated by metallic sodium and redistilled. The reactions were carried out under a N_2 atmosphere. NMR spectra were recorded on an EC-360A instrument at 60 MHz (^1H NMR: CCl_4/TMS, ^{19}F NMR: $CCl_4/CFCl_3$ ext, high field is positive). IR spectra were recorded on IR-440, and MS spectra were obtained on MS-4021 spectrometers.

All the compounds except **Ia** and **Ib** reported below are new.

ω-Chloro-octafluorobutylbenzene **Ia**: Typical Procedure: To 5 ml benzene were added 725 mg (2 mmole) $Cl(CF_2)_4I$, 96 mg (4 mmole) NaH, 110 mg (0.1 mmole) $Ni(PPh_3)_4$ under N_2. The mixture was stirred at 80 °C for 6h, hydrolyzed with a saturated solution of NH_4Cl and extracted several times with ether. The combined ethereal solution was dried with Na_2SO_4, and filtered through a short silica gel column and evaporated, affording 600 mg (96%) **Ia**. The analytical sample was obtained by distillation. b.p. 52 °C/15 mmHg. IR (neat): 3075, 1609, 1500, 1455, 1314-1010, 962 cm^{-1}. MS: m/z 312(M), 293, 277, 158, 127(100), 85, 77. ^1H NMR: δ(ppm) 6.90-7.65(m), ^{19}F NMR: δ(ppm) 68.3(t, 2F, J=12.5Hz), 111(t, 2F, J=12Hz), 119.5(t, 2F, J=11.5Hz), 121.1(t, 2f, J=12Hz). Analysis Found: C, 38.40; H, 1.63; Cl, 11.23; F, 48.45. $C_{10}H_5ClF_8$ Calc.: C, 38.40; H, 1.60; Cl, 11.36; F, 48.64%.

The following compounds were prepared similarly except that dioxane was used as solvent in the preparation of **Ic**, **Id**, **Ie**, **If** and **Ig**.

ω-Chloro-dodecafluorohexylbenzene **Ib**: b.p. 59-61 °C/15 mmHg. IR (neat): 3075, 1600, 1500, 1456, 1340, 1300-1000, 978 cm^{-1}. MS: m/z 412(M), 393, 377, 158, 127(100), 85, 77. ^1H NMR: δ(ppm) 6.90-7.75(m). ^{19}F NMR: δ(ppm) 68.1(t, 2F, J=11.5Hz), 110.5(t, 2F, J=12Hz), 120(m. 2F), 120.9(m. 6F). Analysis Found: C, 34.91; H, 1.23; Cl, 8.58; F, 55.38. $C_{12}H_5ClF_{12}$ Calc.: C, 34.91; H, 1.21; Cl, 8.61; F, 55.27%.

2-(ω-Chloro-octafluorobutyl)furan **Ic**: b.p. 143 °C. IR (neat): 1600, 1500, 1395, 1320, 1300, 1060-1260 cm^{-1}. MS: m/z 304, 303, 302(M), 301, 283, 267, 148, 135, 117(100), 85. ^{1}H NMR: δ(ppm) 6.42(m, 1H, H4), 6.82(d, 1H, J=2.8Hz), 7.48(s, 1H, H5). ^{19}F NMR: δ(ppm) 66.7(t, 2F, J=13.4Hz), 110(t, 2F, J=11.6Hz), 118.6(m, 2F), 120.5(m, 2F). Analysis Found: C, 31.80; H, 1.07; Cl, 11.43; F, 50.13. $C_8H_3ClF_8O$ Calc.: C, 31.79; H,0.99; Cl, 11.75; F, 50.33%.

2-(ω-Chloro-dodecafluorohexyl)furan **Id**: b.p. 69-71 °C/20 mmHg. IR (neat): 1600, 1500, 1395, 1300, 1260-1050 cm^{-1}. MS: m/z 404, 403, 402(M), 383, 367, 148, 135, 117(100), 85. ^{1}H NMR: δ(ppm) 6.32(m, 1H, H4), 6.69(d, 1H, J=2.8Hz, H3), 7.36(s, 1H, H5). ^{19}F NMR: δ(ppm) 66.2(t, 2F, J=12.7Hz), 109.6(t, 2F, J=11.2Hz), 118.6(m, 2F), 120(m, 4F), 120.9(m, 2F). Analysis Found: C, 30.31; H, 0.86; Cl, 8.57; F, 56.50. $C_{10}H_3ClF_{12}O$ Calc.:C, 29.85; H, 0.75; Cl, 8.83; F, 56.72%.

2-(ω-chloro-hexadecafluorooctyl)furan **Ie**: b.p. 63-65 °C/8 mmHg. IR (neat): 1595, 1495, 1390, 1300-1060 cm^{-1}. MS: m/z 504, 503, 502(M), 483, 467, 148, 135, 117(100), 85. ^{1}H NMR δ(ppm) 6.41 (m, 1H, H4), 6.82(d, 1H, J=2.9Hz), 7.47(s, 1H, H5). ^{19}F NMR: δ(ppm) 66.0(t, 2F, J=13.0Hz), 110.6(t, 2F, J=11.0Hz), 119.5 (m, 2F), 120.7(m, 8F), 121.8(m, 2F). Analysis Found: C, 28.99; H, 0.68; Cl, 6.89; F, 59.99. $C_{12}H_3ClF_{16}O$ Calc.: C, 28.69; H, 0.60; Cl, 7.07; F, 60.56%.

2-(ω-Chloro-dodecafluorohexyl)thiophene **If**: b.p. 60-62 °C/10 mmHg. IR (neat): 1535, 1435, 1360, 1300-1080 cm^{-1}. MS: m/z 420, 419, 418(M), 399, 383, 134(100). ^{1}H NMR: δ(ppm) 7.00 (m, 1H, H4), 7.47(m, 2H, H3,5). ^{19}F NMR: δ(ppm) 66.7(t, 2F, J=12.5Hz), 99.5 (t, 2F, J=11.5Hz), 118.7(m, 2F), 119.8(m, 6F). Analysis Found: C, 28.42; H, 0.71; Cl, 8.28; F, 54.45; S, 7.43. $C_{10}H_3ClF_{12}S$ Calc.: C, 28.71; H, 0.72; Cl, 8.49; F, 54.55; S, 7.66%.

2-(ω-Chloro-dodecafluorohexyl)pyrrole **Ig**: b.p. 68-70 °C/1 mmHg. IR (neat): 3500, 1570, 1460, 1423, 1315, 1280-1020 cm^{-1}. ^{1}H NMR: δ(ppm) 6.25(m, 1H, H4), 6.87(m, 1H, H5), 8.25-9.00(1H, NH). ^{19}F NMR: δ(ppm) 66.4(t, 2F, J=12.1Hz), 105.7 (t, 2F, J=11.2Hz), 118.4(m, 2F), 119.6(m, 4F), 120.5(m, 2F). Analysis Found: C, 30.51; H, 0.98; Cl, 8.71; F, 56.76; N, 3.78. $C_{10}H_4ClF_{12}N$ Calc.: C, 29.93; H, 1.00; Cl, 8.85; F, 56.86; N, 3.50%.

2-(ω-Chloro-decafluorocaproyl)pyrrole **IIg**: b.p. 80-82 °C/1 mmHg. IR (neat): 3305, 1660, 1545, 1430, 1400, 1280-1060 cm^{-1}. MS: m/z 381, 380, 379(M), 360, 108, 95(100). ^{1}H NMR: δ(ppm) 6.37(m, 1H, H5), 7.25(m, 2H, H3,4), 10.30-11.10(1H, NH). ^{19}F NMR: δ(ppm) 66.5(t, 2F, J=13Hz), 114.0(t,2F,J=12.1Hz), 118.7(m, 4F), 119.7(m, 2F). Analysis Found: C, 32.13; H, 1.00; Cl, 9.18; F, 49.92; N, 3.84. $C_{10}H_4ClF_{10}NO$ Calc.: C, 31.66; H, 1.06; Cl, 9.37; F, 50.13; N, 3.69%.

REFERENCES

1 G. V. D. Tiers, J. Am. Chem. Soc., 82 (1960), 5513.
2 E. S. Huyser, E. Bedard, J. Org. Chem., 29 (1964), 1588.
3 A. B. Cowell, C. Tamborski, J. Fluorine Chem., 17 (1981), 345.
4 J. J. Drysdale, D. D. Coffmann, J. Am. Chem. Soc., 82 (1960), 5111.
5 J. M. Birchall. G. P. Iruin, R. A. Boysen, J. Chem. Soc. Perkin II, (1975), 435.
6 Y. Kobayashi, I. Kumadaki, A. Ohsawa, S. Murakami, T. Nakano, Chem. Pharm. Bull., 26 (1978), 1247.
7 Y. Girard, J. G. Atkinson, P. C. Belanger, J. J. Fuentes, J. Rokach, C. S. Rooney, D. C. Remy, D. A. Hunt, J. Org. Chem., 48 (1983), 3220.
8 S. Fujii, Y. Maki, H. Kimoto, J. Fluorine Chem., 35 (1987), 437.
9 H. Kimoto, S. Fujii, J. Org. Chem., 47 (1982), 2867.
10 P. L. Coe, N. E. Milner, J. Fluorine Chem., 2 (1972/73), 167.
11 T. Fuchikami, I. Ojima, J. Fluorine Chem., 22 (1983), 541.
12 Qing-Yun Chen, Zai-Ming Qiu, Youji Huaxue, (1987),44.
13 T. Umenoto, Y. Kuriu, H. Shuyama, Chem. Lett., (1981), 1663.
14 T. Umenoto, O. Miyans, Bull. Chem. Soc. Jpn., 57 (1984) 3361.
15 L. M. Yagupolskii; I. I. Maletina, N. V. Kondratenko, V. V. Orda, Synthesis, (1978), 853.
16 C. Zhao, G. M. EL-Taliawi, C. Walling, J. Org. Chem., 48 (1983), 4908.
17 M. Yoshida, H. Amemiya, M. Kobayashi, H. Sawada, H. Hagii, K. Aoshima. J. Chem. Soc. Chem. Commun., (1985), 234.
18 H. Sawada, M. Yoshida, H. Hagii, K. oshima, M. Kobayashi, Bull. Chem. Soc. Jpn., 59 (1986), 215.
19 Y.-Z. Huang, Q.-L. Zhou, Tetrahedron Lett., 27 (1986) 2397.
20 Y.-Z. Huang, Q.-L. Zhou, J. Org. Chem., 52 (1987), 3552.
21 Q.-L. Zhou, Y.-Z. Huang, J. Fluorine Chem., 39 (1988), 87.
22 R. A. Schum, Inorg. Synth., 13 (1972), 124.