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DIRECT PERFLUOROALKYLATION OF FUNCTIONALIZED BENZENES WITH PERFLUOROALKYL HALIDES AND COPPER BRONZE

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SUMMARY

Perfluoroalkyl halides were found to react with functionalized benzenes in the presence of copper bronze to give the corresponding perfluoroalkylated products directly in moderate to good yields. The reaction may involve 'active species' other than perfluoroalkylcopper species. Synthetic utility and possible mechanisms of the present one-step reaction are discussed.

INTRODUCTION

In 1960s, several methods for the direct introduction of a perfluoroalkyl group into benzene and other aromatic compounds were reported, e.g., thermolysis or peroxide promoted thermolysis of perfluoroalkyl iodides [1,2], photolysis of perfluoroalkyl iodide, hexafluoroacetone or perfluoroalkylsulfonyl halide [3,4,5], and nickel carbonyl promoted themolysis of perfluoroacyl chloride [6]. However, vigorous conditions were necessary to promote these reactions. In 1972, Coe and Milner reported another direct route to perfluoroalkyl benzenes under relatively mild conditions using perfluoroalkylcopper species as reagents [7]. Nevertheless, from a synthetic point of view, this reaction has some drawbacks: i) the preparation of perfluoroalkylcopper species requires excess copper and strict control of the reaction conditions, ii) large excess of substrate is necessary to promote the reaction and iii) the yields of perfluoroalkylations are rather low(5-36%).

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In the course of our study on the development of new and convenient methods for the syntheses of perfluoroalkylbenzenes bearing a variety of functional groups, we looked again at Coe and Milner's reaction and succeeded in finding an effective and convenient route to these compounds without isolating perfluoroalkylcopper species. Now, we wish to describe here a convenient one-step synthesis of various perfluoroalkylbenzenes from perfluoroalkyl halides, benzenes bearing a variety of substituents and copper bronze.

RESULTS AND DISCUSSION

First, we carried out the perfluoroalkylation of acetanilide (1a) as a typical case and looked at the effects of reaction variables on the product yield.

The perfluoroalkylation of acetanilide (1a) with perfluorooctyl iodide ($C_8F_{17}I$) in the presence of copper bronze in dimethylsulfoxide (DMSO) proceeded readily at 100°C to give a mixture of *o*-, *m*-, and *p*-perfluorooctylacetanilide (2a) and 1-*H*-perfluorooctane (3). The distribution and yields of these products were found to depend on the reaction variables such as solvent, the ratio of starting materials, and additive. The results are listed in Table 1.

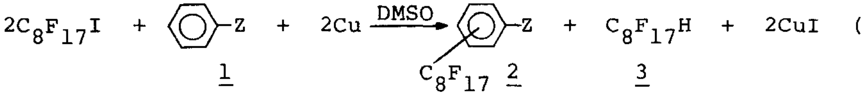
The use of DMSO as solvent seems crucial in the present reaction. Other aprotic solvents such as N,N-dimethylformamide (DMF), dioxane, collidine, pyridine, hexamethylphosphoramide (HMPA), and triethylamine, gave only a trace or small amount of 2a in addition to the predominant formation of 3. In studying the effect of the ratio of the starting materials on the yield of the product, good results were obtained at a ratio of 1a:$C_8F_{17}I$:Cu being 2:1:1 ∿ 1:1:1 (Entries 1 and 2). Increase in the ratio of copper bronze had virtually no effect upon the distribution and yield of 2a. When a half molar amount of 1a was employed with $C_8F_{17}I$ and Cu, the yield of the product was 44% (based on $C_8F_{17}I$; 88% based on 1a) accompanied by 3 (42% based on $C_8F_{17}I$)(Entry 3). From this result, we can deduce that the basic stoichiometry of the present reaction could be described by the equation shown in eq. 1.

TABLE 1

Perfluorooctylation of acetanilide (1a)[a]

Entry	1a (mmol)	$C_8F_{17}I$ (mmol)	Cu (mg-atom)	Additive (mmol)	Solvent	Yield (%)[b] 2a (*o*: *m* :*p*)	Yield (%)[b] 3	Recovered $C_8F_{17}I$ (%)
1	1	1	1		DMSO	58(12:16:72)	29	6
2	1	1	1		DMSO	56(22:19:59)	31	6
3	1/2	1	1		DMSO	44(21:19:60)	42	0
4	2	1	0		DMSO	<1	8	90
5	1	1	1	$Pd(OAc)_2$ (0.01)	DMSO	58(19:20:61)	24	10
6	1	1	1	$Pd(OAc)_2$ (0.1)	DMSO	51(30:19:51)	25	20
7	2	1	1		DMF	14	80	0
8	2	1	1		Dioxane	4	53	36
9	2	1	1		Collidine	3	65	19
10	2	1	1		Pyridine	2	70	0
11	2	1	1		HMPA	<1	95	0
12	2	1	1		Et_3N	<1	90	0

[a] All reactions were run at 100°C for 16 hr. [b] Based on perfluorooctyl iodide used.



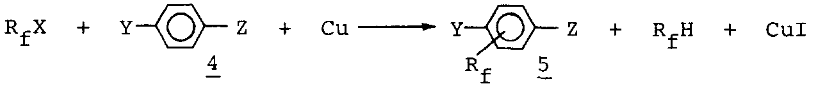
(1)

a: Z=NHAc; b: Z=NH_2; c: Z=NMe_2; d: Z=OCH_2COOMe;
e: Z=OH, f: Z=COOEt

The *para* isomer of 2a was obtained as major product in every case examined. The formation of *para* isomer was increased to some extent on using excess 1a with perfluorooctyl iodide. The addition of palladium acetate somewhat decreased the reaction rate, but rather increased the selectivity of production of 2a as well as the ratio of the *ortho* isomer.

As suitable conditions for the reaction of 1a were found, next we carried out the perfluoroalkylation of other benzenes bearing a variety of functional groups under similar conditions (eq. 1 and eq. 2). It turned out that functional groups such as hydroxy, amino, alkoxy, alkoxycarbonyl, halogen, and carbamoyl groups, were unaffected during the reaction. It should be particularly noted that hydroxy and amino groups which have active hydrogens do not interfere with the reaction. The results are summarized in Table 2.

As Table 2 shows, when monofunctionalized benzenes (2b-f) were employed (Entry 13-17), the formation of *meta* isomer was not observed at all except the case of methyl phenoxyacetate (Entry 15): The reaction with 1a also gave a small amount of *meta* isomer (Table 1). Similarly, difunctionalized benzenes (4a-c) were readily perfluoroalkylated (Entry 18-22)(eq. 2). When *p*-chloroaniline (4c) was enployed, the perfluoroalkyl was introduced preferentially (in case $R_f = C_8F_{17}$) or exclusively (in case $R_f = C_3F_7$) into the *ortho* position to the amino group. It is worth mentioning that perfluorooctyl bromide ($C_8F_{17}Br$) did react with 4c to give the desired product (5c: $R_f = C_8F_{17}$)



(2)

a: Y=Z=OMe; b: Y=Z=OH; c: Y=Cl, Z=NH_2

TABLE 2

Perfluoroalkylation of functionalized benzenes[a]

Entry	R_fX	Y	Z	Yield(%)[b] $\underline{2}$(*o*: *m* :*p*) or $\underline{5}$(*o*:*m*)	R_fH	Recovered R_fX(%)
13	$C_8F_{17}I$	H	NH_2	58(12:16:72)	44	0
14	$C_8F_{17}I$	H	NMe_2	38(39: 0:61)	54	0
15	$C_8F_{17}I$	H	OCH_2COOMe	40(40:20:40)	18	0
16	$C_8F_{17}I$	H	OH	38(48: 0:52)	19	13
17	$C_8F_{17}I$	H	COOEt	37(29: 0:71)	29	24
18	$C_8F_{17}I$	OMe	OMe	57	33	0
19	$C_8F_{17}I$	OH	OH	55	43	0
20	$C_8F_{17}I$	Cl	NH_2	55(90:10)	36	0
21	$C_8F_{17}Br$[c]	Cl	NH_2	50(77:23)	27	8
22	C_3F_7I	Cl	NH_2	45(100:0)	21	23

[a] All reactions were run with 1.0 mmol of perfluoroalkyl halide, 2.0 mmol of functionalized benzene, and 1.0 mmol of copper bronze in 2 ml of DMSO at 100°C for 16 hr unless otherwise noted. [b] Yields were based on perfluoroalkyl halide used. [c] Reaction was run at 150°C.

in almost the same yield to that attained by using $C_8F_{17}I$: As far as we know, this is the first example of the direct perfluoroalkylation of a benzene nucleus using perfluoroalkyl <u>bromide</u>. An attempted trifluoromethylation of <u>4c</u> using trifluoromethyl iodide (CF_3I) resulted in the formation of only a trace of <u>5c</u> ($R_f = CF_3$).

For possible machanisms of the reaction, we can consider the following free radical pathways from eq. 1.

$$2R_fX + 2Cu(metal) \longrightarrow 2R_f\cdot + 2CuX \qquad (a)$$

$$R_f\cdot + ArH \longrightarrow R_fArH\cdot \qquad (b)$$

$$R_fArH\cdot \longrightarrow R_fAr + H\cdot \qquad (c)$$

$$H\cdot + R_f\cdot \longrightarrow R_fH \qquad (d)$$

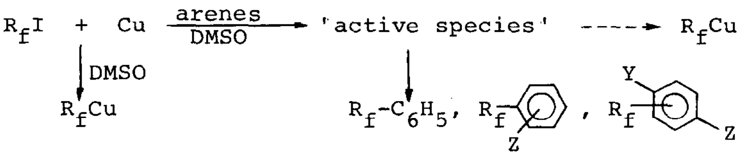
$$2R_fX + 2Cu(metal) + ArH \longrightarrow R_fAr + R_fH + 2CuX$$

$$2H\cdot \longrightarrow H_2 \qquad (e)$$

According to the stoichiometry of this machanism, the yield of R_fAr should not exceed 50% based on R_fX used. However, in several cases we have examined, yields of more than 50% were realized as shown in Tables 1 and 2. These results could be accommodated by taking into account the termination step (e), i.e., generation of molecular hydrogen.

As Coe and Milner reported that "treatment of benzene with $C_7F_{15}I$ and copper, without pre-forming $C_7F_{15}Cu$, gave only a small conversion to $C_7F_{15}C_6H_5$ under the same conditions as those when $C_7F_{15}Cu$ completely reacted" [7], the present results seem inconsistant with those obtained by Coe and Milner. Accordingly, we tried to clarify whether the present reaction involved perfluoroalkylcopper species or not, and carried out the following experiments. (1) $C_8F_{17}Cu$ prepared from $C_8F_{17}I$ and copper bronze ($\geq$ 75% activity) was allowed to react with 1,5 and 20 equivalents of benzene in DMSO at 100°C for 15 h, and (2) a mixture of benzene, $C_8F_{17}I$ and copper bronze (2:1:1 and 20:1:1) was heated at 100°C for 16 h. In experiment (1), the yields of $C_8F_{17}C_6H_5$ based on $C_8F_{17}I$ were 2%, 7% and 31%, respectively: For the estimation of the activity of $C_8F_{17}Cu$, we employed the facile substitution reaction of iodobenzene with $C_8F_{17}Cu$, which should proceed in virtually quantitative yield. In experiment (2), the yields of $C_8F_{17}C_6H_5$ were 34% (39% based on $C_8F_{17}I$ consumed)(C_6H_6:$C_8F_{17}I$:Cu = 2:1:1) and 20% (36% based on $C_8F_{17}I$ consumed)(C_6H_6:$C_8F_{17}I$:Cu = 20:1:1), respectively: It should be noted that the reaction rate was decreased when large excess of benzene was used, possibly due to solvent effects. When acetanilide was employed as substrate, a similar difference was observed: Only 4% of $C_8F_{17}C_6H_4NHAc$ (2a) based on $C_8F_{17}I$ was obtained *via* $C_8F_{17}Cu$ (≥ 75% activity) whereas 56% of 2a was obtained by the direct reaction (Table 1, entry 2). Next, competitive reactions using iodobenzene and aniline (1:1) were carried out: When $C_8F_{17}Cu$ was used, the $C_8F_{17}C_6H_5/C_8F_{17}C_6H_4NH_2$ (2b) ratio was 97.1/2.9 whereas the $C_8F_{17}C_6H_5$/2b ratio was 75.9/24.1 on reacting $C_8F_{17}I$, iodobenzene and copper bronze.

The results mentioned above may imply that the direct reaction, at least, does involve an 'active species' other than the perfluoroalkylcopper species, which is probably generated prior to the formation of the perfluoroalkylcopper species.



(3)

Although a detailed understanding of the mechanism of the direct perfluoroalkylation of benzene nuclei must await further investigation, the present reaction has turned out to serve as a convenient and effective method for the syntheses of perfluoroalkylbenzenes bearing a variety of functional groups without preparing perfluoroalkylcopper species.

EXPERIMENTAL

General

NMR spectra [chemical shifts in parts per million (ppm) from internal tetramethylsilane for ^{1}H and from internal fluorotrichloromethane for ^{19}F; δ is positive for downfield shifts in all cases] were recorded for ^{1}H on a Varian EM-390 spectrometer and for ^{19}F on a Varian XL-100-15A spectrometer. Mass spectra were recorded on a Hitachi RMU-6MG spectrometer at 70 eV. IR spectra were measured on a JASCO A-202 spectrometer. GLC analyses were carried out with a Shimadzu GC-7A instrument, using a glass column (1.2 × 0.3 mm) packed with SE-30 (30%), DC-550 (30%), Apiezon Grease L (30%), and PEG-6000 (20%) on Uniport B. A Varian Aerograph Model 920 gas chromatograph with a thermal conductivity detector was used for separation of the products.

Perfluoroalkyl halides ($C_8F_{17}I$, $C_8F_{17}Br$, and C_3F_7I) were purchased from PCR Inc. and used without further purification. Copper bronze was prepared by a previously reported procedure [8]. Other starting materials and solvents were used as received unless otherwise noted.

Perfluoroalkylation of functionalized benzenes

The following procedure is typical. A mixture of perfluorooctyl iodide (546 mg, 1.0 mmol), acetanilide (270 mg, 2.0 mmol), and copper bronze (63.5 mg, 1.0 mg-atom) in DMSO (2 ml) was heated at 100°C for 16 h in a Pyrex ampoule. The reaction mixture was diluted with ether (10 ml), and hydrolyzed by using aqueous ammonium chloride. The organic layer was separated, and aqueous layer was extracted with ether (2 × 5 ml). The combined extracts were washed with water and dried over anhydrous sodium sulfate. Yields of the products were determined by quantitative GLC analyses, and the reaction conditions and yields of the products are listed in Tables 1 and 2. The products were isolated by preparative GLC or column chromatography on silica gel. The structures of the isolated compounds were determined on the basis of their spectra and elemental analyses. It should be noted that DMSO used as solvent in these reactions is not degassed. In some cases, the use of degassed DMSO gave lower yields of the products.

2-Perfluorooctylacetanilide (*o*-2a): m.p. 89-90°. IR (KBr): 3450, 2530, 1670, 1500, 1400, 1305, 1250, 1220, 1140, 1110, 1090, 940, 765, 660, 635, 600, 555 cm^{-1}. Mass m/e (rel. int.): M^{+} 533(5), 512(7), 511(22), 143(21), 142(100), 141(6), 114(7), 69(7), 43(73). ^{1}H NMR (CD$_3$OD): δ 2.13(s, 3H), 7.4-7.9 ppm(m, 4H). ^{19}F NMR (CD$_3$OD): δ -80.7(t, 3F), -105.4(m, 2F), -120.9(m, 10F), -125.5 ppm(bs, 2F). Analysis: Found: C, 34.72; H, 1.53; N, 2.46%. $C_{16}H_8F_{17}NO$ requires C, 34.74; H, 1.46; N, 2.53%.

3-Perfluorooctylacetanilide (*m*-2a): m.p. 104-106° IR (KBr): 3450, 2430, 1640, 1490, 1390, 1305, 1220, 1200, 1155, 1085, 960, 890, 795, 705, 690, 660, 650, 560, 525 cm^{-1}. Mass m/e (rel. int.): M^{+} 553(6), 511(33), 492(5), 143(9), 142(100), 141 (5), 114(7), 69(7), 43(63). ^{1}H NMR (CD$_3$OD): δ 2.15(s, 3H), 7.36(bd, J_{HH} 8Hz, 1H), 7.53(bt, J_{HH} 8Hz, 1H), 7.83(bd, J_{HH} 8Hz, 1H), 8.00 ppm(bs, 1H). ^{19}F NMR (CD$_3$OD): δ -80.7(t, 3F), -109.8 (t, 2F), -120.4(m, 2F), -121.0(m, 6F), -121.9(m, 2F), -125.5 ppm(m, 2F). Analysis: Found: C, 34.70; H, 1.67; N, 2.58%. $C_{16}H_8F_{17}NO$ requires C, 34.74; H, 1.46; N, 2.53%.

4-Perfluorooctylacetanilide (*p*-2a): m.p. 134-135°. IR (KBr): 3500, 2440, 1660, 1615, 1520, 1445, 1395, 1240, 1195, 1145, 1115, 660 cm^{-1}. Mass m/e (rel. int.): M^{+} 553(6), 511(11), 492 (7), 143(17), 142(100), 114(7), 69(6), 43(60). ^{1}H NMR (CD$_3$OD): δ 2.17(s, 3H), 7.60 and 7.73 ppm(A_2B_2, J_{HH} 8Hz, 4H). ^{19}F NMR (CD$_3$OD): δ -80.7(t, 3F), -109.4(t, 2F), -120.4(m, 2F), -121.1 (m, 6F), -121.9(m, 2F), -125.5 ppm(m, 2F). Analysis: Found: C, 34.63; H, 1.47; N, 2.53%. $C_{16}H_8F_{17}NO$ requires C, 34.74; H, 1.46; N, 2.53%.

2-Perfluorooctylaniline (*o*-2b): m.p. 49.5-50.5°. IR (KBr): 3520, 3410, 1635, 1585, 1500, 1460, 1370, 1330, 1290, 1250, 1220, 1140, 1110, 1085, 940, 760, 660, 645, 620, 555, 530, 460 cm^{-1}. Mass m/e (rel. int.): M^{+} 511(11), 143(10), 142(100), 102(5), 69(9). ^{1}H NMR (CD_3COCD_3): δ 5.1(bs, 2H), 6.68(bt, J_{HH} 8Hz, 1H), 6.86(bd, J_{HH} 8Hz, 1H), 7.23(bd, J_{HH} 8Hz, 1H), 7.29 ppm(bt, J_{HH} 8Hz, 1H). ^{19}F NMR (CD_3COCD_3): δ -80.7(t, 3F), -107.4(bs, 2F), -121.2(m, 8F), -122.3(m, 2F), -125.7 ppm(m, 2F). Analysis: Found: C, 32.87; H, 1.21; N, 2.88%. $C_{14}H_6F_{17}N$ requires C, 32.90; H, 1.18; N, 2.74%.

4-Perfluorooctylaniline (*p*-2b): m.p. 42-43° IR (KBr): 3510, 3420, 1630, 1520, 1370, 1300, 1200, 1150, 1115, 960, 940, 840, 830, 655 cm^{-1}. Mass m/e (rel. int.): M^+ 511(7), 492(15), 173 (6), 143(9), 142(100), 141(5), 69(7). ^{1}H NMR (CD_3COCD_3): δ 5.3(bs, 2H), 6.75 and 7.25 ppm(A_2B_2, J_{HH} 8Hz, 4H). ^{19}F NMR (CD_3COCD_3): δ -80.8(t, 3F), -108.1(t, 2F), -120.9(m, 2F), -121.5(m, 6F), -122.3(m, 2F), -125.8 ppm(m, 2F). Analysis: Found: C, 32.82; H, 1.19; N, 2.75%. $C_{14}H_6F_{17}N$ requires C, 32.90; H, 1.18; N, 2.74%.

2-Perfluorooctyl-N,N-dimethylaniline (*o*-2c): colorless oil. IR (neat): 1690, 1600, 1580, 1495, 1450, 1370, 1290, 1240, 1210, 1150, 1070, 940, 775, 705, 650, 560 cm^{-1}. Mass m/e (rel int.): M^+ 539(37), 538(28), 520(13), 171(100), 127(10), 120(12 109(10), 91(17), 69(19), 43(14), 42(18). ^{1}H NMR ($CDCl_3$): δ 2.66(s, 6H), 7.1-7.7 ppm(m, 4H). ^{19}F NMR ($CDCl_3$): δ -81.3(t, 3F), -104.7(bs, 2F), -120.5(m, 2F), -122.1(m, 6F), -123.1(m, 2F), -126.5 ppm(m, 2F). Analysis: Found: C, 35.71; H, 1.95; N, 2.61%. $C_{16}H_{10}F_{17}N$ requires C, 35.64; H, 1.87; N, 2.60%.

4-Perfluorooctyl-N,N-dimethylaniline (*p*-2c): m.p. 68-68.5°. IR (KBr): 1615, 1535, 1370, 1305, 1200, 1150, 1110, 930, 810, 720, 650 cm^{-1}. Mass m/e (rel. int.): M^+ 539(13), 170(100), 69 (80). ^{1}H NMR ($CDCl_3$): δ 3.02(s, 6H), 6.65 and 7.45 ppm(A_2B_2, J_{HH} 8Hz, 4H). ^{19}F NMR ($CDCl_3$): δ -81.3(t, 3F), -109.6(t, 2F), -122.4(m, 8F), -123.1(m, 2F), -126.5 ppm(m, 2F). Analysis: Found: C, 35.90; H, 2.01; N, 2.79%. $C_{16}H_{10}F_{17}N$ requires C, 35.64; H, 1.87; N, 2.60%.

Methyl 2-perfluorooctylphenoxyacetate (*o*-2d): m.p. 55.5-57.0° IR (KBr): 1760, 1610, 1505, 1470, 1315, 1255, 1220, 1150, 1120, 1095, 945, 765, 670 cm^{-1}. Mass m/e (rel. int.): M$^+$ 584(78), 525(96), 505(27), 215(100), 176(49), 145(63), 126(34), 114(27), 73(22), 69(57), 59(56), 45(84). ^{1}H NMR (CD_3COCD_3): δ 3.70(s, 3H), 4.81(s, 2H), 7.11(bd, J_{HH} 8Hz, 1H), 7.14(bt, J_{HH} 8Hz, 1H), 7.55(bd, J_{HH} 8Hz, 1H), 7.60 ppm(bt, J_{HH} 8Hz, 1H). ^{19}F NMR (CD_3COCD_3): δ -80.7(t, 3F), -106.6(m, 2F), -120.3(m, 2F), -121.3(m, 6F), -122.2(m, 2F), -125.8 ppm(m, 2F). Analysis: Found: C, 35.10; H, 1.65%. $C_{17}H_9F_{17}O_3$ requires C, 34.95; H, 1.55%.

Methyl 3-perfluorooctylphenoxyacetate (*m*-2d): m.p. 44.5-45.5°. IR (KBr): 1760, 1600, 1500, 1455, 1310, 1220, 1160, 1095, 980, 965, 895, 790, 720, 690, 660 cm^{-1}. Mass m/e (rel. int.): M$^+$ 584(13), 188(10), 187(100), 158(11), 145(28), 127(11), 73(19), 69(21), 59(10), 45(94). ^{1}H NMR (CD_3COCD_3): δ 3.70(s, 3H), 4.82 (s, 2H), 7.20(bs, 1H), 7.26(m, 2H), 7.54 ppm(bt, J_{HH} 8Hz, 1H). ^{19}F NNR (CD_3COCD_3): δ -80.7(t, 3F), -109.7(t, 2F), -121.3(m, 10F), -125.7 ppm(m, 2F). Analysis: Found: C, 34.90; H, 1.61%. $C_{17}H_9F_{17}O_3$ requires C, 34.95; H, 1.55%.

Methyl 4-perfluorooctylphenoxyacetate (*p*-2d): m.p. 72-73° IR (KBr): 1770, 1610, 1520, 1440, 1310, 1230, 1200, 1150, 1090, 960, 940, 860, 810, 660, 560 cm^{-1}. Mass m/e (rel. int.): M$^+$ 584(7), 216(11), 215(100), 145(8), 126(9), 73(12), 69(12), 45 (25). ^{1}H NMR ($CDCl_3$): δ 3.77(s, 3H), 4.64(s, 2H), 6.96 and 7.49 ppm(A_2B_2, J_{HH} 8Hz, 4H). ^{19}F NMR ($CDCl_3$): δ -81.3(t, 3F), -110.2(t, 2F), -121.8(m, 2F), -122.3(m, 6F), -123.1(m, 2F), -126.6 ppm(m, 2F). Analysis: Found: C, 35.09; H, 1.62%. $C_{17}H_9F_{17}O_3$ requires C, 34.95; H, 1.55%.

2-Perfluorooctylphenol (*o*-2e): m.p. 49-52° (lit. [9] m.p. 54-54.5°). IR (KBr): 3450, 1610, 1460, 1375, 1310, 1250, 1200, 1150, 1115, 940, 765, 660, 650, 520 cm^{-1}. Mass m/e (rel. int.): M$^+$ 512(8), 145(15), 144(8), 143(100), 95(15), 69(10). ^{1}H NMR ($CDCl_3$): δ 5.9(bs, 1H), 6.93(bd, J_{HH} 8Hz, 1H), 6.97(bt, J_{HH} 8Hz, 1H), 7.36(bd, J_{HH} 8Hz, 1H), 7.40 ppm(bt, J_{HH} 8Hz, 1H). ^{19}F NMR ($CDCl_3$): δ -81.3(t, 3F), -108.5(m, 2F), -122.2(m, 8F), -123.2(m, 2F), -126.6 ppm(m, 2F).

4-Perfluorooctylphenol (*p*-2e): m.p. 68-71° (lit.[9] m.p. 71-73°). IR (KBr): 3450, 1600, 1510, 1455, 1370, 1300, 1200, 1140, 950, 930, 840, 800, 730, 660 cm^{-1}. Mass m/e (rel. int.): M$^+$ 512(4), 174(6), 144(8), 143(100), 69(9). ^{1}H NMR (CDCl$_3$): δ 5.5(bs, 1H), 6.88 and 7.43 ppm(A$_2$B$_2$, J$_{HH}$ 8Hz, 4H). ^{19}F NMR (CDCl$_3$): δ -81.3(t, 3F), -110.1(t, 3F), -121.8(m, 2F), -122.3 (m, 6F), -123.2(m, 2F), -126.6 ppm(m, 2F).

Ethyl 2-perfluorooctylbenzoate (*o*-2f): colorless oil. IR (neat): 1740, 1385, 1315, 1250, 1210, 1155, 1025, 765, 725, 715, 660, 656, 540 cm^{-1}. ^{1}H NMR (CDCl$_3$): δ 1.40(t, J$_{HH}$ 7Hz, 2H), 3.38(q, J$_{HH}$ 7Hz, 2H), 7.5-8.3 ppm(m, 4H). ^{19}F NMR (CDCl$_3$): δ -81.3(t, 3F), -111.2(m, 2F), -122.1(m, 8F), -123.2(m, 2F), -126.6 ppm(m, 2F). Analysis: Found: C, 36.06; H, 1.72%. $C_{17}H_9F_{17}O_2$ requires C, 35.93; H, 1.60%.

Ethyl 4-perfluorooctylbenzoate (*p*-2f): m.p. 63-63.5° IR (KBr): 1725, 1305, 1285, 1235, 1205, 1150, 1060, 1030, 955, 870, 780, 710, 700, 660 cm^{-1}. ^{1}H NMR (CDCl$_3$): δ 1.38(t, J$_{HH}$ 7Hz, 3H), 3.37(q, J$_{HH}$ 7Hz, 2H), 7.64 and 8.13 ppm(A$_2$B$_2$, J$_{HH}$ 8Hz, 4H). ^{19}F NMR (CDCl$_3$): δ -81.3(t, 3F), -111.6(t, 2F), -121.6(m, 2F), -122.3(m, 6F), -123.1(m, 2F), -126.5 ppm(m, 2F). Analysis: Found: C, 35.90; H, 1.58%. $C_{17}H_9F_{17}O_2$ requires C, 35.93; H, 1.60%.

3-Perfluorooctyl-1,4-dimethoxybenzene (5a: $R_f=C_8H_{17}$): colorless oil. IR (neat): 1690, 1595, 1510, 1475, 1430, 1375, 1330, 1300, 1250, 1210, 1150, 1055, 970, 890, 820, 750, 710, 660, 560, 535 cm^{-1}. Mass m/e (rel. int.): M$^+$ 556(56), 187(100), 172(32), 144 (11), 139(72), 138(11), 109(17), 69(18). ^{1}H NMR (CDCl$_3$): δ 3.74(s, 3H), 3.77(s, 3H), 6.8-7.1 ppm(m, 3H). ^{19}F NMR (CDCl$_3$): δ -81.3(t, 3F), -108.0(bs, 2F), -121.6(m, 2F), -122.1(m, 6F), -123.1(m, 2F), -126.5 ppm(m, 2F). Analysis: Found: C, 34.50; H, 1.66%. $C_{16}H_9F_{17}O_2$ requires C, 34.55; H, 1.63%.

3-Perfluorooctyl-1,4-dihydroxybenzene (5b: $R_f=C_8F_{17}$): m.p. 121-122.5°. IR (KBr): 3380, 1455, 1390, 1305, 1240, 1215, 1150, 780, 655, 550 cm^{-1}. Mass m/e (rel. int.): M$^+$ 528 (18), 189(13), 161(12), 160(9), 159(100), 83(12), 69(17). ^{1}H NMR (CD$_3$OD): δ

6.58(s, 1H), 6.81 ppm(m, 2H). ^{19}F NMR (CD_3OD): δ -80.8(t, 3F), -107.3(m, 2F), -121.2(m, 8F), -122.1(m, 2F), -125.7 ppm(m, 2F).

2-Perfluorooctyl-4-chloroaniline (*o*-5c: R_f=C_8F_{17}): m.p. 73-74°. IR (KBr): 3550, 3440, 1630, 1495, 1420, 1305, 1230, 1200, 1140, 1080, 960, 895, 815, 710, 655, 535 cm^{-1}. Mass m/e (rel. int.): M^+ 547(7), 545(22), 178(33), 176(100), 69(13). ^{1}H NMR ($CDCl_3$): δ 5.18(bs, 2H), 6.6 and 7.1(A_2B_2, J_{HH} 8Hz, 2H), 7.15 ppm(s, 1H). ^{19}F NMR ($CDCl_3$): δ -81.4(t, 3F), -109.2(t, 2F), -122.0(m, 8F), -123.0(m, 2F), -126.4 ppm(m, 2F). Analysis: Found: C, 30.98; H, 0.85; N, 2.65%. $C_{14}H_5ClF_{17}N$ requires C, 30.82; H, 0.92; N, 2.57%.

2-Perfluoropropyl-4-chloroaniline (*o*-5c: R_f=C_3F_7): colorless oil. IR (near): 3550, 3460, 1635, 1500, 1420, 1350, 1240, 1110, 945, 920, 890, 820, 755, 700 cm^{-1}. Mass m/e (rel. int.): M^+ 297(12), 295(38), 178(33), 176(100), 88(14). ^{1}H NMR ($CDCl_3$): δ 4.2(bs, 2H), 6.64(d, J_{HH} 7Hz, 1H), 7.27 ppm(m, 2H). ^{19}F NMR ($CDCl_3$): δ -80.7(t, 3F), -110.3(m, 2F), -126.8 ppm(m, 2F). Analysis: Found: C, 36.71; H, 1.71; H, 4.72%. $C_9H_5ClF_7N$ requires C, 36.57; H, 1.71, N, 4.74%.

Reactions of perfluorooctylcopper with substituted benzene

(a) Preparation of perfluorooctylcopper

In a 20 ml Schlenk flask fitted with a septum, a mixture of perfluorooctyl iodide (3.28 g, 6.0 mmol), freshly prepared copper bronze (838 mg, 13.2 mg-atom) in DMSO (12 ml) distilled from calcium hydride was degassed, and heated at 110°C with stirring under argon for 1 h. After the reaction mixture was cooled to room temperature, the precipitated cuprous iodide and excess copper were separated by centrifugation to give 13.5 ml of a pale greenish-yellow solution of perfluorooctylcopper.

In order to estimate the activity of this reagent, we carried out the reaction with iodobenzene. A 2 ml portion of the perfluorooctylcopper solution prepared as described above was mixed with iodobenzene (204 mg, 1.0 mmol), and the mixture was heated at 100°C with stirring for 15 h under argon, and then hydrolyzed with aqueous ammonium chloride. The GLC and ^{19}F NMR analyses of the reaction mixture revealed the formation of perfluorooctylbenzene (0.67 mmol) and 1-H-perfluorooctane (3)(0.12 mmol) which should already be yielded in the perfluorooctylcopper forming reaction. Consequently, the activity of the perfluorooctylcopper thus prepared is estimated to be 0.335 M which corresponds to the 75% yield formation of perfluorooctylcopper based on the perfluorooctyl iodide used, provided that the reaction with iodobenzene proceeds in virtually quantitative yield.

(b) Reaction with acetanilide

A mixture of the perfluorooctylcopper solution in DMSO (2 ml) and acetanilide (135 mg, 1.0 mmol) was heated in a 10 ml pyrex glass ampoule at 100°C for 15 h to give perfluorooctylacetanilide (2a)(0.04 mmol, 4%), 1-H-perfluorooctane (3)(0.65 mmol, 73%) and perfluorohexadecane (0.05 mmol, 11%), which were identified on the basis of ^{19}F NMR and GLC analyses. The yields of the products were determined by GLC analyses based on the perfluorooctyl iodide initially used.

(c) Competitive reaction with a 1:1 mixture of iodobenzene and aniline

In a similar manner, a mixture of the perfluorooctylcopper solution in DMSO (2 ml), iodobenzene (204 mg, 1.0 mmol) and aniline (93 mg, 1.0 mmol) was heated at 100°C for 15 h. The GLC analysis of the reaction mixture revealed the formations of perfluorooctylbenzene (0.60 mmol, 67%), Perfluorooctylaniline (2b) (0.02 mmol, 2%) and 1-H-perfluorooctane (3)(0.15 mmol, 20%): Yields are based on the perfluorooctyl iodide initially used.

(d) Reaction with 1, 5 and 20 equivalents of benzene

The reactions of the perfluorooctylcopper solutions (2 ml each) with 1, 5 and 20 equivalents of benzene, i.e., 70 mg (0.9 mmol), 350 mg (4.5 mmol) and 1.40 g (18 mmol), respectively, were carried out in a similar manner to that described above at 100°C for 15 h. The reaction with 1 equivalent of benzene gave 0.02 mmol of perfluorooctylbenzene (2%), 1-H-perfluorooctane (3) (0.58 mmol, 65%) and perfluorohexadecane (0.07 mmol, 15%); the reaction with 5 equivalents of benzene gave 0.06 mmol of perfluorooctylbenzene (7%), 1-H-perfluorooctane (3) (0.64 mmol, 72%) and perfluorohexadecane (0.06 mmol, 13%); the reacthon with 20 equivalents of benzene gave 0.34 mmol of perfluorooctylbenzene (30%) and 1-H-perfluorooctane (0.50 mmol, 56%): Yields are based on the perfluorooctyl iodide initially used.

Direct perfluorooctylation of benzene

A mixture of perfluorooctyl iodide (546 mg, 1.0 mmol), copper bronze (63.5 mg, 1.0 mg-atom) and benzene (156 mg, 2.0 mmol) in DMSO (2 ml) was heated in a 10 ml Pyrex glass ampoule with stirring at 100°C for 16 h. GLC analysis of the reaction mixture revealed the formations of perfluorooctylbenzene (0.34 mmol, 39% yield based on the perfluorooctyl iodide consumed) and 1-H-perfluorooctane (0.30 mmol, 34% yield based on the perfluorooctyl iodide used), and 0.12 mmol of perfluorooctyl iodide was recovered, i.e., 88% conversion.

When 20 equivalents of benzene (1.56 g, 20 mmol) was used, 0.45 mmol of perfluorooctyl iodide was recovered, i.e., 55% conversion, and 0.20 mmol of perfluorooctylbenzene and 0.15 mmol of 1-H-perfluorooctane were obtained, i.e., 36% and 27% yields, respectively, based on the perfluorooctyl iodide consumed.

Competitive direct perfluorooctylation of a 1:1 mixture of iodobenzene and aniline

Similarly, a mixture of perfluorooctyl iodide (546 mg, 1.0 mmol), copper bronze (63.5 mg, 1.0 mg-atom), iodobenzene (204 mg, 1.0 mmol) and aniline (93 mg, 1.0 mmol) in DMSO (2 ml) was heated at 100°C for 16 h. GLC analysis of the reaction mixture revealed that 0.33 mmol of perfluorooctyl iodide was recovered, i.e., 67% conversion and 0.41 mmol of perfluorooctylbenzene and 0.13 mmol of perfluorooctylaniline (2b) were formed, i.e., 61% and 19% yields, respectively, besed on the perfluorooctyl iodide consumed.

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