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Preparation of organozinc compounds from 3-chloroheptafluorotoluene and zinc: the participation of C–F bonds

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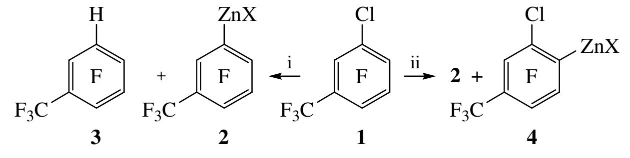
Organozinc compounds were obtained from 3-chloroheptafluorotoluene and Zn in DMF; the C–Cl bond is mainly involved in this reaction; the addition of $SnCl_2$ changes the main reaction course in the direction of the participation of the C–F bond (*para* to the CF_3 group).

Perfluoroarenes react with zinc in dimethylformamide (DMF) in the presence of metal salts ($SnCl_2$, $CuCl_2$ or $ZnBr_2$) to give perfluorozincarenes as the formal result of fluorine atom substitution with zinc in the aromatic ring.[1] Chloropentafluorobenzene reacted with zinc at the C–Cl bond to give pentafluorophenylzinc chloride under similar conditions.[1]

We found that polychlorofluoroarenes react with Zn in DMF upon heating without addition of salts; in all cases, the formation of polyfluoroaromatic organozinc compounds at C–Cl bonds took place, whereas C–F bonds were unaffected.[2] Here, the formation of organozinc compounds with the participation of the C–F bond of the aromatic ring of a polychlorofluoroarene under the action of Zn and $SnCl_2$ is considered.

We studied the reaction of 3-chloroheptafluorotoluene **1** with Zn in dry DMF in order to obtain organozinc compounds.[†] It was found that the interaction of compound **1** with Zn(Cu) in



3 **2** **1** **4**

a X = Cl
b X = 3-$CF_3C_6F_4$

a X = Cl
b X = 3-$CF_3C_6F_4$,
2-Cl-4-$CF_3C_6F_3$

Scheme 1 *Reagents and conditions*: DMF, 70 °C; i, Zn; ii, Zn/$SnCl_2$.

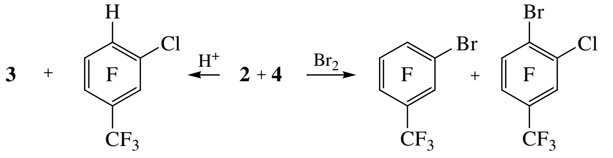
aqueous DMF took place with participation of the C–Cl bond to give the product of hydrodechlorination.[2]

Compound **1** reacted with Zn in dry DMF to give predominantly organozinc compounds **2**[‡] (Scheme 1) as result of the participation of the C–Cl bond in the reaction (run 1, Table 1). Note that 3-*H*-heptafluorotoluene **3** as a product of formal hydrolysis of **2** was also observed in the reaction. Unexpectedly, the addition of ~10–11 mol% $SnCl_2$ (relative to **1**) to zinc changed the reaction course (runs 2, 3; Table 1). In this case, organozinc compounds **4**[§] were obtained as the major products along with smaller amounts of **2** (Scheme 1).

These data are in agreement with the results of treatment of a mixture of organozinc compounds **2** and **4** with hydrochloric acid and bromine;[¶] this treatment gave the hydrolysis products **3**, 1-chloro-2,4,5-trifluoro-3-(trifluoromethyl)benzene **5**[††] and bromo compounds [1-bromo-2,3,4,6-tetrafluoro-5-(trifluoromethyl)benzene **6**[‡‡] and 1-bromo-2-chloro-3,5,6-trifluoro-4-(trifluoromethyl)benzene **7**[§§]], respectively (Table 2, Scheme 2).

An increase of the relative quantity of $SnCl_2$ to 100 or 300 mol% (runs 4, 5; Tables 1, 2) insignificantly affects the correlation between two competitive locations of metallation of arene **1**; it follows from the ratio of reaction products, which were obtained by the hydrolysis of a mixture of organozinc compounds (ratios of 31:69 and 26:74 in favour of fluorine atom substitution).

Proportion of fluorine atom substitution in compound **1** reduced but kept a considerable value when tin powder was used instead of $SnCl_2$ for the formation of organozinc compounds (run 6, Table 1). In this case, the consumption of compound **1** was reduced in comparison with the use of Zn–$SnCl_2$ or only Zn. Thus, the addition of $SnCl_2$ promotes the formation of organozinc compounds with the participation of a C–F bond of toluene **1** (the 4-position); it is in agreement with the orientation, which was observed in the nucleophilic substitution reaction of **1** with dimethyl amine, where the dimethyl amine group enters mainly at the 4-position to give *N*-[2-chloro-3,5,6-trifluoro-4-(trifluoromethyl)phenyl]-*N*,*N*-dimethylamine **8**.[¶¶] At the same time, no reaction between $SnCl_2$ or Sn/$SnCl_2$ and **1** in a DMF solution (70 °C) in the absence of Zn was found to detect the formation of organostannane compounds or products of substitution of fluorine atoms by chlorine in **1**. In this connection, the assumption of the initial nucleophilic substitution of fluorine atoms with chlorine at the 4-position of arene **1** under the action of



5 **6** **7**

Scheme 2

[†] *General procedure.* DMF was stored over KOH, fractionally distilled under reduced pressure, and the main fraction was stored over CaH_2. Compound **1** (95%) contained ~4% 2-*H*-3-chlorohexafluorotoluene (GC/MS and NMR). To a mixture of Zn dust (fivefold amount over stoichiometry) or Zn dust together with $SnCl_2$ or another addition, DMF (0.4 ml per 1 mmol of **1**) compound **1** was added. The mixture was stirred by a magnetic stirrer in a closed flask immersed in a thermostat. After completion of the reaction and subsequent precipitation process, the solution was decanted and the ^{19}F NMR spectrum of the solution was recorded (Table 1). The ^{19}F and ^{1}H NMR spectra were obtained on a Bruker WP-200SY instrument at 188.3 and 200 MHz for reaction mixtures containing organozinc compounds in DMF, as well as in other cases for solutions in CCl_4; the internal standards were C_6F_6 (162.9 ppm from CCl_3F) and HMS (0.04 ppm from TMS). The ^{19}F chemical shifts are reported *vs.* CCl_3F.

[‡] *[2,3,4,6-Tetrafluoro-5-(trifluoromethyl)phenyl]zinc chloride* **2a**. ^{19}F NMR, δ: ~ –55.5 (quasitriplet, 3F, CF_3, $^{4}J_{CF_3-F(4)}$ ~ 22 Hz, $^{4}J_{CF_3-F(6)}$ ~ 22 Hz), –89.5 (qdd, 1F, F-6, $^{4}J_{CF_3-F(6)}$ 21.3 Hz, $^{5}J_{3,6}$ 14.6 Hz, $^{4}J_{4,6}$ 3.9 Hz), –102.9 (dd, 1F, F-2, $^{3}J_{2,3}$ 31.2 Hz, $^{4}J_{2,4}$ 9.3 Hz), –138.3 (qddd, 1F, F-4, $^{4}J_{CF_3-F(4)}$ 23.5 Hz, $^{3}J_{3,4}$ 18.6 Hz, $^{4}J_{2,4}$ 9.2 Hz, $^{4}J_{4,6}$ 3.8 Hz), –165.6 (ddd, 1F, F-3, $^{3}J_{2,3}$ 31.3 Hz, $^{3}J_{3,4}$ 18.6 Hz, $^{5}J_{3,6}$ 14.6 Hz). Spectrum of the reaction mixture also contains the signals of **2b** (X = 3-$CF_3C_6F_4$): –55.5, –89.9, –103.3, –139.2, –165.9. Fine structure of the signals is similar to **2a** excepting $^{3}J_{2,3}$ 32.3 Hz.

[§] *[2-Chloro-3,5,6-trifluoro-4-(trifluoromethyl)phenyl]zinc chloride* **4a**. ^{19}F NMR, δ: –55.6 (quasitriplet, 3F, CF_3, $^{4}J_{CF_3-F(3)}$ ~ 22 Hz, $^{4}J_{CF_3-F(5)}$ ~ 22 Hz), –114.9 (dd, 1F, F-6, $^{3}J_{5,6}$ 31.0 Hz, $^{5}J_{3,6}$ 18.5 Hz), –115.8 (qdd, 1F, F-3, $^{4}J_{CF_3-F(3)}$ 22.1 Hz, $^{5}J_{3,6}$ 18.5 Hz, $^{4}J_{3,5}$ ~ 4.5 Hz), –138.5 (dqd, 1F, F-5, $^{3}J_{5,6}$ 31.0 Hz, $^{4}J_{CF_3-F(5)}$ 22.4 Hz, $^{4}J_{3,5}$ ~ 4 Hz). Spectrum of the reaction mixture also contains the signals of **4b** (X = 2-Cl-4-$CF_3C_6F_3$): –55.6, –115.5, –116.1, –139.2. Fine structure of the signals is similar to **4a** excepting $^{3}J_{5,6}$ ~ 32 Hz. For mixtures of **2** and **4**, the signals of **2b** and **4b** (X = 3-$CF_3C_6F_4$, 2-Cl-4-$CF_3C_6F_3$) are close overlapping sets assigned to the structures of Ar_2Zn and ArAr′Zn types.

[¶] Hydrogen derivatives were obtained by treatment of the solution and solid material after decantation of the solution with dilute HCl. Bromo derivatives were synthesised in the following manner: to a mixture of bromine (an equimolar amount *vs.* compound **1**) in DMF the decanted solution was added. The solid material was washed with a small amount of DMF (3–5 ml) and the solution was added to the above mixture. Reaction mixtures were steam distilled; if necessary, the organic layer was separated and treated with a 10% aqueous solution of Na_2SO_3 until the disappearance of its colour to remove the excess of bromine. Then, the organic layer was dried over $CaCl_2$.

[††] *Compound* **5**. Reaction mixture (run 4, Table 2) was fractionated *in vacuo*. Fraction (79–79.5 °C/35 Torr) contained 96% compound **5**. ^{19}F NMR, δ: –57.6 (quasitriplet, 3F, CF_3, $^{4}J_{CF_3-F(2)}$ ~ 22.7 Hz, $^{4}J_{CF_3-F(4)}$ ~ 22.7 Hz), –116.6 (qddd, 1F, F-2, $^{4}J_{CF_3-F(2)}$ 22.4 Hz, $^{5}J_{2,5}$ 13.7 Hz, $^{4}J_{F(2)-H}$ 6.6 Hz, $^{4}J_{2,4}$ ~ 2.5 Hz), –135.8 (qddd, 1F, F-4, $^{4}J_{CF_3-F(4)}$ 22.8 Hz, $^{3}J_{4,5}$ 20.5 Hz, $^{4}J_{F(4)-H}$ 7.8 Hz, $^{4}J_{2,4}$ 2.5 Hz), –138.5 (ddd, 1F, F-5, $^{3}J_{4,5}$ 20.4 Hz, $^{5}J_{2,5}$ 13.6 Hz, $^{3}J_{F(5)-H}$ 9.0 Hz). ^{1}H NMR, δ: 7.49 (quasiquartet, broadened peaks, 23.2 Hz). IR (CCl_4, ν/cm^{-1}): 3124, 3071, 1633, 1498, 1315, 1207, 1158, 922, 872, 834. HRMS for C_7HClF_6: found, 233.96741; calc., 233.96709.

[‡‡] *Compound* **6**. Reaction mixture (run 3, Table 2) was fractionated *in vacuo*. Fraction (69–69.5 °C/18 Torr) contained 98% compound **6**. ^{19}F NMR, δ: –57.6 (quasitriplet, 3F, CF_3, $^{4}J_{CF_3-F(4)}$ ~ 22.5 Hz, $^{4}J_{CF_3-F(6)}$ ~ 22.5 Hz), –108.8 (qddd, 1F, F-6, $^{4}J_{CF_3-F(6)}$ ~ 22.5 Hz, $^{5}J_{3,6}$ ~ 9.5 Hz, $^{4}J_{4,6}$ ~ 4 Hz, $^{4}J_{2,6}$ ~ 1.5 Hz), –118.4 (dd, 1F, F-2, $^{3}J_{2,3}$ 21.7 Hz, $^{4}J_{2,4}$ 10.2 Hz), –133.8 (qddd, 1F, F-4, $^{4}J_{CF_3-F(4)}$ 22.7 Hz, $^{3}J_{3,4}$ 20.9 Hz, $^{4}J_{2,4}$ 10.0 Hz, $^{4}J_{4,6}$ 3.7 Hz), –160.4 (quasitriplet d, 1F, F-3, $^{3}J_{2,3}$ ~ 21.3 Hz, $^{3}J_{3,4}$ ~ 21.3 Hz, $^{5}J_{3,6}$ 9.7 Hz). IR (CCl_4, ν/cm^{-1}): 1638 (m), 1609, 1502, 1474, 1318, 1214, 1184, 1158, 1090, 918. HRMS for C_7BrF_7: found, 295.90721; calc., 295.90716. MS, *m*/*z* (%): 298 (M^+, 96) 296 (M^+, 100), 279 (M^+ – F, 38), 277 (M^+ – F, 41), 248 (M^+ – CF_2, 19), 246 (M^+ – CF_2, 19), 217 (M^+ – Br, 51). Found (%): C, 28.11; Br, 26.86; F, 45.02. Calc. for C_7BrF_7 (%): C, 28.31; Br, 26.91; F, 44.78.

[§§] *Compound* **7**. Reaction mixture (run 3, Table 2) was fractionated *in vacuo* to give a fraction (95–96.5 °C/17 Torr) containing 96% compound **7** and 1% compound **6**. ^{19}F NMR, δ: –57.9 (t, 3F, CF_3, $^{4}J_{CF_3-F(3)}$ 22.4 Hz, $^{4}J_{CF_3-F(5)}$ 22.4 Hz), –112.4 (qdd, 1F, F-3, $^{4}J_{CF_3-F(3)}$ 22.4 Hz, $^{5}J_{3,6}$ 11.7 Hz, $^{4}J_{3,5}$ 2.7 Hz), –126.9 (dd, 1F, F-6, $^{3}J_{5,6}$ 21.9 Hz, $^{5}J_{3,6}$ 11.7 Hz), –135.0 (quasiquintet d, 1F, F-5, $^{4}J_{CF_3-F(5)}$ ~ 22.4 Hz, $^{3}J_{5,6}$ ~ 22.4 Hz, $^{4}J_{3,5}$ 2.7 Hz). IR (CCl_4, ν/cm^{-1}): 1625, 1593 (weak), 1471, 1313, 1159 (m), 1090, 949, 873. HRMS for C_7ClBrF_6: found, 311.87766; calc., 311.87761. MS, *m*/*z* (%): 316 (M^+, 24), 314 (M^+, 100), 312 (M^+, 75), 295 (M^+ – F, 22), 293 (M^+ – F, 18), 279 (M^+ – Cl, 16), 277 (M^+ – Cl, 18), 264 (M^+ – CF_2, 14), 262 (M^+ – CF_2, 11), 235 (M^+ – Br, 9), 233 (M^+ – Br, 27). Found (%): C, 26.54; F, 36.17. Calc. for C_7ClBrF_6 (%): C, 26.82; F, 36.37.

[¶¶] *Reaction of compound* **1** *with* $HNMe_2$. 16.2 mmol $HNMe_2$ (2.21 g of a 33% aqueous solution) was added to a solution of **1** in 12.6 ml of DMF and shaken. After four days, the resulting mixture was diluted with 12 ml of 5% aqueous HCl, the organic layer was separated and dried over Na_2SO_4. Liquid (2.28 g) contained 80% compound **8** according to GLC and GC-MS. ^{19}F NMR, δ: –57.2 (quasitriplet, 3F, CF_3, $^{4}J_{CF_3-F(3)}$ ~ 21.8 Hz, $^{4}J_{CF_3-F(5)}$ ~ 21.8 Hz), –116.3 (qdd, 1F, F-3, $^{4}J_{CF_3-F(3)}$ 21.6 Hz, $^{5}J_{3,6}$ 9.5 Hz, $^{4}J_{3,5}$ 2.3 Hz), –138.4 (qdd, 1F, F-5, $^{4}J_{CF_3-F(5)}$ ~ 22 Hz, $^{3}J_{5,6}$ 18.9 Hz, $^{4}J_{3,5}$ 2.3 Hz), –150.9 (m, 1F, F-6, 35 Hz breadth and 16 peaks at least).

Table 1 Reaction of 3-chloroheptafluorotoluene **1** with Zn (70 °C, 8 h).

Run	Compound **1**/ g (mmol)	Addition		Concentrations (ratio) of products in the reaction mixture[a,b]					Ratio **4**:**2**[b]
		mol%	g (mmol)	**1**	**2** (**a**:**b**)	**3**	**4** (**a**:**b**)	**5**	
1	4.04 (16.0)	—	—	4.4	92.0 (7:3)	3.5	—[c]	0	~0[c]
2	3.20 (12.7)	$SnCl_2$, 10	0.24 (1.3)	0.5	36.0 (5.5:4.5)	1.4	59.0 (~5.5:4.5)	3.1	62:38
3[d]	6.65 (26.3)	$SnCl_2$, 11	0.57 (3.0)	0	32.9 (5.5:4.5)	0.4	61.8 (5.5:4.5)	4.9	65:35
4	4.04 (16.0)	$SnCl_2$, 100	3.00 (15.8)	0	36.9 (6.5:3.5)	0.7	57.8 (~6.5:3.5)	4.6	61:39[e]
5	4.04 (16.0)	$SnCl_2$, 300	9.10[f] (48.0)	—	—	—	—	—	—[g]
6	4.04 (16.0)	Sn, 10	0.19 (1.6)	41.6	30.1 (6:4)	2.3	25.3 (6:4)	0.7	46:54

[a] Ratios of **2a** and **2b**, **4a** and **4b** are given by polyfluoroaromatic fragments considering organozinc compounds as molecules with such a fragment. [b] Values were found by ^{19}F NMR spectroscopy. [c] Precise estimate failed because of a very small quantity of **4**. [d] 27 h. [e] After the reaction, a decanted solution contained only partly organometallic compounds; the significant portion of the reaction mixture was likely in a solid phase untested by ^{19}F NMR. [f] 12.1 ml of DMF (0.8 ml per 1 mmol of **1**) was also used in the reaction. [g] Reaction mixture is thick mass; compound **1** was mainly detected in solution by ^{19}F NMR spectroscopy.

Table 2 Treatment of reaction mixtures of organozinc compounds **2** and **4** by Br_2 and HCl.[a]

Run	Reagent/g (mmol)	Yield of product mixture/g	Concentrations (yield) of reaction product mixture according to GLC (%)					Ratio **7**:**6**[b]
			1	**3**	**5**	**6**	**7**	
1	Br_2, 2.6 (16.3)	3.80	5.1 (4.8)	2.6 (2.8)	—	84.1 (67.3)	0.7 (0.5)	<1:100
2	Br_2, 2.1 (13.1)	2.23	—	1.4 (1.2)	3.2 (2.4)	33.7 (20.0)	55.8 (31.3)	61:39
3[c]	Br_2, 3.7 (23.2)	5.75	—	5.6 (6.6)	15.4 (16.9)	28.3 (24.5)	43.4 (35.6)	59:41
4	HCl[d]	2.97	—	26.1 (22.2)	63.7 (50.4)	—	—	69:31[e]
5	HCl[d]	2.90	14.9 (10.7)	19.6 (16.3)	59.6 (46.1)	—	—	74:26[e]
6	Br_2, 2.6 (16.3)	3.88	26.0 (25.0)	1.5 (1.7)	1.6 (1.7)	35.6 (29.1)	30.1 (23.3)	44:56

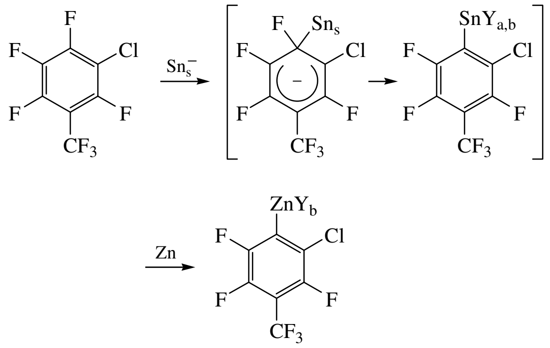
[a] Reaction mixtures were taken from experiments, which are given in Table 1. [b] According to ^{19}F NMR spectra. [c] 22.3 mmol of organozinc compounds (run 3, Table 1) was used for the reaction with Br_2. The rest of solution was treated with 10% HCl to give 0.49 g of a mixture of **3** and **5** in a ratio of 38:62 (^{19}F NMR). [d] 15 ml of 10% HCl was used. [e] Ratio **5**:**3**.

chloride ions and subsequent formation of organometallics from the corresponding 4-chloro derivative appears to be unlikely.

We also found that octafluorotoluene **9** reacts with Zn in DMF in the presence of SnF_2, *i.e.*, in the absence of chloride ions, to give bis(4-heptafluorotolyl)zinc **10**; the latter was treated with bromine to give 4-bromoheptafluorotoluene **11** in a good yield. The reaction took place with Zn–Sn powder mixture but occured slowly. Without addition of Sn, organozinc compound **10** is formed from **9** and Zn in a very small yield.[†††]

The formation of organozinc compounds **2** in the reaction of **1** with Zn in the absence of $SnCl_2$ can be rationalised by a radical anion process by analogy with the mechanism of formation of Grignard reagents and organozinc compounds.[3,4]

At the same time, the influence of the addition of $SnCl_2$ on the main route of the reaction of **1** with the participation of a C–F bond would be expected to take place as a result of the contribution of a nucleophilic mechanism. A possible route is shown in Scheme 3. A concerted mechanism is also likely (*cf.* ref. 5). It is known that octafluorotoluene is much more reactive than chloropentafluorobenzene in nucleophilic reactions.[6] In this connection, a nucleophilic mechanism for chloropentafluorobenzene seems incompetitive with a radical anion process and only the C–Cl bond of chloropentafluorobenzene takes part in the reaction. As a result of a nucleophilic attack, intermediate organostannane compounds could be formed; they are probably converted into organozinc compounds. A similar mechanism could be suggested for the reaction of toluene **9** with Zn and SnF_2.



$Y_a = Sn_s$, F
$Y_b = Cl$, $3\text{-}CF_3C_6F_4$, $2\text{-}Cl\text{-}4\text{-}CF_3C_6F_3$

Scheme 3

References

1 A. O. Miller, V. I. Krasnov, D. Peters, V. E. Platonov and R. Miethchen, *Tetrahedron Lett.*, 2000, **41**, 3817.
2 V. I. Krasnov and V. E. Platonov, *Zh. Org. Khim.*, 2000, **36**, 1524 (*Russ. J. Org. Chem.*, 2000, **36**, 1488).
3 B. J. Wakefield, in *Comprehensive Organic Chemistry*, ed. D. N. Jones, Pergamon Press, Oxford, New York, Toronto, Sydney, Paris, Frankfurt, 1979, vol. 3, p. 975.
4 A. Guijarro, D. M. Rosenberg and R. D. Rieke, *J. Am. Chem. Soc.*, 1999, **121**, 4155.
5 M. I. Slaked, T. Broun, B. Newmann and H.-G. Stammler, *New J. Chem.*, 2003, **27**, 313.
6 G. M. Brooke, *J. Fluorine Chem.*, 1997, **86**, 1.

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[†††] *Reaction of octafluorotoluene* **9** *with Zn–SnF_2, Zn–Sn and Zn.* The mixture of Zn (4.05 g, 62.0 mmol), SnF_2 (0.20 g, 1.3 mmol), toluene **9** (3.00 g, 12.7 mmol) was placed in closed flask (10 ml), magnetically stirred at 70 °C for 8 h and then stored overnight. According to ^{19}F NMR, the starting compound converted completely. The main product was found to be bis(4-heptafluorotolyl)zinc **10**.[1] The obtained solution was added to a solution of bromine (2.05 g, 12.8 mmol) in 1.4 ml of DMF. Steam distillation gave 96.9% (GLC) 4-bromoheptafluorotoluene **11** in 90% yield (3.39 g after drying over $CaCl_2$). Reaction of **9** with Zn and Sn (powder, 0.15 g, 1.26 mmol) was carried out under conditions of the previous experiment. According to ^{19}F NMR, a solution of fluoroaromatics included **9** (77%) and **10** (19%) (per aromatic moiety). A mixture (2.32 g) obtained by treatment with a solution of Br_2 (0.88 g, 5.5 mmol) contained 30.7% (GLC) compound **11** and 63.8% compound **9**; estimated yields were 19 and 49%, respectively.

Reaction of **9** with Zn was performed by the above procedure. The reaction mixture contained compound **10** (2%) (per aromatic moiety) and compound **9** (95%). Bromine (0.40 g, 2.50 mmol) was added to the solution. The above treatment resulted in the mixture (2.63 g) containing 4.5% compound **11** and 90.6% compound **9** (yields by NMR: 3 and 80%, respectively).