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Synthesis of perfluorobiphenyl tetracarboxylic acids *via* the $CuCl_2$-assisted homocoupling of organozinc reagents

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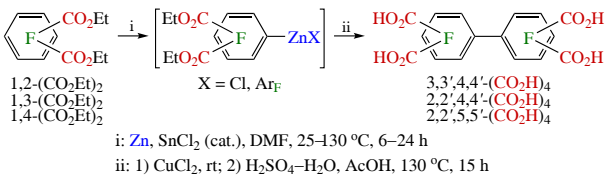
New organozinc reagents were obtained from ethyl esters of tetrafluorophenylene dicarboxylic acids in the reaction with Zn and $SnCl_2$ in DMF. Tetraethyl perfluorobiphenyl tetracarboxylates were synthesized from these organozinc reagents under the action of $CuCl_2$ and then were hydrolyzed into perfluorobiphenyl tetracarboxylic acids.



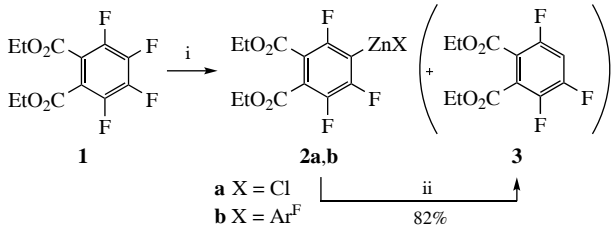
Keywords: organofluorine compounds, zinc, organozinc reagents, biphenyl, tetracarboxylic acids, homocoupling.

Biphenyl tetracarboxylic acids find applications in coordination chemistry, materials science, and environmental studies. These tetraacids facilitate the formation of metal–organic frameworks designed for applications in selective adsorption.[1–5] Moreover, they are utilized for the preparation of various coordination polymers for the use as luminescent sensors.[6–11] The introduction of fluorine atoms into organic molecules significantly alters their physical and chemical properties due to the unique characteristics of fluorine atom such as its high electronegativity, small atomic size, and the strength of the carbon–fluorine bond.[12–16]

Earlier, we have developed a method for preparing perfluoroaromatic organozinc compounds and demonstrated their utility in a range of reactions for the synthesis of polyfluoroarenes with various functional groups.[17–20] For example, using an organozinc compound obtained from ethyl pentafluorobenzoate, we synthesized octafluorobiphenyl-4,4′-dicarboxylic acid,[21,22] and from this acid coordination polymers with different architectures were constructed.[22,23]

To the best of our knowledge, there is little information regarding polyfluorinated biphenyl tetracarboxylic acids, the only example being the patented[24] synthesis of 2,2′,5,5′,6,6′-hexafluorobiphenyl-3,3′,4,4′-tetracarboxylic acid. The claimed overall yield from the starting perfluoroarene was rather modest.

In this communication, we report on the reaction of diethyl esters of tetrafluorophenylene dicarboxylic acids with zinc metal to obtain polyfluoroaromatic organozinc reagents for the synthesis of perfluorobiphenyl tetracarboxylic acids. To assess the reactivity of tetrafluorophenylene dicarboxylates toward organozinc compound we began with the reaction of diethyl 3,4,5,6-tetrafluorophthalate **1** (Scheme 1). Compound **1** did not react with Zn powder in DMF neither at room temperature nor under heating at 70 °C. We have previously[17] found that the addition of catalytic amounts of $SnCl_2$ facilitated the organozinc compound formation from perfluoroarenes. Using this approach, we carried out the reaction of diester **1** with Zn in DMF in the presence of $SnCl_2$ (10 mol%) at room temperature that resulted in [3,4-bis(ethoxycarbonyl)-2,5,6-trifluorophenyl]-zinc chloride **2a** and bis[3,4-bis(ethoxycarbonyl)-2,5,6-trifluorophenyl]zinc **2b**. The reaction was accompanied by the formation of minor quantities of diethyl 3,4,6-trifluorophthalate **3**, a product of the organozinc reagent quenching due to the presence of residual moisture. The conversion of starting compound **1** was almost complete after heating at 70 °C for 6 h (Table 1). When the solution of organozinc species **2a**,**b** in DMF was quenched with 2 M HCl, compound **3** was produced in high yield (see Scheme 1).



Scheme 1 *Reagents and conditions*: i, Zn, DMF, $SnCl_2$ (see Table 1); ii, 2 M HCl, room temperature.

Exposure of the solution of **2a**,**b** in DMF to $CuCl_2$ resulted in tetraethyl 2,2′,5,5′,6,6′-hexafluorobiphenyl-3,3′,4,4′-tetracarboxylate **4**, which then was hydrolyzed by heating with a mixture of sulfuric and acetic acids to produce the corresponding tetraacid **5** (Scheme 2).

Diethyl 2,3,5,6-tetrafluoroterephthalate **6**, in contrast to its isomer **1**, did not react with Zn under the conditions mentioned above (Scheme 3). We managed to obtain the required biaryl tetraester **7**, albeit in a low (7%) yield, only by severe heating (130 °C) compound **6** with Zn in DMF with catalytic amounts of $SnCl_2$ followed by treatment with $CuCl_2$ (the obtained crude reaction mixture contained much resinous material). When purified tetraester **7** was subjected to acidic hydrolysis, the corresponding tetraacid **8** was quantitatively obtained (see Scheme 3).

Table 1 Optimization of reaction of compound **1** with Zn.

Entry	$SnCl_2$ (mol%)	T/°C	t/h	**2**/**3**/**1** ratio[a]
1	–	25	15	0 : 0 : 100
2	–	70	8	0 : 0 : 100
3	10	25	15	94 : 4 : 2
4	10	70	6	96.5 : 3.5 : 0

[a] Determined by ^{19}F NMR spectroscopy.

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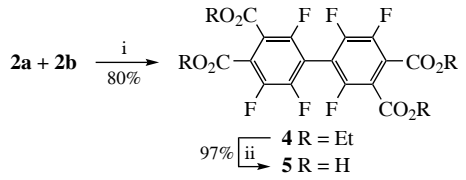
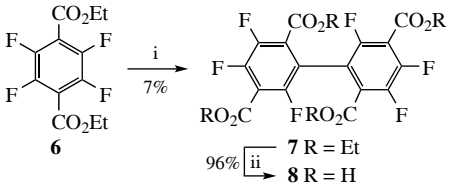


Scheme 2 *Reagents and conditions*: i, $CuCl_2$, room temperature; ii, H_2O, H_2SO_4, AcOH, 130 °C, 15 h.

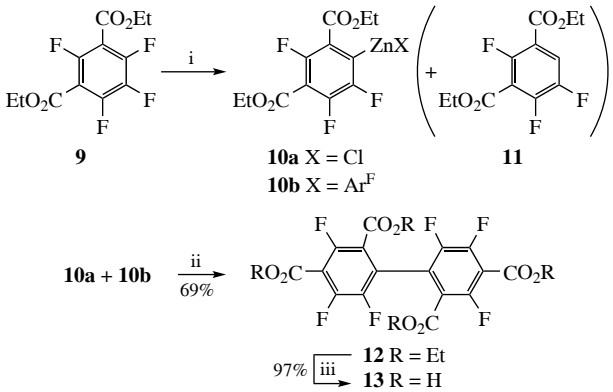


Scheme 3 *Reagents and conditions*: i, Zn, $SnCl_2$ (10 mol%), DMF, 130 °C, 24 h, then $CuCl_2$; ii, H_2SO_4, H_2O, AcOH, 130 °C, 15 h.

Diethyl 2,4,5,6-tetrafluoroisophthalate **9** upon stirring with Zn and $SnCl_2$ in DMF at room temperature was completely transformed into organozinc species **10a**,**b** (Scheme 4), the minor by-product being diethyl 2,4,5-trifluoroisophthalate **11**. Exposure of the solution of **10a**,**b** in DMF to $CuCl_2$ resulted in tetraethyl 3,3′,5,5′,6,6′-hexafluorobiphenyl-2,2′,4,4′-tetracarboxylate **12** (Scheme 4). It should be noted that diester **9** was available to us as a mixture with its isomer **6**, the diesters having been obtained from a mixture of perfluoro *m*- and *p*-xylenes in the 2.6 : 1 ratio. Isomer **6** was not involved in the reaction with Zn at room temperature nor did it undergo any further transformations; so product **12** was easily separated from **6** by column chromatography. Compound **12** was then successfully hydrolyzed in acidic medium to the target tetracarboxylic acid **13**.

We should note that the regioselectivity of organozinc compound formation in the cases of compounds **1** and **9**, as well as the low reactivity of *para*-isomer **6**, is in conformity with the patterns observed previously on reactions of perfluoroarenes with Zn.[17–19]

In conclusion, diethyl tetrafluorophenylene dicarboxylates were converted into organozinc compounds by the reaction with Zn in DMF in the presence of catalytic amounts of $SnCl_2$. Tetrafluoro- (iso)phthalates reacted smoothly, while the reaction of isomeric terephthalate derivative required extensive heating. Using a two-step sequence that involved a homocoupling of the organozincs with $CuCl_2$ followed by acidic hydrolysis of the resulting tetraethyl perfluorobiphenyl tetracarboxylates, perfluorobiphenyl tetra-carboxylic acids were synthesized. These perfluorobiphenyl tetracarboxylic acids can be utilized as ligands for the preparation of new metal–organic frameworks.



Scheme 4 *Reagents and conditions*: i, Zn, $SnCl_2$ (10 mol%), DMF, room temperature, 15 h; ii, $CuCl_2$; iii, H_2O, H_2SO_4, AcOH, 130 °C, 15 h.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.71267/mencom.7682.

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