

One-pot synthesis of *m*-terphenyl-2'-carbaldehydes

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Abstract

An efficient and straightforward one pot synthesis of *m*-terphenyl-2'-carbaldehyde derivatives via cascade reaction of aryl Grignard magnesium bromide with 1,3-dichloriodobenzene is described. Via the reactions three carbon-carbon bonds are constructed and *m*-terphenyls are obtained in good yields.

Keywords: One pot synthesis, cascade reaction, *m*-terphenyl-2'-carbaldehyde, 1,3-dichloriodobenzene, carbon-carbon bond construction

Introduction

The *m*-terphenyl moiety is an important structure for concave molecules.¹ If a functional group is introduced into the 2'-position of a *m*-terphenyl, the outer benzene rings shield this functional group. The shielding is extremely efficient if the outer benzene rings carry further substituents in the *ortho* positions (Figure 1).¹

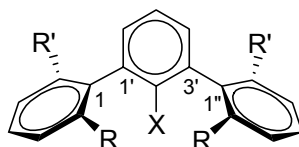
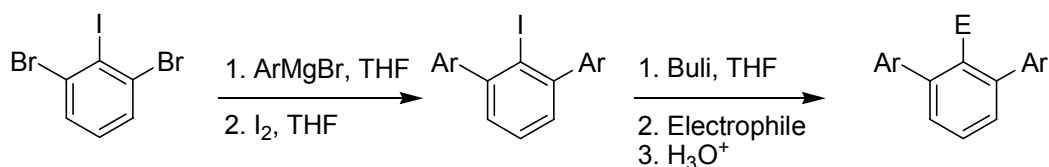


Figure 1

Some *m*-terphenyls with acidic substituents in the 2'-position have been introduced as selective proton donors for diastereoselective and regioselective protonations.² In addition, these compounds are useful intermediates for constructing optical active cyclophans,^{3,4} cyclic ketons,⁵⁻⁸

dendrimers,⁹ and liquid crystals.¹⁰ Thus, several approaches have been developed for their synthesis. Hart developed a method for the synthesis of *m*-terphenyls that may be substituted in all *ortho*-positions of the outer aryl rings.^{11,12} The key intermediate of Hart's method is the 2'-Grignard reagent, which can be quenched by iodine to give the 2'-iodide substituted compound. Starting from the iodide compound, various 2'-substituted *m*-terphenyls have been synthesized via the lithium derivative. Limited studies were carried out with aryl magnesium halides and other 1,2,3-trihalobenzenes such as 2,6-dichloriodobenzene and only moderate yields of the products were obtained.^{4,11-13} Furthermore, most reports on the synthesis of 2'-substituted *m*-terphenyl derivatives are limited to the two step procedure (Scheme 1).



Scheme 1. Synthesis of 2'-substituted *m*-terphenyl derivatives via two step procedure.

In the current study, we examine a facile one pot synthesis of *m*-terphenyl-2'-carbaldehydes starting from 1,3-dichloriodobenzene. Cascade reaction of aryl magnesium bromides with 1,2,3-trihalobenzene **1** followed by quenching with electrophile gives *m*-terphenyls **2** in a one pot reaction. By varying the substituents of the aryl groups of the Grignard reagent, different *m*-terphenyl derivatives can be obtained in good yields.

Results and Discussion

Our initial attempts to test the feasibility of this reaction employed readily accessible 1,3-dichloriodobenzene and phenyl magnesium bromide in THF which afforded 2,3-diphenyl magnesium bromide reagent. Then the addition of ethyl formate gave the desired product **2a** in 81% yield (Table 1). We next investigated the scope of the reaction using aryl magnesium bromides with diverse substituents at *ortho*-, *meta*- and *para*-positions. As a result, *m*-terphenyl-2'-carbaldehyde derivatives were obtained in good yields (Table 1). The structures of the isolated products were confirmed by mp, IR, ¹HNMR, ¹³CNMR and elemental analysis.

It should be mentioned that *ortho*-substituted *m*-terphenyls which can be further functionalized or converted to new functional groups are very important. For example, methoxy groups of the rings can be converted easily to phenol derivatives and bridged to finally give bimacrocylic concave *m*-terphenyl structures. Further investigation on involving these *m*-terphenyls in the polymer backbones is under investigation.

Table 1. One pot synthesis of m-terphenyl-2'-carbaldehyde derivatives

Entry	ArMgBr	Time (h)	Product	Yield (%) ^a
1		20		81
2		20		67
3		25		72
4		20		70
5		25		70
6		25		73

^a Isolated yields

Conclusions

In summary, we have developed an efficient and straightforward one pot approach to *m*-terphenyl-2'-carbaldehyde derivatives using readily accessible starting materials. To the best of our knowledge it is the first report on the one pot synthesis of *m*-terphenyl-2'-carbaldehyde derivatives.

Experimental Section

General Procedures. All substrates were purchased from Merck Company. The reactions involving organomagnesium halide reagents were carried out under argon. Solvents were dried by standard methods. Melting points were determined using a Gallenkamp melting point apparatus and are uncorrected. ¹H NMR and ¹³C NMR spectra were recorded on a Bruker FT-400 MHz in CDCl₃. The Infrared absorption spectra were recorded on a FTIR Bruker-Tensor 270 spectrophotometer. Elemental analyses were carried out with Heareus CHN-RAPID instrument.

General procedure for the synthesis of *m*-terphenyl-2'-carbaldehyde derivatives 2a-2f

To a stirred aryl magnesium bromide solution (prepared from aryl bromides (40 mmol) and Mg (40 mmol) in dry THF (40 mL)) was added slowly 1,3-dichloriodobenzene (4 mmol) in THF (10 mL) under argon and the mixture was refluxed for 20-25 hrs. Then ethyl formate (5 mL) was added and the reaction was refluxed for 30 min. The reaction mixture was then cooled with ice, quenched with dilute HCl (30 mL) and extracted with diethyl ether (3×50 mL). Combined organic layers were dried over MgSO₄ and concentrated in vacuo. The resulting residue was purified by recrystallization or column chromatography (diethyl ether– hexane, 20%) to afford the corresponding aldehydes.

1,1',3',1''-Terphenyl-2'-carbaldehyde (2a). Mp 76-77°C; IR (KBr, cm⁻¹): 2850, 2750, 1700, 1600, 1450; ¹H NMR (400 MHz, CDCl₃): δ 9.65 (s, 1H), 7.28 (t, *J* = 7.6 Hz, 1H), 7.09 (m, 12H); ¹³C NMR (100 MHz, CDCl₃): δ 194.0, 144.7, 140.1, 133.6, 131.9, 130.8, 130.0, 128.6, 128.1; Anal. Calcd for C₁₉H₁₄O: C, 88.34; H, 5.46. Found: C, 88.42; H, 5.51.

4,4''-Dimethyl-1,1',3',1''-terphenyl-2'-carbaldehyde (2b). Mp 108-109°C. IR (KBr, cm⁻¹): 2850, 2750, 1700, 1600, 1450; ¹H NMR (400 MHz, CDCl₃): δ 10.00 (s, 1H), 7.59 (t, *J* = 7.6 Hz, 1H), 7.40 (d, *J* = 7.6 Hz, 2H), 7.28 (m, 8H), 2.45 (s, 6H); ¹³C NMR (100 MHz, CDCl₃): δ 194.4, 144.7, 137.9, 137.1, 133.6, 131.9, 130.6, 129.9, 129.3, 21.7; Anal. Calcd for C₂₁H₁₈O: C, 88.08; H, 6.34. Found: C, 87.90; H, 6.40.

4,4''-Fluoro-1,1',3',1''-terphenyl-2'-carbaldehyde (2c). Mp 152-153°C. IR (KBr, cm⁻¹): 2850, 2750, 1700, 1600, 1450; ¹H NMR (400 MHz, CDCl₃): δ 9.61 (s, 1H), 7.28 (t, *J* = 7.6 Hz, 1H), 7.06 (d, *J* = 7.6 Hz, 2H), 7.01 (m, 4H), 6.82 (m, 4H); ¹³C NMR (100 MHz, CDCl₃): δ 193.6,

164.2, 161.7, 143.8, 135.9, 135.8, 133.5, 132.1, 131.7, 131.6, 131.0, 115.7, 115.5; Anal. Calcd for C₁₉H₁₂F₂O: C, 77.54; H, 4.11. Found: C, 77.48; H, 4.20.

3,3''-Dimethyl-1,1',3',1''-terphenyl-2'-carbaldehyde (2d). Mp 95-96°C. IR (KBr, cm⁻¹): 2850, 2750, 1700, 1600, 1450; ¹H NMR (400 MHz, CDCl₃): δ 10.00 (s, 1H), 7.62 (t, *J* = 7.6 Hz, 1H), 7.41 (d, *J* = 7.7 Hz, 2H), 7.35 (t, *J* = 7.5 Hz, 2H), 7.25 (d, *J* = 7.6 Hz, 2H), 7.21 (s, 2H), 7.18 (d, *J* = 7.5 Hz, 2H), 2.45 (s, 6H); ¹³C NMR (100 MHz, CDCl₃): δ 194.3, 144.8, 140.1, 138.3, 133.6, 131.9, 130.7, 128.8, 128.5, 127.2, 21.9; Anal. Calcd for C₂₁H₁₈O: C, 88.08; H, 6.34. Found: C, 87.80; H, 6.30.

2,2''-Dimethoxy-1,1',3',1''-terphenyl-2'-carbaldehyde (2e). Mp 165-166°C. IR (KBr, cm⁻¹): 2850, 2750, 1700, 1600, 1450; ¹H NMR (400 MHz, CDCl₃): δ 9.79 (s, 1H), 7.66 (t, *J* = 7.6 Hz, 1H), 7.42 (t, *J* = 7.4 Hz, 4H), 7.36 (d, *J* = 7.6 Hz, 2H), 7.13 (d, *J* = 7.6 Hz, 2H), 6.96 (d, *J* = 7.6 Hz, 2H), 3.79 (s, 6H); ¹³C NMR (100 MHz, CDCl₃): δ 193.0, 156.4, 139.4, 132.6, 131.2, 131.0, 129.8, 129.5, 129.3, 121.3, 110.9, 55.7; Anal. Calcd for C₂₁H₁₈O₃: C, 79.22; H, 5.70. Found: C, 79.41; H, 5.81.

2,2'',5,5''-Tetramethoxy-1,1',3',1''-terphenyl-2'-carbaldehyde (2f). Mp 186-187°C. IR (KBr, cm⁻¹): 2850, 2750, 1700, 1600, 1450; ¹H NMR (400 MHz, CDCl₃): δ 9.75 (s, 1H), 7.64 (t, *J* = 7.6 Hz, 1H), 7.35 (d, *J* = 7.6 Hz, 2H), 7.03 (s, 2H), 6.92 (d, *J* = 7.6 Hz, 2H), 6.86 (d, *J* = 7.6 Hz, 2H), 3.85 (s, 6H), 3.68 (s, 6H); ¹³C NMR (100 MHz, CDCl₃): δ 192.7, 154.0, 153.4, 152.1, 150.5, 139.0, 132.5, 130.9, 130.0, 117.2, 114.0, 111.8, 111.3, 56.1; Anal. Calcd for C₂₃H₂₂O₅: C, 73.00; H, 5.86. Found: C, 72.64; H, 5.92.

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