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# Regioselective synthesis of highly-substituted biaryls by reaction of vinyl malononitriles with acetylenic esters

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ABSTRACT

The one-pot procedure for synthesis of highly-substituted biaryl derivatives has been described via cyclocondensation reaction between vinyl malononitriles and acetylenic esters. A series of complex biaryls containing one-donor and three-acceptor moieties was obtained with good yields.



## 1. Introduction

The biaryl structural unit is a commonly found motif in biologically active molecules.[1,2] Moreover, biaryl-containing compounds can be used to design novel materials such as organic semiconductors and liquid crystals. Biaryls are also highly useful compound in organic chemistry, natural products,[1a,b,3a] materials science, pharmaceuticals,[3b,c] polymers, electroluminescent conjugated polymer,[3d] Sensors,[3e] ligands of organometallic catalyst,[3f,g] and semiconductors.[4]

Of the biaryl systems, biaryls containing electron donor and electron acceptor moieties such as alkyl, alkoxy, amino, nitrile or ester groups are not only useful in organic synthesis but are also useful as important substrates for chiral liquid crystals,[5] as chiral phases for chromatography,[6] and as optoelectronic materials.[7]

Accordingly, the synthesis of biaryls remains an active area in organic synthesis.[8] Classical methods for the synthesis of biaryls are based on cross coupling of two aromatic rings in the presence of transition-metal catalyst.[9] One of the oldest methods for construction of biaryls is reductive dimerization of aryl halides using copper bronze as reducing agent.[10] Coupling of electron-rich aromatic phenols also leads to the formation of biaryls under oxidative condition in moderate yields.[11] Symmetrical and unsymmetrical biaryls have been synthesized by cross coupling between the electrophilic aryl halid and organometallic species Ar–M (M being Mg, Zn, Sn, and B) in the presence of a palladium catalyst.[12]

Despite the broad synthesis applicability of Suzuki reaction, use of these methods to prepare highly functionalized biaryls places constraints on the choice of reagent, catalysts and/or reaction conditions. However some of the above mentioned methods suffer from at least one of the following draw backs: low yields, expensive catalyst of serious regiochemical ambiguities originating from orienting effect of the substituent, and harsh reaction condition.[13]

Alternatively, efficient approaches developed for the synthesis of biaryls starting from simple acyclic substrates, in which the substitution pattern of the final products dictated by the structures and functionality of the substrates. These general features are common in the most useful benzannulation reactions such as the [3+2+1] DÖtz chromium-mediated benzannulation of Fischer-type carbene complexes,[14] [4+2] cyclization,[15] [4+2] cycloaddition of metalacyclopentadienes and alkynes,[16] transition metal catalyzed [2+2+2] and [4+2] cycloadditions,[17] [4+2] benzannulation of *O*-alkynyl benzaldehyde and alkyne,[18] [3+3] cyclocondensation of bielectrophiles with binucleophiles,[19] 1,6-electrocyclization reaction,[20] [5+1] benzannulation of alkenoyl keteneacetals with nitroalkane,[21] and [4+2] annulations strategy from the Baylis–Hillman reaction.[22]

In the light of the above mentioned chemistry and properties of biaryls, the development of new approaches, which enable access to these entries, are desirable. As part of our ongoing studies on the development of facile methods for synthesis of organic compounds from readily available starting materials,[23] in this letter we found that vinyl malononitriles, can react with dialkyl acetylenedicarboxylates in the presence of a base, leading to highly-substituted biaryls via one-pot addition process (Scheme 1).

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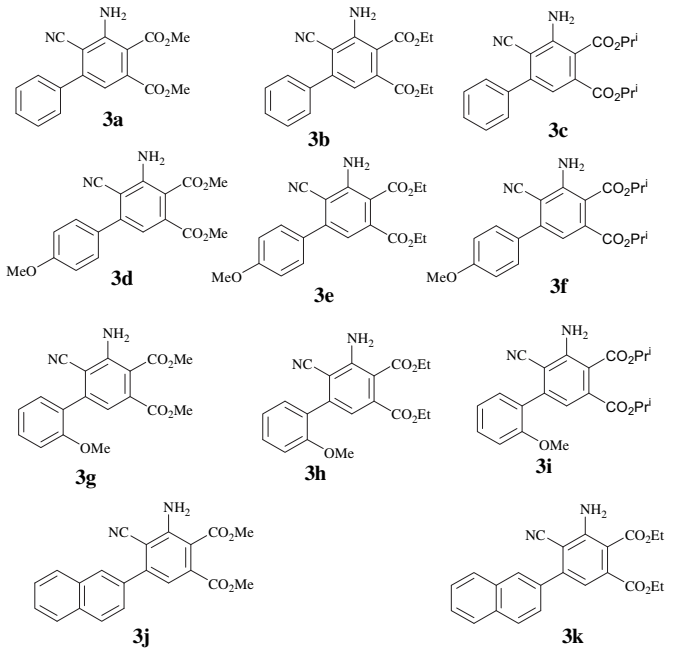
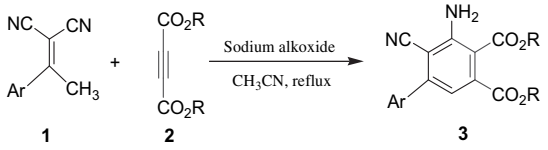



**Scheme 1.** Structure of product **3a–k**.

Thus, a mixture of a vinyl malononitrile **1**, an alkylacetylenedicarboxylate **2**, and sodium alkoxide was heated to reflux at 80 °C in acetonitrile to produce the corresponding biaryl **3** in 50–75% yields (Table 1 and Scheme 1).

**Table 1**
Reaction of vinyl malononitriles **1** with dialkyl acetylenedicarboxylates **2** in the presence of base




| Entry | Ar | R | Product | Yield[a] (%) |
|---|---|---|---|---|
| 1 | $C_6H_4$– | Me | **3a** | 65 |
| 2 | $C_6H_4$– | Ethyl | **3b** | 60 |
| 3 | $C_6H_4$– | Isopropyl | **3c** | 73 |
| 4 | 4-MeO–$C_6H_4$– | Me | **3d** | 73 |
| 5 | 4-MeO–$C_6H_4$– | Ethyl | **3e** | 62 |
| 6 | 4-MeO–$C_6H_4$– | Isopropyl | **3f** | 68 |
| 7 | 2-MeO–$C_6H_4$– | Me | **3g** | 55 |
| 8 | 2-MeO–$C_6H_4$– | Ethyl | **3h** | 62 |
| 9 | 2-MeO–$C_6H_4$– | Isopropyl | **3i** | 75 |
| 10 | 2-Naphthyl– | Me | **3j** | 53 |
| 11 | 2-Naphthyl– | Ethyl | **3k** | 50 |

[a] Isolated yield.

## 2. Results and discussion

For further investigation of the reaction condition, the reaction of vinyl malononitrile and dimethylacetylenedicaboxylate in the presence of a base, was selected as a model (Table 2). As shown in Table 2, temperature, solvent and base loading have an obvious influence on reaction yield. The best result (65% yields) was obtained with 1 equiv of sodium methoxide in $CH_3CN$ at reflux (Table 2, entry 5).

Using the optimized reaction conditions, we proceeded to probe into the scope of the substrates for the formation of highly-substituted biaryls (Table 1).

**Table 2**
Reaction of vinyl malononitriles **1** with dimethyl acetylenedicarboxylates **2**, under various conditions

| Entry | Solvent | Base | Time/h | $T$ (°C) | Yield[a] % |
|---|---|---|---|---|---|
| 1 | $CH_2Cl_2$ | $Et_3N$ | 12 | 25 | 20 |
| 2 | $CH_3CN$ | $Et_3N$ | 12 | 25 | 20 |
| 3 | $CH_2Cl_2$ | $CH_3ONa$ | 12 | 25 | 30 |
| 4 | $CH_3CN$ | $CH_3ONa$ | 12 | 25 | 35 |
| 5 | $CH_3CN$ | $CH_3ONa$ | 10 | 80 | 65 |
| 6 | $CH_3OH$ | $CH_3ONa$ | 10 | 65 | 50 |
| 7 | $CH_3CN$ | $K_2CO_3$ | 12 | 80 | 40 |

[a] Isolated yield.

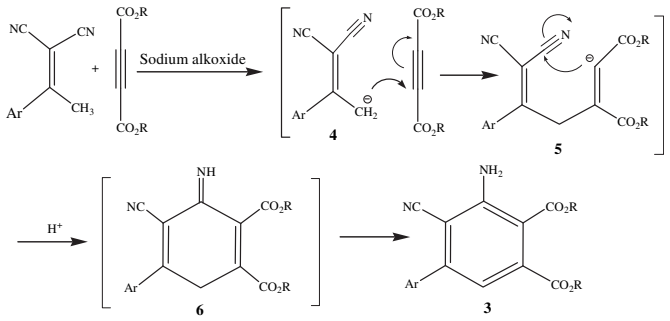
When other dialkyl acetylenedicarboxylates was used instead of DMAD, the base should be exchanged to appropriate alkoxide in order to avoid ester exchange reaction (Table 2).

The structures of the products **3a–k** (Scheme 1) were deduced from their elemental analyses, IR, mass, $^1$H NMR, and $^{13}$C NMR spectra. The mass spectra of these compounds displayed molecular ion peaks at the appropriate $m/z$ (%) values.

The IR spectrum of **3a** showed absorption at 2200 cm$^{-1}$ due to CN (triple bond) group, and two sharp bands at 3450 and 3362 cm$^{-1}$ due to asymmetric and symmetric vibrations of the $NH_2$ group and two ester carbonyls at 1712 and 1618 cm$^{-1}$, respectively.

The $^1$H NMR spectrum of **3a** exhibited two singlet readily recognized as arising from two methoxy protons ($\delta$=3.73 ppm and 3.93 ppm) and a broad singlet for two amine protons, and a characteristic singlet ($\delta$=6.87 ppm) due to an aromatic proton, along with a multiplet for the other aromatic protons ($\delta$=7.2–7.7 ppm).

The $^{13}$C NMR spectrum of **3a** showed 15 distinct resonances in agreement with the suggested structure. The $^1$H NMR and $^{13}$C NMR spectra of **3b–k** are similar to those of **3a** except for the R and Ar groups, which exhibit characteristic signals with appropriate chemical shifts. Mechanistically, the reaction can be interpreted as follows. The carbanion **4** generated by the deprotonation of vinyl malononitriles **1** by sodium alkoxide and adds to dialkyl acetylenedicarboxylates **2** in tandem, to furnish the vinyl anion **5**. Then, the vinyl anion **5** attacked the carbon center of the triple bond in CN by an interamolecular nucleophilic addition to produce imine **6**, and then isomeration of **6**, gave highly-substituted biaryls **3** (Scheme 2).




**Scheme 2.** Proposed mechanism for the formation of compounds **3**.

In summary, we have introduced a novel one-pot synthesis of dialkyl-5-amino-6-cyanobiphenyl-3,4-dicarboxylates and dialkyl-3-amino-4-cyano-5-(2-naphthyl)phthalate of potential interest. According to this new strategy, poly functionalized biphenyls and terphenyls could be prepared by cyclocondensation reaction between vinyl malonitriles and acetylenic esters in the presence of base. Remarkably, the presented one-pot procedure tolerates amine, carbonitril, and alkoxycarbonyl functional groups.

## 3. Experimental

### 3.1. General

Melting points were measured on an Electrothermal 9100 apparatus and are uncorrected. Elemental analyses for C, H, and N were performed using a Heraeus CHN–O-Rapid analyzer. IR spectra were measured on a Perkin-Elmer 783 infrared spectrophotometer. $^1$H and $^{13}$C NMR spectra were measured with BRUKER DRX-500 AVANCE spectrometer at 500 and 125.77 MHz, BRUKER DRX-300 AVANCE spectrometer at 300.13 and 75.46 MHz, respectively. Mass spectra were recorded on a Shimadzu GC–MS-QP5050 mass spectrometer operating at an ionization potential of 70 eV. Acetylenic esters were obtained from Merck (Germany) and Fluka (Buchs, Switzerland) and all materials were used without further purification.

### 3.2. General procedure for the synthesis of products

A 25 mL flask was charged with vinyl malononitrile (1 mmol), dialkylacetylenedicarboxylate (1 mmol), 10 mL of $CH_3CN$, and sodium alkoxy (1 mmol). The solution was heated under reflux. After the reaction was completed (10 h), $CH_3CN$ was removed under reduced pressure. The product was purified by silica gel column chromatography (*n*-hexanes/EtOAc, 8:1 for **3a**–**i**) and (*n*-hexanes/EtOAc/$Et_3N$, 10:2:0.1 for **3j** and **3k**) to yield the polysubstituted biarile **3**.

*3.2.1. Dimethyl-5-amino-6-cyanobiphenyl-3,4-dicarboxylate of (**3a**).* White powder (2.02 g, 65%); mp: 85–87 °C; $R_f$ (5:2 *n*-hexane/EtOAc) 0.46; IR (KBr) cm$^{-1}$: 3450 and 3362 ($NH_2$), 2200 (CN), 1730 and 1712 (2C=O). Anal. Calcd for $C_{17}H_{14}N_2O_4$ (310.31): C, 65.80; H, 4.55; N, 9.03%. Found: C, 65.4; H, 4.4; N, 9.1%; $^1$H NMR (500.13 MHz, $CDCl_3$): $\delta$ (ppm) 3.89 (s, 3H), 3.90 (s, 3H), 6.37 (br s, 2H, NH2), 6.87 (s, 1H), 7.47–7.56 (m, 5H); $^{13}$C NMR (125.77 MHz, $CDCl_3$) $\delta$ (ppm) 52.6, and 52.8 (2$OCH_3$), 98.8 (CN), 109.6 and 116.0 (2C), 117.3, 128.4, 128.8, and 129.6 (4CH), 137.2, 139.5, 150.0, and 151.6 (4CH), 166.7 and 168.4 (2C=O); MS, *m*/*z* (%): 310 ($M^+$, 76), 279 ($M^+$−OMe, 42), 248 ($M^+$−2OMe, 16.2), 220 ($M^+$−$CO_2$Me−OMe, 100), 192($M^+$−2$CO_2$Me, 57).

*3.2.2. Diethyl-5-amino-6-cyanobiphenyl-3,4-dicarboxylate (**3b**).* Yellow powder (2.03 g, 60%); mp: 75–77 °C; $R_f$ (5:2 *n*-hexane/EtOAc) 0.54; IR (KBr) cm$^{-1}$: 3450 and 3310 ($NH_2$), 2200 (CN), 1710 and 1695 (2C=O). Anal. Calcd for $C_{19}H_{18}N_2O_4$ (338.37): C, 67.44; H, 5.36; N, 8.28%. Found: C, 67.6; H, 5.4; N, 8.2%; $^1$H NMR (500.13 MHz, $CDCl_3$) $\delta$ (ppm) 1.36 (t, *J*=5.0 Hz, 3H), 1.38 (t, *J*=5.0 Hz, 3H), 4.36 (quartet, $^3J_{HH}$=5.0 Hz, 4H), 4.37 (quartet, $^3J_{HH}$=5.0 Hz, 4H), 6.34 (br s, 2H, $NH_2$), 6.89 (s, 1H), 7.37–7.56 (m, 5H); $^{13}$C NMR (125.77 MHz, $CDCl_3$) $\delta$ (ppm) 13.9 and 14.1 (2$CH_3$), 61.8 and 61.9 (2$OCH_2$), 98.6 (CN), 109.8 and 116.1 (2C), 117.0, 128.4, 128.83, and 129.5 (4CH), 137.3, 139.9, 149.8, and 151.7 (4C), 166.9 and 167.9 (C=O); MS, *m*/*z* (%): 338 ($M^+$, 100), 293 ($M^+$−OEt, 18.5), 264 ($M^+$−OEt−Et, 58), 248 ($M^+$−2OEt, 29), 220 ($M^+$−$CO_2$Et−OEt, 96), 192 ($M^+$−2$CO_2$Et, 70).

*3.2.3. Diisopropyl-5-amino-6-cyanobiphenyl-3,4-dicarboxylate(**3c**).* White powder (2.67 g, 73%); mp: 129–131 °C; $R_f$ (5:2 *n*-hexane/EtOAc) 0.74; IR (KBr) cm$^{-1}$: 3490 and 3350 ($NH_2$), 2200 (CN), 1725 and 1695 (C=O). Anal. Calcd for $C_{21}H_{22}N_2O_4$ (366.42): C, 68.84; H, 6.05; N, 7.65%. Found: C, 68.4; H, 6.1; N, 7.7%; $^1$H NMR (500.13 MHz, $CDCl_3$) $\delta$ (ppm) 1.36 (d, *J*=5.0 Hz, 6H), 1.37 (d, *J*=5.0 Hz, 6H), 5.24 (m, 2H), 6.34 (br s, 2H, NH2), 6.83 (s, 1H), 7.45–7.55 (m, 5H); $^{13}$C NMR (125.77 MHz, $CDCl_3$) $\delta$ (ppm) 21.6 and 21.8 (2$CH_3$), 69.7 and 70.0 (2OCH), 98.4 (CN), 110.5 and 116.2 (2C), 117.1, 128.4, 128.8, and 129.5 (4CH), 137.5, 140.0, 149.5, and 151.5 (4C), 165.9 and 167.1 (2C=O); MS, *m*/*z* (%): 366 ($M^+$, 100), 324 ($M^+$−$CH_2CHCH_3$, 16), 282 ($M^+$−2$CH_2CHCH_3$, 29), 264 ($M^+$−OCH($CH_3$)$_2$−$CH_2CHCH_3$, 37), 220 ($M^+$−$CO_2$CH($CH_3$)$_2$−OCH($CH_3$)$_2$, 19), 192 ($M^+$−2$CO_2$CH($CH_3$)$_2$, 33).

*3.2.4. Dimethyl-5-amino-6-cyano-4′-methoxybiphenyl-3,4-dicarboxylate (**3d**).* White powder (2.48 g, 73%); mp: 135–137 °C; $R_f$ (5:2 *n*-hexane/EtOAc) 0.34; IR (KBr) cm$^{-1}$: 3448 and 3343 ($NH_2$), 2200 (CN), 1730 and 1695 (2C=O). Anal. Calcd for $C_{18}H_{16}N_2O_5$ (340.33): C, 63.52; H, 4.74; N, 8.23%. Found: C, 63.3; H, 4.8; N, 8.1%; $^1$H NMR (500.13 MHz, $CDCl_3$) $\delta$ (ppm) 3.83 (s, 3H), 3.86 (s, 3H), 3.87 (s, 3H), 6.36 (br s, 2H, $NH_2$), 6.83 (s, 1H), 6.98 (d, *J*=8.3 Hz, 2H), 7.50 (d, *J*=8.3 Hz, 2H); $^{13}$C NMR (125.77 MHz, $CDCl_3$) $\delta$ (ppm) 52.6, 52.8 and 55.4 (3$OCH_3$), 98.3 (CN), 108.9 (C), 114.3 (CH), 116.4 (C), 117.0 (CH), 129.5 (C), 129.8 (CH), 139.5, 149.7, 151.8, and 160.8 (4C), 166.7 and 168.5 (2C=O); MS, *m*/*z* (%): 340 ($M^+$, 100), 309 ($M^+$−OMe, 35), 250 ($M^+$−$CO_2$Me−OMe, 82), 222 ($M^+$−2$CO_2$Me, 53).

*3.2.5. Diethyl-5-amino-6-cyano-4′-methoxybiphenyl-3,4-dicarboxylate (**3e**).* Yellow powder (2.28 g, 62%); mp: 115 °C; $R_f$ (5:2 *n*-hexane/EtOAc) 0.48; IR (KBr) cm$^{-1}$: 3436 and 3325 ($NH_2$), 2200 (CN), 1720 and 1700 (2C=O). Anal. Calcd for $C_{20}H_{20}N_2O_5$ (368.39): C, 65.21; H, 5.47; N, 7.60%. Found: C, 65.0; H, 5.5; N, 7.7%; $^1$H NMR (500.13 MHz, $CDCl_3$) $\delta$ (ppm) 1.36 (m, 6H), 3.85 (s, 3H), 4.34 (m, 4H), 6.38 (br s, 2H, $NH_2$), 6.82 (s, 1H), 6.99 (d, *J*=7.7 Hz, 2H), 6.99 (d, *J*=7.7 Hz, 2H); $^{13}$C NMR (125.77 MHz, $CDCl_3$) $\delta$ (ppm) 13.9 and 14.1 (2$CH_3$), 55.4 ($OCH_3$), 61.8 and, 61.9 (2$OCH_2$), 98.2 (CN), 109.1 (C), 114.3 (CH), 116.4 (C), 117.0 (CH), 129.6 (C), 129.8 (CH), 139.9, 149.6, 151.8, and 160.8 (4C), 166.4 and 168.0 (2C=O); MS, *m*/*z* (%): 368 ($M^+$, 100), 323 ($M^+$−OEt, 11), 294 ($M^+$−OEt−Et, 43), 250 ($M^+$−$CO_2$Et−OEt, 70), 222 ($M^+$−2$CO_2$Et, 45).

*3.2.6. Diisopropyl-5-amino-6-cyano-4′-methoxybiphenyl-3,4-dicarboxylate (**3f**).* White powder (2.70 g, 68%); mp: 77 °C; $R_f$ (5:2 *n*-hexane/EtOAc) 0.57; IR (KBr) cm$^{-1}$: 3457 and 3343 ($NH_2$), 2200 (CN), 1715 and 1690 (2C=O). Anal. Calcd for $C_{22}H_{24}N_2O_5$ (396.45): C, 66.65; H, 6.10; N, 7.07%. Found: C, 66.8; H, 6.0; N, 7.0%; $^1$H NMR (500.13 MHz, $CDCl_3$) $\delta$ (ppm) 1.35–1.37 (m, 12H), 3.68 (s, 3H), 5.22 (m, 2H), 6.33 (br s, 2H, $NH_2$), 6.76 (s, 1H), 7.01 (d, *J*=8.3 Hz, 2H), 7.51 (d, *J*=8.3 Hz, 2H); $^{13}$C NMR (125.77 MHz, $CDCl_3$) $\delta$ (ppm) 21.6 and 21.7 (2$CH_3$), 55.4 ($OCH_3$), 69.6 and 69.9 (2OCH), 98.1 (CN), 109.9 (C), 114.3 (CH), 116.6 (C), 116.95(CH), 129.7 (C), 129.8 (CH), 140.2, 149.3, 151.6, and 160.7 (4C), 165.9 and 167.3 (2C=O); MS, *m*/*z* (%): 396 ($M^+$, 100), 354 ($M^+$−$CH_2CHCH_3$, 20), 312 ($M^+$−2$CH_2CHCH_3$, 31), 294 ($M^+$−OCH($CH_3$)$_2$−$CH_2CHCH_3$, 23), 222 ($M^+$−2$CO_2$CH($CH_3$)$_2$, 20).

*3.2.7. Dimethyl-5-amino-6-cyano-2′-methoxybiphenyl-3,4-dicarboxylate (**3g**).* White powder; (1.87 g, 55%); mp: 129 °C; $R_f$ (5:2 *n*-hexane/EtOAc) 0.35; IR (KBr) cm$^{-1}$: 3460 and 3350 ($NH_2$), 2200 (CN), 1730 and 1700 (2C=O). Anal. Calcd for $C_{18}H_{16}N_2O_5$ (340.33): C, 63.52; H, 4.74; N, 8.23%. Found: C, 63.3; H, 4.8; N, 8.1%; $^1$H NMR (500.13 MHz, $CDCl_3$) $\delta$ (ppm) 3.83 (s, 3H), 3.88 (s, 6H), 6.23 (br s, 2H, $NH_2$), 6.84 (s, 1H), 7.0 (m, 2H), 7.24 (d, *J*=7.2 Hz, 1H), 7.41 (t, *J*=7.6 Hz, 1H); $^{13}$C NMR (125.77 MHz, $CDCl_3$) $\delta$ (ppm) 52.6, 52.7, and 55.4 (3$OCH_3$), 101.2 (CN), 109.9 (C), 111.4 (CH), 115.9 (C), 118.4 and 120.8 (2CH), 126.4 (C), 130.3 and 131.0 (2CH), 139.0, 147.4, 150.7, and 156.3 (4C), 166.8 and 168.4 (2C=O); MS, *m*/*z* (%): 340 ($M^+$, 100), 309 ($M^+$−OMe, 36), 250 ($M^+$−$CO_2$Me−OMe, 92), 222 ($M^+$−2$CO_2$Me, 36).

*3.2.8. Diethyl-5-amino-6-cyano-2′-methoxybiphenyl-3,4-dicarboxylate (**3h**).* Yellow powder (2.28 g, 62%); mp: 104 °C; $R_f$ (5:2 *n*-hexane/EtOAc) 0.42; IR (KBr) cm$^{-1}$: 3460 and 3340 ($NH_2$), 2210 (CN), 1720 and 1690 (C=O). Anal. Calcd for $C_{20}H_{20}N_2O_5$ (368.39): C, 65.21; H, 5.47; N, 7.60%. Found: C, 64.9; H, 5.6; N, 7.5%; $^1$H NMR (500.13 MHz, $CDCl_3$) $\delta$ (ppm) 1.33–1.37 (m, 6H), 3. 4.34 (m, 4H), 6.25 (br s, 2H, $NH_2$), 6.82 (s, 1H), 7.0 (m, 2H), 7.25 (m, 1H), 7.41 (m, 1H); $^{13}$C NMR (125.77 MHz, $CDCl_3$) $\delta$ (ppm) 13.9 and 14.1 (2$CH_3$), 55.5 ($OCH_3$), 61.8 and 61.8 (2$OCH_2$), 101.0 (CN), 110.1 (C), 111.4 (CH), 116.0 (C), 118.3 and 120.8 (2CH), 126.5 (C), 130.3 and 130.9 (2CH), 139.4,

147.2, 150.8, and 156.3 (4C), 166.5 and 168.0 (2C=O); MS, *m*/*z* (%): 368 ($M^+$, 100), 323 ($M^+$−OEt, 14), 294 ($M^+$+1−$CO_2$Et, 28), 250 ($M^+$−$CO_2$Et−OEt, 77), 222 ($M^+$−2$CO_2$Et, 22).

*3.2.9. Diisopropyl-5-amino-6-cyano-4′-methoxybiphenyl-3,4-dicarboxylate (**3i**).* Yellow oil; (2.97 g, 75%); mp: 77–78 °C; $R_f$ (5:2 *n*-hexane/EtOAc) 0.57; IR (KBr) $cm^{-1}$: 3460 and 3355 ($NH_2$), 2210 (CN), 1725, 1695, (2C=O). Anal. Calcd for $C_{22}H_{24}N_2O_5$ (396.45): C, 66.65; H, 6.10; N, 7.07%. Found: C, 66.3; H, 6.2; N, 7.1%; $^1$H NMR (500.13 MHz, $CDCl_3$) $\delta$ (ppm) 1.31–1.36 (m, 12H), 3.82 (s, 3H), 5.22 (m, 2H), 6.19 (br s, 2H, $NH_2$), 6.77 (s, 1H), 7.01–7.05 (m, 2H), 7.23–7.25 (m, 1H), 7.39–7.41 (m, 1H); $^{13}$C NMR (125.77 MHz, $CDCl_3$) $\delta$ (ppm) 21.6 and 21.7 ($2CH_3$), 55.4 ($OCH_3$), 69.5 and 69.9 (2OCH), 100.9 (CN), 111.4 (CH), 116.0 (C), 118.2 and 120.8 (2CH), 126.6 (C), 130.3 and 130.9 (2CH), 139.7, 146.8, 150.6, and 156.4 (4C), 166.0 and 167.16 (2C=O); MS, *m*/*z* (%): 396 ($M^+$, 100), 354 ($M^+$−$CH_2CHCH_3$, 40), 312 ($M^+$−2$CH_2CHCH_3$, 55), 294 ($M^+$−$OCH(CH_3)_2$−$CH_2CHCH_3$, 53), 222 ($M^+$−2$CO_2CH(CH_3)_2$, 22).

*3.2.10. Dimethyl-3-amino-4-cyano-5-(2-naphthyl) phthalate (**3j**).* White powder (1.91 g, 53%); mp: 85–86 °C; $R_f$ (5:2:0.2 *n*-hexane/EtOAc/$Et_3N$) 0.44; IR (KBr) $cm^{-1}$: 3450 and 3350 ($NH_2$), 2200 (CN), 1725 and 1700 (2C=O), 1600, 1250. Anal. Calcd for $C_{21}H_{16}N_2O_4$ (360.37): C, 69.99; H, 4.48; N, 7.77%. Found: C, 70.2; H, 4.5; N, 7.7%; $^1$H NMR (300.13 MHz, DMSO-$d_6$): $\delta$ (ppm) 3.83 (s, 3H), 3.84 (s, 3H), 6.80 (br s, 2H, $NH_2$), 7.00 (s, 1H), 7.57–7.70 (m, 3H), 7.98–8.02 (m, 3H), 8.15 (s, 1H); $^{13}$C NMR (75.46 MHz, DMSO-$d_6$) $\delta$ (ppm) 52.8 ($OCH_3$), 98.0 (CN), 111.8 and 116.1 (2C), 116.4 (CH), 125.8, 126.8, and 127.2 (3C), 127.61 (CH), 128.0 and 128.2 (2C), 128.4 (CH), 132.5, 132.9, 134.5, and 137.6 (4CH), 148.8 (C), 150.7 (CH), 166.2 and 167.1 (2C=O); MS, *m*/*z* (%): 360 ($M^+$, 100), 329($M^+$−OMe, 27), 270 ($M^+$−$CO_2$Me−OMe, 61), 242 ($M^+$−2$CO_2$Me, 93).

*3.2.11. Diethyl-3-amino-4-cyano-5-(2-naphthyl) phthalate (**3k**).* Yellow powder (2.06 g, 53%); mp: 75–77 °C; $R_f$ (5:2:0.2 *n*-hexane/EtOAc/$Et_3N$) 0.64; IR (KBr) $cm^{-1}$: 3450 and 3350 ($NH_2$), 2200 (CN), 1720 and 1700 (2C=O). Anal. Calcd for $C_{23}H_{20}N_2O_4$ (388.43): C, 71.12; H, 5.19; N, 7.21%. Found: C, 70.8; H, 5.3; N, 7.3%; $^1$H NMR (300.13 MHz, DMSO-$d_6$) $\delta$ (ppm) 1.27 (t, $^3J_{HH}$=6.8 Hz, 6H), 4.29 (m, 4H), 6.81 (br s, 2H, $NH_2$), 6.98 (s, 1H), 7.58–7.69 (m, 3H), 7.97–8.06 (m, 3H), 8.1 (s, H); $^{13}$C NMR (75.46 MHz, DMSO-$d_6$) $\delta$ (ppm) 13.6 and 13.8 ($2CH_3$), 61.7 ($OCH_2$), 97.9 (CN), 111.5 and 116.1 (2C), 116.4 (CH), 125.9, 126.8, and 127.1 (3C), 127.6 (CH), 128.0 and 128.2 (2C), 128.4 (CH), 132.5, 132.9, 134.6, and 138.2 (4CH), 148.9 (C), 150.9 (CH), 166.8 and 166.7 (2C=O); MS, *m*/*z* (%): 388 ($M^+$, 100), 343 ($M^+$−OEt, 97), 314 ($M^+$−OEt−Et, 48), 298 ($M^+$−2OEt, 5), 270 ($M^+$−$CO_2$Et−OEt,49.6), 242 ($M^+$−2$CO_2$Et, 78).

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## Supplementary data

Copies of the IR, mass, $^1$H NMR, and $^{13}$C NMR spectra for products are available. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2010.03.052.

## References and notes

1. (a) Torssell, K. G. B. *Natural Product Chemistry*; Wiley: Chichester, UK, 1983; (b) Thomson, R. H. *The Chemistry of Natural Products*; Blackie and Son: Glasgow, 1985; (c) Denmark, S. E.; Wu, Z. *Org. Lett.* **1999**, *1*, 1495–1498.
2. Bringmann, G.; Mortimer, A. J. P.; Keller, P. A.; Gesser, M. J.; Garner, J.; Breuning, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 5384.
3. (a) Baudoin, O.; GuHritte, F. *Stud. Nat. Prod. Chem.* **2003**, *29*, 355–417; (b) Rao, A. V. R.; Gurjar, M. K.; Reddy, K. L.; Rao, A. S. *Chem. Rev.* **1995**, *95*, 2135–2167; (c) Nicolaou, K. C.; Boddy, C. N. C.; BrJse, S.; Winssinger, N. *Angew. Chem.* **1999**, *111*, 2230–2287; *Angew. Chem., Int. Ed.* **1999**, *38*, 2096–2152; (d) Roncali, J. *Chem. Rev.* **1992**, *92*, 711–738; (e) Mei, X.; Wolf, C. *J. Am. Chem. Soc.* **2006**, *128*, 13326–13327; (f) Brunel, J. M. *Chem. Rev.* **2005**, *105*, 857–897; (g) Berthod, M.; Mignani, G.; Woodward, G.; Lemaire, M. *Chem. Rev.* **2005**, *105*, 1801–1836.
4. Kraft, A.; Grimsdale, A. C.; Holmes, A. B. *Angew. Chem., Int. Ed.* **1998**, *37*, 402–428.
5. (a) Yamamuro, K.; Ono, S.; Tabushi, I. *Tetrahedron Lett* **1988**, *29*, 1797–1798; (b) Yamamuro, K.; Ono, S.; Ogoshi, H.; Masuda, H.; Kuroda, Y. *Synlett* **1989**, 18–19.
6. Mikes, F.; Boshart, G. *J. Chromatogr.* **1978**, *149*, 455–464.
7. Reviews: (a) Chelma, D. S.; Zyss, J. *Nonlinear Optical Properties of Organic Molecules and Crystals*; Academic: Orlando, FL, 1987; (b) Elsenbauer, R. L.; Schacklett, L. W. In *Handbook of Conducting Polymers*; Skotheim, T. A., Ed.; Marcel Dekker: New York, NY, 1986; Vol. 1, Chapter 7.
8. (a) Cicero, D.; Lembo, A.; Leoni, A.; Tagliatesta, P. *New J. Chem.* **2009**, *33*, 2162–2165; (b) Akai, S.; Ikawa, T.; Takayanagi, S.-I.; Morikawa, Y.; Mohri, S.; Tsubakiyama, M.; Egi, M.; Wada, Y.; Kita, Y. *Angew. Chem., Int. Ed.* **2008**, *47*, 7673–7676; (c) Ram, R. N.; Kumar, N. *Tetrahedron* **2008**, *64*, 10267–10271; (d) Adib, M.; Mohammadi, B.; Mahdavi, M.; Abbasi, A. R.; Riazati Kesheh, M. *Synlett* **2007**, 2497–2500; (e) Xue, D.; Li, J.; Zhang, Z.-T.; Deng, J.-G. *J. Org. Chem.* **2007**, *72*, 5443–5445; (f) Yi, C.; Blum, C.; Liu, S.-X.; Frei, G.; Neels, A.; Renaud, P.; Leutwyler, S.; Decurtins, S. *J. Org. Chem.* **2008**, *73*, 3596–3599.
9. (a) Negishi, E.; De Meijere, A. *Handbook of Organopalladium Chemistry for Organic Synthesis*; Wiley Interscience: New York, NY, 2002; (b) De Meijere, A.; Diederich, F. *Metal-Catalyzed Cross-Coupling Reactions*; Wiley-VCH: Weinheim, 2004; Vols. 1 and 2.
10. Ullmann, F.; Bielecki, J. *Chem. Ber.* **1901**, *34*, 2174–2185.
11. Taylor, W. I.; Battersby, A. R. *Oxidative Coupling of Phenols*; Dekker: New York, NY, 1967; Vol. 1.
12. Hassan, J.; Se vignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359–1469.
13. Goel, A.; Singh, F. V. *Tetrahedron Lett.* **2005**, *46*, 5585–5587.
14. (a) Dötz, K. H.; Tomuschat, P. *Chem. Soc. Rev.* **1999**, *28*, 187–198; (b) Wang, H.; Huang, J.; Wulff, W. D.; Rheingold, A. L. *J. Am. Chem. Soc.* **2003**, *125*, 8980–9891; (c) Vorogushin, A. V.; Wulff, W. D.; Hansen, H.-J. *J. Am. Chem. Soc.* **2002**, *124*, 6512–6513.
15. (a) Danheiser, R. L.; Brisbois, R. G.; Kowalczyk, J. J.; Miller, R. F. *J. Am. Chem. Soc.* **1990**, *112*, 3093–3100; (b) Danheiser, R. L.; Gee, S. K. *J. Org. Chem.* **1984**, *49*, 1672–1674.
16. (a) Xi, Z.; Sato, K.; Gao, Y.; Lu, J.; Takahashi, T. *J. Am. Chem. Soc.* **2003**, *125*, 9568–9569; (b) Takahashi, T.; Ishikawa, M.; Huo, S. *J. Am. Chem. Soc.* **2002**, *124*, 388–389.
17. (a) Bonaga, L. V. R.; Zhang, H.-C.; Moretto, A. F.; Ye, H.; Gauthier, D. A.; Li, J.; Leo, G. C.; Maryanoff, B. E. *J. Am. Chem. Soc.* **2005**, *127*, 3473–3485; (b) For a review, see Ref. 7.
18. Asao, N.; Nogami, T.; Lee, S.; Yamamoto, Y. *J. Am. Chem. Soc.* **2003**, *125*, 10921–10925; (b) Asao, N.; Takahashi, K.; Lee, S.; Kasahara, T.; Yamamoto, Y. *J. Am. Chem. Soc.* **2002**, *124*, 12650–12651; (c) Asao, N.; Aikawa, H.; Yamamoto, Y. *J. Am. Chem. Soc.* **2004**, *126*, 7458–7459.
19. (a) Langer, P.; Bose, G. *Angew. Chem., Int. Ed.* **2003**, *42*, 4033–4036; (b) Katritzky, A. R.; Li, J.; Xie, L. *Tetrahedron.* **1999**, *55*, 8263–8293.
20. (a) Serra, S.; Fuganti, C.; Moro, A. *J. Org. Chem.* **2001**, *66*, 7883–7888; (b) Turnbull, P.; Moore, H. W. *J. Org. Chem.* **1995**, *60*, 644–679.
21. (a) Bi, X.; Dong, D.; Liu, Q.; Pan, W.; Zhao, L.; Li, B. *J. Am. Chem. Soc.* **2005**, *127*, 4578–4579; (b) Barun, O.; Nandi, S.; Panda, K.; Ila, H.; Junjappa, H. *J. Org. Chem.* **2002**, *67*, 5398–5401.
22. Lee, M. J.; Lee, K. Y.; Gowrisankar, S.; Kim, J. N. *Tetrahedron Lett.* **2006**, *47*, 1355–1358; Winterfeldt, E. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 423–434.
23. (a) Esmaeili, A. A.; Bodaghi, A. *Tetrahedron* **2003**, *59*, 1169; (b) Esmaeili, A. A.; Darbanian, M. *Tetrahedron* **2003**, *59*, 9169–9174; (c) Esmaeili, A. A.; Zendegani, H. *Tetrahedron* **2005**, *61*, 4031; (d) Esmaeili, A. A.; Amini, S.; Bodaghi, A. *Synlett* **2007**, 1452; (e) Esmaeili, A. A.; Nasseri, M. A.; Vesalipoor, H.; Bijanzadeh, H. *ARKIVOC* **2008**, *xv*, 343; (f) Esmaili, A. A.; Vesalipoor, H. *Synthesis* **2009**, 1635.