Supporting Information

for

Organobase-catalyzed three-component reactions for the synthesis of 4H-2-aminopyrans, condensed pyrans and polysubstituted benzenes

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Experimental
General

Melting points reported are uncorrected and were determined with a Sanyo (Gallaenkamp) instrument. Infrared spectra were recorded as KBr pellets on a Jasco FTIR 6300 instrument and absorption bands are reported in cm⁻¹. ¹H and ¹³C NMR spectra were determined with a Bruker DPX instrument at 400 MHz for ¹H NMR and 100 MHz for ¹³C NMR as CDCl₃ or DMSO-d₆ solutions with TMS as internal standard. Chemical shifts are reported in δ (ppm). Mass spectra and accurate mass were measured using a GC–MS DFS Thermo spectrometer with the EI (70 eV) mode. X-ray crystallographic structure determinations were performed by using Rigaku Rapid II and Bruker X8 Prospector single crystal X-ray diffractometers. All X-ray crystal structural data can be obtained free of charge from the Cambridge Crystallographic Data Centre at www.ccdc.cam.ac.uk. All reactions were monitored by thin-layer chromatography (TLC) with ethyl acetate/petroleum ether 1:1 as the solvent and continued until all starting materials were consumed.

Synthesis of 6-amino-5-cyano-4-phenyl-4H-pyran-3-carboxylic acid ethyl ester) (9).

A mixture of ethyl propiolate (4a) (0.98 g, 0.01 mol) and 2-benzylidenemalononitrile (7a) (1.54 g, 0.01 mol) in EtOH (25 mL) in the presence of L-proline (0.23 g, 20%) was stirred at reflux for 3–4 h, cooled and then poured into ice-water. The formed solid was collected by filtration and recrystallized from EtOH to give 9 as faint yellow crystals in 85% yield; mp. 189-90 °C. El-HRMS: m/z = 270.09 (MH⁺); C₁₅H₁₄N₂O₃ requires: m/z = 270.29 (MH⁺); IR: 3383, 3322 (NH₂), 2195 (CN), 1706 (CO); ¹H NMR (400 MHz, DMSO-d6): δ = 1.07 (t, 3H, J = 8.0 Hz, CH₃), 3.97 (q, 2H, J = 8.0 Hz, CH₂), 4.23 (s, 1H, CH),
7.02 (br, 2H, NH₂, D₂O exchangeable), 7.16-7.34 (m, 5H, Ph-H), 7.71 (s, 1H, CH); \(^{13}\)C NMR (100 MHz, DMSO-d₆): \(\delta = 164.5, 158.6, 147.7, 144.2, 133.3, 129.5, 128.4, 126.9, 111.3, 60.2, 57.3, 37.1, 13.8\). MS: \(m/z\) (%) 270 (M⁺, 50), 256 (30), 193 (80), 130 (100), 103 (70), 69 (85). CCDC 851560 contains the supplementary crystallographic data.

Synthesis of 5-amino-4,6-dicyano-biphenyl-2-carboxylic acid ethyl ester (13a).

A mixture of ester 9 (2.70 g, 0.01 mol) and malononitrile (0.66 g, 0.01 mol) in EtOH (25 mL) in the presence of piperidine (0.5 mL) was stirred at reflux for 3–4 h, cooled and then poured into ice-water. The formed solid was collected by filtration and recrystallized from AcOH to give 13a as faint yellow crystals in 75% yield; mp. 185-86 °C. EI-HRMS: \(m/z = 291.10\) (MH⁺); C₁₇H₁₃N₃O₂ requires: \(m/z = 291.31\) (MH⁺); IR (KBr1): 3393, 3344 (NH₂), 2237 (CN), 2225 (CN), 1700 (CO); \(^{1}\)H NMR (400 MHz, DMSO-d₆): \(\delta = 0.85\) (t, 3H, \(J = 8.0\) Hz, CH₃), 3.90 (q, 2H, \(J = 8.0\) Hz, CH₂), 7.25-7.28 (m, 2H, Ph-H), 7.44-7.48 (m, 5H, Ph-H, NH₂, D₂O exchangeable), 8.21 (s, 1H, CH); \(^{13}\)C NMR (100 MHz, DMSO-d₆): \(\delta = 164.2, 153.8, 152.2, 140.0, 137.6, 128.5, 128.0, 127.9, 118.7, 115.5, 114.8, 98.3, 95.1, 60.5, 13.3\). MS: \(m/z\) (%) 291 (M⁺, 40), 263 (15), 246 (100), 217 (10), 191 (25), 164 (30), 140 (5), 77 (5).

Synthesis of 5-amino-4'-nitro-4,6-dicyano-biphenyl-2-carboxylic acid ethyl ester (13b).

A mixture of ethyl propiolate (4a, 0.98 g, 0.01 mol) and 2-(4-nitrobenzylidene)-malononitrile (7b, 3.98 g, 0.02 mol) in EtOH (25 mL) in the presence of L-proline (0.23 g, 20%) was stirred at reflux for 3–4 h, cooled and then poured into ice-water. The
formed solid was collected by filtration and recrystallized from EtOH to give 13b as yellow crystals in 60% yield; mp. 271-73 °C. EI-HRMS: m/z = 336.18 (MH⁺); C₁₇H₁₂N₄O₄ requires: m/z = 336.31 (MH⁺); IR: 3372, 3319 (NH₂), 2224 (CN), 2211 (CN), 1700 (CO); ¹H NMR (400 MHz, DMSO-d₆): δ = 1.36 (t, 3H, J = 8.0 Hz, CH₃), 4.36 (q, 2H, J = 8.0 Hz, CH₂), 7.61 (d, 2H, Ph-H), 7.65 (br, 2H, NH₂, D₂O exchangeable), 8.31 (d, 2H, Ph-H), 8.64 (s, 1H, CH); ¹³C NMR (100 MHz, DMSO-d₆): δ = 164.1, 153.8, 150.5, 147.4, 144.7, 140.4, 133.3 (2C), 129.5 (2C), 117.4, 115.2, 114.4, 98.0, 95.9, 61.6, 14.0. MS: m/z (%) 336 (M⁺, 100), 308 (60), 291 (70), 275 (20), 245 (80), 217 (30), 189 (30), 163 (20), 152 (10), 83 (10), 57 (5). CCDC 876576 contains the supplementary crystallographic data.

Synthesis of 2-amino-4-(cyanomethyl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (18).

A mixture of dimedone (14, 1.40 g, 0.01 mol), 3-(piperidin-1-yl)acrylonitrile (15, 1.36 g, 0.01 mol) and malononitrile (0.66 g, 0.01 mol) in EtOH (25 mL) in the presence of L-proline (0.23 g, 20%) or DABCO (0.22 g, 20%) was stirred at reflux for 4 h, cooled and then poured into ice-water. The formed solid was collected by filtration and recrystallized from EtOH to give 18 as white crystals in 87% yield; mp. 232-33 °C. EI-HRMS: m/z = 257.08 (MH⁺); C₁₄H₁₅N₃O₂ requires: m/z = 257.11 (MH⁺); IR: 3410, 3296 (NH₂), 2243 (CN), 2187 (CN), 1680 (CO); ¹H NMR (400 MHz, DMSO-d₆): δ = 1.05 (s, 3H, CH₃), 1.06 (s, 3H, CH₃), 2.19-2.89 (m, 6H, CH₂, CH₂, CH₂), 3.45 (br, 1H, CH), 7.27 (br, 2H, NH₂, D₂O exchangeable); ¹³C NMR (100 MHz, DMSO-d₆): δ = 196.42, 164.76, 160.22, 119.04, 118.39, 109.69, 53.20, 49.90, 31.77 (2C), 28.84, 27.55, 26.07, 24.10.
Synthesis of 7,7-dimethyl-2-(piperidin-1-yl)-7,8-dihydroquinolin-5(6H)-one (21).

A mixture of dimedone (14, 1.40 g, 0.01 mol) and 3-(piperidin-1-yl)acrylonitrile (15, 1.36 g, 0.01 mol) EtOH (25 mL) containing 5 drops of piperidine was stirred at reflux for 4 h, cooled and then poured into ice-water. The formed solid was collected by filtration and recrystallized from EtOH to give 21 as yellow crystals in 97% yield; mp 145-47 °C; EI-HRMS: m/z = 258.36 (MH⁺); C₁₆H₂₂N₂O requires: m/z = 258.36 (MH⁺); IR: 1653 (CO); \(^1\)H-NMR (DMSO): 0.99 (s, 6H, 2CH₃), 1.53-1.63 (m, 6H, pip-H), 2.34 (s, 2H, CH₂), 2.70 (s, 2H, CH₂), 3.67 (br, 2H, pip-H), 6.73 (d, 1H, J = 8, CH), 7.82 (d, 1H, J = 8, CH); \(^1^3\)C-NMR (DMSO): 194.95 (CO), 162.73, 159.52, 135.24, 116.20, 104.58, 51.07, 46.11, 44.97 (2C), 32.48, 27.93 (2C), 25.29 (2C), 24.19. MS: m/z (%) 258 (M⁺, 100), 229 (90), 215 (45), 203 (40), 175 (55), 145 (10), 119 (10), 91 (15), 84 (35). CCDC 811998 contains the supplementary crystallographic data.

Synthesis of ethyl 3-amino-4-cyano-6,6-dimethyl-8-oxo-5,6,7,8-tetrahydronaphthalene-2-carboxylate (26).

A mixture of dimedone (14, 1.40 g, 0.01 mol), ethyl propiolate (4a, 0.98 g, 0.01 mol) and malononitrile (0.66 g, 0.01 mol) in EtOH (25 mL) in the presence of L-proline (0.23 g, 20%) or DABCO (0.22 g, 20%) was stirred at reflux for 4 h, cooled and then poured into ice-water. The formed solid was collected by filtration and recrystallized from EtOH to give 27 as faint yellow crystals in 75% yield; mp. 255-56 °C. EI-HRMS: m/z = 286.16
(MH⁺); C₁₆H₁₆N₂O₃ requires: m/z = 286.33 (MH⁺); IR: 3430, 3322 (NH₂), 2210 (CN), 1720 (CO), 1677 (CO); ¹H NMR (400 MHz, DMSO-d6): δ = 1.04 (s, 6H, 2CH₃), 1.33 (t, 3H, J = 8.0 Hz, CH₃), 2.44 (s, 2H, CH₂), 2.63 (s, 2H, CH₂), 4.34 (q, 2H, J = 8.0 Hz, CH₂), 7.86 (br, 2H, NH₂, D₂O exchangeable); ¹³C NMR (100 MHz, DMSO-d6): δ = 194.05, 166.14, 154.99, 153.32, 134.40, 130.45, 129.28, 120.05, 115.17, 109.55, 61.20, 50.47, 33.06, 27.52 (2C), 14.07. MS: m/z (%) 286 (M⁺, 100), 271 (15), 240 (40), 230 (90), 215 (50), 202 (25), 184 (50), 157 (20), 129 (30), 102 (15), 55 (15). CCDC 923273 contains the supplementary crystallographic data.

General procedure for the syntheses of 27a and 27b.

Independent mixtures of 9a and 9b (0.01 mol), each containing hydroxylamine hydrochloride (0.01 mol) and sodium acetate (0.01 mol), in EtOH (25 mL) were stirred at reflux for 3 h, cooled and then poured into ice-water. The formed solids were collected by filtration and recrystallized from EtOH to give 28a and 28b as white crystals.

Ethyl 5-(N'-hydroxycarbamimidoyl)-6-(hydroxyimino)-4-phenyl-5,6-dihydro-4H-pyran-3-carboxylate (27a).

Yield 65%; mp. 213-15 ⁰C. EI-HRMS: m/z = 319.11 (MH⁺); C₁₅H₁₇N₃O₅ requires: m/z = 319.32 (MH⁺); IR: 3483 (2OH), 3387, 3284 (NH₂), 1675 (CO); ¹H NMR (400 MHz, DMSO-d6): δ = 1.38 (t, 3H, J = 8.0 Hz, CH₃), 3.69 (q, 2H, J = 8.0 Hz, CH₂), 4.22 (s, 1H, CH) 5.45 (br, 2H, NH₂, D₂O exchangeable), 7.17-7.29 (m, 5H, Ph-H), 7.35 (d, J = 4.0 Hz, 1H, CH), 9.22 (s, 1H, OH, D₂O exchangeable), 9.30 (d, J = 4.0 Hz, 1H, CH), 10.08 (s, 1H, OH, D₂O exchangeable); ¹³C NMR (100 MHz, DMSO-d6): δ = 166.25, 151.25,
147.52, 143.01, 142.64, 128.35 (2C), 127.04 (2C), 126.43, 102.49, 58.99, 44.49, 14.32. MS: m/z (%) 319 (M⁺, 50), 301 (40), 258 (60), 242 (30), 197 (55), 155 (15), 140 (25), 115 (35), 81 (55), 69 (100). CCDC 923277 contains the supplementary crystallographic data.

Ethyl 5-(N-hydroxycarbamimidoyl)-6-(hydroxyimino)-2-methyl-4-phenyl-5,6-dihydro-4H-pyran-3-carboxylate (27b).

Yield 70%; mp. 249-50 °C. EI-HRMS: m/z = 333.13 (MH⁺); C₁₉H₁₉N₃O₅ requires: m/z = 333.34 (MH⁺); IR: 3482 (OH) 3379 (OH), 3271, 3081 (NH₂), 1660 (CO); ¹H NMR (400 MHz, DMSO-d₆): δ = 1.06 (t, 3H, J = 8.0 Hz, CH₃), 2.38 (s, 3H, CH₃), 3.91 (q, 2H, J = 8.0 Hz, CH₂), 4.34 (br, 1H, CH) 5.43 (br, 2H, NH₂, D₂O exchangeable), 7.16-7.25 (m, 5H, Ph-H), 8.68 (br, 1H, CH), 9.21 (s, 1H, OH, D₂O exchangeable), 9.98 (s, 1H, OH, D₂O exchangeable); ¹³C NMR (100 MHz, DMSO-d₆): δ = 166.95, 151.28, 147.83, 143.68, 142.66, 128.20 (2C), 127.14 (2C), 126.22, 99.35, 58.73, 44.48, 40.74, 18.98, 14.21. MS: m/z (%) 333 (M⁺, 50), 315 (100), 296 (25), 273 (65), 257 (35), 236 (25), 211 (55), 184 (25), 168 (15), 140 (20), 128 (25), 103 (15), 77 (20).

General procedure for the syntheses of 28a and 28b.

Independent solutions of 28a and 28b (0.01 mol) in DMF (25 mL) were stirred at reflux for 4 h, cooled and then poured into ice-water. The formed solids were collected by filtration and recrystallized from EtOH to give 28a and 28b as white crystals.
Ethyl 6-amino-5-carbamoyl-4-phenylnicotinate (28a).

Yield 80%; mp. 193-95 °C. El-HRMS: m/z = 285.11 (MH⁺); C₁₅H₁₅N₃O₃ requires: m/z = 285.28 (MH⁺); IR: 3396, 3259 (NH₂), 3147, 3041 (NH₂), 1741 (CO), 1641 (CO); ¹H NMR (400 MHz, DMSO-d₆): δ = 1.14 (t, 3H, J = 8.0 Hz, CH₃), 3.99 (q, 2H, J = 8.0 Hz, CH₂), 6.78 (br, 2H, NH₂, D₂O exchangeable), 7.17-7.38 (m, 7H, Ph-H, NH₂, D₂O exchangeable), 7.57 (s, 1H, CH). ¹³C NMR (100 MHz, DMSO-d₆): δ = 163.54, 144.34, 135.73, 129.57, 128.63 (2C), 127.85, 127.72 (2C), 126.79, 105.68, 83.76, 59.90, 44.29, 14.12. MS: m/z (%) 385 (M⁺, 5), 384 (35), 256 (20), 241 (15), 213 (10), 185 (15), 171 (10), 129 (45), 111 (15), 83 (40), 73 (100).

Ethyl 6-amino-5-carbamoyl-2-methyl-4-phenylnicotinate (28b).

Yield 83%; mp. 252-54 °C. El-HRMS: m/z = 299.12 (MH⁺); C₁₆H₁₇N₃O₃ requires: m/z = 299.33 (MH⁺); IR: 3478, 3418 (NH₂), 3367, 3315 (NH₂), 1695 (CO), 1670 (CO); ¹H NMR (400 MHz, DMSO-d₆): δ = 0.74 (t, 3H, J = 8.0 Hz, CH₃), 2.31 (s, 3H, CH₃), 3.79 (q, 2H, J = 8.0 Hz, CH₂), 61.5 (br, 2H, NH₂, D₂O exchangeable), 7.19-7.36 (m, 7H, Ph-H, NH₂, D₂O exchangeable); ¹³C NMR (100 MHz, DMSO-d₆): δ = 168.27, 168.14, 155.68, 154.05, 146.05, 137.57, 128.12 (2C), 127.73, 127.66 (2C), 117.61, 113.88, 60.15, 22.44, 13.31. MS: m/z (%) 299 (M⁺, 100), 382 (25), 254 (20), 237 (35), 210 (10), 181 (10), 154 (10), 129 (15), 77 (5). CCDC 923276 contains the supplementary crystallographic data.
General procedure for the syntheses of 31a and 31b.

Independent mixtures of 9a and 9b (0.01 mol) containing ammonium acetate (0.25 g) in AcOH (25 mL) were stirred at reflux for 4 h, cooled and then poured into ice-water. The formed solids were collected by filtration and recrystallized from EtOH to give 31a and 31b as faint yellow crystals.

Ethyl 6-amino-5-cyano-4-phenylnicotinate (31a).

Yield 82%; mp. 178-80 °C. El-HRMS: m/z = 267.03 (MH+); C15H13N3O2 requires: m/z = 267.10 (MH+); IR: 3363, 3312 (NH2), 2265 (CN), 1960 (CO); 1H NMR (400 MHz, DMSO-d6): δ = 0.86 (t, 3H, J = 8.0 Hz, CH3), 3.90 (q, 2H, J = 8.0 Hz, CH2), 7.27-7.46 (m, 5H, Ph-H), 7.70 (br, 2H, NH2, D2O exchangeable), 8.67 (s, 1H, CH); 13C NMR (100 MHz, DMSO-d6): δ = 164.96, 162.11, 156.69, 155.48, 137.23, 129.04, 128.44 (2C), 128.16 (2C), 115.93, 114.81, 90.95, 60.60, 13.91. MS: m/z (%) 267 (M+, 35), 239 (10), 222 (100), 194 (10), 167 (10), 140 (35), 113 (10), 88 (5), 77 (20). CCDC 876575 contains the supplementary crystallographic data.

Ethyl 6-amino-5-cyano-2-methyl-4-phenylnicotinate (31b).

Yield 88%; mp. 234-35 °C. El-HRMS: m/z = 281.11 (MH+); C16H15N3O2 requires: m/z = 281.31 (MH+); IR: 3385, 3323 (NH2), 2220 (CN), 1713 (CO); 1H NMR (400 MHz, DMSO-d6): δ = 0.75 (t, 3H, J = 8.0 Hz, CH3), 2.39 (s, 3H, CH3), 3.84 (q, 2H, J = 8.0 Hz, CH2), 7.31-7.49 (m, 7H, Ph-H, NH2, D2O exchangeable); 13C NMR (100 MHz, DMSO-d6): δ = 166.84, 159.93, 159.75, 153.74, 136.18, 129.07, 128.39 (2C), 127.79 (2C), 117.50, 115.89, 87.08, 60.61, 23.23, 13.24. MS: m/z (%) 281 (M+, 45), 236 (100), 209 (10), 191
CCDC 923278 contains the supplementary crystallographic data.

Synthesis of ethyl 5-cyano-6-((dimethylamino)methyleneamino)-2-methyl-4-phenyl-4H-pyran-3-carboxylate (32b).
A mixture of 9b (2.84 g, 0.01 mol) and dimethylformamide dimethylacetal (DMFDMA) (1.19 g, 0.01 mol) in DMF (25 mL) was stirred at reflux for 3 h, cooled and then poured into ice-water. The formed solid was collected by filtration and recrystallized from EtOH to give 33b as yellow crystals in 81% yield; mp. 156-58 °C. El-HRMS: m/z = 339.15 (MH⁺); C₁₉H₂₁N₃O₃ requires: m/z = 339.39 (MH⁺); IR: 2197 (CN), 1713 (CO); ¹H NMR (400 MHz, DMSO-d₆): δ = 1.04 (t, 3H, J = 8.0 Hz, CH₃), 2.38 (s, 3H, CH₃), 2.96 (s, 3H, CH₃), 3.11 (s, 3H, CH₃), 3.95 (q, 2H, J = 8.0 Hz, CH₂), 4.40 (s, 1H, CH), 7.17-7.34 (m, 5H, Ph-H) 8.25 (s, 1H, CH); ¹³C NMR (100 MHz, DMSO-d₆): δ = 165.54, 158.14, 157.60, 154.85, 144.30, 128.49 (2C), 127.46 (2C), 127.01, 119.46, 106.33, 73.27, 60.13, 40.42, 40.17, 34.21, 18.26, 13.75. MS: m/z (%) 339 (M⁺, 35), 310 (15), 295 (5), 262 (100), 234 (35), 99 (20).

Synthesis of ethyl 4-amino-5-phenyl-5H-pyrano[2,3-d]pyrimidine-6-carboxylate (33a).
A mixture of 9a (2.70 g, 0.01 mol) and dimethylformamide dimethylacetal (DMFDMA) (1.19 g, 0.01 mol) in DMF (25 mL) was stirred at reflux for 4–6 h and concentrated in vacuo. A solution of the residue in AcOH (25 mL) containing ammonium acetate (0.25 g) was stirred at reflux for 3 h, cooled and then poured into ice-water. The formed solid was collected by filtration and recrystallized from EtOH to give 34a as white crystals in
80% yield; mp. 207 °C. EI-HRMS: \( m/z = 297.11 \) (MH\(^+\)); \( \text{C}_{16}\text{H}_{15}\text{N}_3\text{O}_3 \) requires: \( m/z = 297.11 \) (MH\(^+\)); IR: 3370, 3344 (NH\(_2\)), 1712 (CO); \(^1\text{H} \) NMR (400 MHz, DMSO-\(d_6\)): \( \delta = 1.46 \) (t, 3H, \( J = 8.0 \) Hz, CH\(_3\)), 4.07 (q, 2H, \( J = 8.0 \) Hz, CH\(_2\)), 4.91 (s, 1H, CH), 6.94 (br, 2H, NH\(_2\), D\(_2\)O exchangeable), 7.16-7.36 (m, 5H, Ph-H), 7.85 (s, 1H, CH), 8.08 (s, 1H, CH); \(^{13}\text{C} \) NMR (100 MHz, DMSO-\(d_6\)): \( \delta = 164.68, 162.68, 161.02, 157.48, 149.01, 142.71, 128.25 \) (2C), 128.17 (2C), 126.96, 112.76, 95.82, 73.07, 33.80, 13.97. MS: \( m/z \) (%): 297 (M\(^+\), 100), 268 (50), 252 (10), 220 (100), 192 (40), 165 (10), 140 (5), 69 (10). CCDC 923279 contains the supplementary crystallographic data.

Synthesis of ethyl 4-amino-7-methyl-5-phenyl-5H-pyrano[2,3-\(d\)]pyrimidine-6-carboxylate (33b).

A mixture of 32b (3.39 g, 0.01 mol) and ammonium acetate (0.25 g) in AcOH (25 mL) was stirred at reflux for 3 h, cooled and then poured into ice-water. The formed solid was collected by filtration and recrystallized from EtOH to give 33b as yellow crystals in 83%; mp. 152-54 °C. EI-HRMS: \( m/z = 311.12 \) (MH\(^+\)); \( \text{C}_{17}\text{H}_{17}\text{N}_3\text{O}_3 \) requires: \( m/z = 311.34 \) (MH\(^+\)); IR: 3449, 3358 (NH\(_2\)), 1683 (CO); \(^1\text{H} \) NMR (400 MHz, DMSO-\(d_6\)): \( \delta = 1.18 \) (t, 3H, \( J = 8.0 \) Hz, CH\(_3\)), 2.41 (s, 3H, CH\(_3\)), 4.05 (q, 2H, \( J = 8.0 \) Hz, CH\(_2\)), 4.94 (s, 1H, CH), 7.16 (br, 2H, NH\(_2\), D\(_2\)O exchangeable), 7.18-7.33 (m, 5H, Ph-H), 8.05 (s, 1H, CH); \(^{13}\text{C} \) NMR (100 MHz, DMSO-\(d_6\)): \( \delta = 165.63, 162.16, 161.03, 158.28, 156.41, 143.82, 128.15 \) (2C), 128.06 (2C), 126.70, 108.44, 96.21, 60.21, 35.32, 18.69, 13.93. MS: \( m/z \) (%): 311 (M\(^+\), 95), 282 (35), 266 (10), 234 (100), 206 (25), 188 (20), 161 (10), 137 (20), 121 (10), 95 (15), 81 (50), 69 (100).
General procedure for the syntheses of 37a–c.

Independent mixtures of diethyl acetylenedicarboxylate (4b, 1.70 g, 0.01 mol) and arylidenemalononitriles 7a–c (0.02 mol) in EtOH (25 mL) in the presence of 1,4-diazabicyclo[2,2,2]octane (DABCO) (0.22 g, 20%) were stirred at reflux for 3–4 h, cooled and then poured into ice-water. The formed solids were collected by filtration and recrystallized from EtOH to give 37a–c.

5-Amino-4,6-dicyano-biphenyl-2,3-dicarboxylic acid diethyl ester (37a).

Faint yellow crystals, yield 85%; mp. 180-81 °C. EI-HRMS: m/z = 363.28 (MH⁺);
C₂₀H₁₇N₃O₄ requires: m/z = 363.37 (MH⁺); IR: 3347, 3248 (NH₂), 2229 (CN), 2227 (CN), 1747 (CO), 1730 (CO); ¹H NMR (400 MHz, DMSO-d₆): δ = 0.77 (t, 3H, J = 8.0 Hz, CH₃), 1.28 (t, 3H, J = 8.0 Hz, CH₃), 3.83 (q, 2H, J = 8.0 Hz, CH₂), 4.32 (q, 2H, J = 8.0 Hz, CH₂), 7.31-7.48 (m, 5H, Ph-H), 7.52 (br, 2H, NH₂, D₂O exchangeable); ¹³C NMR (100 MHz, DMSO-d₆): δ = 164.6, 164.5, 153.3, 150.5, 140.6, 136.2, 129.1, 128.2 (2C), 128.0 (2C), 119.7, 114.3, 113.6, 99.2, 93.4, 62.7, 61.2, 13.5, 13.1. MS: m/z (%) 363 (M⁺, 70), 318 (15), 290 (100), 272 (15), 245 (25), 218 (20), 191 (15), 164 (15), 152 (5), 97 (5), 57 (5). CCDC 861197 contains the supplementary crystallographic data.

5-Amino-4'-nitro-4,6-dicyano-biphenyl-2,3-dicarboxylic acid diethyl ester (37b).

Faint yellow crystals, yield 75%; mp. 191-93 °C. EI-HRMS: m/z = 408.11 (MH⁺);
C₂₀H₁₆N₄O₆ requires: m/z = 408.10 (MH⁺); IR: 3351, 3250 (NH₂), 2228 (CN), 2219 (CN), 1751 (CO), 1730 (CO); ¹H NMR (400 MHz, DMSO-d₆): δ = 0.81 (t, 3H, J = 8.0 Hz, CH₃), 1.29 (t, 3H, J = 8.0 Hz, CH₃), 3.85 (q, 2H, J = 8.0 Hz, CH₂), 4.33 (q, 2H, J = 8.0
Hz, CH₂), 7.68 (d, 2H, Ph-H), 7.74 (br, 2H, NH₂, D₂O exchangeable), 8.35 (d, 2H, Ph-H); ¹³C NMR (100 MHz, DMSO-d₆): δ = 164.5, 163.8, 153.4, 149.0, 147.8, 143.3, 141.8, 129.8 (2C), 123.3 (2C), 118.0, 114.0, 113.4, 99.0, 94.2, 62.7, 61.4, 13.5, 13.1. MS: m/z (%): 408 (M⁺, 70), 380 (10), 363 (15), 335 (100), 308 (10), 270 (10), 245 (25), 217 (30), 189 (50), 163 (15), 151 (5). CCDC 861198 contains the supplementary crystallographic data.

5-Amino-4'-chloro-4,6-dicyano-biphenyl-2,3-dicarboxylic acid diethyl ester (37c).

Faint yellow crystals, yield 75%; mp. 160-61 °C. EI-HRMS: m/z = 397.73 (MH⁺); C₂₀H₁₆ClN₃O₄ requires: m/z = 397.82 (MH⁺); IR: 3338, 3211 (NH₂), 2222 (CN), 1689 (CO), 1684 (CO; ¹H NMR (400 MHz, DMSO-d₆): δ = 0.83 (t, 3H, J = 8.0 Hz, CH₃), 1.28 (t, 3H, J = 8.0 Hz, CH₃), 3.86 (q, 2H, J = 8.0 Hz, CH₂), 4.34 (q, 2H, J = 8.0 Hz, CH₂); ¹³C NMR (100 MHz, DMSO-d₆): δ = 164.5, 164.3, 153.3, 149.5, 141.1, 135.2, 134.0, 130.0 (2C), 128.3 (2C), 119.1, 114.3, 113.6, 99.3, 93.7, 62.7, 61.3, 13.5, 13.1. MS: m/z (%) 397 (M⁺, 55), 369 (5), 352 (15), 324 (100), 306 (5), 279 (15), 252 (25), 225 (10), 217 (15), 189 (25), 162 (5), 69 (40).

Synthesis of 4,6-dicyano-5-(dimethylamino-methyleneamino)-biphenyl-2,3-dicarboxylic acid diethyl ester (38).

A mixture of 37a (3.63 g, 0.01 mol) and dimethylformamide dimethylacetal (DMFDMA) (1.19 g, 0.01 mol) in DMF (25 mL) was stirred at reflux for 3 h, cooled and then poured into ice-water. The formed solid was collected by filtration and recrystallized from EtOH
to give 39 as white crystals in 88% yield; mp. 155-57 ºC. Ei-HRMS: m/z = 418.16 (MH+); C_{23}H_{22}N_{4}O_{4} requires: m/z = 418.16 (MH+); IR: 2227 (CN), 2225 (CN), 1727 (CO), 1635 (CO); \(^1\)H NMR (400 MHz, DMSO-\(d_6\)): \(\delta = 0.81\) (t, 3H, \(J = 8.0\) Hz, CH\(_3\)), 1.28 (t, 3H, \(J = 8.0\) Hz, CH\(_3\)), 3.06 (s, 3H, CH\(_3\)), 3.15 (s, 3H, CH\(_3\)), 3.89 (q, 2H, \(J = 8.0\) Hz, CH\(_2\)), 4.34 (q, 2H, \(J = 8.0\) Hz, CH\(_2\)), 7.35-7.51 (m, 5H, Ph-H), 8.20 (s, 1H, CH); \(^{13}\)C NMR (100 MHz, DMSO-\(d_6\)): \(\delta = 164.83, 164.30, 159.74, 156.69, 149.23, 139.13, 135.86, 129.13, 128.39 (2C), 128.28 (2C), 125.37, 115.45, 114.65, 109.8, 103.39, 62.89, 61.58, 40.13, 34.26, 13.55, 13.15. MS: m/z (%) 418 (M\(^+\), 35), 392 (20), 373 (15), 345 (20), 302 (20), 273 (10), 230 (15), 202 (5), 69 (10), 57 (15).


A mixture of 38 (4.18 g, 0.01 mol) and ammonium acetate (0.25 g) in AcOH (25 mL) was stirred at reflux for 3 h, cooled and then poured into ice-water. The formed solid was collected by filtration and recrystallized from EtOH to give 39 as orange crystals in 80% yield; mp. 352-55 ºC. Ei-HRMS: m/z = 315.07 (MH+); C_{17}H_{9}N_{5}O_{2} requires: m/z = 315.29 (MH+); IR: 3279, 3141 (NH\(_2\)), 3098 (NH), 1770 (CO), 1735 (CO); \(^1\)H NMR (400 MHz, DMSO-\(d_6\)): \(\delta = 7.52-7.56\) (m, 5H, Ph-H), 8.65 (s, 1H, CH), 8.94 (br, 1H, NH, \text{D}_2\text{O exchangeable}), 12.06 (br, 2H, NH\(_2\), \text{D}_2\text{O exchangeable}); \(^{13}\)C NMR (100 MHz, DMSO-\(d_6\)): \(\delta = 172.08, 170.30, 166.36, 160.51, 159.42, 155.39, 147.19, 135.01, 133.16, 129.24 (2C), 127.94 (2C), 126.94, 116.26, 115.25, 110.37. MS: m/z (%) 315 (M\(^+\), 100), 287 (10), 261 (20), 244 (5), 217 (10), 189 (20), 163 (10), 97 (10), 69 (5). CCDC 923275 contains the supplementary crystallographic data.
Synthesis of ethyl 1,7-diamino-6-(N-hydroxycarbamimidoyl)-3-oxo-5-phenyl-3H-isooindole-4-carboxylate (40).

A mixture of 37a (3.63 g, 0.01 mol) and hydroxylamine hydrochloride (0.69 g, 0.01 mol) in EtOH (25 mL) in presence of sodium acetate (0.01 mol) was stirred at reflux for 4 h, cooled and then poured into ice-water. The formed solid was collected by filtration and recrystallized from EtOH to give 40 as yellow crystals in 70% yield; mp. 268-69 °C. El-HRMS: $m/\text{z} = 367.35$ (MH$^+$); C$_{18}$H$_{17}$N$_5$O$_4$ requires: $m/\text{z} = 367.36$ (MH$^+$); IR (KBr): 3462 (OH), 3411, 3396 (NH$_2$), 3365, 3334 (NH$_2$), 3236, 3212 (NH$_2$), 1736 (CO), 1713 (CO); $^1$H NMR (400 MHz, DMSO-d$_6$): $\delta = 0.91$ (t, 3H, $J = 8.0$ Hz, CH$_3$), 3.94 (q, 2H, $J = 8.0$ Hz, CH$_2$), 6.29 (br, 2H, NH$_2$, D$_2$O exchangeable), 7.25-7.67 (m, 9H, Ph-H, 2NH$_2$, D$_2$O exchangeable), 11.27 (br, 1H, OH, D$_2$O exchangeable); $^{13}$C NMR (100 MHz, DMSO-d$_6$): $\delta = 170.13$, 167.44, 166.94, 165.38, 143.15, 142.69, 138.96, 129.33, 129.02, 128.82 (2C), 128.15, 127.76 (2C), 118.93, 109.92, 60.81, 13.53. MS: $m/\text{z}$ (%) 368 (M$^+$, 20), 353 (100), 336 (20), 305 (20), 290 (85), 264 (10), 219 (10), 192 (10), 164 (15), 152 (10), 57 (5).