Isocyanide-Based Four-Component Synthesis of Benzo[*a*]pyrano[2,3-*c*]phenazines

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Abstract: An efficient and simple method for the synthesis of biologically interesting benzo[*a*]pyrano[2,3-*c*]phenazines by a four-component reaction of *o*-phenylenediamines, 2-hydroxynaphthalene-1,4-dione, isocyanides, and dialkyl acetylenedicarboxylates in *N*,*N*-dimethylformamide at 100 °C is reported.

Key words: isocyanide, benzo[*a*]pyrano[2,3-*c*]phenazine, dialkyl acetylenedicarboxylates, phenazine, phenylenediamines

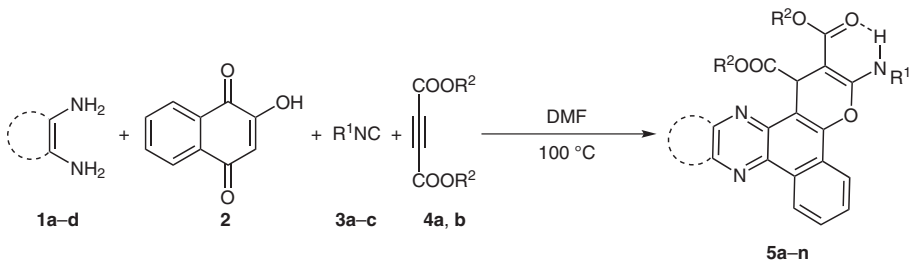
Within the past decade, the resurgence of interest in multicomponent reactions (MCRs) has been driven, not only due to their convergent nature, superior atom economy, and straightforward experimental procedures, but also because of their value in pharmaceutical industry for the construction of low-molecular-weight compound libraries through combinatorial strategies and parallel synthesis.[1,2] Isocyanide-based multicomponent reactions are particularly interesting as they are more versatile and diverse than other MCRs.[3] The great potential of isocyanides for the development of multicomponent reactions lies in the diversity of the available bond-forming processes, functional group tolerance, and the high levels of chemo-, regio-, and stereoselectivity often observed. MCRs involving isocyanides have emerged as valuable tools for the preparation of structurally diverse chemical libraries of drug-like heterocyclic compounds.[4–8] In this context, phenazine derivatives show interesting features that make them attractive for use in isocyanide-based multicomponent reactions.

More than 6000 phenazine-containing compounds have been identified and reported during the past century.[9] Several hundreds of the known phenazines possess biological activity, including antimalarial,[10,11] trypanocidal,[12] fungicidal,[13] and antiplatelet[14] effects, and are either isolated from natural sources or synthetically constructed. Some benzophenazines are dual inhibitors of topoisomerase I and II, two key enzymes that affect the topology of DNA at different points in the cell cycle.[15–18] Also, the antitumor activity of pyridophenazinediones and pyridazinophenazinedione derivatives was reported.[19,20] Due to the wide range biological activity of phenazines, research in this area continues to thrive and mostly is directed toward the synthesis of compounds with enhanced biological activity.[9,21–27] A literature survey reveals that a limited number of synthetic routes for the preparation of benzopyranophenazines have been reported. Recently, the two-step synthesis of benzopyranophenazines under harsh conditions and with long reaction time was described by Perez-Sacau and co-workers.[28] To the best of our knowledge, there is only one report of the synthesis of benzopyranophenazines via a multicomponent reaction.[29]

Although isocyanide-based multicomponent reactions have been applied for the synthesis of various heterocycles,[30] to date, the synthesis of benzo[*a*]pyrano[2,3-*c*]phenazines has not been reported by this route.

As part of our current studies on the development of multicomponent reactions,[31–35] in this paper, we report an efficient method for the preparation of benzo[*a*]pyrano[2,3-*c*]phenazines, which proceeds via the formation of five new bonds, [2 N–C + 2 C–C + C–O] by a isocyanide-based four-component strategy.

A mixture of phenylenediamines **1**, 2-hydroxynaphthalene-1,4-dione (**2**), isocyanides **3**, and dialkyl acetylenedicarboxylates **4** in the absence of any catalyst in *N*,*N*-dimethylformamide under thermal and one-pot conditions



Scheme 1 The synthesis of benzo[*a*]pyrano[2,3-*c*]phenazines **5**

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leads to the formation of benzo[*a*]pyrano[2,3-*c*]phenazine derivatives **5a–k** after 20 hours in good yields (Scheme 1). When the 2,3-diaminomaleonitrile **1d** was used, the desired 5*H*-benzo[*h*]pyrano[3,2-*f*]quinoxaline-5,6-dicarboxylates **5l–n** were obtained in good yields.

To explore the scope and limitations of the reaction and obtain various substituted benzo[*a*]pyrano[2,3-*c*]phenazines, we extended the procedure to four diamines **1a–d**, three isocyanides **3a–c**, and two acetylenic esters **4a**,**b** (Scheme 1). In this method, fourteen new compounds **5** were selectively synthesized by the one-pot, four-component condensation reaction in good yields. The results are summarized in Table 1. ^{1}H NMR spectra of the crude products clearly indicated the formation of benzo[*a*]pyrano[2,3-*c*]phenazine **5**. As anticipated from our original results, these reactions proceeded very cleanly under mild conditions, and no undesirable side reactions were observed. In addition, as the starting materials are ready accessible, a modular approach to the synthesis of benzopyranophenazine is possible. The workup of these very clean reactions involves only filtration and simple washing with diethyl ether.

Table 1 The Synthesis of Benzopyranophenazines **5**

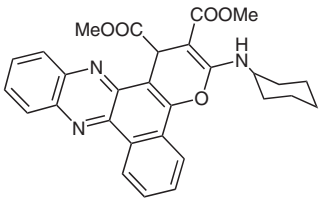
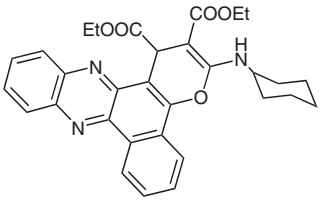
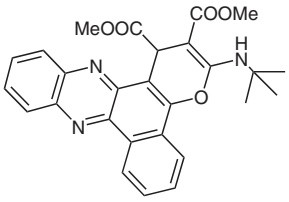
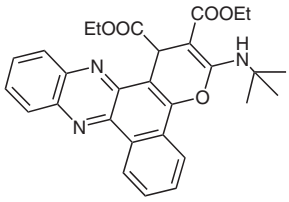
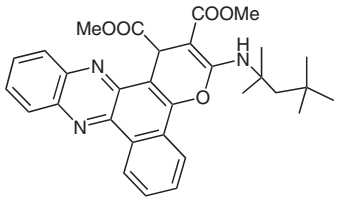
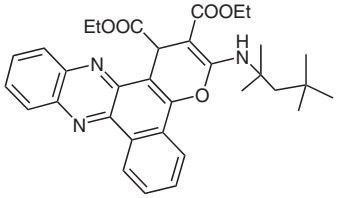
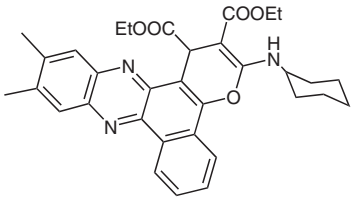
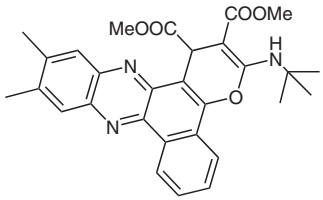
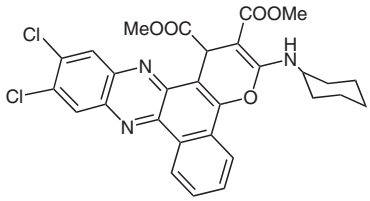
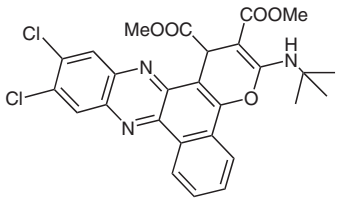
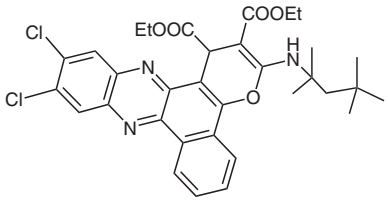
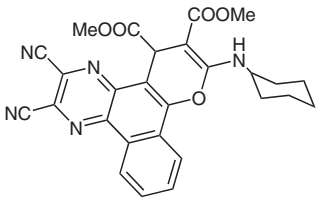
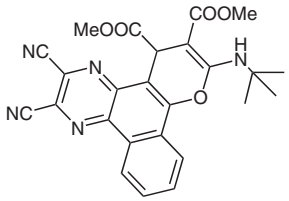
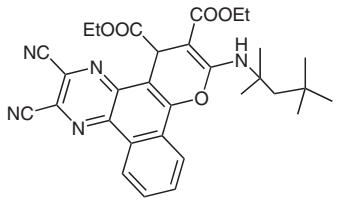
Product **5**		Yield (%)
5a		84
5b		86
5c		85
5d		86
5e		80
5f		92
5g		85
5h		81
5i		90
5j		80
5k		95
5l		83

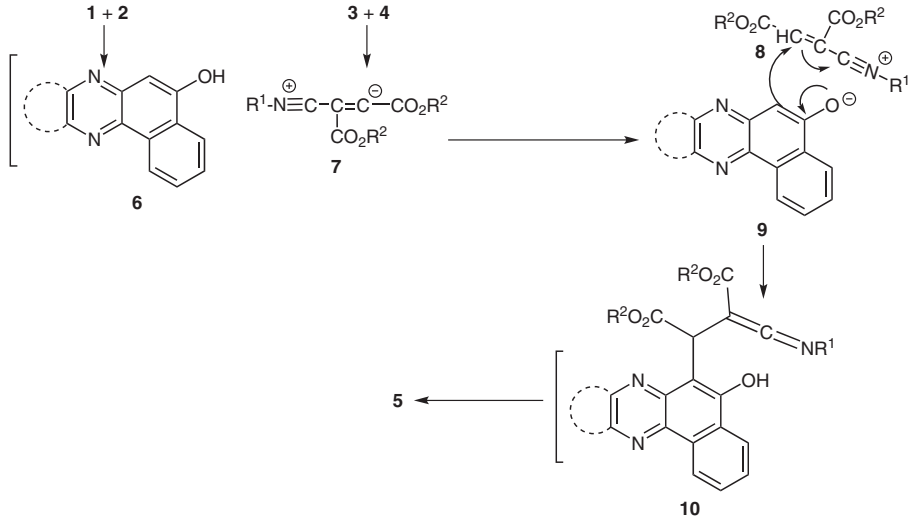
Table 1 The Synthesis of Benzopyranophenazines **5** (continued)

Product **5**		Yield (%)
5m		94
5n		95

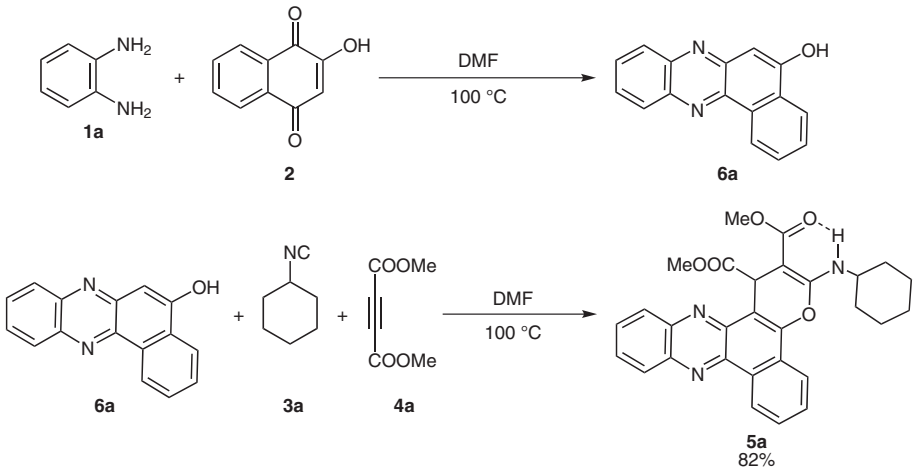
All compounds described in the paper were synthesized for the first time and the products were characterized by IR, mass spectroscopy, NMR, and elemental analysis.

We have not established a detailed mechanism for the formation of benzopyranophenazine **5**, however, a reasonable possibility is shown in Scheme 2. The formation of **5** is expected to proceed via initial condensation of **1** and **2** to afford benzo[*a*]phenazin-5-ol **6**. Then, the 1:1 zwitterionic ionic intermediate **7**, formed from the isocyanide and the acetylenic ester, is protonated by **6** to furnish intermediate **8**, which is attacked by the anion of the CH-acidic **9** in a Michael fashion to produce ketenimine **10**. The latter then can undergo cyclization under the reaction conditions to afford the benzopyranophenazine **5**. Indeed, we demonstrated that this process can be conducted stepwise by condensing **1a** with **2** and isolating benzo[*a*]phenazin-5-ol **6a** in a quantitative yield. Compound **6a** was further reacted with cyclohexyl isocyanide (**3a**) and dimethyl acetylenedicarboxylate (**4a**) under the same reaction conditions and gave a comparable yield of **5a** (Scheme 3).

In conclusion, we have described an efficient and one-pot synthesis of benzo[*a*]pyrano[2,3-*c*]phenazines starting from simple and readily available precursors under neutral conditions without activation or modifications. The



Scheme 2 Proposed mechanism of the reaction



Scheme 3 Benzo[*a*]phenazin-5-ol **6** as intermediate in the reaction

products are of potential synthetic and pharmacological interest. The simplicity of the presented procedure makes it an interesting alternative to the complex multistep approaches for the synthesis of phenazine derivatives. Moreover, it is worth noting that in total two C–C, two N–C, and one C–O bonds were formed with concomitant creation of a fused phenazine ring in this one-pot, four-component process.

The chemical used in this work were obtained from Fluka and Merck and were used without purification. Melting points were measured on an Electrothermal 9100 apparatus and are uncorrected. Mass spectra were recorded on a Finnigan-MAT 8430 mass spectrometer operating at an ionization potential of 70 eV. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DRX-300 Avance spectrometer at 300.13 and 75.47 MHz. ^{1}H and ^{13}C NMR spectra were obtained in solns in DMSO-d_6 and $CDCl_3$ using TMS as internal standard. IR spectra were recorded using an FTIR apparatus, Bomem MB-series. Elemental analyses were performed using a Heracus CHN-O-Rapid analyzer.

Benzopyranophenazines 5; General Procedure

To a magnetically stirred soln of diamine **1** (1 mmol) and 2-hydroxynaphthalene-1,4-dione (**2**, 1 mmol) in DMF (3 mL) at 100 °C were added, after 2 h, isocyanide 3 (1 mmol) and dialkyl acetylenedicarboxylate **4** (1 mmol). The mixture was finally stirred for 20 h at 100 °C. After completion of the reaction, the mixture was cooled to r.t. The solvent was evaporated and the residue was washed with Et_2O (10 mL) to afford the pure product **5**.

Dimethyl 3-(Cyclohexylamino)-1*H*-benzo[*a*]pyrano[2,3-*c*]phenazine-1,2-dicarboxylate (5a)

Yellow powder; yield: 418 mg (84%); mp 225–227 °C.

IR (KBr): 3267, 1742, 1677 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.38–2.23 (m, 10 H, 5 Cy-CH_2), 3.63 (s, 3 H, OCH_3), 3.89 (s, 3 H, OCH_3), 4.10 (br s, 1 H, CHN), 5.78 (s, 1 H, CH), 7.84–8.36 (m, 7 H, H_{Ar}), 8.85 (d, *J* = 7.4 Hz, 1 H, NH), 9.38–9.41 (m, 1 H, H_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.6, 24.7, 25.6, 33.6, 33.9, 36.7, 50.6, 51.2, 52.3, 72.2, 112.7, 121.5, 125.6, 126.3, 128.6, 129.5, 129.6, 130.0, 130.1, 131.1, 141.1, 141.7, 142.6, 147.4, 160.1, 170.1, 174.1.

MS (EI, 70eV): *m*/*z* = 497 (M^+).

Anal. Calcd for $C_{29}H_{27}N_3O_5$: C, 70.01; H, 5.47; N, 8.45. Found: C, 69.90; H, 5.41; N, 8.36.

Diethyl 3-(Cyclohexylamino)-1*H*-benzo[*a*]pyrano[2,3-*c*]phenazine-1,2-dicarboxylate (5b)

Yellow powder; yield: 452 mg (86%); mp 184–186 °C.

IR (KBr): 3240, 1720, 1669 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.21 (t, *J* = 5.6 Hz, 3 H, CH_3), 1.42–2.22 (m, 13 H, 5 Cy-CH_2, CH_3), 4.09 (br s, 3 H, CHN, OCH_2), 4.35 (ABq, *J* = 5.6 Hz, 2 H, OCH_2), 5.74 (s, 1 H, CH), 7.85–8.33 (m, 7 H, H_{Ar}), 8.87 (br s, 1 H, NH), 9.40 (br s, 1 H, H_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.3, 14.8, 24.7, 25.6, 33.6, 33.9, 37.0, 50.5, 59.6, 60.8, 72.3, 112.7, 121.6, 125.5, 126.4, 128.6, 129.4, 129.5, 129.9, 130.1, 131.1, 140.5, 141.0, 141.9, 142.6, 147.4, 159.9, 169.8, 174.2.

MS (EI, 70eV): *m*/*z* = 525 (M^+).

Anal. Calcd for $C_{31}H_{31}N_3O_5$: C, 70.84; H, 5.94; N, 7.99. Found: C, 70.72; H, 5.99; N, 7.93.

Dimethyl 3-(*tert*-Butylamino)-1*H*-benzo[*a*]pyrano[2,3-*c*]phenazine-1,2-dicarboxylate (5c)

Yellow powder; yield: 401 mg (85%); mp 237–239 °C.

IR (KBr): 3200, 1737, 1671 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.60 (s, 9 H, CH_3), 3.49 (s, 3 H, OCH_3), 3.77 (s, 3 H, OCH_3), 5.64 (s, 1 H, CH), 7.97–8.37 (m, 7 H, H_{Ar}), 9.09 (s, 1 H, NH), 9.28–9.31 (m, 1 H, H_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 30.6, 36.4, 51.2, 51.3, 52.3, 52.5, 72.9, 112.7, 122.0, 125.7, 126.2, 128.4, 128.5, 129.2, 129.5, 129.6, 130.0, 131.1, 140.4, 141.1, 141.6, 142.6, 142.7, 147.7, 161.4, 170.3, 174.0.

MS (EI, 70eV): *m*/*z* = 471 (M^+).

Anal. Calcd for $C_{27}H_{25}N_3O_5$: C, 68.78; H, 5.34; N, 8.91. Found: C, 68.85; H, 5.41; N, 8.84.

Diethyl 3-(*tert*-Butylamino)-1*H*-benzo[*a*]pyrano[2,3-*c*]phenazine-1,2-dicarboxylate (5d)

Yellow powder; yield: 430 mg (86%); mp 239–241 °C.

IR (KBr): 3200, 1721, 1669 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.08 (t, *J* = 6.9 Hz, 3 H, CH_3), 1.31 (t, *J* = 6.4 Hz, 3 H, CH_3), 1.60 (s, 9 H, CH_3), 3.97 (m, 2 H, OCH_2), 4.25 (ABq, *J* = 6.4 Hz, 2 H, OCH_2), 5.60 (s, 1 H, CH), 8.00–8.38 (m, 7 H, H_{Ar}), 9.14 (s, 1 H, NH), 9.34–9.37 (m, 1 H, H_{Ar}).

^{13}C NMR: due to very low solubility **5d**, the ^{13}C NMR data could not be recorded.

MS (EI, 70eV): *m*/*z* = 499 (M^+).

Anal. Calcd for $C_{29}H_{29}N_3O_5$: C, 69.72; H, 5.85; N, 8.41. Found: C, 69.63; H, 5.92; N, 8.50.

Dimethyl 3-(2,4,4-Trimethylpentan-2-ylamino)-1*H*-benzo[*a*]pyrano[2,3-*c*]phenazine-1,2-dicarboxylate (5e)

Yellow powder; yield: 423 mg (80%); mp 197–199 °C.

IR (KBr): 3300, 1744, 1674 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 0.96 (s, 9 H, CH_3), 1.62 (s, 3 H, CH_3), 1.65 (s, 3 H, CH_3), 2.02 (s, 2 H, CH_2), 3.47 (s, 3 H, OCH_3), 3.77 (s, 3 H, OCH_3), 5.65 (br s, 1 H, CH), 7.98–8.38 (m, 7 H, H_{Ar}), 9.20 (s, 1 H, NH), 9.27–9.30 (m, 1 H, H_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 31.1, 31.4, 31.6, 31.8, 36.4, 51.2, 52.2, 53.1, 56.1, 72.6, 113.0, 122.1, 125.8, 126.2, 128.6, 129.5, 129.5, 129.6, 130.0, 131.2, 140.4, 141.2, 141.6, 141.7, 147.8, 161.1, 161.4, 170.3, 173.9.

MS (EI, 70eV): *m*/*z* = 527 (M^+).

Anal. Calcd for $C_{31}H_{33}N_3O_5$: C, 70.57; H, 6.30; N, 7.96. Found: C, 70.50; H, 6.36; N, 7.88.

Diethyl 3-(2,4,4-Trimethylpentan-2-ylamino)-1*H*-benzo[*a*]pyrano[2,3-*c*]phenazine-1,2-dicarboxylate (5f)

Yellow powder; yield: 512 mg (92%); mp 176–178 °C.

IR (KBr): 3400, 1731, 1666 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 0.96 (s, 9 H, CH_3), 1.05 (t, *J* = 7 Hz, 3 H, CH_3), 1.30 (t, *J* = 7.1 Hz, 3 H, CH_3), 1.61 (s, 3 H, CH_3), 1.64 (s, 3 H, CH_3), 2.03 (s, 2 H, CH_2), 3.95 (m, 2 H, OCH_2), 4.24 (ABq, *J* = 7 Hz, 2 H, OCH_2), 5.62 (s, 1 H, CH), 7.99–8.39 (m, 7 H, H_{Ar}), 9.25 (s, 1 H, NH), 9.34–9.36 (m, 1 H, H_{Ar}).

^{13}C NMR: due to very low solubility **5f**, the ^{13}C NMR data could not be recorded.

MS (EI, 70eV): *m*/*z* = 555 (M^+).

Anal. Calcd for $C_{33}H_{37}N_3O_5$: C, 71.33; H, 6.71; N, 7.56. Found: C, 71.44; H, 6.76; N, 7.49.

Diethyl 3-(Cyclohexylamino)-11,12-dimethyl-1*H*-benzo[*a*]pyrano[2,3-*c*]phenazine-1,2-dicarboxylate (5g)
Yellow powder; yield: 471 mg (85%); mp 200–205 °C.

IR (KBr): 3400, 1721, 1671 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.20 (t, *J* = 6.9 Hz, 3 H, CH_3), 1.42–2.23 (m, 19 H, 5 Cy-CH_2, 3 CH_3), 4.09 (br s, 3 H, CHN, OCH_2), 4.39 (ABq, *J* = 6.9 Hz, 2 H, OCH_2), 5.75 (s, 1 H, CH), 7.84–8.21 (m, 5 H, H_{Ar}), 8.87 (d, *J* = 7.2 Hz, 1 H, NH), 9.38 (br s, 1 H, H_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.3, 14.8, 20.6, 24.7, 25.6, 33.6, 33.9, 37.0, 50.5, 59.5, 60.7, 72.4, 112.8, 121.4, 125.3, 126.2, 128.1, 128.2, 128.3, 128.4, 129.6, 131.3, 139.8, 140.2, 140.4, 141.0, 141.1, 141.8, 146.8, 160.0, 169.8, 174.1.

MS (EI, 70eV): *m*/*z* = 553 (M^+).

Anal. Calcd for $C_{33}H_{35}N_3O_5$: C, 71.59; H, 6.37; N, 7.59. Found: C, 71.51; H, 6.30; N, 7.53.

Dimethyl 3-(*tert*-Butylamino)-11,12-dimethyl-1*H*-benzo[*a*]pyrano[2,3-*c*]phenazine-1,2-dicarboxylate (5h)
Yellow powder; yield: 405 mg (81%); mp 223–227 °C.

IR (KBr): 3350, 1729, 1667 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 1.68 (s, 9 H, CH_3), 2.57 (s, 6 H, CH_3), 3.61 (s, 3 H, OCH_3), 3.89 (s, 3 H, OCH_3), 5.84 (s, 1 H, CH), 7.28–8.42 (m, 5 H, H_{Ar}), 9.20 (s, 1 H, NH), 9.40 (br s, 1 H, H_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.5, 20.6, 30.6, 36.5, 51.2, 52.2, 52.5, 73.0, 112.9, 121.9, 125.4, 126.0, 128.1, 128.2, 128.3, 129.6, 131.3, 140.4, 140.6, 140.9, 141.0, 141.9, 147.1, 161.6, 170.3, 174.0.

MS (EI, 70eV): *m*/*z* = 499 (M^+).

Anal. Calcd for $C_{29}H_{29}N_3O_5$: C, 69.72; H, 5.85; N, 8.41. Found: C, 69.61; H, 5.92; N, 8.32.

Dimethyl 11,12-Dichloro-3-(cyclohexylamino)-1*H*-benzo[*a*]pyrano[2,3-*c*]phenazine-1,2-dicarboxylate (5i)
Yellow powder; yield: 510 mg (90%); mp 253–255 °C (dec).

IR (KBr): 3200, 1730, 1668 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.39–2.22 (m, 10 H, 5 Cy-CH_2), 3.62 (s, 3 H, OCH_3), 3.89 (s, 3 H, OCH_3), 4.09 (br s, 1 H, CHN), 5.67 (s, 1 H, CH), 7.82–8.43 (m, 5 H, H_{Ar}), 8.83 (d, *J* = 7.5 Hz, 1 H, NH), 9.27 (d, *J* = 7.3 Hz, 1 H, H_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.6, 25.5, 33.6, 33.8, 36.5, 50.6, 51.2, 52.4, 72.1, 121.6, 125.7, 126.5, 128.9, 129.7, 130.6, 134.0, 134.7, 139.5, 141.0, 141.1, 142.3, 148.2, 159.9, 169.9, 173.8.

MS (EI, 70eV): *m*/*z* = 566 (M^+).

Anal. Calcd for $C_{29}H_{25}Cl_2N_3O_5$: C, 61.49; H, 4.45; N, 7.42. Found: C, 61.55; H, 4.31; N, 7.48.

Dimethyl 3-(*tert*-Butylamino)-11,12-dichloro-1*H*-benzo[*a*]pyrano[2,3-*c*]phenazine-1,2-dicarboxylate (5j)
Yellow powder; yield: 433 mg (80%); mp 237–239 °C.

IR (KBr): 3200, 1737, 1671 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 1.59 (s, 9 H, CH_3), 3.50 (s, 3 H, OCH_3), 3.76 (s, 3 H, OCH_3), 5.54 (s, 1 H, CH), 7.95–8.52 (m, 5 H, H_{Ar}), 9.06 (s, 1 H, NH), 9.15 (d, *J* = 7.2 Hz, 1 H, H_{Ar}).

^{13}C NMR: due to very low solubility **5j**, the ^{13}C NMR data could not be recorded.

MS (EI, 70eV): *m*/*z* = 540 (M^+).

Anal. Calcd for $C_{27}H_{23}Cl_2N_3O_5$: C, 60.01; H, 4.29; N, 7.78. Found: C, 60.11; H, 4.21; N, 7.86.

Diethyl 11,12-Dichloro-3-(2,4,4-trimethylpentan-2-ylamino)-1*H*-benzo[*a*]pyrano[2,3-*c*]phenazine-1,2-dicarboxylate (5k)
Yellow powder; yield: 594 mg (95%); mp 195–205 °C.

IR (KBr): 3300, 1723, 1669 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.03 (s, 9 H, CH_3), 1.18 (s, 3 H, CH_3), 1.43 (s, 3 H, CH_3), 1.66 (s, 3 H, CH_3), 1.71 (s, 3 H, CH_3), 2.06 (s, 2 H, CH_2), 4.06 (br s, 2 H, OCH_2), 4.27–4.39 (m, 2 H, OCH_2), 5.73 (s, 1 H, CH), 7.89–9.33 (m, 7 H, H_{Ar}, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.2, 14.8, 31.2, 31.6, 31.8, 36.5, 53.1, 56.1, 56.2, 59.7, 60.8, 72.6, 96.1, 122.3, 125.9, 128.9, 129.8, 130.6, 130.7, 134.0, 141.1, 169.7, 169.8, 173.6.

MS (EI, 70eV): *m*/*z* = 624 (M^+).

Anal. Calcd for $C_{33}H_{35}Cl_2N_3O_5$: C, 63.46; H, 5.65; N, 6.73. Found: C, 63.55; H, 5.71; N, 6.68.

Dimethyl 2,3-Dicyano-7-(cyclohexylamino)-5*H*-benzo[*h*]pyrano[3,2-*f*]quinoxaline-5,6-dicarboxylate (5l)
Yellow powder; yield: 414 mg (83%); mp 198–202 °C (dec).

IR (KBr): 3200, 2150, 1741, 1677 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.26–2.20 (m, 10 H, 5 Cy-CH_2), 3.64 (s, 3 H, OCH_3), 3.86 (s, 3 H, OCH_3), 4.06 (br s, 1 H, CHN), 5.63 (s, 1 H, CH), 7.97–8.33 (m, 3 H, H_{Ar}), 8.77 (d, *J* = 7.3 Hz, 1 H, NH), 9.25 (d, *J* = 7.9 Hz, 1 H, H_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.5, 25.4, 31.4, 33.5, 33.8, 35.9, 36.5, 50.8, 51.3, 52.6, 71.9, 112.6, 113.6, 113.8, 122.0, 126.4, 127.1, 129.0, 130.3, 132.6, 140.0, 141.7, 151.1, 159.4, 162.5, 169.4, 173.0.

MS (EI, 70eV): *m*/*z* = 497 (M^+).

Anal. Calcd for $C_{27}H_{23}N_5O_5$: C, 65.18; H, 4.66; N, 14.08. Found: C, 65.11; H, 4.61; N, 13.99.

Dimethyl 7-(*tert*-Butylamino)-2,3-dicyano-5*H*-benzo[*h*]pyrano[3,2-*f*]quinoxaline-5,6-dicarboxylate (5m)
Yellow powder; yield: 444 mg (94%); mp 210–211 °C (dec).

IR (KBr): 3200, 2231, 1739, 1668 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.65 (s, 9 H, CH_3), 3.64 (s, 3 H, OCH_3), 3.87 (br s, 3 H, OCH_3), 5.65 (s, 1 H, CH), 8.00–8.53 (m, 3 H, H_{Ar}), 9.12 (s, 1 H, NH), 9.25 (d, *J* = 7.4 Hz, 1 H, H_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 30.6, 35.6, 51.4, 52.6, 52.8, 72.7, 112.6, 113.6, 113.8, 122.5, 126.5, 126.9, 128.2, 129.1, 130.2, 130.6, 132.6, 140.0, 141.6, 151.3, 160.6, 169.7, 172.9.

MS (EI, 70eV): *m*/*z* = 471 (M^+).

Anal. Calcd for $C_{25}H_{21}N_5O_5$: C, 63.69; H, 4.49; N, 14.85. Found: C, 63.75; H, 4.45; N, 14.93.

Diethyl 2,3-Dicyano-7-(2,4,4-trimethylpentan-2-ylamino)-5*H*-benzo[*h*]pyrano[3,2-*f*]quinoxaline-5,6-dicarboxylate (5n)
Yellow powder; yield: 528 mg (95%); mp 221–223 °C.

IR (KBr): 3400, 2200, 1743, 1670 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.02 (s, 9 H, CH_3), 1.24 (t, *J* = 6.5 Hz, 3 H, CH_3), 1.42 (t, *J* = 6.5 Hz, 3 H, CH_3), 1.66 (s, 3 H, CH_3), 1.71 (s, 3 H, CH_3), 2.03 (br s, 2 H, CH_2), 4.08 (m, 2 H, OCH_2), 4.33 (ABq, *J* = 6.5 Hz, 2 H, OCH_2), 5.62 (s, 1 H, CH), 8.00–8.55 (m, 3 H, H_{Ar}), 9.24–9.28 (m, 2 H, NH, H_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1, 14.7, 31.1, 31.4, 31.7, 31.8, 36.0, 53.4, 56.4, 60.0, 61.3, 72.4, 112.8, 113.7, 113.9, 122.5, 126.5, 127.0, 128.2, 129.1, 130.2, 130.6, 132.5, 140.0, 141.8, 151.4, 160.4, 169.4, 172.9.

MS (EI, 70eV): *m*/*z* = 555 (M^+).

Anal. Calcd for $C_{31}H_{33}N_5O_5$: C, 67.01; H, 5.99; N, 12.60. Found: C, 67.09; H, 6.06; N, 12.66.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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