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INVERSE-ELECTRON-DEMAND DIELS-ALDER REACTIONS OF CONDENSED PYRIDAZINES, PART 1. SYNTHESIS OF PHTHALAZINE DERIVATIVES FROM PYRIDAZINO[4,5-*d*]PYRIDAZINES.

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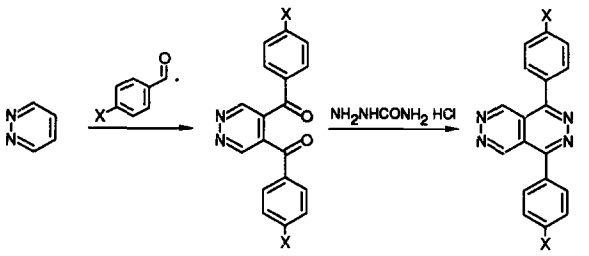
Abstract: The 1,4-diarylpyridazino[4,5-*d*]pyridazine derivatives **1a,b** were found to undergo [4+2] cycloaddition reactions with a variety of electron-rich dienophiles like enamines and ketene acetals to afford phthalazine derivatives in good to high yields.

During the past two decades, the inverse-electron-demand variant of the Diels-Alder reaction has been attracting strongly increasing interest.[1] Especially in the field of heterocyclic chemistry, this reaction type has proven to be of particular value. There are numerous examples of ring transformations involving thermally induced (inter- and intramolecular) [4+2] cycloaddition reactions of monocyclic π-electron-deficient heteroaromatic azadienes such as 1,2,4,5-tetrazines,[1,2] 1,2,3-triazines,[1,3] 1,2,4-triazines,[1,4] 1,3,5-triazines,[1,5] pyridazines,[1,6] pyrimidines,[1,7] pyrazines,[1,8] and pyridines[1,9] with electron-rich dienophiles such as enamines, alkenes, alkynes, ketene acetals etc. On the other hand, there are only few reports describing inverse-electron-demand Diels-Alder reactions of condensed N-heteroaromatic systems like benzo-, pyrimido-, benzofuro-, and benzothieno-fused 1,2,4-triazines,[10-13] several phthalazines,[14] 1,2,3-triazolo[4,5-*d*]pyridazines,[15] and imidazo[4,5-*d*]pyridazines.[16] In the latter examples of annelated pyridazines, the required reaction temperatures are rather high (up to 220°C) and/or the yields of products are only modest.[14-16]

As the magnitude of the $HOMO_{dienophile}/LUMO_{diene}$ energy gap plays a key role in the rate-determing cycloaddition step in such reactions, the annelation of a six-membered π-deficient heteroaromatic ring to positions 4,5 of the pyridazine nucleus should result in a considerable decrease of the LUMO energy (similar to the introduction of electron-withdrawing substituents) and thus to a pronounced azadiene reactivity of the bicyclic system. In the present paper, this is demonstrated by high-yield [4+2] cycloaddition reactions of 1,4-diarylpyridazino[4,5-*d*]pyridazines with a variety of electron-rich C=C dienophiles.

The synthesis of the requisite tetraazanaphthalenes of type **1** (cf. Scheme 1) has been reported by Heinisch et al.[17] and consists of radicalic aroylation of pyridazine, followed by cyclisation of the resulting diketones with semicarbazide.

Scheme 1.

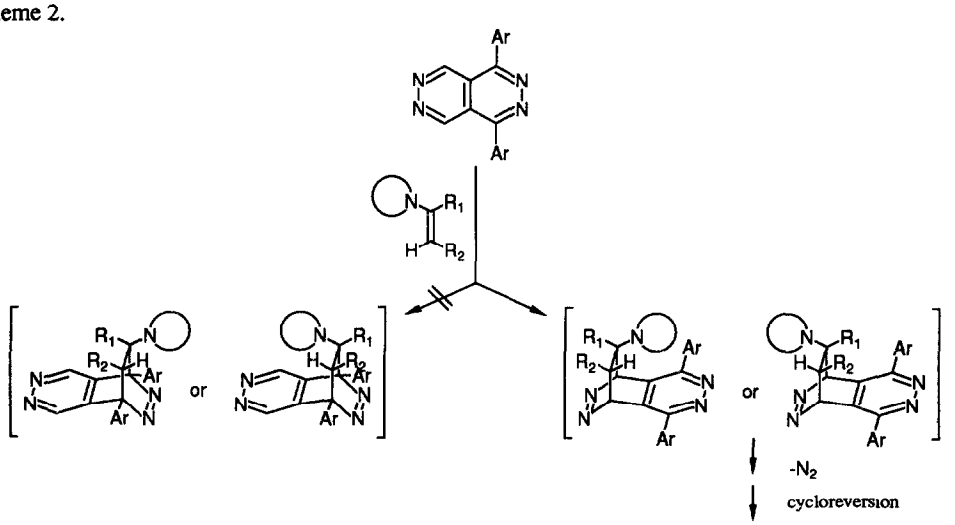


1 X = H, OCH_3

Treatment of 1,4-diphenylpyridazino[4,5-*d*]pyridazine (**1a**) with a twofold excess of cyclic enamines like 1-pyrrolidino-1-cyclopentene in boiling ethanol - conditions which have been described for comparable cycloaddition reactions of nitropyrimidines[18] - led to complete conversion within periods ranging from 10 minutes to 2 hours (cf. Table). As expected, with six-membered enamines the reaction rates were significantly lower than with the highly reactive cyclopentanone-derived reagent. The same order of reactivity was observed on treatment of 1,4-bis(4-methoxyphenyl)pyridazino[4,5-*d*]pyridazine (**1b**) with the same dienophiles. In general, the refluxing periods required for complete consumption of **1b** (reaction monitoring by HPLC) were about three times as long as compared with compound **1a**. Obviously, this effect is due to the electron-donating properties of the methoxy substituents, resulting in a higher LUMO energy of the system.

For steric reasons, addition of the dienophile across C-5/C-8 of the tetraazanaphthalene skeleton was expected to predominate compared to addition across C-1/C-4 (Scheme 2). Indeed, in all instances only reaction products resulting from attack on the less hindered pyridazine ring were isolated.

Scheme 2.



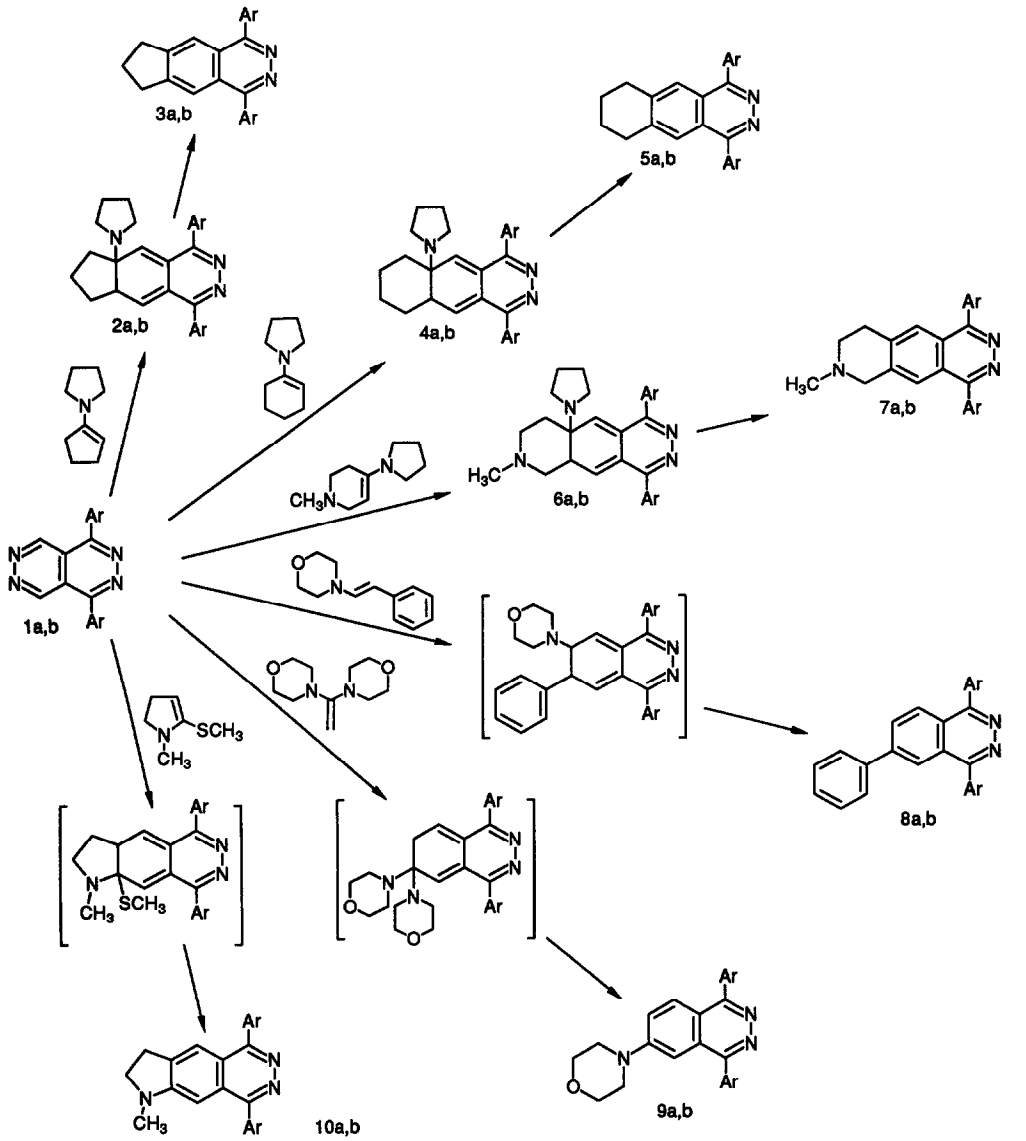
The initially formed, highly strained [4+2] cycloadducts immediately eliminate molecular nitrogen to afford cycloamino-substituted (condensed) dihydrophthalazine derivatives. When enamine reagents derived from cyclic ketones were used, these primary reaction products (**2a,b**, **4a,b**, **6a,b**) could be isolated as stable, colourless solids in 75-94% yield. Initial attempts to aromatise compounds **2**, **4**, **6** by heating in toluene were unsuccessful. However, in the case of the cyclopentane- and cyclohexane-fused dihydrophthalazines **2a,b** and **4a,b**, addition of trifluoroacetic acid to the solutions effected smooth elimination of pyrrolidine within 1 hour of refluxing, affording the condensed phthalazines **3a,b** and **5a,b**, respectively, in high yields. On the other hand, application of this procedure (heating in toluene/CF_3COOH) to the N-methylpiperidine-annelated compounds **6a,b** resulted in immediate decomposition of the material. In these cases, aromatisation finally could be accomplished by heating compounds **6** in the absence of a solvent to a temperature slightly above their melting points (see Experimental).

Initial attempts to react the azadienes **1a,b** with N-styrylmorpholine or 1,1-dimorpholinoethene (a ketene aminal), respectively, in a similar manner as described above (refluxing in ethanol) failed. Observed conversion rates were very low, obviously owing to concurrent hydrolytic/solvolytic consumption of the dienophilic reagents. However, employment of an aprotic solvent (1,4-dioxane) together with a larger (i.e. 4-fold) excess of dienophile and prolonged reaction times (cf. Table) were found to permit the transformation of the starting pyridazino[4,5-*d*]pyridazines into phthalazine derivatives. On treatment of compounds **1a,b** with N-styrylmorpholine, the initially formed dihydrophthalazines proved to be very unstable, leading to the isolation of the elimination products **8a,b** in 57-67% overall yield. In the case of 1,1-dimorpholinoethene as dienophile, not even traces of an aminal-like dihydrophthalazine intermediate could be detected. Instead, the 1,4-diaryl-6-morpholinophthalazines **9a,b** were obtained in high yields.

Also ketene N,S-acetals react readily with azadienes of type **1**, as demonstrated by the smooth conversion of **1a,b** into the pyrrolophthalazine derivatives **10a,b**. Again, the reactions were carried out in dry 1,4-dioxane; the dienophile was generated *in situ* by treatment of 2-methylmercapto-1-methyl-1-pyrrolinium iodide with the strong base 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU). Spontaneous aromatisation of the cycloadducts *via* elimination of methylmercaptane afforded compounds **10** in about 90% yield.

In conclusion, the described inverse-electron-demand Diels-Alder reactions of pyridazino[4,5-*d*]pyridazines proceed under relative mild conditions, due to the pronounced π-electron-deficient character of this tetraazanaphthalene system. Thus, this reaction type was found to provide a simple and convenient method for the transformation of (easily available) 1,4-diarylpyridazino[4,5-*d*]pyridazines into condensed/substituted phthalazine derivatives. The structures of all new compounds are in full agreement with their spectral and microanalytical data.[19] Further investigations on the utility of fused pyridazines in [4+2] cycloaddition reactions are in progress.

Scheme 3



1-10 **a** Ar = C_6H_5
b Ar = 4-$C_6H_4OCH_3$

Table. Cycloaddition Reactions of the 1,4-Diarylpyridazino[4,5-*d*]pyridazines **1**: Reaction Conditions, Products, and Yields.

Starting Compound	Solvent	Temp. (°C)	Reaction Time	Reaction Product	Yield (%)
1a	ethanol	78	10 min	**2a**	94
1a	ethanol	78	1.5 h	**4a**	93
1a	ethanol	78	2.0 h	**6a**	91
1a	dioxane	101	3 d	**8a**	67
1a	dioxane	101	16 h	**9a**	93
1a	dioxane	101	30 min	**10a**	92
1b	ethanol	78	30 min	**2b**	93
1b	ethanol	78	5.0 h	**4b**	90
1b	ethanol	78	6.0 h	**6b**	75
1b	dioxane	101	10 d	**8b**	57
1b	dioxane	101	3 d	**9b**	88
1b	dioxane	101	1.5 h	**10b**	88

EXPERIMENTAL

Melting points (uncorrected) were determined on a Kofler hot-stage microscope. ^{1}H-NMR spectra were recorded on a Varian EM 390 (90 MHz) or a Bruker AC 80 (80 MHz) spectrometer (TMS as internal reference, δ-values in ppm), high-resolution mass spectra on a Finnigan MAT 8230 (equipped with a data system SS300). Column chromatography was carried out on Merck Kieselgel 60, 0.063-0.200 mm (70-230 mesh ASTM). Analytical HPLC separations were accomplished using a 12.5 cm x 4.0 mm column, filled with 5µm Merck LiChrosorb RP18; mobile phase: methanol/water (70-90% methanol), 1.0 ml/min; detection at 254 nm. Light petroleum refers to the fraction of bp 50-70°C. Microanalyses were performed at the Institute of Physical Chemistry (Microanalytical Laboratory), University of Vienna.

Cycloaddition Reactions of the Pyridazino[4,5-*d*]pyridazines **1a,b** with Cyclic Enamines. General Procedure for the Preparation of Compounds **2a,b**, **4a,b**, and **6a,b**.

A solution of **1a**[17] (284 mg; 1 mmol) or **1b**[17] (344 mg; 1 mmol), respectively, and 2 mmol of 1-pyrrolidino-1-cyclopentene,[20] 1-pyrrolidino-1-cyclohexene,[20] or 1,2,5,6-tetrahydro-1-methyl-4-pyrrolidinopyridine,[21] respectively, in ethanol (10 ml) was refluxed for the period given in the Table. The solvent was removed under reduced pressure and the residue was purified by column chromatography (eluent: dichloromethane/methanol, 95:5 for **2a,b**, **4a,b**, 90:10 for **6a,b**).

5a,7,8,8a-Tetrahydro-1,4-diphenyl-8a-pyrrolidino-6*H*-cyclopenta[*g*]phthalazine (**2a**).

Yield: 94%; colourless crystals, mp 172-174°C (methanol).

^{1}H-NMR ($CDCl_3$) δ 7.75-7.20 (m, 10 H, C_6H_5), 6.22 (unresolved, 1 H, H-9), 4.44 (d, J = 12.4 Hz, 1 H, H-5), 3.20-1.00 (m, 15 H, H-5a, N-CH_2-C, C-CH_2-C).

Anal. Calcd. for $C_{27}H_{27}N_3$: C, 82.41; H, 6.92; N, 10.68. Found: C, 82.47; H, 6.92; N, 10.46.

5a,7,8,8a-Tetrahydro-1,4-bis(4-methoxyphenyl)-8a-pyrrolidino-6*H*-cyclopenta[*g*]phthalazine (**2b**).
Yield: 93%; colourless crystals, mp 180-183°C (methanol).
^{1}H-NMR ($CDCl_3$) δ 7.75-6.80 (m, 8 H, $C_6\underline{H}_4OCH_3$), 6.23 (unresolved, 1 H, H-9), 4.43 (d, J = 10.9 Hz, 1 H, H-5), 3.88 (s, 3 H, OCH_3), 3.85 (s, 3 H, OCH_3), 3.15-1.00 (m, 15 H, H-5a, N-CH_2-C, C-CH_2-C).
Anal. Calcd. for $C_{29}H_{31}N_3O_2$: C, 76.79; H, 6.89; N, 9.26. Found: C, 76.68; H, 6.99; N, 9.26.

5a,6,7,8,9,9a-Hexahydro-1,4-diphenyl-9a-pyrrolidinobenzo[*g*]phthalazine (**4a**).
Yield: 93%; colourless crystals, mp 203-207°C (ethanol).
^{1}H-NMR ($CDCl_3$) δ 7.85-7.35 (m, 10 H, C_6H_5), 6.31 (unresolved, 1 H, H-10), 4.05 (unresolved, 1 H, H-5), 2.70-1.00 (m, 17 H, H-5a, N-CH_2-C, C-CH_2-C).
Anal. Calcd. for $C_{28}H_{29}N_3$: C, 82.52; H, 7.17; N, 10.31. Found: C, 82.22; H, 7.39; N, 10.16.

5a,6,7,8,9,9a-Hexahydro-1,4-bis(4-methoxyphenyl)-9a-pyrrolidinobenzo[*g*]phthalazine (**4b**).
Yield: 90%; colourless crystals, mp 200-202°C (methanol).
^{1}H-NMR ($CDCl_3$) δ 7.75-6.85 (m, 8 H, $C_6\underline{H}_4OCH_3$), 6.33 (unresolved, 1 H, H-10), 4.05 (unresolved, 1 H, H-5), 3.89 (s, 3 H, OCH_3), 3.88 (s, 3 H, OCH_3), 2.70-1.00 (m, 17 H, H-5a, N-CH_2-C, C-CH_2-C).
Anal. Calcd. for $C_{30}H_{33}N_3O_2$: C, 77.06; H, 7.11; N, 8.99. Found: C, 76.82; H, 7.34; N, 8.87.

5a,6,7,8,9,9a-Hexahydro-7-methyl-1,4-diphenyl-9a-pyrrolidinopyrido[3,4-*g*]phthalazine (**6a**).
Yield: 91%; pale yellow crystals, mp 202-205°C (ethyl acetate).
^{1}H-NMR ($CDCl_3$) δ 7.85-7.35 (m, 10 H, C_6H_5), 6.34 (unresolved, 1 H, H-10), 3.86 (unresolved, 1 H, H-5), 3.20-1.40 (m, 18 H, H-5a, N-CH_2-C, NCH_3, C-CH_2-C).
Anal. Calcd. for $C_{28}H_{30}N_4$: C, 79.59; H, 7.16; N, 13.26. Found: C, 79.36; H, 7.24; N, 13.20.

5a,6,7,8,9,9a-Hexahydro-1,4-bis(4-methoxyphenyl)-7-methyl-9a-pyrrolidinopyrido[3,4-*g*]phthalazine (**6b**).
Yield: 75%; pale yellow crystals, mp 216-218°C (ethyl acetate).
^{1}H-NMR ($CDCl_3$) δ 7.80-6.85 (m, 8 H, $C_6\underline{H}_4OCH_3$), 6.36 (unresolved, 1 H, H-10), 3.89 (s, 4 H, H-5, OCH_3), 3.88 (s, 3 H, OCH_3), 3.20-1.40 (m, 18 H, H-5a, N-CH_2-C, NCH_3, C-CH_2-C).
Anal. Calcd. for $C_{30}H_{34}N_4O_2$: C, 74.66; H, 7.10; N, 11.61. Found: C, 74.43; H, 6.72; N, 11.63.

7,8-Dihydro-1,4-diphenyl-6*H*-cyclopenta[*g*]phthalazine (**3a**).
A solution of compound **2a** (197 mg; 0.5 mmol) and trifluoroacetic acid (68 mg; 0.6 mmol) in toluene (10 ml) was refluxed for 1 h. The solvent was removed under reduced pressure and the residue was partitioned between a saturated aqueous solution of sodium hydrogencarbonate and dichloromethane. The organic layer was washed with water, dried, and evaporated to afford almost colourless crystals (93%), mp 198-200°C (ethanol).
^{1}H-NMR ($CDCl_3$) δ 8.00-7.40 (m, 12 H, H-5, H-9, C_6H_5), 3.20-2.90 (m, 4 H, C-CH_2-C_{ar}), 2.40-1.90 (m, 2 H, C-CH_2-C).
Anal. Calcd. for $C_{23}H_{18}N_2$: C, 85.68; H, 5.63; N, 8.69. Found: C, 85.54; H, 5.88; N, 8.65.

7,8-Dihydro-1,4-bis(4-methoxyphenyl)-6*H*-cyclopenta[*g*]phthalazine (**3b**).
Preparation as described for **3a**, starting from compound **2b** (227 mg; 0.5 mmol). Yield: 98%; colourless crystals, mp 194-195°C (methanol).

^{1}H-NMR ($CDCl_3$) δ 7.93 (s, 2 H, H-5, H-9), 7.85-7.65 (BB' part of an AA'BB' system, J = 8.7 Hz, 4 H, $C_6H_4OCH_3$), 7.20-7.00 (AA' part of an AA'BB' system, J = 8.7 Hz, 4 H, $C_6H_4OCH_3$), 3.92 (s, 6 H, OCH_3), 3.25-2.90 (m, 4 H, C-CH_2-C_{ar}), 2.40-1.90 (m, 2 H, C-CH_2-C).
Anal. Calcd. for $C_{25}H_{22}N_2O_2$: C, 78.51; H, 5.80; N, 7.32. Found: C, 78.36; H, 5.85; N, 7.28.

6,7,8,9-Tetrahydro-1,4-diphenylbenzo[g]phthalazine (**5a**).
Preparation as described for **3a**, starting from compound **4a** (204 mg; 0.5 mmol). Yield: 95%; colourless crystals, mp 220-223°C (ethanol).
^{1}H-NMR ($CDCl_3$) δ 7.90-7.40 (m, 12 H, H-5, H-10, C_6H_5), 3.10-2.75 (m, 4 H, C-CH_2-C_{ar}), 2.00-1.65 (m, 4 H, C-CH_2-C).
Anal. Calcd. for $C_{24}H_{20}N_2$: C, 85.68; H, 5.99; N, 8.33. Found: C, 85.34; H, 6.13; N, 8.33.

6,7,8,9-Tetrahydro-1,4-bis(4-methoxyphenyl)benzo[g]phthalazine (**5b**).
Preparation as described for **3a**, starting from compound **4b** (234 mg; 0.5 mmol). Yield: 96%; colourless crystals, mp 230-233°C (methanol).
^{1}H-NMR ($CDCl_3$) δ 7.81 (s, 2 H, H-5, H-10), 7.85-7.65 (BB' part of an AA'BB' system, J = 8.7 Hz, 4 H, $C_6H_4OCH_3$), 7.20-6.95 (AA' part of an AA'BB' system, J = 8.7 Hz, 4 H, $C_6H_4OCH_3$), 3.92 (s, 6 H, OCH_3), 3.15-2.80 (m, 4 H, C-CH_2-C_{ar}), 2.05-1.70 (m, 4 H, C-CH_2-C).
Anal. Calcd. for $C_{26}H_{24}N_2O_2$: C, 78.76; H, 6.10; N, 7.07. Found: C, 78.57; H, 6.22; N, 7.13.

6,7,8,9-Tetrahydro-7-methyl-1,4-diphenylpyrido[3,4-g]phthalazine (**7a**).
Compound **6a** (211 mg; 0.5 mmol) was heated in a Kugelrohr distillation apparatus to 240°C for 30 min. The oily residue was purified by column chromatography (eluting with dichloromethane/methanol, 95:5) to afford a tan solid (74%), mp 180-185°C.
^{1}H-NMR ($CDCl_3$) δ 7.95-7.40 (m, 12 H, H-5, H-10, C_6H_5), 3.75 (s, 2 H, N-CH_2-C_{ar}), 3.13, 2.75 (each t, J = 5.9 Hz; 6 H, N-CH_2-C, C-CH_2-C_{ar}), 2.47 (s, 3 H, NCH_3).
For elemental analysis, the corresponding perchlorate was prepared by addition of perchloric acid to a methanolic solution of **7a**. Evaporation of the solvent, followed by recrystallisation from water/charcoal afforded colourless crystals, mp 211-215°C (decomp.).
Anal. Calcd. for $C_{24}H_{22}N_3ClO_4 \cdot 1/4\ H_2O$: C, 63.16; H, 4.97; N, 9.21. Found: C, 63.03; H, 5.11; N, 9.03.

6,7,8,9-Tetrahydro-1,4-bis(4-methoxyphenyl)-7-methylpyrido[3,4-g]phthalazine (**7b**).
Compound **6b** (241 mg; 0.5 mmol) was heated in a Kugelrohr distillation apparatus to 220°C for 45 min. The oily residue was purified by column chromatography (eluting with dichloromethane/methanol, 95:5) to afford pale yellow crystals (49%), mp 202-205°C (ethanol/diisopropyl ether).
^{1}H-NMR ($CDCl_3$) δ 7.95-7.60 (m, 6 H, H-5, H-10, $C_6H_4OCH_3$), 7.20-7.00 (AA' part of an AA'BB' system, J = 8.7 Hz, 4 H, $C_6H_4OCH_3$), 3.92 (s, 6 H, OCH_3), 3.76 (s, 2 H, N-CH_2-C_{ar}), 3.14, 2.76 (each t, J = 5.8 Hz; 6 H, N-CH_2-C, C-CH_2-C_{ar}), 2.48 (s, 3 H, NCH_3).
HRMS Calcd. for $C_{26}H_{25}N_3O_2$: m/z 411.1947. Found: 411.1928.
Anal. Calcd. for $C_{26}H_{25}N_3O_2 \cdot 1/8\ H_2O$: C, 75.48; H, 6.15; N, 10.16. Found: C, 75.37; H, 6.35; N, 10.05.

1,4,6-Triphenylphthalazine (**8a**).
A solution of **1a** (142 mg; 0.5 mmol) and N-styrylmorpholine[22] (378 mg; 2 mmol) in dry 1,4-dioxane (10 ml) was refluxed for 72 h. The solvent was removed under reduced pressure and the residue was subjected to column chromatography (eluting with ethyl acetate/light petroleum, 2:3) to afford almost colourless crystals (67%), mp 176-178°C (ethanol).
^{1}H-NMR ($CDCl_3$) δ 8.29 (unresolved, 1 H, H-5), 8.25-8.00 (m, 2 H, H-7, H-8), 7.95-7.30 (m, 15 H, C_6H_5).

HRMS Calcd. for $C_{26}H_{18}N_2$: m/z 358.1469. Found: 358.1457.
Anal. Calcd. for $C_{26}H_{18}N_2 \cdot 1/4\ H_2O$: C, 86.04; H, 5.14; N, 7.72. Found: C, 86.07; H, 5.04; N, 7.75.

1,4-Bis(4-methoxyphenyl)-6-phenylphthalazine (8b).
A solution of **1b** (172 mg; 0.5 mmol) and N-styrylmorpholine[22] (378 mg; 2 mmol) in dry 1,4-dioxane (10 ml) was refluxed for 10 d; every 48 h, another 1 mmol portion of enamine was added. The solvent was removed under reduced pressure and the residue was subjected to column chromatography (eluting with ethyl acetate/light petroleum, 2:3) to afford pale yellow crystals (57%), mp 183-185°C (ethanol).
^{1}H-NMR ($CDCl_3$) δ 8.33 (d, J = 1.6 Hz, 1 H, H-5), 8.26 (d, J = 9.8 Hz, 1 H, H-8), 8.05 (dd, J_1 = 9.8 Hz, J_2 = 1.6 Hz, 1 H, H-7), 7.95-7.70 (BB' part of an AA'BB' system, J = 8.7 Hz, 4 H, $C_6\underline{H_4}OCH_3$), 7.65-7.30 (m, 5 H, C_6H_5), 7.20-7.00 (AA' part of an AA'BB' system, J = 8.7 Hz, 4 H, $C_6\underline{H_4}OCH_3$), 3.92 (s, 6 H, OCH_3).
HRMS Calcd. for $C_{28}H_{22}N_2O_2$: m/z 418.1681. Found: 418.1686.
Anal. Calcd. for $C_{28}H_{22}N_2O_2 \cdot 1/8\ H_2O$: C, 79.93; H, 5.33; N, 6.66. Found: C, 79.78; H, 5.20; N, 6.68.

6-Morpholino-1,4-diphenylphthalazine (9a).
A solution of **1a** (142 mg; 0.5 mmol) and 1,1-dimorpholinoethene[23] (396 mg; 2 mmol) in dry 1,4-dioxane (10 ml) was refluxed for 16 h. The solvent was removed under reduced pressure and the residue was triturated with methanol to afford almost colourless crystals (93%), mp 250-252°C (1-propanol).
^{1}H-NMR ($CDCl_3$) δ 8.00 (d, J = 9.2 Hz, 1 H, H-8), 7.90-7.35 (m, 11 H, H-7, C_6H_5), 7.28 (d, J = 2.6 Hz, 1 H, H-5), 4.00-3.70 (m, 4 H, O-CH_2-C), 3.40-3.10 (m, 4 H, N-CH_2-C).
HRMS Calcd. for $C_{24}H_{21}N_3O$: m/z 367.1684. Found: 367.1680.
Anal. Calcd. for $C_{24}H_{21}N_3O \cdot 1/4\ H_2O$: C, 77.50; H, 5.83; N, 11.30. Found: C, 77.45; H, 5.89; N, 11.16.

1,4-Bis(4-methoxyphenyl)-6-morpholinophthalazine (9b).
A solution of **1b** (172 mg; 0.5 mmol) and 1,1-dimorpholinoethene[23] (396 mg; 2 mmol) in dry 1,4-dioxane (10 ml) was refluxed for 72 h; every 24 h, another 1 mmol portion of reagent was added. The solvent was removed under reduced pressure and the residue was subjected to column chromatography (eluting with dichloromethane/methanol, 96:4) to afford pale yellow crystals (88%), mp 227-229°C (ethanol).
^{1}H-NMR ($CDCl_3$) δ 8.02 (d, J = 9.1 Hz, 1 H, H-8), 7.85-7.60 (m, 4 H, $C_6\underline{H_4}OCH_3$), 7.44 (dd, J_1 = 9.1 Hz, J_2 = 2.5 Hz, 1 H, H-7), 7.31 (d, J = 2.5 Hz, 1 H, H-5), 3.91 (s, 6 H, OCH_3), 3.90-3.70 (m, 4 H, O-CH_2-C), 3.40-3.10 (m, 4 H, N-CH_2-C).
Anal. Calcd. for $C_{26}H_{25}N_3O_3$: C, 73.05; H, 5.89; N, 9.83. Found: C, 73.17; H, 5.71; N, 9.81.

2,3-Dihydro-1-methyl-5,8-diphenyl-1*H*-pyrrolo[2,3-g]phthalazine (10a).
To a solution of **1a** (142 mg; 0.5 mmol) in dry 1,4-dioxane (10 ml) were added 1-methyl-2-methylmercapto-1-pyrrolin-1-ium iodide[24] (514 mg; 2 mmol) and DBU (304 mg; 2 mmol). The mixture was refluxed for 30 min, then the solvent was removed under reduced pressure. The residue was subjected to column chromatography (eluting with dichloromethane/methanol, 96:4) to afford yellow crystals (92%), mp 229-231°C (methanol).
^{1}H-NMR ($CDCl_3$) δ 7.95-7.35 (m, 11 H, H-4, C_6H_5), 6.62 (s, 1 H, H-9), 3.75-3.40 (m, 2 H, N-CH_2-C), 3.30-2.95 (m, 2 H, C-CH_2-C), 2.83 (s, 3 H, NCH_3).
HRMS Calcd. for $C_{23}H_{19}N_3$: m/z 337.1579. Found: 337.1563.
Anal. Calcd. for $C_{23}H_{19}N_3 \cdot 1/2\ H_2O$: C, 79.74; H, 5.82; N, 12.13. Found: C, 79.39; H, 5.61; N, 12.41.

2,3-Dihydro-5,8-bis(4-methoxyphenyl)-1-methyl-1*H*-pyrrolo[2,3-g]phthalazine (**10b**).
Preparation as described for **10a**, starting from compound **1b** (172 mg; 0.5 mmol). Reaction time: 1.5 h; yellow crystals (88%), mp 258-262°C (ethanol).
^{1}H-NMR ($CDCl_3$) δ 7.85-7.55 (m, 5 H, H-4, $C_6H_4OCH_3$), 7.20-6.95 (AA' part of an AA'BB' system, J = 8.7 Hz, 4 H, $C_6H_4OCH_3$), 6.66 (s, 1 H, H-9), 3.90 (s, 6 H, OCH_3), 3.70-3.40 (m, 2 H, N-CH_2-C), 3.30-2.95 (m, 2 H, C-CH_2-C), 2.85 (s, 3 H, NCH_3).
HRMS Calcd. for $C_{25}H_{23}N_3O_2$: m/z 397.1790. Found: 397.1782.
Anal. Calcd. for $C_{25}H_{23}N_3O_2 \cdot 1/4\ H_2O$: C, 74.70; H, 5.89; N, 10.45. Found: C, 74.40; H, 5.73; N, 10.26.

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