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Synthesis and *In-vitro* Antitumor Activity of 1-[3-(Indol-1-yl)prop-1-yn-1-yl]phthalazines and Related Compounds

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Abstract: A series of novel 3-(indol-1-yl)prop-1-yn-1-yl-substituted phthalazines and related azines was prepared *via* a concise pathway by palladium-catalyzed cross-coupling of appropriate halo-azines and *N*-propargylindoles. Some of the compounds exhibited significant antitumor activity in an *in-vitro* assay.

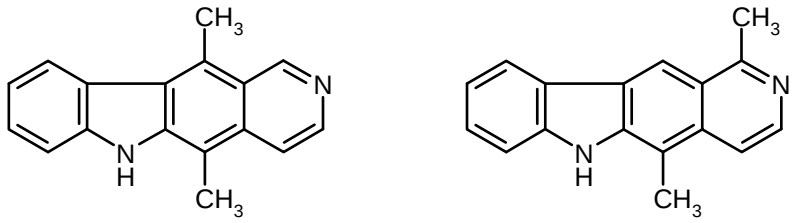
Keywords: 1-[3-(indol-1-yl)prop-1-yn-1-yl]phthalazines, *N*-propargylindoles, palladium-catalyzed cross-coupling, Sonogashira reaction, antitumor activity.

Introduction

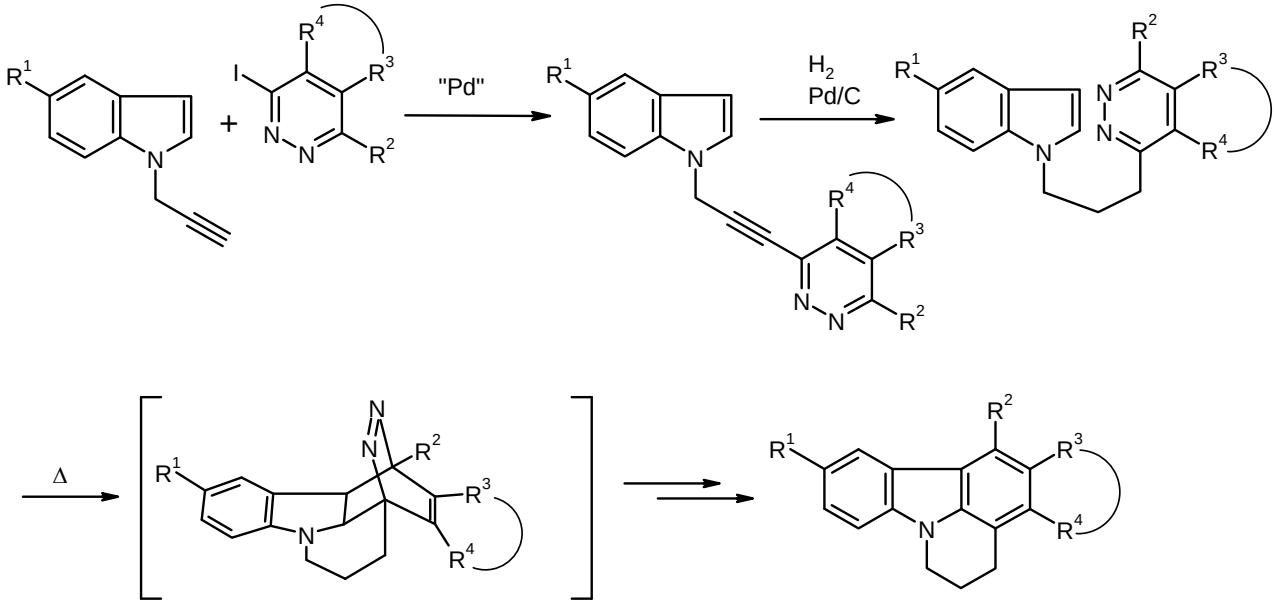
During the course of a research program at our department, focusing on the synthesis and antitumor activity of polycyclic hetarenes, especially condensed carbazoles of the ellipticine/olivacine type [1-5] (cf. Figure 1) and polycyclic quinones [6-8], we recently described the preparation of novel pentacyclic ellipticine analogs *via* a route featuring an intramolecular inverse-electron-demand Diels-Alder reaction of indolylpropyl-substituted 1,2-diazines as the key step (Scheme 1) [9]. In a routine *in-vitro* screening for cytotoxic activity, not only the target compounds, but also one of the intermediates, namely 1-[3-(indol-1-yl)prop-1-yn-1-yl]phthalazine, showed significant tumor cell-growth inhibition. Therefore, this compound with a 1,3-disubstituted propyne unit as the central element was selected as a new lead structure for further exploratory investigations. Here, we report on the synthesis and the

results of preliminary *in-vitro* antitumor tests of a focused compound library featuring the same propyne motif with one electron-rich and one electron-deficient hetarene attached at the terminal carbon atoms.

Figure 1. Structures of the alkaloids, *ellipticine* and *olivacine*.



Scheme 1. Synthesis of bridged ellipticine/olivacine analogs [9].



Results and Discussion

Syntheses

Following the first step of the pathway above (Scheme 1), the target compounds were prepared essentially by a Sonogashira cross-coupling reaction of an appropriate propargyl-substituted indole or indoline synthon with an iodohetarene or bromohetarene, respectively. Two series of compounds were synthesized, keeping always one of the two heterocyclic subunits constant (either the indole or the azine) and varying the other one. The propynyl-substituted educts were obtained in good yields by

treatment of the N-unsubstituted precursors with propargyl bromide in toluene/50% sodium hydroxide, using tetrabutylammonium bromide as a phase-transfer catalyst [10].

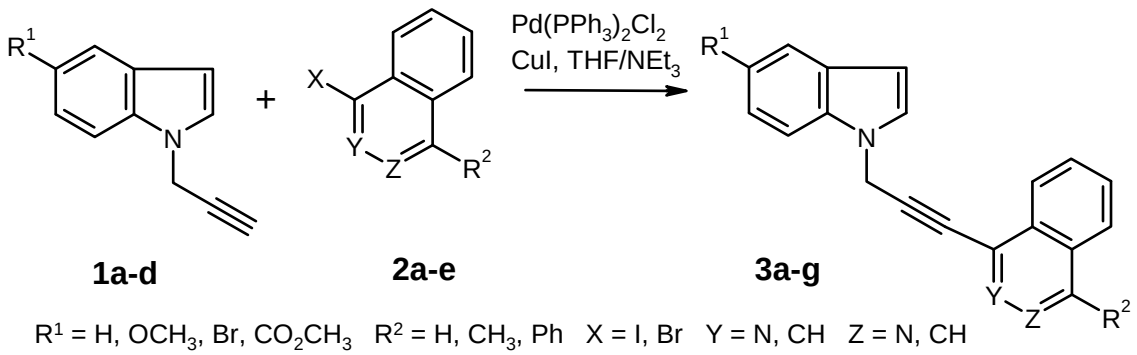
An improved synthesis of 1-iodophthalazine

During the preparation of the requisite starting materials, it turned out that the transformation of 1-chlorophthalazine into 1-iodophthalazine by treatment of the former with potassium iodide and hydroiodic acid in acetone, as described by Hirsch and Orphanos [11], gives very unreliable results if the original work-up procedure is applied (dissolving the initially formed hydroiodide salt of 1-iodophthalazine in water, followed by neutralization and filtration of the free base). In several runs, the compound underwent complete decomposition within a very short time. We found that this crude material is highly acid-sensitive and is prone to an autocatalytic decomposition process if exposed to traces of acid. Therefore, it is essential to keep the pH after liberation of the free base strictly alkaline. Instead of collecting the product by filtration, it is extracted quickly into dichloromethane and the organic extract is immediately basified by addition of triethylamine (see Experimental section). Evaporation of this solution gives a pure product which can be stored under refrigeration for several weeks.

Palladium-catalyzed cross-coupling reactions

As the educts for the Sonogashira cross-coupling reaction (see Scheme 2), the following azines were chosen besides 1-iodophthalazine (**2a**): 1-iodo-4-methylphthalazine (**2b**) [12], 1-iodo-4-phenylphthalazine (**2c**) [13], 1-iodoisoquinoline (**2d**) [14], and 4-bromoisoquinoline (**2e**) [15]. As the acetylenic building blocks, *N*-propargyl-substituted 5-methoxyindole (**1a**) [9], 5-bromoindole (**1b**), methyl indole-5-carboxylate (**1c**) [16], and indoline (**1d**) [17] were employed.

Scheme 2. Synthesis of the target compounds (**3**) by Sonogashira cross-coupling.



In all cases, bis(triphenylphosphine)palladium(II)dichloride and copper(I)iodide were used as catalysts, and the reactions were run in tetrahydrofuran/triethylamine under an argon atmosphere at room temperature (except for 3-bromoisoquinoline: reflux temperature) with TLC monitoring. Extended reaction times were found to result in a substantial drop of yields, mainly because of increased decomposition and/or a base-promoted alkyne/allene rearrangement of the products [18] (the latter process was particularly problematic in the case of the 5-bromoindole derivative **3f**). Whereas

conversion rates were generally good, yields in some cases were only moderate owing to substantial losses during the purification process. Product structures, reaction conditions and yields of isolated material as well as the results of *in-vitro* antitumor screening (see below), including the values for the previously prepared analogs **3h-j** [9] are summarized in Table 1.

Table 1. Structures, reaction conditions, yields, and biological activities for the title compounds.

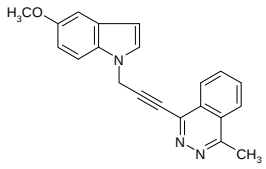
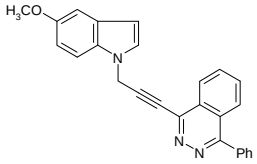
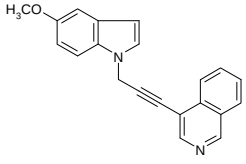
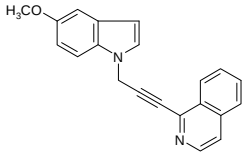
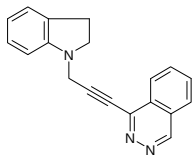
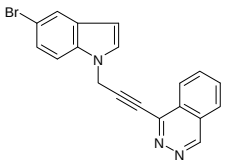
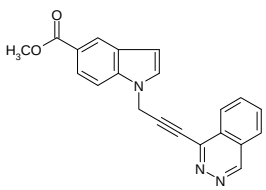
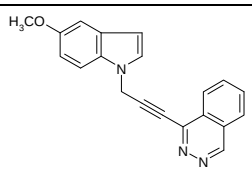
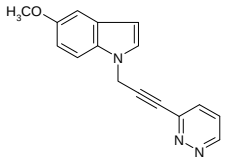
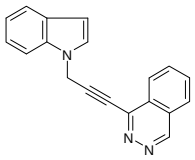
Product		Reaction conditions or reference	Yield (%)	Tumor cell growth inhibition (%) [a)]				
				KB	SK OV-3	SF-268	NCI H460	RKO P 27
	**3a**	r.t., 20 h	47	91	13	93	85	96
	**3b**	r.t., 6 h	55	99	61	99	95	100
	**3c**	reflux, 7 d	34	19	6	8	18	28
	**3d**	r.t., 48 h	75	n.d.	n.d.	n.d.	27	31
	**3e**	r.t., 5 h	80	19	28	26	74	45
	**3f**	r.t., 4 h	30	54	50	63	68	64
	**3g**	r.t., 5 h	15	23	41	41	64	54
	**3h**	lit. [9]	-	97	58	81	97	90

Table 1. Cont.

	**3i**	lit. [9]	-	28	13	11	36	28
	**3j**	lit. [9]	-	86	53	88	93	78

[a)] Tumor cell lines used: KB: cervical carcinoma; SF-268: CNS cancer; RKOP27: colon adenocarcinoma; SK OV-3: ovarial carcinoma; NCI H-460: non-small-cell lung cancer.

Biological Activity

All compounds were subjected to a preliminary screening for antitumor activity at a fixed sample concentration of 3.16 µg/mL, using the XTT *in-vitro* assay [19]. As can be concluded from the results (see Table 1), replacement of the phthalazine unit by a monocyclic 1,2-diazine (**3i**) or by an isoquinoline (**3c**, **3d**) leads to a marked drop in activity, whereas substitution of the phthalazine at position 4 [methyl (**3a**) or phenyl (**3b**)] is well tolerated. In the indole part of the molecule, the 5-methoxy substituent appears to be most favorable among the variations studied. Replacement of an indole by an indoline structure (**3e**) results in lower activity.

Conclusions

Sonogashira reaction of 1-iodophthalazines and related haloazines with the terminal acetylene unit of *N*-propargylindoles provides a convenient access to the title compounds, which are of pharmaceutical interest due to their activity in an *in-vitro* antitumor screen. Further investigations will be required for a more detailed evaluation of these agents.

Experimental

General

Melting points (uncorrected) were determined on a Kofler hot-stage microscope (Reichert). ^{1}H-NMR spectra were recorded on a Bruker Avance DPX 200 (200 MHz) or on a Varian UnityPlus 300 (300 MHz) spectrometer. IR spectra were taken on a Perkin-Elmer 1605 FT-IR instrument. Mass spectra were obtained on a Shimadzu QP5050A DI 50 instrument, high-resolution mass spectra were recorded on a Finnigan MAT 8230 spectrometer at the Institute of Organic Chemistry, University of Vienna. Column chromatography was carried out on Merck Kieselgel 60, 0.063–0.200 mm, thin layer chromatography was done on Merck aluminium sheets pre-coated with Kieselgel F_{254}. Microanalyses were performed at the Microanalytical Laboratory, Faculty of Chemistry, University of Vienna.

5-Bromo-1-prop-2-yn-1-yl-1H-indole (**1c**). To a solution of 5-bromoindole (1.96 g, 10 mmol) and propargyl bromide (2.23 g of a 80% solution in toluene; 15 mmol) in toluene (30 mL) were added tetrabutylammonium bromide (0.161 g, 0.5 mmol) and 50% aqueous NaOH (6 mL). The two-phase system was stirred vigorously for 3 h at room temperature, then it was diluted with toluene (10 mL) and the phases were separated. The organic layer was washed several times with water and then with brine. It was dried over Na_2SO_4 and the solvent was removed under reduced pressure to give the product (2.179 g, 93%) as an almost colorless oil which darkened slowly on storage. IR (KBr): 3290, 2125, 1564, 1507, 1465, 1189, 1053, 898, 752 cm^{-1}; MS (EI, 70 eV) *m/z*: 235 (M^+, 46%), 233 (M^+, 49), 196 (12), 194 (10), 154 (100), 127 (18), 115 (33), 88 (22), 62 (19); ^{1}H-NMR ($CDCl_3$) δ: 7.77 (d, $J_{4–6}$ = 1.8 Hz, 1H, 4-H), 7.36–7.26 (m, 2H, 6-H, 7-H), 7.21 (d, $J_{2–3}$ = 3.3 Hz, 2-H), 6.48 (d, $J_{2–3}$ = 3.3 Hz, 1H, 3-H), 4.86 (d, *J* = 2.6 Hz, 2H, CH_2), 2.42 (t, *J* = 2.6 Hz, 1H, C≡CH). HRMS (EI, 70 eV) *m/z* calcd. for $C_{11}H_8BrN$ (M^+): 232.9840. Found: 232.9844.

1-Iodophthalazine (**2a**) [11]. *Modified Procedure.* A mixture of 1-chlorophthalazine (2.75 g, 17 mmol), potassium iodide (5.0 g, 30 mmol), 57% hydroiodic acid (3.4 mL) and acetone (50 mL) was stirred in the dark at room temperature for 96 h. The yellow precipitate (**2a**·HI) was collected by filtration, washed with diethyl ether, and dried *in vacuo*. The material was then suspended in ice-water and the mixture was stirred for 15 min and made alkaline with dilute ammonium hydroxide. It was extracted several times with CH_2Cl_2 and the combined extracts were repeatedly washed with a solution of sodium thiosulfate (0.5 g) in 1% ammonium hydroxide, then with brine. Triethylamine (2 mL) was added to the CH_2Cl_2 extract, then it was dried over Na_2SO_4. Evaporation of the volatile components gave **2a** (3.153 g, 74%) as yellow crystals, mp 87–96 °C (lit. [11]: 78 °C), which were stored in a deep freezer and which were used for the subsequent steps without further purification.

Synthesis of Compounds **3** *by Pd-Catalyzed Cross-Coupling Reaction. General Procedure.* To a solution of the aryl halide **2a**, **2b**, **2c**, **2d**, or **2e** (2.6 mmol), respectively, and the appropriate alkyne **1a**, **1b**, **1c**, or **1d** (3.25 mmol), respectively, in dry THF (6 mL) were added triethylamine (1.0 mL, 7.2 mmol), CuI (0.015 g, 3 mol%) and $Pd(PPh_3)_2Cl_2$ (0.055 g, 3 mol%), and the mixture was flushed with argon. It was then stirred under an argon atmosphere under the conditions (room temperature or reflux) and for the time listed in Table 1. The insoluble material was filtered off and washed carefully with THF. The combined filtrates were evaporated under reduced pressure and the residue was purified by column chromatography (eluent: ethyl acetate or ethyl acetate/light petroleum).

1-[3-(5-Methoxy-1H-indol-1-yl)prop-1-yn-1-yl]-4-methylphthalazine (**3a**). Prepared from 5-methoxy-1-prop-2-yn-1-yl-1*H*-indole (**1a**) and 1-iodo-4-methylphthalazine (**2b**); yield: 0.408 g (47%), recrystallization from ethyl acetate/light petroleum gave almost colorless crystals, mp 166–168 °C. IR (KBr): 2921, 2231, 1620, 1484, 1383, 1239, 1153, 1029, 848, 799, 771, 619 cm^{-1}; MS (EI, 70 eV) *m/z*: 327 (M^+, 19%), 312 (10), 296 (2), 284 (6), 164 (6), 152 (15), 142 (9), 127 (7), 103 (4), 77 (7), 70 (13), 61 (14), 45 (24), 43 (100); ^{1}H-NMR ($CDCl_3$) δ: 8.09 (d, *J* = 8.7 Hz, 1H, phthalazine 8-H), 8.06 (d, *J* = 9.3 Hz, 1H, phthalazine 5-H, shows positive NOE on irradiation at 3.02 ppm), 7.92–7.80 (m, 2H, phthalazine 6-H, 7-H), 7.47 (d, $J_{6–7}$ = 9.0 Hz, 1H, indole 7-H), 7.31 (d, $J_{2–3}$ = 3.0 Hz, 1H, indole 2-H), 7.15 (d, $J_{4–6}$ = 2.1 Hz, 1H, indole 4-H), 6.96 (dd, $J_{6–7}$ = 9.0 Hz, $J_{4–6}$ = 2.4 Hz, 1H, indole 6-H), 6.52 (d,

$J_{2–3}$ = 3.0 Hz, 1H, indole 3-H), 5.28 (s, 2H, CH_2), 3.88 (s, 3H, OCH_3), 3.02 (s, 3H, 4-CH_3). Anal. calcd. for $C_{21}H_{17}N_3O \cdot 0.25\ H_2O$: C, 76.00; H, 5.31; N, 12.60. Found: C, 76.04; H, 5.22; N, 12.45.

1-[3-(5-Methoxy-1H-indol-1-yl)prop-1-yn-1-yl]-4-phenylphthalazine (**3b**). Prepared from 5-methoxy-1-prop-2-yn-1-yl-1*H*-indole (**1a**) and 1-iodo-4-phenylphthalazine (**2c**); yield: 0.552 g (55%), recrystallization from ethyl acetate gave almost colorless crystals, mp 150–152 °C. IR (KBr): 3057, 2939, 2236, 1619, 1576, 1485, 1386, 1239, 1151, 1028, 702, 653 cm^{-1}; MS (EI, 70 eV) *m/z*: 389 (M^+, 100%), 374 (24), 358 (10), 346 (22), 244 (20), 213 (50), 194 (56), 187 (42), 173 (33), 165 (12), 147 (27), 132 (34), 104 (19), 77 (18), 51 (17), 43 (20); ^{1}H-NMR ($CDCl_3$) δ: 8.19–8.16 (m, 1H, phthalazine 8-H), 8.09–8.05 (m, 1H, phthalazine 5-H, shows positive NOE on irradiation at 7.75 ppm), 7.88–7.83 (m, 2H, phthalazine 6-H, 7-H), 7.77–7.74 (m, 2H, phenyl 2-H, 6-H), 7.60–7.56 (m, 3H, phenyl 3-H, 4-H, 5-H, shows positive NOE on irradiation at 7.75 ppm), 7.49 (d, $J_{6–7}$ = 8.9 Hz, 1H, indole 7-H), 7.33 (d, $J_{2–3}$ = 3.3 Hz, 1H, indole 2-H), 7.16 (d, $J_{4–6}$ = 2.4 Hz, 1H, indole 4-H), 6.97 (dd, $J_{6–7}$ = 8.9 Hz, $J_{4–6}$ = 2.4 Hz, 1H, indole 6-H), 6.54 (d, $J_{2–3}$ = 3.3 Hz, 1H, indole 3-H), 5.31 (s, 2H, CH_2), 3.88 (s, 3H, OCH_3). Anal. calcd. for $C_{26}H_{19}N_3O$: C, 80.19; H, 4.92; N, 10.79. Found: C, 79.98; H, 4.99; N, 10.55.

4-[3-(5-Methoxy-1H-indol-1-yl)prop-1-yn-1-yl]isoquinoline (**3c**). Prepared from 5-methoxy-1-prop-2-yn-1-yl-1*H*-indole (**1a**) and 4-bromoisoquinoline (**2e**); yield: 0.284 g (34%), recrystallization from ethyl acetate/light petroleum gave brownish crystals, mp 131–133 °C. IR (KBr): 2903, 2825, 2244, 1620, 1488, 1241, 1150, 794, 753, 715, 580 cm^{-1}; MS (EI, 70 eV) *m/z*: 312 (M^+, 60%), 296 (2), 281 (3), 201 (4), 166 (100), 156 (9), 139 (36), 103 (5), 89 (6), 76 (6), 43 (14); ^{1}H NMR ($CDCl_3$) δ: 9.28 (br s, 1H, isoquinoline 1-H), 8.75 (br s, 1H, isoquinoline 3-H), 8.11 (d, $J_{7–8}$ = 8.4 Hz, 1H, isoquinoline 8-H), 7.98 (d, $J_{5–6}$ = 7.8 Hz, 1H, isoquinoline 5-H), 7.74 (t, *J* = 7.7 Hz, 1H, isoquinoline 7-H, shows positive NOE on irradiation at 8.11 ppm), 7.65 (t, *J* = 7.3 Hz, 1H, isoquinoline 6-H), 7.46 (d, $J_{6–7}$ = 8.9 Hz, 1H, indole 7-H, shows positive NOE on irradiation at 5.25 ppm), 7.32 (d, $J_{2–3}$ = 3.3 Hz, 1H, indole 2-H, shows positive NOE on irradiation at 5.25 ppm), 7.15 (d, $J_{4–6}$ = 2.4 Hz, 1H, indole 4-H), 6.96 (dd, $J_{6–7}$ = 8.9 Hz, $J_{4–6}$ = 2.4 Hz, 1H, indole 6-H), 6.52 (d, $J_{2–3}$ = 3.3 Hz, 1H, indole 3-H), 5.25 (s, 2H, CH_2), 3.88 (s, 3H, OCH_3). Anal. calcd for $C_{21}H_{16}N_2O \cdot 0.25\ H_2O$: C, 79.60; H, 5.25; N, 8.84. Found: C, 79.66; H, 5.50; N, 8.46.

1-[3-(5-Methoxy-1H-indol-1-yl)prop-1-yn-1-yl]isoquinoline (**3d**). Prepared from 5-methoxy-1-prop-2-yn-1-yl-1*H*-indole (**1a**) and 1-iodoisoquinoline (**2d**); yield: 0.620 g (75%), recrystallization from ethyl acetate/light petroleum gave almost colorless crystals, mp 155–157 °C. IR (KBr): 3048, 2953, 2235, 1620, 1578, 1551, 1486, 1350, 1242, 1153, 1028, 830, 747, 723, 666 cm^{-1}; MS (EI, 70 eV) *m/z*: 312 (M^+, 34%), 297 (6), 281 (2), 269 (9), 184 (11), 166 (44), 146 (11), 139 (38), 134 (15), 103 (7), 89 (6), 76 (9), 61 (13), 45 (26), 43 (100); ^{1}H-NMR ($CDCl_3$) δ: 8.51 (d, $J_{3–4}$ = 5.4 Hz, 1H, isoquinoline 3-H), 8.22 (dd, $J_{7–8}$ = 8.4 Hz, $J_{6–8}$ = 1.2 Hz, 1H, isoquinoline 8-H), 7.82 (d, $J_{5–6}$ = 8.1 Hz, 1H, isoquinoline 5-H), 7.72–7.69 (m, 1H, isoquinoline 6-H, shows positive NOE on irradiation at 7.82 ppm), 7.67–7.63 (m, 1H, isoquinoline 4-H, shows positive NOE on irradiation at 8.51 ppm), 7.61–7.55 (m, 1H, isoquinoline 7-H, shows positive NOE on irradiation at 8.22 ppm), 7.47 (d, $J_{6–7}$ = 8.9 Hz, 1H, indole 7-H), 7.32 (d, $J_{2–3}$ = 3.3 Hz, 1H, indole 2-H), 7.14 (d, $J_{4–6}$ = 2.4 Hz, 1H, indole 4-H), 6.96 (dd, $J_{6–7}$ = 8.9 Hz, $J_{4–6}$ = 2.4 Hz, 1H, indole 6-H), 6.51 (d, $J_{2–3}$ = 3.3 Hz, 1H, indole 3-H), 5.26 (s, 2H, CH_2), 3.88 (s,

3H, OCH_3). Anal. calcd. for $C_{21}H_{16}N_2O \cdot 0.2\ H_2O$: C, 79.83; H, 5.23; N, 8.87. Found: C, 79.82; H, 5.22; N, 8.59.

1-[3-(2,3-Dihydro-1H-indol-1-yl)prop-1-yn-1-yl]phthalazine (**3e**). Preparation from 1-prop-2-yn-1-ylindoline (**1d**) and 1-iodophthalazine (**2a**); yield: 0.592 g (80%), recrystallization from ethyl acetate gave brownish crystals, mp 94–95 °C. IR (KBr): 3043, 2830, 2227, 1606, 1484, 1353, 1237, 1138, 757, 594 cm^{-1}; MS (EI, 70 eV) *m/z*: 285 (M^+, 2%), 168 (100), 141 (13), 114 (11), 91 (23), 77 (6), 65 (16), 51 (5); ^{1}H-NMR ($CDCl_3$) δ: 9.43 (s, 1H, phthalazine 4-H), 7.93–7.73 (m, 4H, phthalazine 5-H, 6-H, 7-H, 8-H), 7.21–7.16 (m, 2H, indoline 4-H, 6-H, shows positive NOE on irradiation at 3.05 ppm), 6.85–6.76 (m, 2H, indoline 5-H, indoline 7-H), 4.38 (s, 2H, $C{\equiv}CCH_2$), 3.60 (t, J = 8.1 Hz, 2H, indoline 2-H, shows positive NOE on irradiation at 3.05 ppm), 3.05 (t, J = 8.1 Hz, 2H, indoline 3-H). Anal. calcd. for $C_{19}H_{15}N_3$: C, 79.98; H, 5.30; N, 14.73. Found: C, 79.93; H, 5.47; N, 14.68.

1-[3-(5-Bromo-1H-indol-1-yl)prop-1-yn-1-yl]phthalazine (**3f**). Preparation from 5-bromo-1-prop-2-yn-1-yl-1*H*-indole (**1b**) and 1-iodophthalazine (**2a**); yield: 0.281 g (30%), recrystallization from ethyl acetate gave almost colorless crystals, mp 154–158 °C. IR (KBr): 3097, 2955, 2239, 1465, 1394, 1353, 1282, 1185, 1051, 899, 758, 594 cm^{-1}; MS (EI, 70 eV) *m/z*: 363 (M^+, 13%), 361 (M^+, 12), 282 (8), 195 (14), 167 (7), 141 (34), 127 (36), 114 (15), 97 (11), 84 (20), 69 (25), 58 (93), 57 (39), 43 (100); ^{1}H NMR ($CDCl_3$) δ: 9.48 (s, 1H, phthalazine 4-H), 8.06 (d, $J_{7–8}$ = 8.1 Hz, 1H, phthalazine 8-H), 7.99–7.86 (m, 3H, phthalazine 5-H, 6-H, 7-H), 7.81 (d, $J_{4–6}$ = 1.6 Hz, 1H, indole 4-H), 7.45 (d, $J_{6–7}$ = 8.7 Hz, 1H, indole 7-H), 7.38 (dd, $J_{6–7}$ = 8.7 Hz, $J_{4–6}$ = 1.6 Hz, 1H, indole 6-H), 7.34 (d, $J_{2–3}$ = 3.3 Hz, 1H, indole 2-H), 6.55 (d, $J_{2–3}$ = 3.3 Hz, 1H, indole 3-H), 5.31 (s, 2H, CH_2). Anal. calcd. for $C_{19}H_{12}N_3Br$: C, 63.00; H, 3.34; N, 11.60. Found: C, 62.75; H, 3.34; N, 11.34.

Methyl 1-(3-Phthalazin-1-ylprop-2-yn-1-yl)-1H-indole-5-carboxylate (**3g**). Preparation from methyl 1-prop-2-yn-1-yl-1*H*-indole-5-carboxylate (**1c**) and 1-iodophthalazine (**2a**); modified work-up procedure: after completion of the reaction, the solid material (**3g** + triethylammonium iodide) was filtered off and washed with diethyl ether. It was then dissolved in CH_2Cl_2 and this solution was washed with 0.5 N HCl, then with water. The extract was dried over Na_2SO_4 and evaporated under reduced pressure to give the product (0.133 g, 15%) as brownish crystals, mp 97 °C (decomposition). IR (KBr): 2948, 2241, 1710, 1610, 1434, 1310, 1196, 1097, 754, 595 cm^{-1}; MS (EI, 70 eV) *m/z*: 341 (M^+, 23%), 282 (10), 175 (50), 165 (10), 144 (100), 141 (36), 116 (73), 89 (39), 72 (29), 58 (66), 44 (81); ^{1}H-NMR ($CDCl_3$) δ: 9.49 (s, 1H, phthalazine 4-H), 8.45 (d, $J_{4–6}$ = 0.9 Hz, 1H, indole 4-H), 8.10–7.85 (m, 5H, indole 6-H, phthalazine 5-H, 6-H, 7-H, 8-H), 7.58 (d, $J_{6–7}$ = 8.7 Hz, 1H, indole 7-H, shows positive NOE on irradiation at 5.35 ppm), 7.41 (d, $J_{2–3}$ = 3.4 Hz, 1H, indole 2-H, shows positive NOE on irradiation at 5.35 ppm), 6.71 (d, $J_{2–3}$ = 3.4 Hz, 1H, indole 3-H), 5.35 (s, 2H, CH_2), 3.95 (s, 3H, OCH_3). HRMS (EI, 70 eV) *m/z* calcd. for $C_{21}H_{15}N_3O_2$ (M^+): 341.1164. Found: 341.1167.

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