Transformations of Methyl 2-[(*E*)-2-(Dimethylamino)-1-(methoxycarbonyl)ethenyl]-1-methyl-1*H*-indole-3-carboxylate

by **David Bevk**, **Uroš Grošelj**, **Anton Meden, Jurij Svete***, and **Branko Stanovnik***

Faculty of Chemistry and Chemical Technology, University of Ljubljana, P. O. Box 537, SI-1001 Ljubljana, Slovenia
(phone: +386 1 2419 100; fax: +386 1 2419 220; branko.stanovnik@fkkt.uni-lj.si and jurij.svete@fkkt.uni-lj.si)

A simple and efficient synthesis of novel 2-heteroaryl-substituted 1*H*-indole-2-carboxylates and γ-carbolines, compounds **1**–**3**, from methyl 2-(2-methoxy-2-oxoethyl)-1-methyl-1*H*-indole-3-carboxylate (**4**) by the enaminone methodology is presented.

Introduction. – Inhibition of the kinase insert domain receptor (KDR) may be useful for the prevention and treatment of tumor-induced angiogenesis. A number of potent and selective KDR inhibitors such as compounds **I**–**IV** (*Fig. 1*) have been identified. Compounds **Ia**–**Ic**, *e.g.*, are potential drug candidates in a range of cancer indications [1–3], and an efficient synthesis of their key pharmacophore, *i.e.*, 1*H*-indol-2-yl-substituted 1*H*-quinolin-2-ones, has been described recently, starting from *para*-substituted nitrobenzene and 2-substituted 3-formylquinolines [4]. The novel flavono-indole alkaloid lotthanongine (**II**) has been isolated from the roots of *Trigonostemon reidioides* (Euphorbiaceae) [5], and four β-indoloquinoline alkaloids, bouchardatine (**III**), rutaecarpine (**IVa**), 1-hydroxyrutaecarpine (**IVb**), and 1,2-dihydrorutaecarpine (**IVc**), have been isolated from the aerial parts of *Bouchardatia neurococca* [6].

Conventional approaches to 2-arylindoles typically rely upon cross-coupling of indol-2-yl halides, boronic acids, or stannates and silanes [7]. Although effective methods are available for the preparation of 1*H*-indol-2-ylboronic acid and silanes [8], the major limitation with most of these approaches are the additional steps needed for the preparation of coupling partners to enter Pd-catalyzed reactions. While a number of other classical methods (*e.g.*, those of *Fischer*, *Madelung*, *Bischler*, *Reissert*, *Nenitzescu*, or *Leimgruber–Batcho* [9]) have been successfully employed for the synthesis of 2-substituted indoles, each has its limitation due to either construction of the starting materials or harsh reaction conditions, which may interfere with other sensitive functional groups often located in the target molecule. Therefore, mild synthetic methods providing rapid assembly of the indole ring and tolerating a wide range of functional groups continue to offer significant advantages.

A number of fluorescent 3-aryl-1-methylquinolinones, including 3-(1*H*-indol-2-yl)-1-methylquinolin-2(1*H*)-one, have been synthesized by regiospecific photocoupling of 3-halo-1-methylquinolinones with aromatic and hetero-aromatic compounds [10]. And a number of fluorescent 3-arylcoumarins, including 3-(1-methyl-1*H*-indol-2-yl)-2*H*-1-

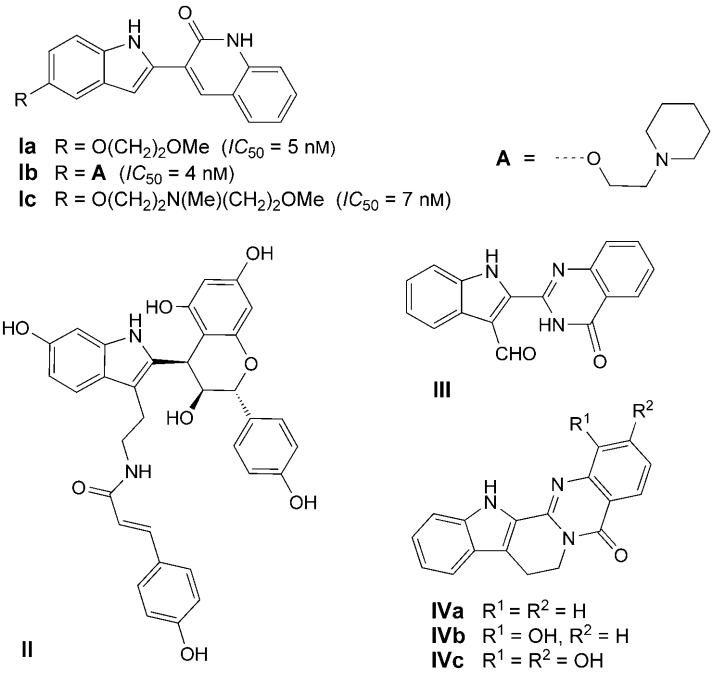


Fig. 1. *Known inhibitors of the kinase insert domain receptor* (KDR)

benzopyran-2-one, have been prepared by photo-coupling of 3-bromocoumarin with aromatic and heteroaromatic compounds [11].

Recently a series of 2-substituted alkyl 3-(dimethylamino)prop-2-enoates (and related enaminones) have been prepared as versatile reagents for the preparation of various dehydro-alanine derivatives, heterocyclic systems, and natural-product analogues. In extension, chiral cyclic enamino lactams and lactones, derived from an α-amino acid and (+)-camphor, have been used in the synthesis of functionalized heterocycles such as hetero-arylalanines, hetero-arylalaninols, hetero-arylpropanediols, 3-heteroaryl-substitued (+)-camphor derivatives, and heterocyclic compounds with and α-amino acid or a dipeptide structural element incorporated into the ring system [12][13].

In the present paper, we describe an extension of our research on 2-substituted alkyl 3-(dimethylamino)prop-2-enoates and related enaminones. These versatile reagents have been used for the preparation of various heterocyclic systems [12] and natural products and their analogues such as 3-substituted indoles, dipodazines [14], aplysinopsins [15], and meridianins [16], or employed in combinatorial syntheses of heterocycles and *N*-acyldehydroalanine esters [17]. Here, we present an efficient synthesis of the 2-heteroaryl-substituted novel indoles **1**–**3** (*Scheme*)[1]).

[1]) For systematic names, see the *Exper. Part*.

Results and Discussion. – 1. *Synthesis.* As shown in the *Scheme below*, methyl 2-(2-methoxy-2-oxoethyl)-1-methyl-1*H*-indole-3-carboxylate (**4**) [18] was transformed with dimethylformamide dimethylacetal (DMF-DMA) in MeOH into the enamino-substituted compound **5** in 88% yield. The latter turned out to be a versatile intermediate for a series of transformations: when **5** was heated with 2-aminopyridine in AcOH, cyclization to the 4*H*-pyrido[1,2-*a*]pyrimidine derivative **1** occurred (27% yield). Similarly, when **5** was heated in the presence of 1,3-dimethylbarbituric acid (=1,3-dimethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione), the heterocyclic system **2** was obtained. Finally, **5** could be further transformed in H_2O into the corresponding enol **6a**. Analogously, in the presence of alcohols (ROH) and AcCl, the enol ethers **6b**–**d** were isolated in moderate yields. With aromatic amines in MeOH/HCl, compound **5** afforded the enamines **7a**–**e** in 61–98% yield, and the latter (**7a**,**b**) could be cyclized in MeOH/MeONa at room temperature to afford the target compounds **3a**,**b**.

2. *Structure Determination*. The structures of all compounds were determined by spectroscopic methods and by elemental analyses. The geometry of the exocyclic C=C bond in compounds **5** and **7c** was established by NMR analysis on the basis of the ^3J(C,H) coupling constants between the olefinic H-atom and the ester C=O group, as determined from the antiphase splitting of cross-peaks in the HMBC spectrum. Generally, the ^3J(C,H) value for nuclei on the same side of the C=C bond was smaller (2–6 Hz) than those for nuclei on opposite sides (8–12 Hz) [12].

In compound **5**, a ^3J(C,H) value of 5 Hz indicated an (*E*)-configured C=C bond (*Fig. 2*). Similarly, for compound **7c**, the magnitude of the coupling constant of the major isomer (5 Hz) indicated (*E*)-configuration, whereas the minor isomer (11 Hz) had the (*Z*)-configuration. Also, in the case of the enol ether **6b** (^3J(C,H) = 3.2 Hz), the proposed (*E*)-configuration was unequivocally confirmed by X-ray-diffraction analysis (*Fig. 3*).

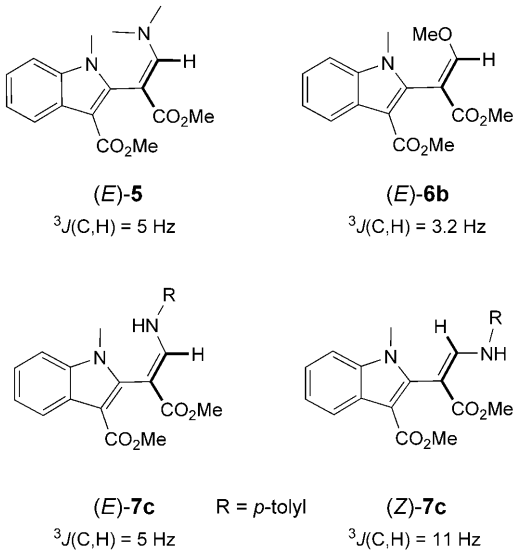
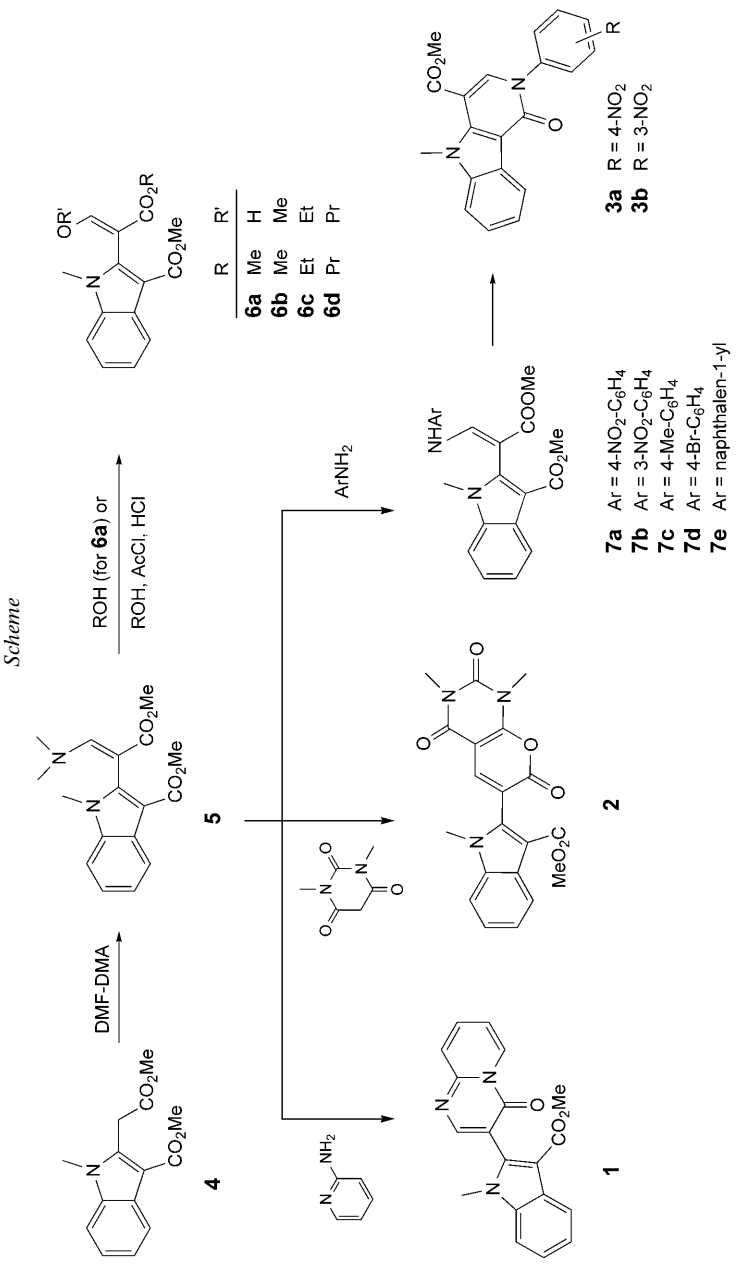


Fig. 2. ^{3}J*(C,H) Values for the discrimination of* (E)*- and* (Z)*-isomers of compounds* **5**–**7**

Scheme


DMF-DMA
ROH (for 6a) or
ROH, AcCl, HCl
ArNH2
4
5
1
2
6a R = Me, R' = H
6b R = Me, R' = Me
6c R = Et, R' = Et
6d R = Pr, R' = Pr
7a Ar = 4-NO2-C6H4
7b Ar = 3-NO2-C6H4
7c Ar = 4-Me-C6H4
7d Ar = 4-Br-C6H4
7e Ar = naphthalen-1-yl
3a R = 4-NO2
3b R = 3-NO2

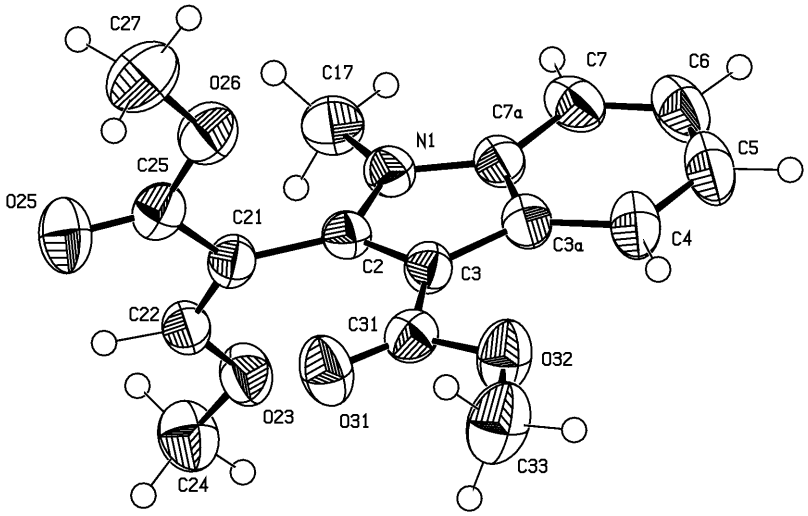


Fig. 3. *X-Ray crystal structure of* **6b** (ORTEP-III plot)

Experimental Part

General. All chemicals and reagents were purchased from *Fluka* or *Aldrich*. Compound **4** was prepared according to a literature procedure [18]. Melting points (m.p.) were determined on a *Kofler* hot-stage micro-melting-point apparatus. IR Spectra were recorded on a *Perkin-Elmer-BX* FT-IR spectrophotometer; in cm^{-1}. ^{1}H- and ^{13}C-NMR Spectra were obtained on a *Bruker Avance DPX-300* apparatus at 300 (^{1}H) and 75.5 (^{13}C) MHz in $CDCl_3$ or (D_6)DMSO soln.; δ in ppm rel. to Me_4Si, *J* in Hz. Elemental analyses were performed on a *Perkin-Elmer CHN Analyser 2400 II*.

*Methyl 2-[(*E*)-2-(Dimethylamino)-1-(methoxycarbonyl)ethenyl]-1-methyl-1*H*-indole-3-carboxylate* (**5**). A soln. of **4** (2.61 g, 10 mmol) and DMF-DMA (2 ml) in MeOH (30 ml) was heated at reflux for 24 h. The solvent was evaporated *in vacuo*, and the residue was crystallized from MeOH/H_2O: 3.86 g (88%). Colorless needles. M.p. 165–167° (MeOH/H_2O). IR (KBr): 2940, 1700, 1600, 1430, 1390, 1280, 1210, 1090, 750. ^{1}H-NMR ($CDCl_3$): 2.73 (br. *s*, Me_2N); 3.62 (*s*, 3 H); 3.64 (*s*, 3 H); 3.88 (*s*, 3 H); 7.27–7.86 (*m*, 3 H of indole); 8.17 (*s*, HC=); 8.17–8.18 (*m*, 1 H of indole). ^{13}C-NMR ($CDCl_3$): 30.1; 31.3; 50.5; 51.1; 86.4; 107.0; 109.5; 121.6; 121.7; 122.3; 126.5; 136.3; 141.9; 152.4; 165.5; 169.1. Anal. calc. for $C_{17}H_{20}NO_4$: C 64.54, H 6.37, N 8.86; found: C 64.74, H 6.53, N 8.76.

*Methyl 1-Methyl-2-(4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)-1*H*-indole-3-carboxylate* (**1**). Compound **5** (158 mg, 0.5 mmol), 2-aminopyridine (47 mg, 0.5 mmol), and AcOH (2 ml) were heated at reflux for 8 h. After cooling, the precipitated product was filtered off and recrystallized from toluene: 45 mg (27%). Yellow crystals. M.p. > 350° (toluene). IR (KBr): 3430, 3050, 1690, 1670, 1520, 1490, 1330, 1190, 1100, 790, 730. ^{1}H-NMR ($CDCl_3$): 3.71 (*s*, MeN); 3.81 (*s*, MeO); 7.28–7.43 (*m*, 5 H); 7.80–7.90 (*m*, 2 H); 8.53 (*s*, 1 H); 9.21–9.24 (*m*, 1 H). Anal. calc. for $C_{19}H_{15}N_3O_3$: C 68.46, H 4.54, N 12.61; found: C 68.68, H 4.38, N 12.66.

*Methyl 2-(2,3,4,7-Tetrahydro-1,3-dimethyl-2,4,7-trioxo-2*H*-pyrano[2,3-*d*]pyrimidin-6-yl)-1-methyl-1*H*-indole-3-carboxylate* (**2**). A mixture of **5** (158 mg, 0.5 mmol), 1,3-dimethylbarbituric acid (78 mg, 0.5 mmol), and AcOH (2 ml) was heated at reflux for 9 h. After cooling, the precipitated product was filtered off and recrystallized from toluene/DMF: 100 mg (51%). Yellow crystals. M.p. 259–260° (toluene/DMF). IR (KBr): 3470, 2960, 1770, 1710, 1670, 1580, 1530, 1440, 1290, 1190, 1110, 910, 770, 750, 480. ^{1}H-NMR ($CDCl_3$): 3.44 (*s*, MeN); 3.64 (*s*, MeN); 3.70 (*s*, MeN); 3.87 (*s*, MeO); 7.26–7.41 (*m*, 4 H of indole); 8.14 (*s*, 1 H); 8.15–8.17 (*m*, 1 H of indole). Anal. calc. for $C_{20}H_{17}N_3O_6$: C 60.76, H 4.33, N 10.63; found: C 60.68, H 4.29, N 10.50.

*Methyl 2-[(*E*)-2-Hydroxy-1-(methoxycarbonyl)ethenyl]-1-methyl-1*H*-indole-3-carboxylate* (**6a**). A soln. of **5** (158 mg, 0.5 mmol) and conc. HCl (20 drops) in MeOH (2 ml) was left standing at r.t. for 12 h. The precipitate was filtered off and recrystallized from MeOH/H_2O: 100 mg (46%). Colorless crystals. M.p. 127–131° (MeOH/H_2O). IR (KBr): 3200, 2950, 1690, 1440, 1400, 1190, 740. ^{1}H-NMR ($CDCl_3$): 3.64 (*s*, Me); 3.74 (*s*, Me); 3.87 (*s*, Me); 7.25–7.38 (*m*, 3 H of indole, =CH); 8.17–8.20 (*m*, 1 H of indole); 12.34 (*d*, *J* = 12.8, OH). Anal. calc. for $C_{15}H_{15}NO_5$: C 62.28, H 5.23, N 4.84; found: C 62.32, H 5.35, N 4.67.

*Methyl 2-[(*E*)-2-Methoxy-1-(methoxycarbonyl)ethenyl]-1-methyl-1*H*-indole-3-carboxylate* (**6b**). MeOH (2 ml) was cooled to −30°, and AcCl (0.5 ml) was added dropwise during mixing on an ice bath. Then, **5** (158 mg, 0.5 mmol) was added, and the mixture was heated at reflux for 3 h: 118 mg (78%). Colorless crystals. M.p. 164–168° (MeOH). IR (KBr): 2950, 1720, 1690, 1640, 1400, 1250, 1210, 1120, 1100, 760, 750, 550. ^{1}H-NMR ($CDCl_3$): 3.63 (*s*, Me); 3.70 (*s*, Me); 3.86 (*s*, Me); 3.82 (*s*, Me); 7.24–7.30 (*m*, 2 H of indole); 7.34–7.37 (*m*, 1 H of indole); 7.74 (*s*, HC=); 8.16–8.19 (*m*, 1 H of indole). ^{13}C-NMR ($CDCl_3$): 30.4; 50.7; 51.8; 62.3; 103.1; 105.7; 109.7; 121.7; 121.8; 122.5; 126.5; 136.9; 138.3; 162.0; 165.3; 166.9. Anal. calc. for $C_{16}H_{17}NO_5$: C 63.36, H 5.65, N 4.62; found: C 65.59, H 5.73, N 4.76.

*Methyl 2-[(*E*)-2-Ethoxy-1-(ethoxycarbonyl)ethenyl]-1-methyl-1*H*-indole-3-carboxylate* (**6c**). EtOH (2 ml) was cooled to −30°, and AcCl (0.5 ml) was added dropwise during mixing on an ice bath. Then, compound **5** (158 mg, 0.5 mmol) was added, and the mixture was heated at reflux for 3 h: 106 mg (67%). Yellow oil. ^{1}H-NMR ($CDCl_3$): 1.19 (*t*, *J* = 7.12, *Me*CH_2O); 1.25 (*t*, *J* = 7.08, *Me*CH_2O); 3.61 (*s*, MeN); 3.84 (*s*, MeO); 4.08 (*q*, *J* = 7.05, MeC*H*$_2$O); 4.14–4.24 (*m*, MeC*H*$_2$O); 7.24–7.36 (*m*, 3 H of indole); 7.79 (*s*, HC=); 8.17–8.20 (*m*, 1 H of indole). ^{13}C-NMR ($CDCl_3$): 14.2; 15.3; 30.4; 50.6; 60.4; 71.3; 102.9; 105.5; 109.6; 121.6; 121.7; 122.3; 126.6; 136.8; 138.7; 160.7; 165.3; 166.5. HR-CI-MS: 331.1425 (M^+, $C_{18}H_{21}NO_5^+$; calc. 331.1420).

*Methyl 1-Methyl-2-[(*E*)-2-propoxy-1-(propoxycarbonyl)ethenyl}-1*H*-indole-3-carboxylate* (**6d**). PrOH (2 ml) was cooled to −30°, and AcCl (0.5 ml) was added dropwise during mixing on an ice bath. Then, compound **5** (158 mg, 0.5 mmol) was added, and the mixture was heated at reflux for 3 h: 92 mg (56%). Yellow oil. ^{1}H-NMR ($CDCl_3$): 0.76–0.92 (*m*, 2 *Me*$(CH_2)_2O$); 1.51–1.65 (*m*, 2 MeC*H*$_2$CH$_2$O); 3.61 (*s*, MeN); 3.83 (*s*, MeO); 3.98 (*dd*, *J* = 6.7, 2.6, MeCH$_2$C*H*$_2$O); 4.01–4.14 (*m*, MeCH$_2$C*H*$_2$O); 7.24–7.36 (*m*, 3 H of indole); 7.29 (*s*, HC=); 8.16–8.21 (*m*, 1 H of indole). ^{13}C-NMR ($CDCl_3$): 9.8; 10.2; 21.9; 23.0; 30.3; 50.5; 66.0; 77.2; 102.7; 105.4; 109.6; 121.5; 121.7; 122.2; 126.6; 136.8; 138.7; 161.0; 165.2; 166.6. HR-CI-MS: 359.1740 (M^+, $C_{20}H_{25}NO_5^+$; calc. 359.1733).

*Methyl 1-Methyl-2-{(*Z*)-1-(methoxycarbonyl)-2-[(4-nitrophenyl)amino]ethenyl}-1*H*-indole-3-carboxylate* (**7a**). A soln. of **5** (158 mg, 0.5 mmol), 4-nitroaniline (69 mg, 0.5 mmol), and conc. HCl (25 drops) in MeOH (2 ml) was left standing at r.t. for 12 h. Then, H_2O (2 ml) was added, and the precipitate was filtered off and recrystallized from MeOH/H_2O: 192 mg (94%). Colorless crystals. M.p. 180–184° (MeOH/H_2O). IR (KBr): 3430, 1690, 1630, 1590, 1520, 1340, 1240, 1100, 840, 750. ^{1}H-NMR ($CDCl_3$): 3.66 (*s*, Me); 3.74 (*s*, Me); 3.87 (*s*, Me); 7.08–7.13 (*m*, 2 arom. H); 7.29–7.38 (*m*, 3 arom. H); 7.59 (*d*, *J* = 12.5, HC=); 8.16–8.19 (*m*, 1 arom. H); 8.20–8.24 (*m*, 2 arom. H); 10.90 (*d*, *J* = 12.5, NH). Anal. calc. for $C_{21}H_{19}N_3O_6$: C 61.61, H 4.68, N 10.26; found: C 61.75, H 4.81, N 10.17.

*Methyl 1-Methyl-2-{(*Z*)-1-(methoxycarbonyl)-2-[(3-nitrophenyl)amino]ethenyl}-1*H*-indole-3-carboxylate* (**7b**). A soln. of **5** (158 mg, 0.5 mmol), 3-nitroaniline (69 mg, 0.5 mmol), and conc. HCl (25 drops) in MeOH (2 ml) was left standing at r.t. for 12 h. Then, H_2O (2 ml) was added, and the precipitate was filtered off and recrystallized from MeOH/H_2O: 200 mg (98%). Colorless crystals. M.p. 155–160° (MeOH/H_2O). IR (KBr): 3430, 1700, 1670, 1530, 1350, 1220, 1100, 790, 730. ^{1}H-NMR ($CDCl_3$): 3.67 (*s*, Me); 3.73 (*s*, Me); 3.88 (*s*, Me); 7.28–7.39 (*m*, 5 arom. H); 7.47–7.52 (*m*, 1 arom. H); 7.59 (*d*, *J* = 12.7, HC=); 7.88–7.92 (*m*, 2 arom. H); 8.16–8.19 (*m*, 1 arom. H); 10.79 (*d*, *J* = 12.7, NH). Anal. calc. for $C_{21}H_{19}N_3O_6$: C 61.61, H 4.68, N 10.26; found: C 61.54, H 4.75, N 10.12.

*(*E*)- and (*Z*)-Isomers of Methyl 1-Methyl-2-[1-(methoxycarbonyl)-2-[(4-methylphenyl)amino]-ethenyl}-1*H*-indole-3-carboxylate* (**7c**). A soln. of **5** (158 mg, 0.5 mmol), 4-methylaniline hydrochloride (72 mg, 0.5 mmol), and conc. HCl (20 drops) in MeOH (2 ml) was left standing at r.t. for 12 h. Then, H_2O (2 ml) was added, and the precipitate was filtered off and recrystallized from MeOH/H_2O. Yield: 115 mg (61%); (*Z*/*E*) 57:43. Colorless crystals. M.p. 116–168° (MeOH/H_2O). IR (KBr): 3200, 1690, 1440, 1400, 1190, 1140, 1100, 760, 740. ^{1}H-NMR ($CDCl_3$; (*Z*)-isomer): 2.31 (*s*, Me); 3.64 (*s*, Me); 3.70 (*s*, Me); 3.85 (*m*, 3 arom. H); 6.95–6.98 (*m*, 2 arom. H); 7.12–7.14 (*m*, 2 arom. H); 7.27–7.43 (*m*, 3

arom. H); 7.53 (*d*, *J* = 13.2, HC=); 8.17–8.20 (*m*, 1 arom. H); 10.56 (*d*, *J* = 13.2, NH). ^{1}H-NMR ($CDCl_3$; (*E*)-isomer): 2.29 (*s*, Me); 3.64 (*s*, Me); 3.72 (*s*, Me); 3.84 (*s*, Me); 6.39 (*d*, *J* = 14.1, NH); 6.83–6.86 (*m*, 2 arom. H); 7.08–7.10 (*m*, 2 arom. H); 7.27–7.43 (*m*, 3 arom. H); 8.24–8.27 (*m*, 1 arom. H); 8.36 (*d*, *J* = 14.1, HC=). Anal. calc. for $C_{22}H_{22}N_2O_4$: C 69.83, H 5.86, N 7.40; found: C 70.08, H 6.14, N 7.34.

*(*E*)- and (*Z*)-Isomers of Methyl 2-[2-[(4-Bromophenyl)amino]-1-(methoxycarbonyl)ethenyl]-1-methyl-1*H*-indole-3-carboxylate* (**7d**). A soln. of **5** (158 mg, 0.5 mmol), 4-bromoaniline (86 mg, 0.5 mmol), and conc. HCl (20 drops) in MeOH (2 ml) was left standing at r.t. for 12 h. Then, H_2O (2 ml) was added, and the precipitate was filtered off and recrystallized from MeOH/H_2O. Yield: 209 mg (94%); (*Z*/*E*) 38 : 62. Colorless crystals. M.p. 189–197° (MeOH/H_2O). IR (KBr): 3280, 1690, 1620, 1440, 1220, 1100, 820, 790, 750. ^{1}H-NMR ($CDCl_3$; (*Z*)-isomer): 3.63 (*s*, Me); 3.72 (*s*, Me); 3.84 (*s*, Me); 6.44 (*d*, *J* = 13.8, NH); 6.80–6.85 (*m*, 2 arom. H); 7.26–7.35 (*m*, 3 arom. H); 7.37–7.41 (*m*, 2 arom. H); 8.22–8.26 (*m*, 1 arom. H); 8.31 (*d*, *J* = 13.8, HC=). ^{1}H-NMR ($CDCl_3$; (*E*)-isomer): 3.64 (*s*, Me); 3.70 (*s*, Me); 3.86 (*s*, Me); 6.92–6.97 (*m*, 2 arom. H); 7.26–7.35 (*m*, 3 arom. H); 7.42–7.45 (*m*, 2 arom. H); 7.51 (*d*, *J* = 13.0, HC=); 8.16–8.19 (*m*, 1 arom. H); 10.59 (*d*, *J* = 13.0, NH). Anal. calc. for $C_{21}H_{19}N_2O_4Br$: C 56.90, H 4.32, N 6.32; found: C 57.08, H 4.52, N 6.33.

*Methyl 1-Methyl-2-[(*Z*)-1-(methoxycarbonyl)-2-(naphthalen-1-ylamino)ethenyl]-1*H*-indole-3-carboxylate* (**7e**). A soln. of **5** (158 mg, 0.5 mmol), naphthalene-1-amine (72 mg, 0.5 mmol), and conc. HCl (20 drops) in MeOH (2 ml) was left standing at r.t. for 12 h. The precipitate was collected by filtration and recrystallized from toluene/heptane: 145 mg (70%). Colorless crystals. M.p. 168–170° (toluene/heptane). IR (KBr): 3460, 1700, 1680, 1620, 1440, 1200, 1100, 790. ^{1}H-NMR ($CDCl_3$): 3.69 (*s*, Me); 3.77 (*s*, Me); 3.87 (*s*, Me); 7.25–7.46 (*m*, 5 arom. H); 7.53–7.62 (*m*, 3 arom. H); 7.77 (*d*, *J* = 12.6, HC=); 7.86–7.89 (*m*, 1 arom. H); 8.16–8.22 (*m*, 2 arom. H); 11.42 (*d*, *J* = 12.6, NH). Anal. calc. for $C_{25}H_{22}N_2O_4$: C 72.45, H 5.35, N 6.76; found: C 72.61, H 5.50, N 6.54.

*Methyl 2,5-Dihydro-5-methyl-2-(4-nitrophenyl)-1-oxo-1*H*-pyrido[4,3-*b*]indole-4-carboxylate* (**3a**). Na (40 mg) was dissolved in MeOH (2 ml), and the resulting soln. was added dropwise to a suspension of **7a** (100 mg, 0.24 mmol) in MeOH (2 ml). The mixture was kept 4 h at r.t., and the precipitate was collected by filtration and recrystallized from MeOH/DMF: 46 mg (50%). Yellow crystals. M.p. 237–238° (MeOH/DMF). IR (KBr): 1710, 1670, 1520, 1350, 1250, 1080, 750. ^{1}H-NMR ((D_6)DMSO): 3.89 (*s*, Me); 3.99 (*s*, MeO); 7.32–7.38 (*m*, 1 arom. H); 7.45–7.51 (*m*, 1 arom. H); 7.73–7.76 (*m*, 1 arom. H); 7.87–7.92 (*m*, 2 arom. H); 8.20–8.24 (*m*, 1 arom. H); 8.30 (*s*, H–C(3)); 8.38–8.43 (*m*, 2 arom. H). Anal. calc. for $C_{20}H_{15}N_3O_5$: C 63.66, H 4.01, N 11.14; found: C 63.53, H 4.18, N 11.04.

*Methyl 2,5-Dihydro-5-methyl-2-(3-nitrophenyl)-1-oxo-1*H*-pyrido[4,3-*b*]indole-4-carboxylate* (**3b**). A soln. of Na (40 mg) in MeOH (2 ml) was added dropwise to a suspension of **7b** (73 mg, 0.18 mmol) in MeOH (2 ml). The mixture was kept for 24 h at r.t. The precipitate was collected by filtration and recrystallized from MeOH/DMF: 67 mg (quant.). Colorless crystals. M.p. 280–282° (MeOH/DMF). IR (KBr): 1720, 1680, 1530, 1350, 1280, 1080, 750. ^{1}H-NMR ((D_6)DMSO): 3.89 (*s*, Me); 4.00 (*s*, MeO); 7.32–7.37 (*m*, 1 arom. H); 7.45–7.51 (*m*, 1 arom. H); 7.73–7.76 (*m*, 1 arom. H); 7.83–7.88 (*m*, 1 arom. H); 8.04–8.08 (*m*, 1 arom. H); 8.21–8.23 (*m*, 1 arom. H); 8.34 (*s*, H–C(3)); 8.35–8.38 (*m*, 1 arom. H); 8.48–8.49 (*m*, 1 arom. H). Anal. calc. for $C_{20}H_{15}N_3O_5$: C 63.66; H 4.01; N 11.14; found: C 63.78; H 4.08; N 11.10.

X-Ray Crystal Structure of **6b**[2]). Single-crystal X-ray-diffraction data of *methyl 2-[(*E*)-2-methoxy-1-(methoxycarbonyl)ethenyl]-1-methyl-1*H*-indole-3-carboxylate* (**6b**) were collected at r.t. on a *Nonius Kappa CCD* diffractometer using the Nonius Collect software [19]. DENZO and SCALEPACK [20] were used for indexing and scaling of the data, and the structure was solved by means of SIR97 [21]. Refinement was done with the Xtal3.4 [22] program package. The crystal structure was refined on *F* values using the full-matrix least-squares procedure. The non-H-atoms were refined anisotropically, and the positions of the H-atoms were geometrically calculated, their positional and isotropic atomic-displace-

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[2]) The crystallographic data for compound **6b** have been deposited with the *Cambridge Crystallographic Data Centre* as deposition number CCDC-608868. The data can be obtained, free of charge, at http://www.ccdc.cam.ac.uk/data_request/cif.

Table. *X-Ray Crystallographic and Refinement Data for* **6b**

Formula	$C_{16}H_{17}NO_5$
M_r	303.31
Crystal system	orthorhombic
Space group	$P\,2_12_12_1$
a, b, c [Å]	8.0709(2), 10.7386(3), 17.6925(5)
$\alpha=\beta=\gamma$ [°]	90.0000
V [Å^3]	1533.41(7)
Z	4
ρ [Mg m^{-3}]	1.314
μ [mm^{-1}]	0.098
Crystal dimension [mm]	$0.40\times0.30\times0.25$
Temperature [K]	293(1)
Wavelength [Å]	0.71073
θ_{max} [°]	27.48
Total reflections	17035
Independent reflections	2043
R_{int}	0.055
Observed reflections	1591
Reflection parameters	199
Threshold criterion	$I>2.0\sigma(I)$
Final R and R_w	0.048, 0.044
$(\Delta/\sigma)_{max}$	0.0005
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	−0.25, 0.24

ment parameters not being refined. Absorption corrections were not necessary. The *Regina* [23] weighting scheme was used. The resulting crystal data and details concerning data collection and refinement are collected in the *Table*. For an ORTEP-III [24] representation, see *Fig. 3*.

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