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Synthesis of New 2-Vinylation Products of Indole via a Michael-Type Addition Reaction with Dimethyl Acetylenedicarboxylate and Their Diels−Alder Reactivity as Precursors of New Carbazoles

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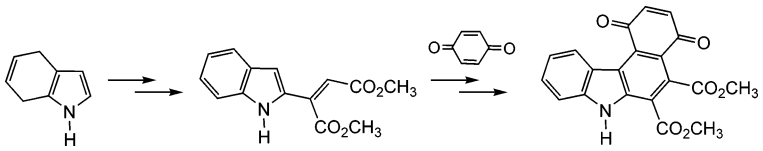
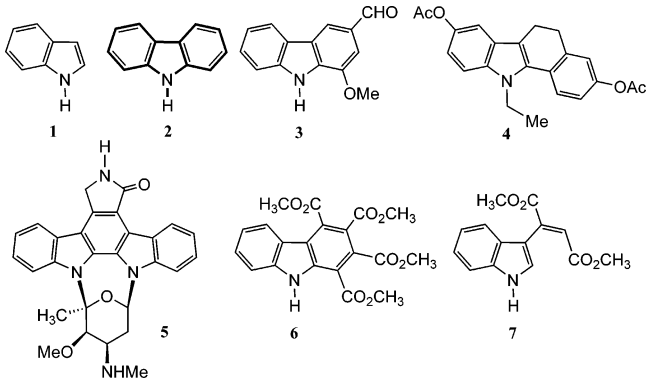


Reaction of 4,7-dihydroindole and dimethyl acetylenedicarboxylate provided a convenient route to functionalized 2-vinylindoles. Diels−Alder reactions of the 2-vinylindoles with naphthoquinone, *p*-benzoquinone, 1,2-dicyano-4,5-dichloroquinone, *N*-phenyltriazolinedione, and tetracyanoethylene were investigated to give [*c*]annelated 1,2-dihydro, 1,2,3,4-tetrahydro, and fully aromatized carbazoles. The structure and formation mechanism of both 2-vinylindoles and their cycloadduct are discussed.

Introduction

The indole (**1**) moiety is a fundamental structural unit of numerous alkaloids and biologically active compounds.[1] Because of their interesting biological activities, carbazole (**2**) alkaloids constitute an important class of natural compounds.[2] Ever since the first isolation of the simple carbazole alkaloid murrayanine (**3**), organic chemists have been interested in the synthesis of carbazole alkaloids.[2,3] Benzo-annulated carbazole ring systems possessing complex structures are found only rarely in natural products.[2] Simple benzo[*a*]carbazoles as **4** have been shown to bind to estrogen receptors and inhibit the growth of mammary tumors of rats.[4] Staurosporine (**5**), which is an indolocarbazole alkaloid, has very interesting biological activities such as antimicrobial, hypotensive, and cytotoxic properties, inhibition of protein kinase C, and platelet aggregation inhibition.[5]



2-Substituted indoles are potential intermediates for many alkaloids and pharmacologically important substances.[6] The Diels−Alder reactions of 2- or 3-vinylindoles represent an attractive methodology for the synthesis of many indole

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alkaloids and annulated carbazole derivatives.[7−9] Acheson et al. reported the reactions of indoles with dimethyl acetylenedicarboxylate (DMAD) in the presence and absence of solvents.[10] Although treatment of indole with DMAD alone gave a complex mixture from which the major component was tetramethyl carbazole-1,2,3,4-tetracarboxylate (**6**), the main product in methanol and in acetic acid was dimethyl indole-3-ylfumarate (**7**), which is the 3-vinylindole derivative. Also, Acheson et al. investigated the reaction of indole with DMAD carried out under high pressure.[11] Besides these reactions, the photocycloaddition of DMAD to the activated indoles was investigated by Neckers et al.[12]

The 3-position of indole is the preferred site for an electrophilic substitution reaction.[13a] Although the methods for the preparation of 3-substituted indoles are well established, there is a need for easier access to 2-substituted indoles. Joule et al. improved an indirect method for the synthesis of the 2-acylindoles via the acylation reaction of the *N*-bromomagnesio derivatives of 4,7-dihydroindole (**8**) or 4,5,6,7-tetrahydroindole (**9**), which in a two-step synthesis reacted like simple dialkylpyrrole derivatives followed by dehydrogenation.[13b] Michael-type addition reactions provide a very reliable method and have been exploited for the formation of the carbon−carbon bond.[14] In addition, this type of reaction has been investigated for the functionalization of indoles. Recently, we reported on Michael addition reactions between 4,7-dihydroindole (**8**) and some α,β-unsaturated compounds, which provides a new pathway to 2-substituted indoles.[15] Recently, Evans et al. extended our methodology to the asymmetric synthesis of 2-substituted indoles.[16] In continuation of our interest in the chemistry of indole, we decided to obtain its 2-Michael addition products with DMAD of the indole (**1**). There is no report on the conjugate addition of 3-unsubstituted indole with electron-deficient olefins to give 2-alkylated derivatives. Compared with the corresponding 3-substituted compounds, 2-vinylindoles are not easily accessible. We wish to report the synthesis and cycloadditions with dienophiles of new 2-vinylindole derivatives (**14** and **15**) by starting from indole (**1**).

Results and Discussion

To synthesize the 2-vinylindole derivatives **14** and **15**, our synthetic approach is based on the dipole change of indole toward electrophilic substitution. Therefore, we reduced the indole with Li−MeOH in liquid NH_3 to give 4,7-dihydroindole (**8**) and 4,5,6,7-tetrahydroindole (**9**).[15,17] We investigated the reaction of the pyrrole derivatives **8** and **9** with DMAD (**10**). The reaction of **8** gave addition products **12** and **13** (in 73% yield) in a 1:2.5 ratio by ^{1}H NMR, which was separated by silica gel column chromatography eluted with ethyl acetate−hexane. A possible mechanism is shown in Scheme 1. The nucleophilic attack of the pyrrole to the C−C triple bond of DMAD would result in the formation of a zwitterionic intermediate **11** which is followed by aromatization of the pyrrole ring to give the Michael adducts **12** and **13**. The structure assignments for isomers **12** and **13** are based on ^{1}H NMR, ^{13}C NMR, NOE ^{1}H NMR, IR, and elemental analysis. The olefin geometry and the placement of the substitution at pyrrole were established by differential ^{1}H NMR nuclear Overhauser enhancement (NOE) experiments. When the vinylic proton (δ 5.87) of *Z*-isomer **13** was irradiated, the NOE between the NH (δ 8.47) and C3−H (δ 6.28) signals was observed. This observation shows that the substituent connected to the pyrrole ring is at the 2-position and that there is an equilibrium between the conformers (**13a** and **13b**) resulting from free rotation about the single bond. For the next step, we attempted the aromatization of the cyclohexadiene ring in **12** and **13** to obtain the vinylindole derivatives **14** and **15**. To achieve this aim, the Michael adduct **12** and 1,2-dicyano-4,5-dichloroquinone (DDQ) were allowed to react in dry benzene for 1 h at room temperature. The oxidation product **14** was isolated in a high yield. The oxidation of **13** to **15** was realized with a similar procedure. We have observed that the geometric isomerization of alkenes in the Michael addition products can be catalyzed with heating of the pure *E*-isomer **14** (or *Z*-isomer **15**) and resulted in the formation of an equilibrium mixture consisting of **14** and **15** (58:42) (Scheme 1). Additionally, we investigated the reactivity of tetrahydroindole **9** toward DMAD (**10**) and isolated the two Michael products **16** and **17** in a ratio of 1:3.3 (total yield 72%) (Scheme 2). The geometry of the olefins and the placement of the substituent connecting the tetrahydroindole were especially determined by NOE studies.

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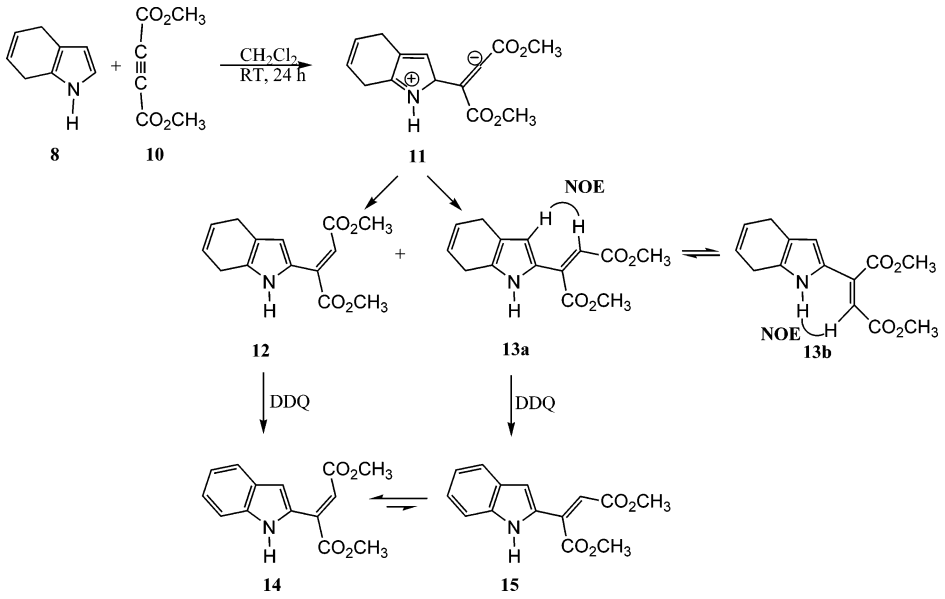
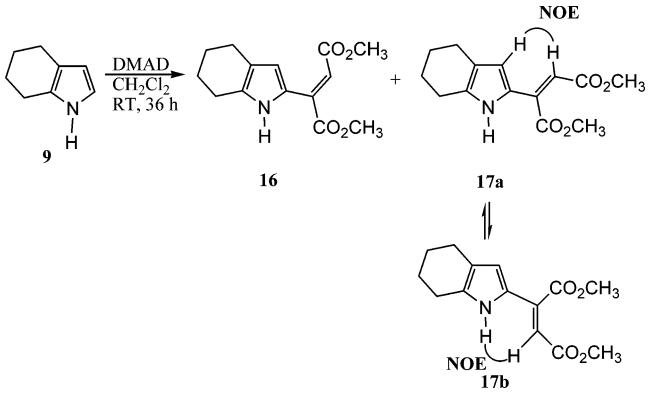
SCHEME 1



SCHEME 2



At the same time, we noticed that the Michael addition products (**12** and **13**) when heated rearrange to the indole derivative **19**. Heating of the isomer (**12** or **13**) in $CHCl_3$ resulted in the formation of the rearrangement product **19** in a quantitative yield. We assume that **19** is formed subsequently by two hydrogen shifts as shown in Scheme 3. The driving force for rearrangement is the formation of the more stable aromatic product. The fact that both **12** and **13** rearrange to **19** provides evidence that **12** and **13** are geometric isomers of each other. The rearrangement product **19** was characterized by the presence of NH signals at δ 8.61 ppm, aromatic protons at 7.35−7.06 ppm, C3−H of the pyrrole ring at 6.38 ppm, doublet of doublet (8.6, 5.8 Hz) of the allylic proton in succinic acid at 4.33 ppm, and two ester methoxy protons at 3.76 and 3.73 ppm. Furthermore, analysis of the AB system arising from CH_2 protons neighboring the asymmetric center in succinic acid shows that the low-field part (3.20 ppm) is split into doublet of doublet (17.1, 8.6 Hz). The B part of the system resonates the high field (3.01 ppm) as doublet of doublet (17.1, 5.8 Hz). Additionally, the NOE signal at 6.38 ppm shows that the dimethyl succinic acid group is attached to the 2-position of the indole ring.

The chemistry of vinylindoles is very important in that they are mostly able to take part in various cycloaddition processes such as a $HOMO_{diene}$-controlled Diels−Alder reaction, which efficiently lead to the construction of polycyclic systems. Heterocyclic quinones are a very important class of compounds from a biological perspective, particularly as antitumor agents.[18] The carbazolquinones also represent an important family of carbazole alkaloids.[2] Therefore, we turned our attention to the syntheses of carbazole quinone derivatives and studied the cycloaddition reactions of vinylindoles **14** (or **15**). First, vinylindole **14** was reacted with the naphthoquinone (**20**) to yield compound **22** as the sole product. The sole product **22** was a secondary product formed from the first addition product **21** by a 1,3-hydrogen shift. Careful examination of the ^1H and ^{13}C NMR spectra of the product showed exclusive formation of a cycloaddition-type product. Especially significant, from the coupling constants of $J_{AB} = 5.9$, $J_{CD} = 5.1$, and $J_{BC} = 7.7$ Hz of protons in the cyclohexene ring, was that an axial−equatorial (cis) relationship between these protons could be deduced. Thus, we consider that the first step of the sequence yielding **22** is a concerted $HOMO_{diene}$−$LUMO_{dienophile}$-controlled Diels−Alder process. And also, the energetically more favorable secondary orbital interaction between a diene and a dienophile controls the stereochemistry in the endo Diels−Alder transition state before the hydrogen shift to form **22**, as described by Pindur et al.[19] The oxidation of **22** with 2 equiv of 1,2-dicyano-4,5-dichloroquinone (DDQ) gave a carbazole derivative **23** in 94% yield (Scheme 4).

In a second approach to carbazole derivative containing quinones, we examined the Diels−Alder reactions of the vinylindole **14** with *p*-benzoquinone (**24**) (Scheme 4). The reaction of **14** with 1 equiv of *p*-benzoquinone (**24**) gave a complex reaction mixture, which contained unreacted starting material **14**, the addition product, and aromatized product **25**.

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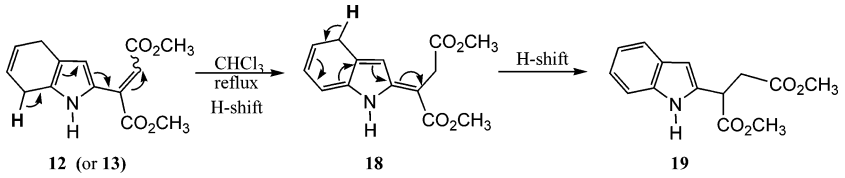
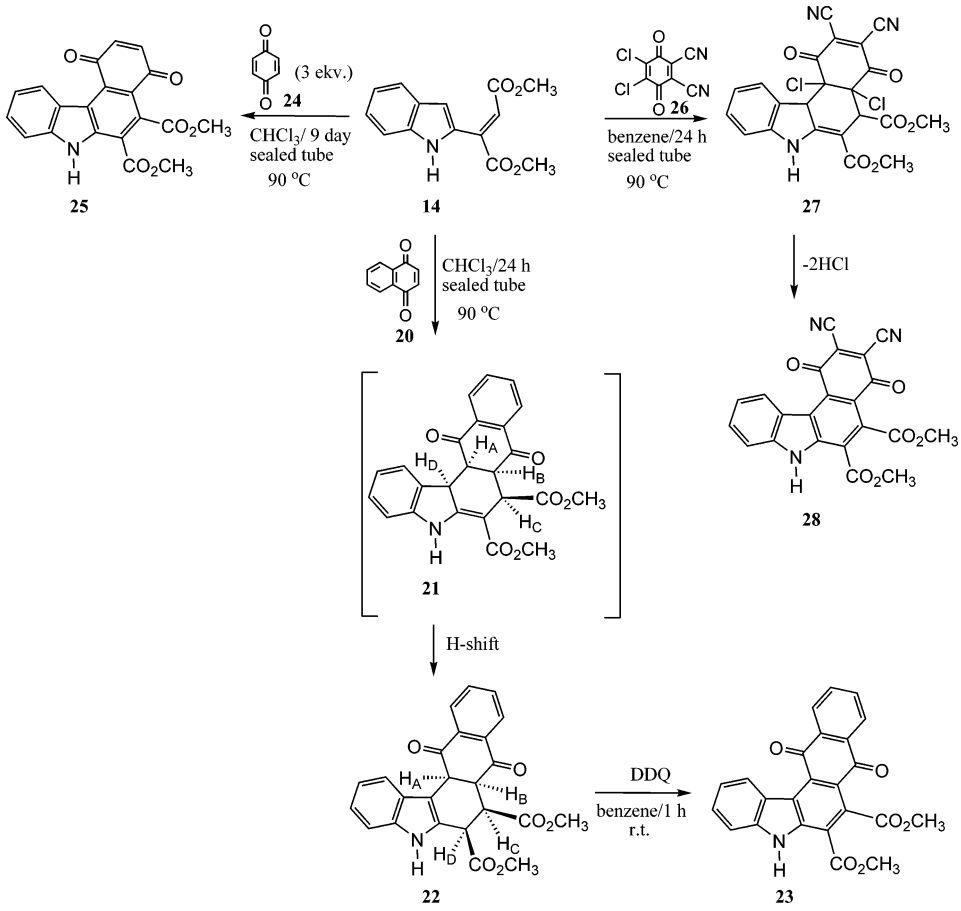
SCHEME 3



SCHEME 4

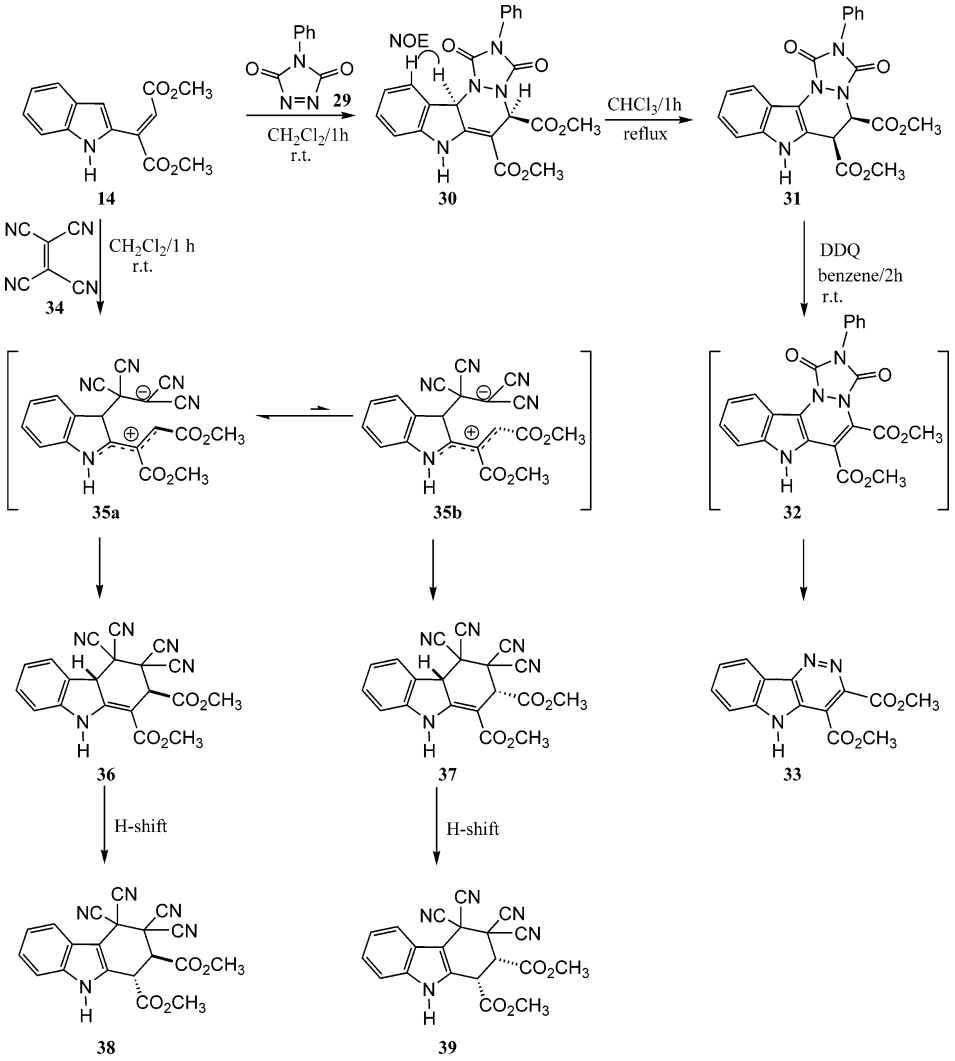


Use of excess *p*-benzoquinone (**24**) allowed us to isolate the aromatized product **25** from the cycloaddition product contained in the in situ oxidation of quinone (Scheme 4). The reaction of **14** in the presence of 1 equiv of DDQ (**26**) resulted in overoxidation of the adduct by the elimination of 2 mol of HCl to the [*c*]annulated carbazole **28** (Scheme 4).

Last, our experiments focused on the cycloaddition of **14** with *N*-phenyltriazolinedione (PTAD) (**29**), and tetracyanoethylene (**34**). The reaction of **14** with PTAD was carried out in dichloromethane at room temperature for 1 h to provide the cycloadduct **30** in quantitative yield. The relative configuration of the ring system for **30** was confirmed by ^{1}H NMR, ^{13}C NMR, NOE ^{1}H NMR, IR, and elemental analysis. Especially significant, the relative configuration at the diaza-cyclohexene ring was assigned on the basis of NOE observations. Irradiation of the methine proton at δ 5.94 ppm produced a strong NOE for one proton of the aromatic ring at 8.30 ppm. These results indicated that we had isolated the [4+2] cycloadduct **30** without a 1,3-H shift. Furthermore, we observed that when the cycloadduct **30** was refluxed in chloroform for 1 h it easily underwent rearrangement to form the isomerization product **31** where a 1,3-H shift has occurred due to the aromatic stabilization of the indole. The observed coupling constants (^3J = 1.1 Hz) between the vicinal protons in the tetrahydro-pyridazine ring of **31** are in agreement with the presence of the cis configuration due to the nearly 90° dihedral angle. Although the NOE of the proton at 5.88 ppm gives only a NOE with a proton at 4.72 ppm, the irradiation of the signal at 4.72 shows the NOE with both the indole N−H and the cis-vicinal C−H. To oxidize the tetrahydro-pyridazine **31** to dihydro-pyridazine **32**, the compound **31** was submitted to DDQ oxidation. However, the expected compound **32** was not observed. Instead, the full aromatized compound **33**, which has a pyridazino[4,3-*b*]indole framework, was formed as the sole product in 71% yield. We assumed that the reaction proceeds via an unusual pathway in which the intermediate **32** may undergo oxidation and hydrolysis to furnish **33** (Scheme 5).

Finally, the vinylindole **14** was treated with tetracyanoethylene (**34**) in dichloromethane at room temperature for 1 h which resulted in the formation of two isomeric products **39** ($J_{\text{cis-vicinal}}$ = 5.6 Hz for protons in the cyclohexene ring) and **38** ($J_{\text{trans-vicinal}}$ = 11.0 Hz) in a ratio of 2:8 according to ^{1}H NMR. In the reaction of **15** with tetracyanoethylene, because the hydrogen shift did not take place stereospecifically, we suggested that

SCHEME 5



the reaction involved an ionic mechanism instead of a nonconcerted mechanism as described in Scheme 5.

In conclusion, we have achieved the synthesis of new isomeric 2-vinylindole derivatives containing trisubstituted vinyl groups and demonstrated their utility in Diels−Alder reactions to produce [*c*]annelated carbazoles. Further applications of these very interesting reactions are being studied.

Experimental Section

General Methods. Solvents were concentrated at reduced pressure. Melting points were uncorrected. Infrared spectra were obtained from KBr pellets or film on a FT-IR spectrophotometer. ^{1}H NMR spectra were obtained in $CDCl_3$ at 200 and 400 MHz using TMS as the internal standard. Elemental analyses were carried out on an elemental analyses apparatus.

Reaction of 4,7-Dihydroindole (8) with Dimethyl Acetylenedicarboxylate (DMAD). A solution of 4,7-dihydroindole (**8**) (500 mg, 4.20 mmol) and DMAD **10** (605 mg, 4.20 mmol) in 10 mL of CH_2Cl_2 was stirred at room temperature for 24 h. After removal of the solvent, the residue was filtered on a short silica gel column (50 g). Eluting with ethyl acetate/hexane (5%) gave 300 mg (27%) of **12**, which was crystallized from CH_2Cl_2/hexane (dark yellow crystals, mp 88−89 °C). Further elution with ethyl acetate/hexane (40%) furnished the product **13** (480 mg, 44%): pale yellow crystals from CH_2Cl_2/hexane (mp 168−169 °C). For **12**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 12.54 (m, NH, 1H), 6.52 (d, J = 2.2 Hz, =CH, H_3, 1H), 5.94−5.80 (m, =CH, H_5, H_6, 2H), 5.82 (s, =CH, 1H), 3.89 (s, OCH_3, 3H), 3.79 (s, OCH_3, 3H), 3.77−3.19 (m, CH_2, H_4 and H_7, 4H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 171.3, 170.6, 140.9, 134.2, 127.5, 127.0, 124.3, 119.5, 118.7, 109.1, 54.8, 54.1, 26.4, 26.3; IR (CH_2Cl_2, cm^{-1}) 3232, 3031, 2962, 2885, 2831, 1735, 1681, 1565, 1519, 1481, 1434, 1365, 1311, 1283, 1203, 1149, 1064, 1025, 979. Anal. Calcd for $C_{14}H_{15}NO_4$: C, 64.36; H, 5.79; N, 5.36. Found: C, 64.42; H, 5.44; N, 5.39. For **13**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.47 (m, NH, 1H), 6.28 (bs, =CH, H_3, 1H), 5.87 (s, =CH, 1H), 5.91−5.77 (m, =CH, H_5, H_6, 2H), 3.95 (s, OCH_3, 3H), 3.72 (s, OCH_3, 3H), 3.28−3.13 (m, CH_2, H_4 and H_7, 4H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 170.3, 168.3, 142.1, 133.2, 127.5, 126.8, 124.0, 119.8, 114.6, 108.7, 54.8, 53.6, 26.4, 25.9; IR (CH_2Cl_2, cm^{-1}) 3355, 3031, 2954, 2885, 2831, 1673, 1604, 1573, 1473, 1434, 1349, 1295, 1241, 1203, 1172, 1141, 1049, 971, 848, 809. Anal. Calcd for $C_{14}H_{15}NO_4$: C, 64.36; H, 5.79; N, 5.36. Found: C, 64.03; H, 6.03; N, 5.45.

Synthesis of Dimethyl Indole-2-ylfumarate (14): Oxidation of 12 with DDQ. A solution of **12** (116 mg, 0.44 mmol) and DDQ (26 mg, 0.12 mmol) in 10 mL of dry benzene was stirred at room temperature for 1 h. After the benzene was evaporated, the residue was filtered on a short silica gel column (5 g) eluting with CH_2Cl_2 (50 mL). The crude product was recrystallized from CH_2Cl_2/hexane (108 mg, 94%, pale brown crystals, mp 74−75 °C): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (dd, J = 7.6, 1.0 Hz, 1H), 7.44 (dd, J = 7.6,

1.0 Hz, 1H), 7.28 (td, J = 7.0, 1.0 Hz, 1H), 7.10 (td, J = 7.6, 1.0 Hz, 1H), 67.02 (bd, J = 1.5 Hz, =CH, 1H), 6.28 (s, =CH, 1H), 3.95 (s, OCH_3, 3H), 3.86 (s, OCH_3, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.5, 168.1, 139.2, 137.8, 130.6, 127.6, 125.6, 122.2, 120.7, 115.9, 112.2, 111.5, 53.4, 52.9; IR (CH_2Cl_2, cm^{-1}) 3249, 2952, 1732, 1697, 1586, 1434, 1346, 1301, 1262, 1209, 1135, 1054, 1020. Anal. Calcd for $C_{14}H_{13}NO_4$: C, 64.86; H, 5.05; N, 5.40. Found: C, 64.58; H, 5.03; N, 5.55.

Synthesis of Dimethyl Indole-2-ylmaleate (15): Oxidation of 13 with DDQ. A solution of **13** (104 mg, 0.40 mmol) and DDQ (92 mg, 0.44 mmol) in 10 mL of dry benzene was stirred at room temperature for 1 h. After the benzene was evaporated, the residue was filtered on a short silica gel column (5 g) eluting with CH_2Cl_2 (70 mL). The crude product was recrystallized from CH_2Cl_2/hexane in a quantitative yield (dark yellow crystals, mp 126−127 °C): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (bs, NH, 1H), 7.59 (bd, J = 8.2 Hz, 1H), 7.35 (bd, J = 8.12 Hz, 1H), 7.26 (bd, J = 8.2 Hz, 1H), 7.11 (bd, J = 8.2 Hz, 1H), 6.79 (bd, J = 1.5 Hz, =CH, H_3, 1H), 6.29 (s, =CH, H_3, 1H), 3.99 (s, OCH_3, 3H), 3.74 (s, OCH_3, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.9, 165.7, 140.3, 138.1, 131.3, 125.3, 122.0, 121.2, 113.6, 112.2, 111.6, 107.8, 53.4, 52.3; IR (CH_2Cl_2, cm^{-1}) 3394, 3363, 2962, 1720, 1612, 1450, 1334, 1272, 1241, 1203, 1172, 1049, 1018, 971. Anal. Calcd for $C_{14}H_{13}NO_4$: C, 64.86; H, 5.05; N, 5.40. Found: C, 64.62; H, 5.14; N, 5.61.

Reaction of 4,5,6,7-Tetrahydroindole (9) with Dimethyl Acetylenedicarboxylate (DMAD). A solution of 4,5,6,7-tetrahydroindole (**9**) (300 mg, 2.47 mmol) and DMAD (355 mg, 2.47 mmol) in 10 mL of CH_2Cl_2 was stirred at room temperature for 36 h. After removal of the solvent, the residue was filtered on a short silica gel column (50 g), and eluting with ethyl acetate/hexane (5%) gave 180 mg (27.5%) of **16**, which was crystallized from CH_2Cl_2/hexane (dark brown crystals, mp 128−129 °C). Further elution with ethyl acetate/hexane (40%) furnished the product **17** (150 mg, 23%, pale brown crystals from CH_2Cl_2/hexane, mp 96−97 °C). For **16**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.45 (d, J = 2.1 Hz, =CH, H_3, 1H), 5.76 (s, =CH, 1H), 3.39 (s, OCH_3, 3H), 3.78 (s, OCH_3, 3H), 2.68 (t, J = 5.7 Hz, CH_2, 2H), 2.52 (t, J = 5.8 Hz, CH_2, 2H), 1.85−1.71 (m, CH_2, H_5 ve H_6, 4H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 171.3, 170.7, 140.8, 137.6, 126.4, 122.7, 108.2, 54.8, 54.0, 25.5, 25.5, 25.0, 24.7; IR (CH_2Cl_2, cm^{-1}) 3353, 2946, 2861, 1738, 1630, 1530, 1438, 1207, 1169, 1007. Anal. Calcd for $C_{14}H_{17}NO_4$: C, 63.87; H, 6.51; N, 5.32. Found: C, 63.70; H, 6.41; N, 5.59. For **17**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.52 (m, NH, 1H), 6.22 (d, J = 2.23 Hz, =CH, H_3, 1H), 5.84 (s, =CH, 1H), 3.93 (s, OCH_3, 3H), 3.72 (s, OCH_3, 3H), 2.57 (t, J = 5.7 Hz, CH_2, 2H), 2.45 (t, J = 5.6 Hz, CH_2, 2H), 1.85−1.51 (m, CH_2, H_5 ve H_6, 4H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 170.4, 168.5, 142.3, 136.6, 126.2, 122.9, 115.7, 107.5, 54.9, 53.7, 25.4, 25.0, 24.9, 24.6; IR (CH_2Cl_2, cm^{-1}) 3376, 2953, 2861, 1738, 1607, 1576, 1438, 1261, 1200, 1176, 1053. Anal. Calcd for $C_{14}H_{17}NO_4$: C, 63.87; H, 6.51; N, 5.32. Found: C, 64.01; H, 6.48; N, 5.61.

2-(1*H*-Indol-2-yl)-succinic Acid Dimethyl Ester (19). A solution of **12** (or **13**) (105 mg, 0.39 mmol) in 20 mL of $CHCl_3$ was refluxed for 2.5 h. After removal of the solvent, the 2-(1*H*-Indol-2-yl)-succinic acid dimethyl ester (**19**) was obtained in quantitative yield (pale yellow crystals from CH_2Cl_2/hexane; mp 101−102 °C): ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.61 (bs, NH, 1H), 7.57 (bd, J = 7.7 Hz, 1H), 7.35 (bd, J = 8.0 Hz, 1H), 7.23−7.06 (m, 2H), 6.38 (bs, =CH, H_3, 1H), 4.33 (dd, J = 8.6 Hz, 5.84 Hz, CH, 1H), 3.76 (s, OCH_3, 3H), 3.73 (s, OCH_3, 3H), 3.20 (dd, J = 17.1 Hz, 8.6 Hz, A-part of AB system, CH_2, 1H), 3.01 (dd, J = 17.1 Hz, 5.8 Hz, B-part of AB system, CH_2, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 174.2, 174.0, 138.2, 135.9, 130.0, 124.2, 122.4, 122.0, 112.9, 103.0, 54.7, 54.1, 42.9, 38.2; IR (CH_2Cl_2, cm^{-1}) 3392, 3037, 2960, 2899, 2852, 1741, 1610, 1579, 1448, 1356, 1271, 1232, 1171, 1016, 870. Anal. Calcd for $C_{14}H_{15}NO_4$: C, 64.36; H, 5.79; N, 5.36. Found: C, 64.60; H, 5.53; N, 5.49.

5,13-Dioxo-5a,6,7,8,12c,13-hexahydro-5*H*-8-aza-indeno[1,2-*a*]-anthracene-6,7-dicarboxylic Acid Dimethyl Ester (22). A solution of dimethyl indole-2-ylfumarate (**14**) (400 mg, 1.54 mmol) and 1,4-naphthoquinone (568 mg, 3.10 mmol) in $CHCl_3$ (10 mL) was placed in a glass tube. The tube was sealed and heated at 90 °C for 2 days. After cooling the mixture to room temperature, the solvent was evaporated and the residue was submitted to silica gel (60 g) column chromatography and eluting with AcOEt/*n*-hexane (10:90) to give the excessive of 1,4-naphthoquinone. Then, the elution of the column with AcOEt/*n*-hexane (40:60) gave the addition product **22** (420 mg, 66%, brown crystals from CH_2Cl_2/hexane, mp 155−156 °C): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (bs, NH, 1H), 8.10 (dd, J = 7.4 Hz, 1.2 Hz, 1H), 7.98 (dd, J = 7.4 Hz, 1.2 Hz, 1H), 7.74−7.66 (m, 2H), 7.48 (d, J = 7.4 Hz, 1H), 7.21 (d, J = 7.4 Hz, 1H), 7.11 (td, J = 7.4 Hz, 1.2 Hz, 1H), 7.06 (td, J = 7.4 Hz, 1.2 Hz, 1H), 4.60 (dd, J = 5.9 Hz, 1.5 Hz, A-part of AB system, CH, 1H), 4.50 (dd, J = 5.1 Hz, 1.5 Hz, A-part of AB system, CH, 1H), 4.04 (dd, J = 7.7 Hz, 5.9 Hz, B-part of AB system, CH, 1H), 3.84 (dd, J = 7.7 Hz, 5.1 Hz, B-part of AB system, CH, 1H), 3.82 (s, OCH_3, 3H), 3.73 (s, OCH_3, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.1, 196.0, 172.4, 171.2, 136.7, 135.1, 134.8, 134.4, 134.2, 128.4, 127.5, 127.2, 126.6, 122.8, 120.4, 119.3, 111.4, 107.0, 53.3, 53.0, 50.5, 46.4, 43. 8, 41.0; IR (CH_2Cl_2, cm^{-1}) 3412, 3072, 2948, 1738, 1712, 1610, 1456, 1275, 1043, 734. Anal. Calcd for $C_{24}H_{19}NO_6$: C, 69.06; H, 4.59; N, 3.36. Found: C, 68.93; H, 4.51; N, 3.47.

5,13-Dioxo-8,13-dihydro-5*H*-8-aza-indeno[1,2-*a*]anthracene-6,7-dicarboxylic Acid Dimethyl Ester (23). A solution of the addition product **22** (200 mg, 0.48 mmol) and DDQ (218 mg, 0.96 mmol) in 10 mL of dry benzene was stirred at room temperature for 3 h. After the benzene was evaporated, the residue was filtered on a short silica gel column (5 g) eluting with CH_2Cl_2 (50 mL). The crude product **23** (188 mg, 95%) was recrystallized from CH_2Cl_2/hexane (165 mg, 83%, yellow crystals from CH_2Cl_2/hexane, mp 183−184 °C): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.73 (bs, NH, 1H), 9.11 (d, J = 8.4 Hz, 1H), 8.30 (bd, J = 8.8 Hz, 1H), 8.18 (bd, J = 8.8 Hz, 1H), 7.89−7.82 (m, 2H), 7.50−7.49 (m, 2H), 7.29−7.25 (m, 1H), 4.18 (s, OCH_3, 3H), 4.07 (s, OCH_3, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.2, 183.6, 173.6, 166.2, 143.8, 142.5, 135.2, 134.9, 134.2, 133.1, 132.8, 132.6, 130.4, 128.1, 127.7, 127.6, 125.2, 123.7, 122.4, 121.1, 113.0, 112.0, 54.5, 50.4; IR (CH_2Cl_2, cm^{-1}) 3437, 2948, 1738, 1687, 1481, 1326, 1275, 1223, 1120, 1043. Anal. Calcd for $C_{24}H_{15}NO_6$: C, 69.73; H, 3.66; N, 3.39. Found: C, 69.56; H, 3.59; N, 3.36.

1,4-Dioxo-4,7-dihydro-1*H*-benzo[*c*]carbazole-5,6-dicarboxylic Acid Dimethyl Ester (25). A solution of dimethyl indole-2-ylfumarate (**14**) (150 mg, 0.58 mmol) and *p*-benzoquinone (187 mg, 1.73 mmol) in $CHCl_3$ (10 mL) was placed in a glass tube. The tube was sealed and heated at 90 °C for 9 days. After cooling the mixture to room temperature, the solvent was evaporated and the residue was eluted by silica gel (5 g) column chromatography with CH_2Cl_2 (50 mL). The product **25** was obtained in quantitative yield (light brown crystals from CH_2Cl_2/hexane, 140 mg, 67%, mp 197−198 °C): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.64 (bs, NH, 1H), 9.23 (d, J = 8.3 Hz, 1H), 7.58 (tdd, J = 8.3 Hz, 7.1 Hz, 1.1 Hz, 1H), 7.50 (d, J = 8.3 Hz, 1H), 7.35 (tdd, J = 8.3 Hz, 7.1 Hz, 1.1 Hz, 1H), 6.98 (d, J = 10.3 Hz, A-part of AB system, =CH, 1H), 6.88 (d, J = 10.3 Hz, B-part of AB system, =CH, 1H), 4.09 (s, OCH_3, 3H), 4.05 (s, OCH_3, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.3, 183.8, 169.3, 165.9, 143.8, 142.3, 139.2, 138.4, 133.6, 131.1, 130.0, 128.2, 123.9, 122.4, 122.2, 121.3, 112.2, 111.8, 53.5, 53.2; IR (CH_2Cl_2, cm^{-1}) 3437, 2948, 1739, 1714, 1481, 1326, 1275, 1223, 1146, 1043. Anal. Calcd for $C_{20}H_{13}NO_6$: C, 66.12; H, 3.61; N, 3.86. Found: C, 66.00; H, 3.82; N, 3.80.

2,3-Dicyano-1,4-dioxo-4,7-dihydro-1*H*-benzo[*c*]carbazole-5,6-dicarboxylic Acid Dimethyl Ester (28). A solution of dimethyl indole-2-ylfumarate (**14**) (140 mg, 0.54 mmol) and DDQ (122 mg, 54 mmol) in benzene (10 mL) was placed in a glass tube. The tube was sealed and heated at 90 °C for 1 day. After cooling the mixture to room temperature, the solvent was evaporated and the residue was filtered on a short silica gel (5 g) column with CH_2Cl_2 (50 mL). The crude product was recrystallized from CH_2Cl_2/hexane

(95 mg, 43%, orange crystals from CH_2Cl_2/*n*-hexane, mp 215−216 °C): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.19 (bs, NH, 1H), 7.48 (td, J = 7.8 Hz, 1.0 Hz, 1H), 7.18−7.14 (m, 2H), 6.99 (d, J = 7.8 Hz, 1H), 3.91 (s, OCH_3, 3H), 3.83 (s, OCH_3, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.4, 177.1, 163.9, 159.2, 150.5, 148.5, 144.9, 143.4, 133.2, 125.2, 124.1, 122.3, 114.0, 113.6, 110.1, 93.7, 91.3, 53.9, 52.9; IR (CH_2Cl_2, cm^{-1}) 3309, 2948, 2227, 1738, 1610, 1532, 1507, 1455, 1352, 1198. Anal. Calcd for $C_{22}H_{11}N_3O_6$: C, 63.93; H, 2.68; N, 10.17. Found: C, 64.07; H, 2.55; N, 9.99.

1,3-Dioxo-2-phenyl-2,3,6,10b-tetrahydro-1*H*,4*H*-2,3a,6,10c-tetraaza-cyclopenta[*c*]fluorene-4,5-dicarboxylic Acid Dimethyl Ester (30). A solution of dimethyl indole-2-ylfumarate (**14**) (250 mg, 0.96 mmol) and PTAD (169 mg, 0.96 mmol) in 10 mL of dry CH_2Cl_2 was stirred at room temperature for 1 h. After the CH_2Cl_2 was evaporated, the addition product **30** was obtained. The crude product was purified by crystallization from CH_2Cl_2/*n*-hexane (280 mg, 66%, white crystals, mp 185−186 °C): ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.32 (bs, NH, 1H), 8.30 (d, J = 7.8 Hz, 1H), 7.56−7.38 (m, 5H), 7.30 (t, J = 7.8 Hz, 1H), 7.04 (td, J = 7.8 Hz, 0.7 Hz, 1H), 6.92 (d, J = 7.8 Hz, 1H), 6.03 (s, CH, 1H), 5.94 (s, CH, 1H), 3.88 (s, OCH_3, 3H), 3.78 (s, OCH_3, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8 (2C), 165.9, 155.9, 153.4, 152.8, 144.3, 131.5, 130.6, 129.5, 128.8, 126.3, 124.1, 122.9, 110.4, 59.1, 54.2, 53.6, 52.3; IR (CH_2Cl_2, cm^{-1}) 3360, 2974, 1713, 1635, 1507, 1429, 1275, 1223. Anal. Calcd for $C_{22}H_{18}N_4O_6$: C, 60.83; H, 4.18; N, 12.90. Found: C, 60.92; H, 4.03; N, 12.63.

1,3-Dioxo-2-phenyl-2,3,5,6-tetrahydro-1*H*,4*H*-2,3a,6,10c-tetraaza-cyclopenta[*c*]fluorene-4,5-dicarboxylic Acid Dimethyl Ester (31). A solution of the PTAD adduct **30** (100 mg, 0.23 mmol) in 10 mL of dry $CHCl_3$ was refluxed for 1 h. After the $CHCl_3$ was evaporated, the rearrangement product **31** was obtained in quantitative yield. The product was crystallized from CH_2Cl_2/*n*-hexane (70 mg, 70%, white crystals, mp 241−242 °C): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, J = 8.2 Hz, 1H), 8.27 (bs, NH, 1H), 7.61 (bd, J = 8.2 Hz, 2H), 7.52 (bt, J = 8.2 Hz, 2H), 7.43 (bt, J = 8.2 Hz, 1H), 7.34 (bd, J = 7.7 Hz, 1H), 7.27 (td, J = 7.7 Hz, 1.0 Hz, 1H), 7.15 (td, J = 7.7 Hz, 1.0 Hz, 1H), 5.88 (d, J = 1.1 Hz, CH, 1H), 4.72 (d, J = 1.1 Hz, CH, 1H), 3.84 (s, OCH_3, 3H), 3.75 (s, OCH_3, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.6, 167.4, 152.4, 146.0, 135.6, 131.5, 129.5, 128.7, 126.3, 124.4, 123.0, 120.9, 117.3, 113.0, 112.8, 111.3, 54.7, 54.1, 53.8, 40.9; IR (CH_2Cl_2, cm^{-1}) 3309, 1764, 1712, 1507, 1429, 1249, 1017. Anal. Calcd for $C_{22}H_{18}N_4O_6$: C, 60.83; H, 4.18; N, 12.90. Found: C, 60.59; H, 4.12; N, 12.75.

Dimethyl 5*H*-Pyridazino[4,3-*b*]indole-3,4-dicarboxylate (33). A solution of the addition product **31** (150 mg, 0.35 mmol) and DDQ (180 mg, 0.79 mmol) in 10 mL of dry benzene was stirred at room temperature for 3 h. After the benzene was evaporated, the residue was diluted with CH_2Cl_2 (100 mL), and the organic phase was washed with $NaHCO_3$ (3 × 50 mL, 5%), washed with water (2 × 50 mL), and dried over $MgSO_4$. After removal of the solvent, the crude product **33** was recrystallized from ethyl acetate/ether (70 mg, 71%, white crystals, mp 193−194 °C): ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.89 (bs, NH, 1H), 8.55 (d, J = 7.7 Hz, 1H), 7.69 (t, J = 7.7 Hz, 1H), 7.58 (t, J = 7.7 Hz, 1H), 7.47 (t, J = 7.7 Hz, 1H), 4.08 (s, OCH_3, 3H), 4.06 (s, OCH_3, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 165.0, 150.3, 147.7, 142.1, 132.8, 131.7, 123.4, 122.9, 119.9, 112.2, 105.9, 53.7, 53.6; IR (CH_2Cl_2, cm^{-1}) 3721, 3412, 3154, 1738, 1610, 1481, 1404, 1326, 1275, 1223, 1198, 1172, 1069. Anal. Calcd for $C_{14}H_{11}N_3O_4$: C, 58.95; H, 3.89; N, 14.73. Found: C, 59.10; H, 3.79; N, 14.58.

***trans*- and *cis*-Dimethyl 3,3,4-Tricyano-4-isocyano-2,3,4,9-tetrahydro-1*H*-carbazole-1,2-dicarboxylate (38 and 39).** A solution of dimethyl indole-2-ylfumarate (**14**) (180 mg, 0.69 mmol) and tetracyanoethylene (89 mg, 0.69 mmol) in 10 mL of dry CH_2Cl_2 was stirred at room temperature for 1 h. After the CH_2Cl_2 was evaporated, the mixture of the addition products **38** and **39** was obtained in a quantitative yield. The crude product was purified by crystallization from CH_2Cl_2/*n*-hexane (200 mg, 75%, brown crystals). For trans isomer **39**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.11 (bs, NH, 1H), 7.86 (d, J = 8.1 Hz, 1H), 7.53−7.34 (m, 3H), 4.72 (d, J = 11.0 Hz, A-part of AX system, CH, 1H), 4.11 (d, J = 11.0 Hz, X-part of AX system, CH, 1H), 4.03 (s, OCH_3, 3H), 3.94 (s, OCH_3, 3H) (for cis isomer **38**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.65 (d, J = 5.6 Hz, A-part of AX system, CH, 1H), 3.92 (s, OCH_3, 3H), 3.87 (s, OCH_3, 3H) and the other signals coincide with signals of trans isomer); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 166.7, 136.4, 127.5, 125.6, 125.5, 123.3, 122.8, 118.2, 112.5, 110.0, 109.7, 108.4, 54.8, 54.7, 46.1, 45.9, 43.4, 40.9; IR (CH_2Cl_2, cm^{-1}) 3412, 2974, 1764, 1584, 1455, 1352, 1249, 11172, 966, 760.

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