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New 3-vinylation products of indole and investigation of its Diels–Alder reactivity: synthesis of unusual Morita–Baylis–Hillman-type products

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ABSTRACT

3-Vinylindoles as precursors of carbazole and bis-indole derivatives were synthesized. Then, to form new carbazoles, Diels–Alder reactivity of these vinylindoles was studied with various dienophiles. During the cycloaddition reaction, unusual Morita–Baylis–Hillman-type products were observed. The structure and the formation mechanism of the products is discussed.

1. Introduction

The indole (**1**) and carbazole (**2**) moieties occur widely in synthetic and natural products.[1–6] Due to a wide range of biological activities, the synthesis of carbazoles and bis-indole alkaloids has received considerable interest. Ever since the first isolation of a simple carbazole alkaloid, murrayanine (**3**), organic chemists have been interested in the synthesis of carbazole alkaloids.[7] An indolocarbazole alkaloid staurosporine (**4**) has very interesting biological activities such as antimicrobial, hypotensive, cytotoxic properties, inhibition of protein kinase C, and platelet aggregation inhibition.[8–10] Vinblastine (**5**) isolated from *Catharanthus roseus*, a more complex annulated system containing the indole ring, has been widely used as an agent for cancer chemotherapy (Fig. 1).[11–13]

Vinylindoles have been shown to act as heterocyclic dienes in $HOMO_{diene}$-controlled Diels–Alder reactions, and therefore, as valuable synthons in highly functionalized carbazole ring systems, indole alkaloids, and carbolines.[14–26] The Michael addition is one of the most important carbon–carbon and carbon-heteroatom bond-forming reactions in organic synthesis.[27–38] For the synthesis of carbazoles and bis-indoles, we are examining the synthesis of new 3-vinylindoles **6**–**9** and investigating their Diels–Alder reactivity. Our retro-synthetic approach to carbazoles and bis-indoles was delineated through the retro-synthetic analysis depicted in Figure 2, which identifies the key step as well as vinylindoles **6**–**9**. Thus, bis-indole **10** could be accessed through the Fisher indolization of the cyclic ketone **11**. The carbazole derivative **11** could be derived from vinylindole **6** by [4+2]-cycloaddition.

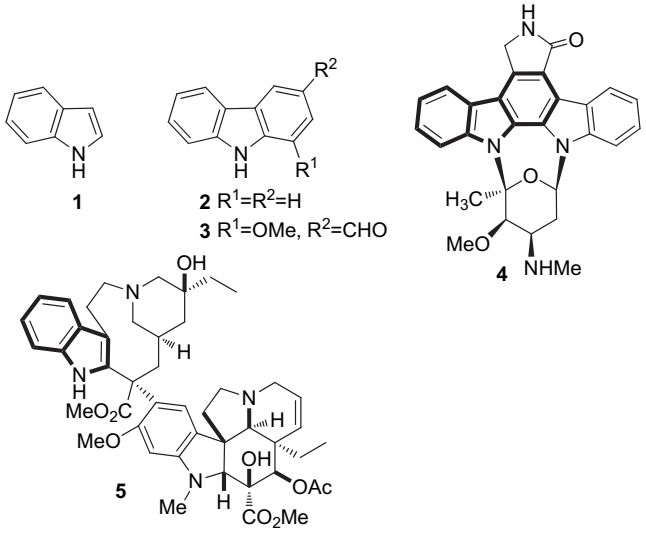

Figure 1. Some indoles and carbazoles.

2. Results and discussions

First, we prepared Michael adduct **13** from the $Bi(NO_3)_3 \cdot 5H_2O$-catalyzed conjugate addition reaction between indole **1** and cyclopent-2-enone **12** (Scheme 1).[39] Reaction of the Michael addition product **13** with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) yielded vinylindole **6**, an α,β-unsaturated ketone (Scheme 1). Although vinylindole **8** was prepared by a similar strategy, molecules **7** and **9** could be synthesized via different routes.

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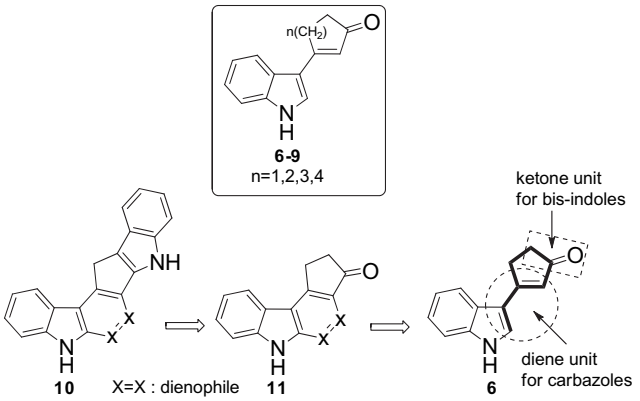
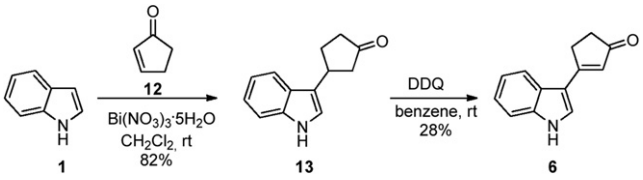
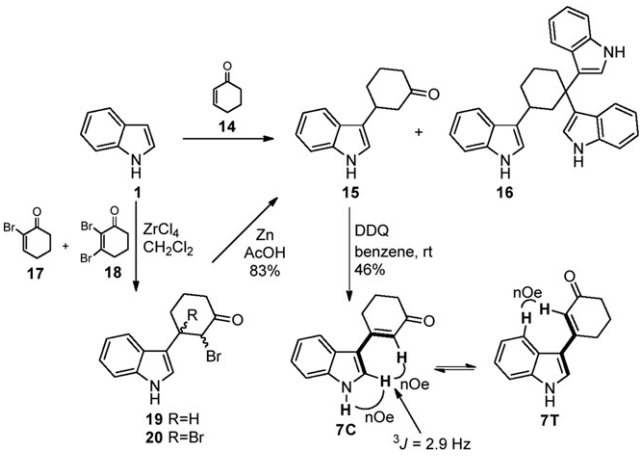


Figure 2. Retro-synthetic approach to carbazoles and bis-indoles.



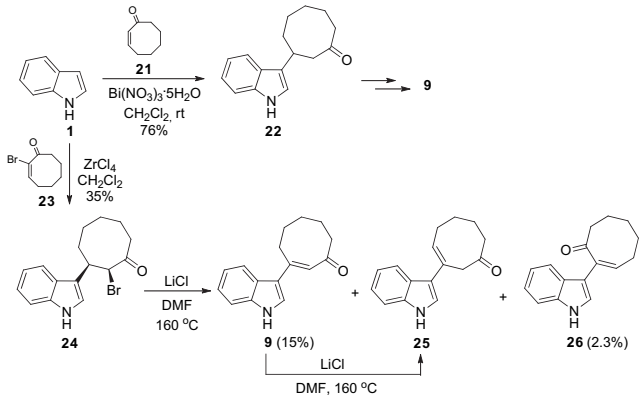
Scheme 1.

Due to the formation of tris-indole **16**[40] as well as Michael adduct **15**[41] from indole **1** and cyclohex-2-enone **14**, we first synthesized bromo compounds **17**[42] and **18**. The $ZrCl_4$-catalyzed reaction of a mixture of bromo compounds **17** and **18** gave a mixture of Michael adducts **19** and **20** (Scheme 2). After reduction of **19** and **20** with Zn–AcOH, DDQ-oxidation of **15** gave vinylindole **7**.[43–45] Structure analysis of vinylindole **7** showed that cisoid (**C**) conformer **7C** is in equilibrium with transoid (**T**) conformer **7T**. The coupling constant for C3-H and nuclear Overhauser enhancement (NOE) experiments for both C3-H in the indole ring and olefinic alpha proton in cyclohexen-2-one of **7** were completely in agreement with the structures depicted in Scheme 2.

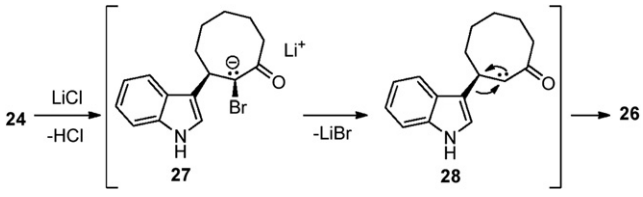


Scheme 2.

For the synthesis of vinylindole **9**, the Michael adduct **22** was prepared from indole **1** and cyclooct-2-en-1-one **21** (Scheme 3).[46] Oxidation of this compound with DDQ gave a complex reaction mixture. Therefore, indole **1** was treated with vinyl bromide **23**[10] in dichloromethane at room temperature, which resulted in the formation of bromo-compound **24** as a single product (Scheme 3). The configuration of bromine atom and indole ring in **24** was determined by the coupling constants of the relevant protons as well as the calculated optimized molecule geometry. The vicinal coupling constant (^3J=2.5 Hz) for a methine proton (a doublet at δ=5.02 ppm) bonding to the bromine atom confirms the *cis* position of the indole ring and the bromine. The calculated dihedral angle (60.50°) by the AM1 method is in agreement with the proposed structure **24**. The reaction of **24** with LiCl was carried out in DMF at 160 °C for 3 h to provide a mixture of three products, which contained vinylindole **9**, isomerization product **25**, and rearrangement product **26**. The mixture was submitted to silica gel column chromatography. Following chromatography, we managed to separate the two vinylindoles, **9** and **26**. Furthermore, isomerization product **25** could be isolated as a mixture with vinylindole **9**. While vinylindoles **9** and **26** were initial products, isomer **25** was formed by isomerization of **9**. To test this isomerization, the reaction of pure **9** with lithium chloride in DMF under the same reaction conditions gave a mixture of **9** and **25** in a ratio of 7:3. Independently, when pure **9** was heated in DMF without base, no isomerization was observed. Product **26** was an unexpected elimination product. For the formation of **26**, we suggest that the mechanism involves a carbene rearrangement via a geminal hydrogen halide elimination as depicted in Scheme 4. The structure of rearrangement product **26** was determined by ^{1}H- and ^{13}C NMR spectroscopy. The most conspicuous feature in the ^{1}H NMR spectra of **26** was a triplet (^3J=5.9 Hz) at 6.41 ppm, which corresponds to the olefinic proton in the cyclooctene ring. The C3-H proton in the pyrrole ring of indole skeleton resonates as a doublet (^3J=2.9 Hz) at 6.98 ppm. The sixteen carbon resonance signals support the suggested structure.



Scheme 3.

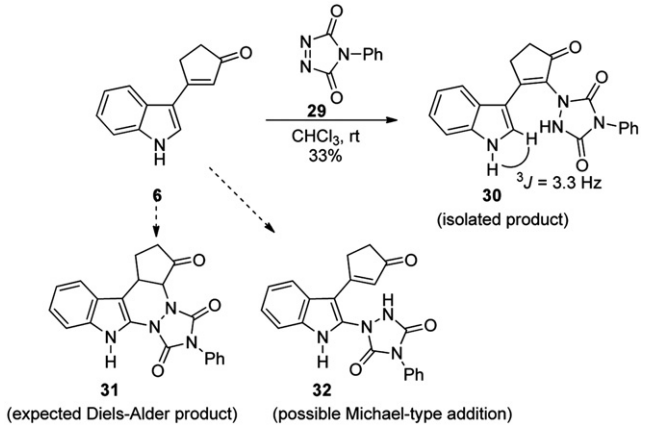


Scheme 4.

Since carbazoles also represent an important family of alkaloids, we turned out our attention to the synthesis of carbazole derivatives and studied the cycloaddition reactions of vinylindoles **6**–**9**. First, the Diels–Alder reactivity of vinylindole **6** was carried out with dieoniphiles such as maleic anhydride, dimethyl acetylenedicarboxylate (DMAD), tetracyanoethylene (TCE), naphthoquinone,

and *p*-benzoquinone under different conditions. However, unreacted starting material was recovered in every case.

Later, vinylindole **6** was reacted with *N*-phenyltriazolinedione (PTAD; **29**), to yield **30** as the only product (Scheme 5). The isolated product was not the expected cycloadduct **31** or possible Michael-type product **32**. A careful examination of the ^{1}H and ^{13}C NMR spectra of the product revealed an exclusive formation of Aza-Baylis–Hillman-type product **30**. The Aza-Baylis–Hillman reaction, a variation of the Morita–Baylis–Hillman, describes the reaction of an electron-deficient alkene, usually an α,β-unsaturated carbonyl compound with an imine in the presence of a nucleophile to give an allylic amine.[47–51] We observed a similar behavior when the reactivity of vinylindoles **7**–**9** with PTAD was investigated. All vinylindoles provided Aza-Baylis–Hillman-type products **33**–**35** as the sole product (Fig. 3). The structures of the products were determined by ^{1}H NMR, ^{13}C NMR, IR, and elemental analysis. The unusual Morita–Baylis–Hillman-type product **30** was characterized by the presence of NH signals (δ=11.09 ppm and 12.30 ppm), aromatic ten protons (δ=8.41–7.18 ppm) and the AA′BB′ system arising from CH_2 protons. In particular, the coupling constant (^{3}J=3.3 Hz) between the olefinic C2-H (doublet at 8.41 ppm) and NH protons in the pyrrole moiety show that the phenyl-urazole ring was joined to the α-position of the cyclopenten-2-one ring.



Scheme 5.

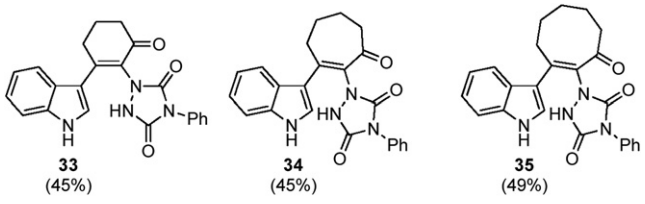
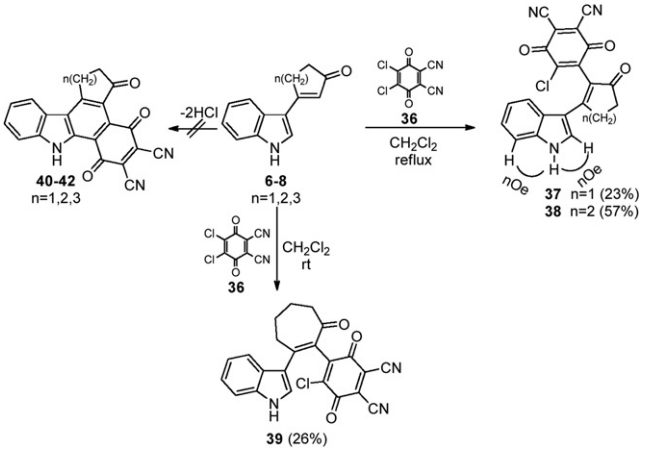
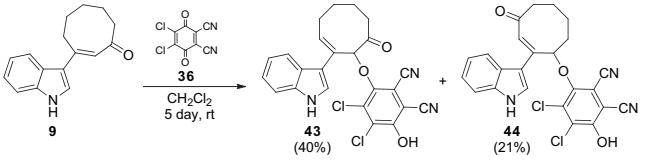


Figure 3. Aza-Morita–Baylis–Hillman-type products.

Next, our experiments focused on the cycloaddition of vinylindoles **6**–**9** with DDQ **36**. The reaction of both **6** and **7** with 1 equiv DDQ in methylene chloride gave a single reaction product, which was the Morita–Baylis–Hillman-type products **37**–**39**, not the expected cycloadducts **40**–**42** (Scheme 6). While the reaction of vinylindole **8** with DDQ allowed us to isolate product **37** together with two products as yet uncharacterized, the reaction of **9** in the presence of DDQ resulted in the formation of two new unusual products **43**–**44**, which were purified via silica gel thin-layer chromatography (Scheme 7). The structures of these compounds were elucidated on the basis of ^{1}H-, and ^{13}C NMR spectroscopic data, extensive double resonance, and NOE experiments. For example, irradiation of the NH proton at 11.91 ppm of molecule **38** caused an enhancement of the C2-H in the pyrrole ring at 7.99 ppm and the aromatic proton at 7.85 ppm. While the OCH neighbouring to the phenolic group for unusual product **43** resonates as a singlet at 6.96 ppm, the olefinic proton in eight-member ring appears the triplet at 6.25 ppm. For the unusual product **44**, whilst the singlet of olefinic proton resonances at 6.55 ppm, the OCH proton appears as a triplet at 5.91 ppm. The resonances of the alkoxy carbons for both compound **43** and **44** are at 86.6 ppm and at 84.6 ppm, respectively.

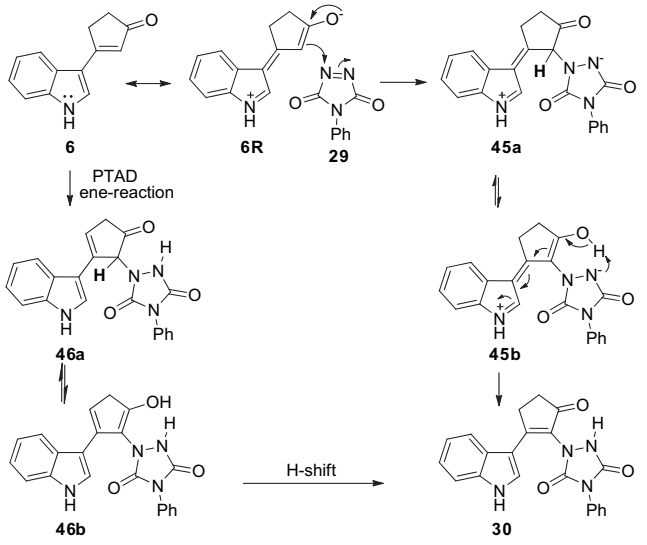


Scheme 6.



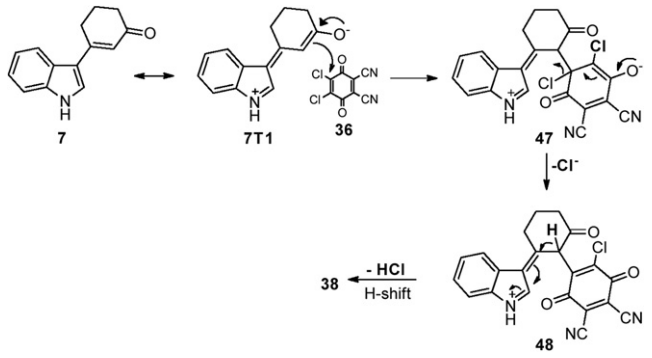
Scheme 7.

For the formation of Aza-Baylis–Hillman-type products **30**, **33**–**35**, we suggest that the reaction involves two mechanisms both an ionic and neutral, as described below (Scheme 8). Firstly, resonance (**R**) structure **6R** of vinylindole **6** adds to the double bond of N=N in the PTAD molecule to furnish intermediate **45a**. The mechanism results in bond tautomerization and proton shift. The second mechanism initiates an ene-reaction between PTAD and the double bond of the α,β-unsaturated ketone and continues as keto–enol tautomerization.



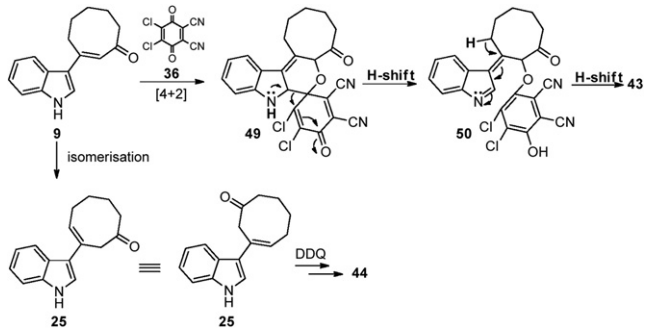
Scheme 8.

A similar formation mechanism is proposed for Morita–Baylis–Hillman-type-products **37**–**39** of DDQ (Scheme 9). However, according to the suggested mechanism, 1 mole of HCl was eliminated during product formation.



Scheme 9.

A mechanism for the formation of the products **43** and **44** from **9** and DDQ is given in Scheme 10. The reaction mechanism involves a Diels–Alder cycloaddition step giving rise to primary cycloadduct **49**, that is, rearranged through a hydrogen shift and bond break towards the more stable phenol structure **43** (Scheme 10). The key step is the behavior of the carbonyl group of DDQ as a dienophile to give products **43** and **44**. We assume that vinylindole **9** isomerizes to vinylindole **25** in the reaction medium. A similar mechanism could also be proposed to yield product **44** with the cycloaddition reaction between vinylindole **25** and DDQ.



Scheme 10.

3. Conclusions

In conclusion, we have described the synthesis of new 3-vinylindole derivatives. These vinyl groups are in α,β-unsaturated cyclic ketones. The results of the present study demonstrate that attempted Diels–Alder reactions of vinylindoles with various dienophiles mainly provided unusual Morita–Baylis–Hillman-type products. In the case of **9**, the secondary products were isolated through primary [4+2]-cycloaddition products. The formation of these unusual products can be attributed to the cyclic structure and ketone functionality of the vinyl group, which changes the geometry and electron density. Due to the unexpected behaviors of this type of 3-vinylindoles, the chemistry of 2-vinylindoles is in progress.

4. Experimental section

4.1. General methods

Melting points were determined on Buchi 539 capillary melting apparatus. Infrared spectra were recorded on a Mattson 1000 FTIR spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on 200 (50) and 400 (100)-MHz Varian spectrometer and are reported in δ units with $SiMe_4$ as internal standard. Elemental analyses were carried out on a Leco CHNS-932 instrument. All optimized geometries were determined using SPARTAN04 software for Windows (version 1.0.0) as the semi-empirical AM1.[52–55]

*4.1.1. 3-(1H-indol-3-yl)cyclopentanone (**13**).* A solution of indole (**1**) (2.85 g, 24.36 mmol), cyclopenten-2-one (**12**; 2 g, 24.39 mmol), and $Bi(NO_3)_3\cdot 5H_2O$ (85 mg, 0.18 mmol) in acetonitrile (20 mL) was placed in a glass tube. The tube was sealed and was heated at 70–80 °C for two days. After cooling the mixture to room temperature, the mixture is filtered and the filtrate was washed with CH_2Cl_2 (50 mL). The organic layer was washed with saturated $NaHCO_3$ (2×25 mL), water (2×25 mL), dried over $MgSO_4$ and the solvent was evaporated. The crude product was recrystallized from CH_2Cl_2/hexane (3.91 g, 82%, red crystals from CH_2Cl_2/*n*-hexane, mp 108–109 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18 (m, NH, 1H), 7.65 (d, *J*=7.7 Hz,=CH, 1H), 7.38 (d, *J*=7.7 Hz,=CH, 1H), 7.25 (t, *J*=7.7 Hz,=CH, 1H), 7.17 (t, *J*=7.7 Hz,=CH, 1H), 6.96 (d, *J*=2.2 Hz,=CH, 1H), 3.73 (p, *J*=7.3 Hz, CH, 1H), 2.77 (dd, *J*=17.8 Hz, 7.3 Hz, CH_2, 1H), 2.58–2.29 (m, CH_2, 4H), 2.19–2.09 (m, CH_2, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 210.0, 137.0, 126.9, 122.6, 120.3, 119.7, 119.3, 118.8, 111.7, 45.6, 38.4, 34.0, 30.1. Anal. Calcd for $C_{13}H_{13}NO$: C, 78.36; H, 6.58; N, 7.03. Found: C, 78.69; H, 6.42; N, 7.12.

*4.1.2. 3-(1H-indol-3-yl)cyclopent-2-enone (**6**).* A solution of **13** (392 mg, 1.97 mmol) and DDQ (447 mg, 1.97 mmol) in dry benzene (10 mL) was stirred at room temperature for 90 min. After the benzene was evaporated, the residue was dissolved by with CH_2Cl_2 (50 mL) and washed with saturated $NaHCO_3$ (2×50 mL), water (2×25 mL), dried over $MgSO_4$ and the solvent was evaporated. The crude product was recrystallized from CH_2Cl_2/hexane (110 mg, 28%, green dust, mp 207–208 °C); ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.93 (m, NH, 1H), 8.05 (d, *J*=2.9 Hz,=CH, 1H), 7.88 (d, *J*=7.9 Hz,=CH, 1H), 7.47 (d, *J*=7.9 Hz,=CH, 1H), 7.21–7.15 (m,=CH, 2H), 6.47 (s,=CH, 1H), 3.10–3.08 (m, AA′ part of AA′BB′ system, CH_2, 2H), 2.38–2.35 (m, BB′ part of AA′BB′ system, CH_2, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 208.7, 169.7, 138.0, 130.2, 125.6, 123.2, 122.1, 121.9, 120.9, 113.1, 112.6, 34.4, 29.8. IR (KBr, cm^{-1}) 3218, 2919, 1727, 1650, 1567, 1432, 1236, 1191, 743. Anal. Calcd for $C_{13}H_{11}NO$: C, 79.16; H, 5.62; N, 7.10. Found: C, 78.90; H, 5.70; N, 7.21.

*4.1.3. Bromination of cyclohexen-1-one (**14**).* To a solution of cyclohexen-1-one (**14**; 2 g, 20.83 mmol) in CH_2Cl_2 (50 mL) was dropped a solution of Br_2 (3.32 g, 20.75 mmol) in CH_2Cl_2 (25 mL) at 0 °C and the mixture stirred for 45 min. After the addition of Br_2, the mixture is stirred at the same temperature for 90 min. Later, NEt_3 (3.54 g, 35.00 mmol) was added dropwise to the reaction mixture at room temperature. After stirring for 90 min, the mixture was washed with brine (100 mL) and HCl (3%, 2×50 mL). The organic layer was dried over $MgSO_4$, and the solvent was removed under vacuum. The crude product was crystallized from ethanol to give a mixture product of **17** and **18** (3.90 g). The ^{1}H NMR integration ratio of the mixture showed that the formation of **17**/**18** (67:33). For the mixture of **17** and **18**; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.43 (t, *J*=4.4 Hz,=CH, 1H), 2.66–2.50 (m, CH_2, 2H), 2.50–2.41 (m, CH_2, 2H), 2.14–2.04 (m, CH_2, 2H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 193.1, 153.0, 125.9, 40.4, 30.4, 24.7.

*4.1.4. Michael addition reaction of indole (**1**) and a mixture of **17**/**18** with $ZrCl_4$-catalyzed.* A solution of indole (**1**) (606 mg, 5.18 mmol) and a mixture of **17**/**18** (950 mg; 67:33) and $ZrCl_4$ (23 mg, 0.20% mmol) in CH_2Cl_2 (10 mL) was stirred for 3 h at room temperature. Then, the mixture was filtered on a short silica gel column (5 g) eluting with CH_2Cl_2 (200 mL). After the solvent was evaporated,

crude product gave a mixture of Michael adducts **19**/**20** (1.20 g). Since the isomers were not subjected to the purification procedure, the spectral data was not obtained.

*4.1.5. 3-(1H-indol-3-yl)cyclohexanone (**15**).* To a magnetically stirred mixture of glacial acetic acid (10 mL) and Zn (1.62 g, 25.00 mmol) at room temperature, a solution of a mixture (1.10 g) of Michael adduct **19**/**20** was dropwise. After addition was completed, the temperature was raised to and maintained at 70 °C for 20 h. Then, the reaction mixture was cooled and treated with ether (150 mL), and the zinc residue was filtered. The ethereal layer was washed with a saturated $NaHCO_3$ (3×50 mL) to remove acetic acid, and dried over $MgSO_4$. The solvent removed under reduced pressure. The reduction product **15** was recrystallized from CH_2Cl_2/hexane (723 mg, 83%, yellow crystals, mp 103–104 °C; Lit.[41] 106–107 °C); ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.17 (m, NH, 1H), 7.65 (d, J=7.4 Hz,=CH, 1H), 7.38 (d, J=8.2 Hz,=CH, 1H), 7.27–7.11 (m,=CH, 2H), 6.98 (d, J=2.4 Hz,=CH, 1H), 3.47 (m, CH, 1H), 2.85 (dd, J=14.1 Hz, 4.6 Hz, A part of AB system, CH_2, 1H), 2.65 (dd, J=14.1 Hz, 10.4 Hz, B part of AB system, CH_2, 1H), 2.50–2.10 (m, CH_2, 2H), 2.09–1.81 (m, CH_2, 2H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 213.9, 138.5, 128.2, 124.2, 122.4, 121.7, 121.4, 121.0, 113.4, 50.1, 43.6, 38.0, 33.8, 26.9. Anal. Calcd for $C_{14}H_{15}NO$: C, 78.84; H, 7.09; N, 6.57. Found: C, 78.99; H, 6.87; N, 6.33.

*4.1.6. 3-(1H-indol-3-yl)cyclohex-2-enone (**7**).* A solution of **15** (440 mg, 2.06 mmol) and DDQ (468 mg, 2.06 mmol) in dry benzene (10 mL) was stirred at 0 °C for 1 h. Then, the stirring was continued at room temperature for 12 h. After the benzene was evaporated, the residue was dissolved by with CH_2CL_2 (100 mL) and washed with saturated $NaHCO_3$ (3×20 mL), water (50 mL), dried over $MgSO_4$ and the solvent was evaporated. The crude product was recrystallized from acetone (200 mg, 46%, yellow dust, mp 166–167 °C); ^{1}H NMR (200 MHz, $CDCl_3$): δ 9.05 (m, NH, 1H), 7.97 (d, J=7.4 Hz,=CH, 1H), 7.57 (d, J=2.6 Hz,=CH, 1H), 7.44 (d, J=6.5 Hz,=CH, 1H), 7.40–7.22 (m,=CH, 2H), 6.74 (s,=CH, 1H), 2.84 (t, J=6.2 Hz, CH_2, 2H), 2.54 (t, J=6.2 Hz, CH_2, 2H), 2.17 (p, J=6.2 Hz, CH_2, 2H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 201.7, 157.3, 139.3, 127.9, 126.9, 125.2, 124.2, 123.6, 123.1, 118.5, 113.8, 39.4, 30.7, 24.7. IR (KBr, cm^{-1}) 3384, 2924, 2852, 1695, 1606, 1583, 1561, 1510, 1485, 1449, 1348, 1331, 1292, 1189, 1078, 967, 876, 822, 738. Anal. Calcd for $C_{14}H_{13}NO$: C, 79.59; H, 6.20; N, 6.63. Found: C, 79.28; H, 6.13; N, 6.67.

4.1.7. 3-(1H-indol-3-yl)cycloheptanone. A solution of indole (**1**) (59 mg, 0.50 mmol), cyclohepten-2-one (56 mg, 0.50 mmol), and $Bi(NO_3)_3{\cdot}5H_2O$ (18 mg, 0.036 mmol) in CH_2Cl_2 (10 mL) was stirred as magnetically at room temperature for two days. The mixture was diluted with CH_2Cl_2 (50 mL). The organic layer was washed with water (3×30 mL), dried over Na_2SO_4 and the solvent was evaporated. The crude product was recrystallized from CH_2Cl_2/hexane (83 mg, 73%, red powder, mp 105–106 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22 (m, NH, 1H), 7.64 (d, J=8.1 Hz,=CH, 1H), 7.34 (d, J=8.1 Hz,=CH, 1H), 7.22–7.12 (m,=CH, 2H), 6.91 (d, J=1.5 Hz,=CH, 1H), 3.30–3.24 (m, CH, 1H), 3.01–2.94 (m, CH_2, 1H), 2.89–2.84 (m, CH_2, 1H), 2.67–2.63 (m, CH_2, 2H), 2.33–2.28 (m, CH_2, 1H), 2.09–2.00 (m, CH_2, 2H), 1.86–1.72 (m, CH_2, 2H), 1.64–1.57 (m, CH_2, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 214.8, 136.7, 126.3, 122.3, 121.6, 120.0, 119.5, 119.2, 111.6, 50.8, 44.3, 38.4, 34.2, 29.5, 24.6. IR (KBr, cm^{-1}) 3385, 2928, 1693, 1458, 1372, 741. Anal. Calcd for $C_{15}H_{17}NO$: C, 79.26; H, 7.54; N, 6.16. Found: C, 79.03; H, 7.41; N, 6.28.

*4.1.8. 3-(1H-indol-3-yl)cyclohept-2-enone (**8**).* A solution of 3-(1*H*-indol-3-yl)cycloheptanone (120 mg, 0.53 mmol) and DDQ (120 mg, 0.53 mmol) in dry benzene (15 mL) was stirred at 0 °C for 3 h. After the solvent was evaporated, the residue was filtered on a silica gel thin layer (50 g) eluting with ethyl acetate/hexane (10%) gave 36 mg (30%) of **8**, which was crystallized from CH_2Cl_2/hexane (30 mg, 25%, yellow crystals, mp: 80–81 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.51 (m, NH, 1H), 7.93 (d, J=8.1 Hz,=CH, 1H), 7.47 (d, J=2.6 Hz,=CH, 1H), 7.41 (dd, J=7.9, 0.9 Hz,=CH, 1H), 7.36–7.19 (m,=CH, 2H), 6.60 (s,=CH, 1H), 2.97–2.94 (m, CH_2, 2H), 2.73–2.70 (m, CH_2, 2H), 2.17–1.88 (m, CH_2, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.9, 153.1, 137.3, 127.2, 125.3, 125.1, 123.4, 121.5, 121.2, 119.2, 111.9, 42.0, 32.1, 25.2, 21.4. IR (KBr, cm^{-1}) 3345, 2926, 2855, 1586, 1457, 1240, 739. Anal. Calcd for $C_{15}H_{15}NO$: C, 79.97; H, 6.71; N, 6.22. Found: C, 80.11; H, 6.40; N, 6.12.

*4.1.9. 3-(1H-indol-3-yl)cycoloctanone (**22**).* A solution of indole (**1**) (106 mg, 0.90 mmol), cycloocten-2-one (112 mg, 0.90 mmol), and $Bi(NO_3)_3{\cdot}5H_2O$ (32 mg, 0.065 mmol) in CH_2Cl_2 (10 ml) was stirred as magnetically at room temperature for two days. After the solvent was removed, the residue was dissolved in ethyl acetate (50 mL). The organic layer was washed with water (3×30 mL), dried over Na_2SO_4 and the solvent was evaporated. The crude product was recrystallized from CH_2Cl_2/hexane (164 mg, 76%, orange powder, mp 119–120 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.27 (m, NH, 1H), 7.73 (dd, J=7.8, 1.1 Hz,=CH, 1H), 7.36 (dd, J=7.8, 1.1 Hz,=CH, 1H), 7.23 (td, J=7.8, 1.1 Hz,=CH, 1H), 7.17 (td, J=7.8, 1.1 Hz,=CH, 1H), 6.95 (d, J=2.2 Hz,=CH, 1H), 3.65–3.59 (m, CH, 1H), 3.00–2.94 (m, CH_2, 1H), 2.74–2.70 (m, CH_2, 1H), 2.69–2.62 (m, CH_2, 1H), 2.52–2.46 (m, CH_2, 1H), 2.17–2.01 (m, CH_2, 2H), 2.00–1.95 (m, CH_2, 1H), 1.83–1.75 (m, CH_2, 1H), 1.67–1.52 (m, CH_2, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 217.3, 136.7, 126.4, 122.3 (CH), 121.4, 120.3 (CH), 119.5 (CH), 119.2 (CH), 111.7 (CH), 48.4 (CH_2), 43.3 (CH_2), 35.9 (CH), 34.3 (CH_2), 28.0 (CH_2), 25.1 (CH_2), 24.6 (CH_2). IR (KBr, cm^{-1}) 3392, 3055, 2928, 2859, 1709, 1619, 1458, 1421, 1338, 1313, 1259, 1229, 1170, 1142, 1126, 1100, 1077, 1047, 1011, 932. Anal. Calcd for $C_{16}H_{19}NO$: C, 79.63; H, 7.94; N, 5.80. Found: C, 79.53; H, 7.82; N, 5.67.

*4.1.10. 2-Bromo-2-cyclooctenone (**23**).* To a solution of cycloocten-2-one (1 g, 8.06 mmol) in CH_2Cl_2 (25 mL) at 0 °C, a solution of Br_2 (1.29 g, 8.06 mmol) in CH_2Cl_2 (25 mL) was added dropwise for 45 min. After the addition was completed, the reaction mixture was stirred at room temperature for 90 min. Then, NEt_3 (0.822 mg, 8.06 mmol) was added dropwise to the reaction mixture at room temperature. After stirring for 90 min, the mixture was washed with brine (100 mL) and HCl (3%, 2×50 mL). The organic layer was dried over $MgSO_4$, and the solvent was removed under vacuum. The crude product was obtained as dark yellow colored liquid (1.20 g, 73%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.81 (t, J=6.9 Hz,=CH, 1H), 2.72 (t, J=6.9 Hz, CH_2, 2H), 2.46–2.42 (m, CH_2, 2H), 1.89–1.83 (m, CH_2, 2H), 1.67–1.56 (m, CH_2, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.7, 140.7, 121.2, 41.6, 30.5, 26.1, 22.7. Anal. Calcd for $C_8H_{11}BrO$: C, 47.32; H, 5.46. Found: C, 47.51; H, 5.41.

*4.1.11. (2S(R),3R(S))-2-Bromo-3-(1H-indol-3-yl)cyclooctanone (**24**).* A solution of indole (**1**) (750 mg, 6.38 mmol), 2-bromo-2-cyclooctenone (**23**; 1.30 g; 6.38 mmol), and $ZrCl_4$ (32 mg, 0.02 mmol) in CH_2Cl_2 (15 mL) was stirred at room temperature for 1 h. After the solvent was removed, the residue was dissolved with ethyl acetate (50 mL).The organic layer was washed with water (3×20 mL), dried over $MgSO_4$ and the solvent was evaporated. Chromatography of the residue on silica gel (20 g) eluting with ethyl acetate/hexane (10:90) furnished the compound 24 (0.72 mg, 35%): (dark brown powder from CH_2Cl_2/hexane; mp 130–131 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 (m, NH, 1H), 7.63 (d, J=7.6 Hz,=CH, 1H), 7.42 (d, J=7.6 Hz,=CH, 1H), 7.26–7.16 (m,=CH, 3H), 5.02 (d, J=2.4 Hz, CHBr, 1H), 4.25 (td, J=5.0, 2.4 Hz, CH, 1H), 3.07–3.00 (m, CH_2, 1H), 2.81–2.76 (m, CH_2, 1H), 2.34–2.27 (m, CH_2, 1H), 2.07–1.75 (m, CH_2, 5H), 1.56–1.52 (m, CH_2, 1H), 1.28–1.21 (m, CH_2, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.8, 136.2, 126.2, 122.9

(CH), 122.5 (CH), 119.9 (CH), 118.0 (CH), 117.9, 111.9 (CH), 68.0 (CHBr), 39.4 (CH_2), 36.7 (CH), 30.7 (CH_2), 29.6 (CH_2), 26.3 (CH_2), 24.6 (CH_2). IR (KBr, cm^{-1}) 3392, 3055, 2928, 2859, 1709, 1619, 1458, 1421, 1338, 1313, 1259, 1229, 1170, 1142, 1126, 1100, 1077, 1047, 1011, 932. Anal. Calcd for $C_{16}H_{18}BrNO$: C, 60.01; H, 5.67; N, 4.37. Found: C, 59.86; H, 5.84; N, 4.30.

*4.1.12. The reaction of (2S(R),3R(S))-2-bromo-3-(1H-indol-3-yl)cyclooctanone (**24**) with LiCl.* A solution of (2*S*(*R*),3*R*(*S*))-2-brom-3-(1*H*-indol-3-yl)cyclooctanone (**24**) (5.51 g, 17.21 mmol) and LiCl (1.09 g, 25.70 mmol) in 50 mL of dimethylformamide (DMF) was stirred at 160 °C for 3 h. The mixture was cooled, and DMF was removed under reduced pressure. The mixture was dissolved with ethyl acetate (50 mL), the organic layer was washed with water (3×20 mL) and dried over $MgSO_4$. The residue (3.38 g) was chromatographed over thin-layer silica gel with ethyl acetate/hexane (10:90). The first fraction was identified as the mixture of **25** and **26** (2.50 g). The second fraction gave the mixture of **9** and **25** (100 mg). The last fraction furnished (*E*)-3-(1*H*-indol-3-yl)cyclooct-2-enone (**9**) (650 mg, 15%; yellow crystals from CH_2Cl_2/hexane, mp 69–70 °C). A sample of the first fraction (300 mg) was subjected to thin-layer silica gel chromatography with ethyl acetate/hexane (25:75). The third band gave (*Z*)-2-(1*H*-indol-3-yl)cyclooct-2-enone (**26**), which was crystallized from ether/hexane (95 mg, 2.3%, pale brown crystals, mp 103–104 °C). For **9**; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.15 (m, NH, 1H), 7.95 (d, *J*=8.1 Hz,=CH, 1H), 7.46 (d, *J*=2.9 Hz,=CH, 1H), 7.40 (d, *J*=8.1 Hz,=CH, 1H), 7.26–7.15 (m,=CH, 2H), 6.96 (s,=CH, 1H), 3.17 (t, *J*=7.0 Hz, CH_2, 2H), 2.97 (t, *J*=7.3 Hz, CH_2, 2H), 1.84–1.75 (m, CH_2, 4H), 1.69–1.64 (m, CH_2, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.5, 149.6, 137.5, 129.1 (CH), 126.3 (CH), 125.1, 123.2 (CH), 121.5 (CH), 121.2 (CH), 119.3, 112.2 (CH), 42.8 (CH_2), 32.2 (CH_2), 25.5 (CH_2), 23.7 (CH_2), 23.2 (CH_2). IR (KBr, cm^{-1}) 3241, 2928, 2851, 1706, 1582, 1517, 1430, 1344, 1255, 1236, 1203, 1157, 1123. Anal. Calcd for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85. Found: C, 80.23; H, 6.95; N, 5.93. For mixture of **9** and **25**;^{1}H NMR (400 MHz, $CDCl_3$): δ 8.80 (m, NH, 1H), 8.31 (m, NH, 1H), 7.97 (d, *J*=7.7 Hz,=CH, 1H), 7.88 (d, *J*=8.1 Hz,=CH, 1H), 7.45 (d, *J*=3.0 Hz,=CH, 1H), 7.40 (d, *J*=8.1 Hz,=CH, 1H), 7.38 (d, *J*=8.6 Hz,=CH, 1H), 7.37–7.15 (m,=CH, 5H), 6.93 (s,=CH, 1H), 6.34 (t, *J*=8.6 Hz,=CH, 1H), 3.63 (s, CH_2, 2H), 3.18 (t, *J*=6.8 Hz, CH_2, 2H), 2.96 (t, *J*=7.3 Hz, CH_2, 2H), 2.58–2.56 (m, CH_2, 2H), 2.46–2.41 (m, CH_2, 2H), 1.90–1.72 (m, CH_2, 8H), 1.70–1.64 (m, CH_2, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 213.7, 203.3, 149.1, 137.4, 137.1, 129.9, 129.4 (CH), 126.8 (CH), 125.9 (CH), 125.3, 125.2, 123.3 (CH), 122.6 (CH), 122.3 (CH), 121.5 (CH), 121.3 (CH), 120.7 (CH), 120.4 (CH), 119.6, 119.2, 112.0 (CH), 111.7 (CH), 47.0 (CH_2), 42.8 (CH_2), 41.9 (CH_2), 32.3 (CH_2), 28.8 (CH_2), 27.9 (CH_2), 25.5 (CH_2), 25.3 (CH_2), 23.7 (CH_2), 23.2 (CH_2). (Note: The signals of **25** are underline). For (*Z*)-2-(1*H*-indol-3-il)cyclooct-2-enone (**26**) ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.54 (m, NH, 1H), 7.84 (dd, *J*=6.6, 1.8 Hz,=CH, 1H), 7.31 (dd, *J*=6.6, 1.8 Hz,=CH, 1H), 7.21–7.16 (m,=CH, 2H), 6.98 (d, *J*=2.9 Hz,=CH, 1H), 6.41 (t, *J*=5.9 Hz,=CH, 1H), 2.61–2.58 (m, CH_2, 2H), 2.47–2.42 (m, CH_2, 2H), 2.00–1.98 (m, CH_2, 2H), 1.78–1.74 (m, CH_2, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 213.8, 137.0, 134.7, 128.5, 125.7, 123.2, 122.6, 120.4, 120.2, 113.0, 111.9, 44.9, 29.7, 29.2, 24.1, 23.1. IR (KBr, cm^{-1}) 3283, 2896, 2821, 1648, 1553, 1482, 1338,1300, 1210, 1196, 1144,1068, 977. Anal. Calcd for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85. Found: C, 80.06; H, 6.98; N, 6.01.

*4.1.13. 1-(2-(1H-Indol-3-yl)-5-oxocyclopent-1-enyl)-4-phenyl-1,2,4-triazolidine-3,5-dione (**30**).* A solution of **6** (50 mg, 0.25 mmol) and PTAD (44 mg, 0.25 mmol) in dry $CHCl_3$ (10 mL) was stirred at room temperature for 5 min. After the reaction was completed, the formed precipitate was filtered through filter paper, and washed with acetone. The product **30** was obtained as a grey powder (31 mg, 33%, mp 290–291 °C); ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.30 (d, *J*=2.8 Hz, NH, 1H), 11.09 (m, NH, 1H), 8.41 (d, *J*=2.8 Hz,=CH, 1H), 7.58–7.40 (m,=CH, 5H), 7.39–7.38 (m,=CH, 1H), 7.25–7.18 (m,=CH, 2H), 3.40–3.38 (m, AA′ part of AA′BB′ system, CH_2, 2H), 2.55–2.53 (m, BB′ part of AA′BB′ system, CH_2, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 201.2, 168.4, 153.3, 152.8, 137.5, 133.2, 132.6, 129.5, 128.5, 127.0, 126.7, 126.2, 123.2, 122.3, 121.4, 113.4, 109.6, 32.8, 28.3. IR (KBr, cm^{-1}) 3260, 2919, 1760, 1704, 1588, 1502, 1424, 1235. Anal. Calcd for $C_{21}H_{16}N_4O_3$: C, 67.73; H, 4.33; N, 15.05. Found: C, 67.48; H, 4.46; N, 15.30.

*4.1.14. 1-(2-(1H-Indol-3-yl)-6-oxocyclohex-1-enyl)-4-phenyl-1,2,4-triazolidine-3,5-dione (**33**).* A solution of **7** (100 mg, 0.47 mmol) and PTAD (82.5 mg, 0.47 mmol) in 10 mL of dry $CHCl_3$ was stirred at room temperature for 5 min. After the reaction was completed, the formed precipitate was filtered through filter paper. The residue was purified by crystallization from acetone (80 mg, 45%, yellow powder, mp 168–170 °C); ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.99 (m, NH, 1H), 9.36 (m, NH, 1H), 8.04 (d, *J*=2.9 Hz,=CH, 1H), 7.87 (d, *J*=8.1 Hz,=CH, 1H), 7.58–7.48 (m,=CH, 5H), 7.41–7.37 (m,=CH, 1H), 7.24–7.14 (m,=CH, 2H), 3.42 (dt, *J*=11.7, 6.0 Hz, A part of AB system, CH_2, 1H), 3.10 (dt, *J*=11.7, 6.0 Hz, B part of AB system, CH_2, 1H), 2.62–2.58 (m, CH_2, 2H), 2.23–2.17 (m, CH_2, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 193.0, 159.2, 154.5, 153.1, 137.5, 132.8, 129.7 (CH), 129.6 (CH), 128.5 (CH), 126.8, 126.7 (CH), 126.2, 122.8 (CH), 121.5 (CH), 121.4 (CH), 113.2 (CH), 112.0, 37.7 (CH_2), 32.1 (CH_2), 22.7 (CH_2). IR (KBr, cm^{-1}) 3252, 2950, 1768, 1704, 1588, 1502, 1424, 1371, 1330, 1240, 1188, 1138, 1023. Anal. Calcd for $C_{22}H_{18}N_4O_3$: C, 68.38; H, 4.70; N, 14.50. Found: C, 68.47; H, 4.62; N, 14.31.

*4.1.15. (Z)-1-(2-(1H-Indol-3-yl)-7-oxocyclohept-1-enyl)-4-phenyl-1,2,4-triazolidine-3,5-dione (**34**).* A solution of **8** (110 mg, 0.48 mmol) and PTAD (86 mg, 0.48 mmol) in 15 mL of dry $CHCl_3$ was stirred at room temperature for 5 min. After completion of the reaction, the formed precipitate was filtered through filter paper and dissolved in acetone. After acetone was removed, residue was purified by crystallization from CH_2Cl_2/hexane (87 mg, 45%, yellow powder, mp 233–234 °C); ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.77 (m, NH, 1H), 10.75 (m, NH, 1H), 7.83 (d, *J*=2.9 Hz,=CH, 1H), 7.62 (d, *J*=7.7 Hz,=CH, 1H), 7.49–7.38 (m,=CH, 3H), 7.37–7.34 (m,=CH, 3H), 7.18–7.14 (m,=CH, 1H), 7.11–7.07 (m,=CH, 1H), 3.10 (m, CH_2, 2H), 2.69 (m, CH_2, 2H), 1.91–1.87 (m, CH_2, 4H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 198.7, 155.4, 153.7, 152.5, 137.5, 132.7, 129.9, 129.7, 129.6, 128.4, 126.6, 126.2, 122.6, 120.9, 120.7, 114.3, 113.0, 32.1, 31.4, 24.4, 20.6. IR (KBr, cm^{-1}) 3283, 2935, 1762, 1698, 1500, 1428, 1245. Anal. Calcd for $C_{23}H_{20}N_4O_3$: C, 68.99; H, 5.03; N, 13.99. Found: C, 69.13; H, 5.01; N, 13.78.

*4.1.16. (Z)-1-(2-(1H-Indol-3-yl)-8-oxocyclooct-1-enyl)-4-phenyl-1,2,4-triazolidine-3,5-dione (**35**).* A solution of **9** (100 mg, 0.42 mmol) and PTAD (72 mg, 0.42 mmol) in 10 mL of $CHCl_3$ was stirred at room temperature for five days. After removal of the solvent, the residue was chromatographed on thin-layer silica gel eluting with acetone/hexane (30:70). The brown band was extracted with ethyl acetate (50 mL), and the solvent was removed. Residue was crystallized from acetone/hexane (82 mg, 49%, pale brown powder, mp 207–208 °C); ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.66 (d, *J*=2.6 Hz, NH, 1H), 10.69 (m, NH, 1H), 7.75 (d, *J*=2.6 Hz,=CH, 1H), 7.63 (d, *J*=7.7 Hz,=CH, 1H), 7.49–7.43 (m,=CH, 3H), 7.38–7.33 (m,=CH, 3H), 7.16–7.12 (m,=CH, 1H), 7.09–7.05 (m,=CH, 1H), 3.30–3.36 (m, CH_2, 2H), 2.98–2.95 (m, CH_2, 2H), 1.80–1.78 (m, CH_2, 2H), 1.72–1.65 (m, CH_2, 4H). APT ^{13}C NMR (100 MHz, d_6-DMSO): δ 197.2 (CO), 154.0, 152.5 (2C), 137.3, 132.8, 131.7, 129.5 (CH), 129.2 (CH), 128.3 (CH), 126.5 (CH), 126.3, 122.4 (CH), 120.7 (CH), 120.5 (CH), 115.1, 113.0 (CH), 42.7 (CH_2), 33.7 (CH_2), 25.3 (CH_2), 23.7 (CH_2), 23.6 (CH_2). IR (KBr, cm^{-1}) 3288, 2900, 2856, 1940, 1765,

1690, 1550, 1430, 1257, 1210, 1158. Anal. Calcd for $C_{24}H_{22}N_4O_3$: C, 69.55; H, 5.35; N, 13.52. Found: C, 69.70; H, 5.23; N, 13.37.

*4.1.17. 4-(2-(1H-Indol-3-yl)-5-oxocyclopent-1-enyl)-5-chloro-3,6-dioxocyclohexa-1,4-diene-1,2-dicarbonitrile (**37**).* A solution of **6** (100 mg, 0.50 mmol) and DDQ (115 mg, 0.50 mmol) in CH_2Cl_2 (15 mL) was placed in a glass tube. The tube was sealed and was heated at 55–60 °C for three days. The reaction mixture was cooled and diluted with CH_2Cl_2 (50 mL). The organic layer was washed with water (3×30 mL) and dried over Na_2SO_4. Then, the solvent was evaporated and the residue was crystallized from acetone/hexane (45 mg, 23%, green powder, mp 250–251 °C); ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.15 (d, J=2.7 Hz, NH, 1H), 8.24 (d, J=2.7 Hz,=CH, 1H), 7.94 (d, J=7.8 Hz,=CH, 1H), 7.51 (d, J=7.8 Hz,=CH, 1H), 7.24–7.14 (m,=CH, 2H), 3.25–3.23 (m, AA′ part of AA′BB′ system, CH_2, 2H), 2.51–2.48 (m, BB′ part of AA′BB′ system, CH_2, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 197.4, 155.4, 150.7, 148.4, 142.9, 137.4, 132.6, 131.8, 129.7, 126.2, 123.2, 121.9, 121.6, 114.2, 113.3, 113.2, 109.9, 106.4, 102.0, 32.3, 25.3. IR (KBr, cm^{-1}) 3394, 2918, 2555, 2314, 2079, 1589. Anal. Calcd for $C_{21}H_{10}ClN_3O_3$: C, 65.04; H, 2.60, N, 10.84. Found: C, 65.16; H, 2.58; N, 11.03.

*4.1.18. 4-(2-(1H-Indol-3-yl)-6-oxocyclohex-1-enyl)-5-chloro-3,6-dioxocyclohexa-1,4-diene-1,2-dicarbonitrile (**38**).* A solution of **7** (100 mg, 0.46 mmol) and DDQ (104 mg, 0.46 mmol) in CH_2Cl_2 (10 mL) was placed in a glass tube. The tube was sealed and was heated at 55–60 °C for three days. The reaction mixture was cooled and the solvent was evaporated and the residue was crystallized from CH_2Cl_2/hexane (106 mg, 57%, brown powder, mp 185–186 °C); ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.91 (m, NH, 1H), 7.99 (d, J=3.1 Hz,=CH, 1H), 7.85 (d, J=7.3 Hz,=CH, 1H), 7.46 (d, J=7.3 Hz,=CH, 1H), 7.17 (t, J=7.3 Hz,=CH, 1H), 7.11 (t, J=7.3 Hz,=CH, 1H), 3.21–3.20 (m, CH_2, 2H), 2.55–2.51 (m, CH_2, 2H), 2.14–2.09 (m, CH_2, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 190.9, 153.9, 150.3, 143.4, 141.3, 137.3, 131.4 (CH), 131.3, 130.1, 126.3, 122.8 (CH), 122.2 (CH), 121.3 (CH), 114.2, 113.6, 113.1 (CH), 111.3, 102.7, 102.6, 37.4 (CH_2), 30.9 (CH_2), 22.5 (CH_2). IR (KBr, cm^{-1}) 2490, 2227, 1692, 1628, 1580, 1549, 1506, 1484, 1410, 1354, 1299, 1257, 1224, 1193, 1124, 1063, 1015, 915. Anal. Calcd for $C_{22}H_{12}ClN_3O_3$: C, 65.76; H, 3.01; N, 10.46. Found: C, 66.99; H, 2.90; N, 10.63.

*4.1.19. The reaction of (E)-3-(1H-indol-3-yl)cyclohept-2-enone (**8**) with DDQ.* A solution of **8** (330 mg, 1.46 mmol) and DDQ (333 mg, 1.46 mmol) in $CHCl_3$ (25 mL) was stirred at room temperature for five days. The precipitate was separated via filtration. After the filtration solvent was concentrated under vacuum, suspended in chloroform (15 mL), and filtered through filter paper. The precipitate afforded **43** as yellow powder (157 mg, 24%, mp 239–240 °C). The filtrate was submitted to thin-layer silica gel chromatography eluting with acetone/hexane (20:80). The first band extracted with ethyl acetate (50 mL) gave **44** as yellow oil (165 mg, 25%). The remaining band was extracted by ethyl acetate (50 mL), the solvent was removed. Recrystallization of the combined residues from ethyl acetate/hexane gave **39** as yellow powder (158 mg, 26%, mp 179–180 °C); (*E*)-4-(2-(1*H*-indol-3-yl)-7-oxocyclohept-1-enyl)-5-chloro-3,6-dioxocyclohexa-1,4-diene-1,2-dicarbonitrile (**39**): ^{1}H NMR (400 MHz, Acetone-d_6): δ 10.81 (m, NH, 1H), 7.82 (d, J=1.8 Hz,=CH, 1H), 7.79 (d, J=7.7 Hz,=CH, 1H), 7.47 (dd, J=7.9, 1.1 Hz,=CH, 1H), 7.18–7.10 (m,=CH, 2H), 3.21–3.18 (m, CH_2, 2H), 2.73–2.72 (m, CH_2, 2H), 2.14–2.00 (m, CH_2, 4H). ^{13}C NMR (100 MHz, Acetone-d_6): δ 195.5, 146.4, 139.4, 137.0, 136.9, 128.1, 128.0, 126.5, 122.1, 121.1, 120.3, 114.1, 112.2, 112.1, 102.7, 40.4, 30.4, 24.2, 20.4 (Note: The four resonance signals of quaternary carbons are coinciding in the olefinic area). IR (KBr, cm^{-1}) 3339, 2924, 2218, 1641, 1583. Anal. Calcd for $C_{23}H_{14}C_lN_3O_3$: C, 66.43; H, 3.39; N, 10.11. Found: C, 66.31; H, 3.48; N, 10.01. The existence of two different products was determined in both the first precipitate and first band. But, the structures of these products were yet not characterized.

*4.1.20. Reaction of (E)-3-(1H-indol-3-yl)cyclooct-2-enone (**9**) with DDQ.* A solution of **9** (220 mg, 0.92 mmol) and DDQ (208 mg, 0.92 mmol) in $CHCl_3$ (20 mL) was placed in a glass tube. The tube was sealed and was heated at 50 °C for three days. The solvent was concentrated under vacuum. The crude products were submitted to thin-layer silica gel chromatography eluting with acetone/hexane (30:70). The first band extracted with ethyl acetate (50 mL) gave **43** (170 mg, 40%), which was recrystallized from methanol (yellow crystals, mp 153–154 °C). The second fraction extracted with ethyl acetate (50 mL) afforded **44** as yellow oil (90 mg, 21%). (*Z*)-3-(2-(1*H*-Indol-3-yl)-8-oxocyclooct-2-enyloxy)-4,5-dichloro-6-hydroxyphthalonitrile (**43**): ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.12 (m, NH, 1H), 7.41 (d, J=2.6 Hz,=CH, 1H), 7.26 (d, J=7.6 Hz,=CH, 1H), 7.04 (t, J=7.6 Hz,=CH, 1H), 6.96 (t, J=7.6 Hz,=CH, 1H), 6.25 (t, J=8.7 Hz,=CH, 1H), 6.19 (s, OCH, 1H), 2.83–2.76 (m, CH_2, 1H), 2.48–2.29 (m, CH_2, 3H), 1.93–1.92 (m, CH_2, 2H), 1.70–1.51 (m, CH_2, 1H), 1.49–1.48 (m, CH_2, 1H). APT ^{13}C NMR (100 MHz, DMSO-d_6): δ 208.1 (CO), 154.4, 149.6, 136.8, 134.1 (CH), 134,0, 129.0, 128.6, 125.4, 124.1 (CH), 122.2 (CH), 119.9 (CH), 119.3 (CH), 115.8, 114.1, 114.0, 112.2 (CH), 109.1, 102.0, 86.9 (OCH), 39.0 (CH_2), 27.4 (CH_2), 27.1 (CH_2), 26.4 (CH_2). IR (KBr, cm^{-1}) 3669, 2935, 2863, 2235, 1707, 1560, 1440, 1420, 1357, 1230, 1129, 1089, 1011, 949, 933. Anal. Calcd for $C_{24}H_{17}Cl_2N_3O_3$: C, 61.82; H, 3.67; N, 9.01. Found: C, 62.01; H, 3.92; N, 8.97.

*4.1.21. (Z)-3-(2-(1H-Indol-3-yl)-4-oxocyclooct-2-enyloxy)-4,5-dichloro-6-hydroxyphthalonitrile (**44**).* ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.70 (d, J=2.6 Hz, NH, 1H), 7.80 (d, J=2.6 Hz,=CH, 1H), 7.74 (d, J=7.3 Hz,=CH, 1H), 7.43 (d, J=7.3 Hz,=CH, 1H), 7.17–7.09 (m,=CH, 2H), 6.55 (s,=CH, 1H), 5.91 (t, J=8.3 Hz, OCH, 1H), 2.84–2.78 (m, CH_2, 1H), 2.67–2.64 (m, CH_2, 1H), 2.14–2.12 (m, CH_2, 1H), 1.76–1.52 (m, CH_2, 4H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 201.1, 165.1, 146.9, 141.3, 137.1, 133.2, 132.5, 129.4, 128.4, 126.0, 122.6, 121.1, 120.3, 118.7, 116.1, 112.9, 112.2, 107.5, 96.3, 84.6, 43.6, 31.8, 23.0, 22.8. APT ^{13}C NMR (100 MHz, DMSO-d_6): δ 201.1 (CO), 165.1, 146.9, 141.3, 137.1, 133.2, 132.5, 129.4 (CH), 128.4 (CH), 126.0, 122.6 (CH), 121.1 (CH), 120.3 (CH), 118.7, 116.1, 112.9 (CH), 112.2, 107.5, 96.4, 84.6 (OCH), 43.6 (CH_2), 31.2 (CH_2), 23.0 (CH_2), 22.8 (CH_2). IR (KBr, cm^{-1}) 3665, 2930, 2850, 2235, 1607, 1557, 1443, 1430, 1351, 1238, 1110, 1050, 920. Anal. Calcd for $C_{24}H_{17}Cl_2N_3O_3$: C, 61.82; H, 3.67; N, 9.01. Found: C, 66.99; H, 3.90; N, 9.93.

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Supplementary data

Supplementary data includes ^{1}H and ^{13}C NMR spectra of compounds. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2010.02.081.

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