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Synthesis of a new series of 2-vinylindoles and their cycloaddition reactivity

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ABSTRACT

The regioselective synthesis of 2-vinylindoles was achieved through the use of 4,7-dihydroindole **19**. Reactions of these 2-vinylindoles as 4π-component gave 2,3-disubstitue indoles as well as the expected Diels–Alder products.

1. Introduction

The vinylindole skeleton appears to be an attractive substrate as diene component in Diels–Alder reactions. For instance, the cycloaddition of vinylindoles with carbon- and heteroatomic dienophiles provides indole alkaloids, carbazoles, [*b*]annelated indole derivatives.[1–19] Prudhomme et al. synthesized structural analogs of granulatimide (**1**) and investigated their biological activities as new checkpoint kinase 1 inhibitors (Fig. 1).[20] Some of the corresponding syntheses, such as cycloadducts **2** and **3**, were carried out through Diels–Alder reactions of *N*-Boc-vinylindoles **4** and **5**.

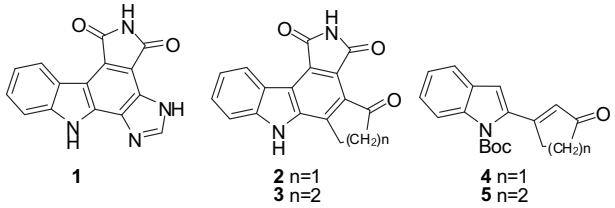
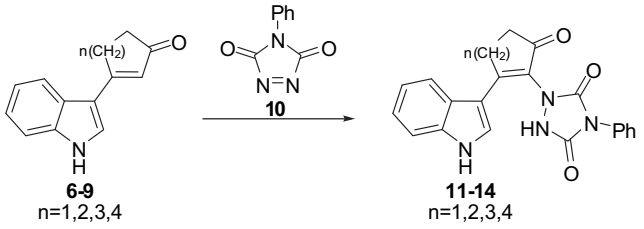


Figure 1. Structures of granulatimide (**1**), vinilyindoles **4** and **5**, and their cycloadducts **2** and **3**.

Recently, we have synthesized new indoles **6–9** containing 3-vinyl functionality and investigated their reactivity (Scheme 1).[21] The Diels–Alder reactivity of the 3-vinylindoles toward various dienophiles leads to unusual Morita–Baylis–Hillman-type products **11–14**, instead of the expected cycloadducts. Interesting mechanistic and synthetic findings have encouraged us to investigate the reactivity and synthesis of 2-vinylindoles **15–18** (Fig. 2). Herein, we report our results.



Scheme 1.

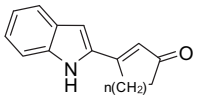


Figure 2. Structures of targeted 2-vinylindoles **15–18**.

Although there are numerous methods to prepare 3-substitue indoles, a limited number of methods have been reported for access to 2-substituted indoles. An indirect method for the synthesis of 2-acylindoles from 4,7-dihydroindole **19** was improved by Joule et al.[22] Recently, we have reported on a new pathway to 2-substituted indoles.[23,24] Our method contains Michael addition reactions between 4,7-dihydroindole **19** and some α,β-unsaturated compounds followed by dehydrogenation. The Michael reaction is one of the most important and reliable carbon–carbon and carbon–heteroatom bond-forming methods in organic synthesis.[25] In addition, this type of reaction has been investigated for the functionalization of indoles.[26–34] In fact, our methodology has been used for the synthesis of asymmetric 2-substituted indoles and functionalizations of indole.[35–43]

2. Results and discussions

To synthesize 2-vinylindole derivatives **15–18**, firstly, 4,7-dihydroindole **19**, the Birch reduction product of indole was obtained.

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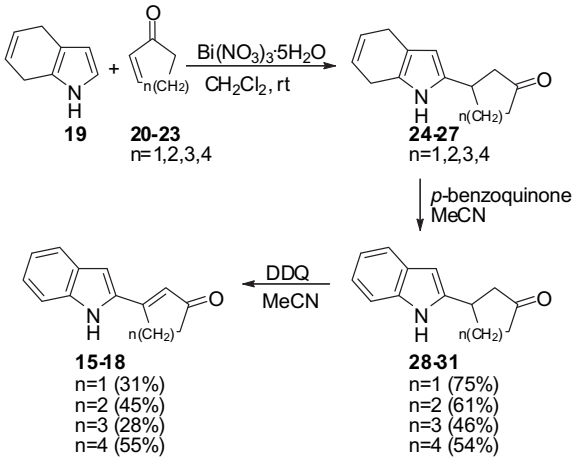
$Bi(NO_3)_3 \cdot 5H_2O$-catalyzed reaction by cyclopent-2-one of the reduced indole **19** gave Michael adduct **24** (Scheme 2). In situ reaction of adduct **24** with *p*-benzoquinone in acetonitrile yielded oxidation product **28**. In a similar manner we synthesized the corresponding compounds **25**–**27** by starting from the appropriate unsaturated cyclic ketone. After key compounds **24**–**27** were synthesized, the preparation of the targeted indoles **15**–**18** was achieved by the oxidation of 2-substitue indoles **24**–**27** with DDQ (2,3-dichloro-5,6-dicyanobenzoquinone), which is a stronger oxidant (Scheme 2). The structures for vinylindoles **15**–**18** are based on ^1H, ^{13}C NMR, NOE ^1H NMR, IR, and elemental analysis. For example, vinylindole **16** was characterized by the presence of a NH signal at δ 9.04 ppm, four benzene protons at 7.45–7.10 ppm, C3–H in the pyrrole ring at 6.95 ppm (d, J=1.1 Hz), and alpha olefinic proton in cyclohexen-2-one ring at 6.49 ppm (s). Furthermore CH_2 protons resonated at 2.86 (t, J=5.7 Hz), 2.55 (t, J=5.7 Hz), and 2.18 (p, J=5.7 Hz). The observed coupling constant (^4J=1.1 Hz) between the NH and C3–H in the pyrrole ring of **16** confirms the presence of substitution at the C-2 position. The olefin geometry and placement of the substitution in the pyrrole were established by differential ^1H NMR nuclear Overhauser enhancement (NOE) experiments. When the olefinic proton (6.49 ppm) of **16** was irradiated, the NH at δ 9.04 ppm gave a NOE signal, whereas a NOE was not observed between C3–H (7.92 ppm) and olefinic (6.49 ppm) signals.

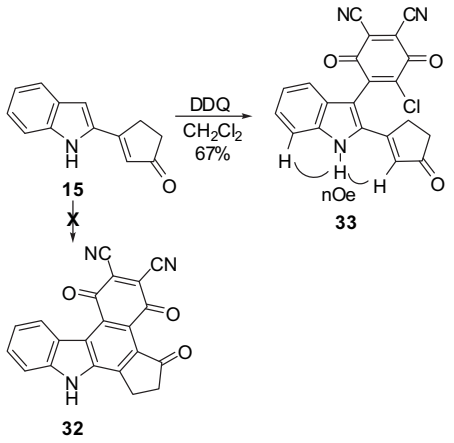


Scheme 2.

Subsequently, our experiments focused on the cycloaddition of 2-vinylindoles **15**–**18**. When vinylindoles **15**–**18** were treated with dieonophiles, such as maleic anhydride, dimethyl acetylenedicarboxylate, tetracyanoethylene, naphthoquinone, and *p*-benzoquinone under different conditions, unreacted starting materials were recovered in every case. Due to the observed positive results, we fully concentrated on the reaction of the vinylindoles with *N*-phenyltriazolinedione (PTAD; **10**) and DDQ.

Vinylindole **15** and DDQ were refluxed in methylene chloride for five days (Scheme 3). After purification, all data showed that the product is not exactly a cycloaddition product **32**. The structure of Michael-type adduct **33** was especially assigned on the basis of the NOE observations. Irradiation of the NH at δ 11.61 ppm produced a strong NOE for one of the aromatic protons at 7.42 ppm and the olefinic proton in cyclopenten-2-one ring at 6.48 ppm. Similarly, Michael adducts **34** and **35** were obtained from the reaction of vinylindoles **16** and **18** with DDQ (Fig. 3).

Next, the reaction of **16** with PTAD was carried out in dichloromethane at room temperature for 24 h to provide Michael adduct **36** (Scheme 4). Under similar conditions, we obtained Michael adduct **37** from the reaction with PTAD of vinylindole **15** (Scheme 4). The relative configuration for Michael adducts **36** and **37** was confirmed by ^1H NMR, ^{13}C NMR, NOE ^1H NMR, IR, and elemental analysis.



Scheme 3.

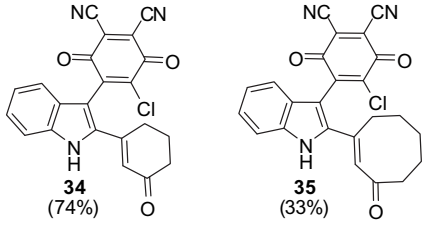
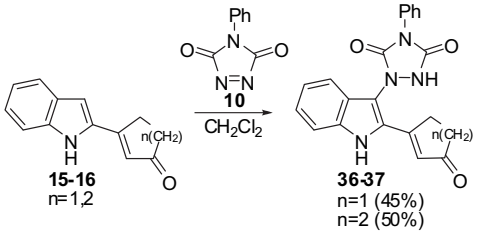
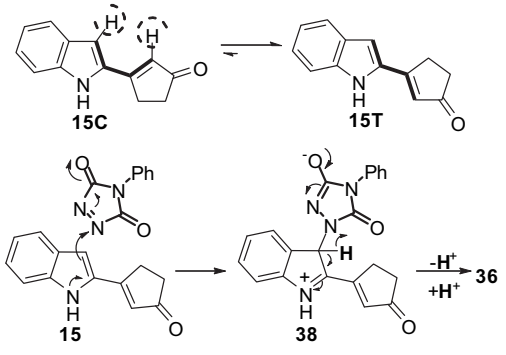


Figure 3. 2,3-Disubstitue indoles **34** and **35**.



Scheme 4.

Clearly, the dienophiles are not captured in cisoid conformation in vinylindoles **15**–**18**. On the other hand, transoid (T) structures for vinylindoles **15**–**18** are more stable than cisoid (C) structures (Scheme 5). We assume that the dynamic equilibrium for 2-vinylindoles is toward transoid structures due to the steric repulsion between C3–H of indole ring and alpha-proton of cycloalken-2-one ring. A reasonable mechanism leading to the formation of Michael addition products is shown below, where it may well proceed via zwitterion **38** (Scheme 5).



Scheme 5.

3. Conclusions

In summary, we synthesized new 2-vinylindoles. It is remarkable that Diels–Alder reactivity of these vinylindoles did not form the expected cycloaddition products or unusual Morita–Baylis–Hillman-type products observed for 3-vinyl analogs. However, Michael addition products, 2,3-disubstitue indoles, were obtained.

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 FT-IR 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.

*4.1.1. 3-(1H-Indol-2-yl)cyclopentanone (**28**).* A solution of 4,7-dihydro-1*H*-indole (**19**; 500 mg, 4.20 mmol), cyclopent-2-en-1-one (**20**; 345 mg, 4.20 mmol) and catalytic amount of $Bi(NO_3)_3\cdot 5H_2O$ in CH_2Cl_2 (15 mL) was stirred magnetically at room temperature for 16 h. After completion of the reaction, the mixture was diluted with dichloromethane (30 mL) and washed with water (2×50 mL), and organic phase was dried over Na_2SO_4. The crude product (790 mg; 93%) was dissolved in CH_2Cl_2 (15 mL) and *p*-benzoquinone (636 mg, 5.88 mmol) was added. The mixture was stirred at the room temperature for two days. After completion of the reaction, the solvent was evaporated and crude product was dissolved with ethyl acetate (30 mL) and the organic phase was washed with NaOH (2 N, 2×30 mL), brine (30 mL), and dried over Na_2SO_4. The solvent was evaporated to give 3-(*1H*-indol-2-yl)cyclopentanone (**28**[23]; 590 mg, 75%).

*4.1.2. 3-(1H-Indol-2-yl)cyclohexanone (**29**).* 3-(1*H*-Indol-2-yl)cyclohexanone (**29**[23]; 145 mg, 61%) was prepared from 4,7-dihydro-1*H*-indole (**19**; 200 mg, 1.67 mmol) and cyclohex-2-en-1-one (**21**, 161 mg, 1.67 mmol) as described for the preparation of **28**.

*4.1.3. 3-(1H-Indol-2-yl)cycloheptanone (**30**).* The Micheal adduct **30** was prepared as described for **28**. For **30** (492 mg, 46%, dark brown crystals from CH_2Cl_2/hexane, mp 134–135 °C): ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.12 (m, NH, 1H), 7.54 (d, *J*=7.4 Hz, =CH, 1H), 7.30 (d, *J*=7.4 Hz, =CH, 1H), 7.14 (br t, *J*=7.4 Hz, =CH, 1H), 7.08 (br t, *J*=7.4 Hz, =CH, 1H), 6.27–6.26 (m, =CH, 1H), 3.17–3.11 (m, CH, 1H), 2.97 (dd, *J*=14.2, 10.4 Hz, A part of AB system, CH_2, 1H), 2.88 (dd, *J*=14.2, 1.6 Hz, B part of AB system, CH_2, 1H), 2.60–2.57 (m, CH_2, 2H), 2.29–2.45 (m, CH_2, 1H), 2.08–2.00 (m, CH_2, 1H), 1.98–1.92 (m, CH_2, 1H), 1.89–1.81 (m, CH_2, 1H), 1.78–1.61 (m, CH_2, 1H), 1.59–1.52 (m, CH_2, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 213.4, 142.9, 136.1, 128.6, 121.7, 120.3, 120.0, 110.8, 98.7, 49.6, 44.2, 37.1, 35.9, 28.5, 24.2. IR (KBr, cm^{-1}) 3390, 3053, 2927, 2857, 1686, 1617, 1584, 1544, 1457, 784, 746. Anal. Calcd for $C_{15}H_{17}NO$: C, 79.26; H, 7.54; N, 6.16. Found: C, 79.42; H, 7.41; N, 7.39.

*4.1.4. 3-(1H-Indol-2-yl)cyclooctanone (**31**).* The Micheal adduct **31** was synthesized as described for **28**. For **31** (220 mg, 54%, dark brown crystals from CH_2Cl_2/hexane, mp 155–156 °C): ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.37 (m, NH, 1H), 7.54 (d, *J*=7.9 Hz, =CH, 1H), 7.32 (dd, *J*=7.9, 1.1 Hz, =CH, 1H), 7.16–7.06 (m, =CH, 2H), 6.27–6.26 (m, =CH, 1H), 3.38–3.33 (m, CH, 1H), 2.96–2.90 (m, CH_2, 1H), 2.75–2.74 (m, CH_2, 1H), 2.72–2.43 (m, CH_2, 2H), 2.12–2.04 (m, CH_2, 2H), 1.98–1.93 (m, CH_2, 1H), 1.77–1.57 (m, CH_2, 4H), 1.45–1.41 (m, CH_2, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 216.2, 143.4, 136.0, 128.6, 121.6, 120.2, 120.0, 110.9, 98.5, 46.1, 44.0, 38.4, 33.5, 28.1, 24.4, 24.4. IR (KBr, cm^{-1}) 3335, 2955, 1678, 1450, 1220. Anal. Calcd for $C_{16}H_{19}NO$: C, 79.63; H, 7.94; N, 5.80. Found: C, 79.91; H, 7.79; N, 5.82.

*4.1.5. 3-(1H-Indol-2-yl)cyclopent-2-enone (**15**).* A solution of **28** (516 mg, 2.59 mmol) and DDQ (590 mg, 2.59 mmol) in 20 mL of dry benzene was stirred at 0 °C for 2 h. After the benzene was evaporated, the crude product was dissolved in CH_2Cl_2 (50 mL) and organic phase was washed with $NaHCO_3$ (2×50 mL), water (2×25 mL) and dried over Na_2SO_4. After removal of the solvent, crude product **15** was recrystallized from acetone/hexane. (157 mg, 31%, pale yellow crystals, mp 179–180 °C): ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.66 (m, NH, 1H), 7.60 (d, *J*=7.9 Hz, =CH, 1H), 7.41 (d, *J*=7.9 Hz, =CH, 1H), 7.22 (t, *J*=7.9 Hz, =CH, 1H), 7.05–7.02 (m, =CH, 2H), 6.55 (s, =CH, 1H), 3.04–3.02 (m, CH_2, 2H), 2.44–2.42 (m, CH_2, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 208.7, 165.6, 138.9, 133.8, 128.4, 125.2, 125.0, 122.1, 120.6, 112.4, 106.3, 35.2, 28.4. IR (KBr, cm^{-1}) 3251, 2919, 2230, 1653, 1590, 1451, 1342, 1280, 1196, 1079. Anal. Calcd for $C_{13}H_{11}NO$: C, 79.16; H, 5.62; N, 7.10. Found: C, 79.13; H, 5.41; N, 7.38.

*4.1.6. 3-(1H-Indol-2-yl)cyclohex-2-enone (**16**).* The vinylindole **16** was prepared as described for **15**. For **16** (65 mg, 45%, pale pink crystals, mp 201–203 °C from ether): ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.04 (m, NH, 1H), 7.45 (dd, *J*=8.2, 0.9 Hz, =CH, 1H), 7.30–7.26 (m, =CH, 1H), 7.14–7.10 (m, =CH, 1H), 6.95 (d, *J*=1.1 Hz, =CH, 1H), 6.49 (s, =CH, 1H), 2.86 (t, *J*=5.7 Hz, CH_2, 2H), 2.55 (t, *J*=5.7 Hz, CH_2, 2H), 2.18 (p, *J*=5.7 Hz, CH_2, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.8, 150.7, 138.2, 135.5, 128.6, 125.1, 121.7, 121.1, 120.8, 111.7, 106.9, 37.8, 26.8, 22.7. IR (KBr, cm^{-1}) 3305, 2929, 2364, 1641, 1591. Anal. Calcd for $C_{14}H_{13}NO$: C, 79.59; H, 6.20; N, 6.63. Found: C, 79.73; H, 6.47; N, 7.39.

*4.1.7. 3-(1H-Indol-2-yl)cyclohept-2-enone (**17**).* The vinylindole **17** was prepared as described for **15**. For **17** (192 mg, 28%, dark brown crystals from acetone/hexane, mp 76–77 °C): ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.42 (m, NH, 1H), 7.53 (d, *J*=7.9 Hz, =CH, 1H), 7.33 (d, *J*=7.9 Hz, =CH, 1H), 7.14 (t, *J*=7.9 Hz, =CH, 1H), 7.00–6.96 (m, =CH, 2H), 6.55 (s, =CH, 1H), 2.94–2.91 (m, CH_2, 2H), 2.60–2.57 (m, CH_2, 2H), 1.85–1.80 (m, CH_2, 2H), 1.78–1.73 (m, CH_2, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 203.7, 148.0, 138.9, 138.1, 128.6, 125.8, 124.3, 121.6, 120.3, 112.1, 106.1, 42.0, 28.7, 25.1, 21.2. IR (KBr, cm^{-1}) 3311, 2936, 2863, 1631, 1591, 1510, 1448, 1418, 1285, 1183, 798, 749. Anal. Calcd for $C_{15}H_{15}NO$: C, 79.97; H, 6.71; N, 6.22. Found: C, 80.13; H, 6.82; N, 6.01.

*4.1.8. (E)-3-(1H-Indol-2-yl)cyclooct-2-enone (**18**).* The vinylindole **18** was prepared as described for **15**. For **18** (120 mg, 55%, yellow crystals from acetone/hexane, mp 163–164 °C): ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.72 (m, NH, 1H), 7.60 (br d, *J*=8.0 Hz, =CH, 1H), 7.38 (dd, *J*=8.0, 0.7 Hz, =CH, 1H), 7.26 (td, *J*=8.0, 1.1 Hz, =CH, 1H), 7.10 (td, *J*=8.0, 1.1 Hz, =CH, 1H), 6.93 (d, *J*=1.5 Hz, =CH, 1H), 6.66 (s, =CH, 1H), 3.19 (t, *J*=7.0 Hz, CH_2, 2H), 2.96 (t, *J*=7.3 Hz, CH_2, 2H), 1.87–1.78 (m, CH_2, 4H), 1.66–1.60 (m, CH_2, 2H). ^{13}C NMR (100 MHz DMSO-d_6): δ 202.2, 143.5, 138.9, 138.6, 128.7, 128.0 (CH), 124.2 (CH), 121.5 (CH), 120.3 (CH), 112.2 (CH), 106.0 (CH), 42.8 (CH_2), 29.1 (CH_2), 25.5 (CH_2), 23.4 ($2CH_2$). IR (KBr, cm^{-1}) 3333, 2924, 1737, 1617, 1578, 1364, 1216. Anal. Calcd for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85. Found: C, 80.13; H, 7.01; N, 5.97.

*4.1.9. 4-Chloro-3,6-dioxo-5-(2-(3-oxocyclopent-1-enyl)-1H-indol-3-yl)cyclohexa-1,4-diene-1,2-dicarbonitrile (**33**).* A solution of **15** (155 mg, 0.79 mmol) and DDQ 178 mg (0.79 mmol) in 20 mL CH_2Cl_2 was refluxed for five days. After CH_2Cl_2 was evaporated, acetone (15 mL) was added to the reaction mixture. The solution with acetone was decanted and the precipitate was dried on paper filter was dried over room conditions to give **33** (206 mg, 67%, yellow

crystals, mp 232–233 °C): ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.61 (br s, NH, 1H), 7.42 (d, J=7.9 Hz, =CH, 1H), 7.22 (t, J=7.9 Hz, =CH, 1H), 6.91 (t, J=7.9 Hz, =CH, 1H), 6.73 (d, J=7.9 Hz, =CH, 1H), 6.58 (s, =CH, 1H), 3.16–3.14 (m, CH_2, 2H), 2.46–2.44 (m, CH_2, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 208.3, 163.4, 157.2, 147.2, 137.3, 135.7, 132.7, 130.9, 126.3, 125.7, 121.2, 118.0, 114.6, 113.4, 112.8, 106.8, 102.5, 34.9, 29.3. IR (KBr, cm^{-1}) 3288, 2924, 2224, 1650, 1586, 1446. Anal. Calcd for $C_{21}H_{10}ClN_3O_3$: C, 65.04; H, 2.60; N, 10.84. Found: C, 64.93; H, 2.89; N, 11.03.

*4.1.10. 4-Chloro-3,6-dioxo-5-(2-(3-oxocyclohex-1-enyl)-1H-indol-3-yl)cyclohexa-1,4-diene-1,2-dicarbonitrile (**34**).* The Michael adduct **34** was prepared as described for **33**. For **34** (140 mg, 74%, orange crystals from acetone, mp 230–232 °C): ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.54 (br s, NH, 1H), 7.39 (d, J=7.8 Hz, =CH, 1H), 7.17 (t, J=7.8 Hz, =CH, 1H), 6.88 (t, J=7.8 Hz, =CH, 1H), 6.68 (d, J=7.8 Hz, =CH, 1H), 6.57 (s, =CH, 1H), 2.92 (t, J=5.7 Hz, CH_2, 2H), 2.38 (t, J=6.6 Hz, CH_2, 2H), 2.08–2.01 (m, CH_2, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 198.9, 156.8, 150.0, 147.6, 136.5, 135.1, 132.6, 130.8, 125.1, 123.7, 123.3, 121.0, 118.5, 117.6, 114.5, 113.2, 112.7, 106.5, 102.8, 37.6, 27.0, 22.8. IR (KBr, cm^{-1}) 3355, 2935, 2229, 1711, 1619, 1583, 1412, 1356, 1239. Anal. Calcd for $C_{22}H_{12}ClN_3O_3$: C, 65.76; H, 3.01; N, 10.46. Found: C, 65.90; H, 3.07; N, 10.38.

*4.1.11. (E)-4-Chloro-3,6-dioxo-5-(2-(3-oxocyclooct-1-enyl)-1H-indol-3-yl)cyclohexa-1,4-diene-1,2-dicarbonitrile (**35**).* The vinylindole **35** was prepared as described for **33**. For **35** (60 mg, 33%, yellow crystals from acetone, mp 185–186 °C): ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.38 (m, NH, 1H), 7.36 (dd, J=7.2 Hz, 1.0 Hz, =CH, 1H), 7.15 (td, J=7.2, 1.0 Hz, =CH, 1H), 6.88 (td, J=7.2, 1.0 Hz, =CH, 1H), 6.71 (s, =CH, 1H), 6.67 (d, J=7.2 Hz, =CH, 1H), 3.22 (t, J=6.6 Hz, CH_2, 2H), 2.82 (t, J=7.2 Hz, CH_2, 2H), 1.74–1.69 (m, CH_2, 4H), 1.53–1.52 (m, CH_2, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 202.5, 157.4, 147.0, 142.6, 135.6, 134.5, 132.3, 131.11, 131.1, 125.5, 124.6, 120.8, 118.8, 117.3, 114.9, 113.1, 112.8, 105.9, 102.2, 43.0, 28.9, 24.5, 23.7, 23.5. IR (KBr, cm^{-1}) 3338, 2941, 2302, 2235, 1622, 1580, 1530, 1415, 1348, 1328, 1269, 1239, 1194, 1169. Anal. Calcd for $C_{24}H_{16}ClN_3O_3$: C, 67.06; H, 3.75; N, 9.78. Found: C, 67.31; H, 3.62; N, 10.01.

*4.1.12. 1-(2-(3-Oxocyclopent-1-enyl)-1H-indol-3-yl)-4-phenyl-1,2,4-triazolidine-3,5-dione (**36**).* A solution of **15** (160 mg, 0.81 mmol) and PTAD (142 mg, 0.81 mmol) in CH_2Cl_2 (20 mL) was stirred magnetically at room temperature for 24 h. After CH_2Cl_2 was evaporated, acetone (15 mL) was added to the reaction mixture. The solution with acetone was decanted and the precipitate was filtered and dried to give **36** (135 mg, 45%, pale yellow crystals, mp 285–286 °C): ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.15 (m, NH, 1H), 11.46 (m, NH, 1H), 7.61–7.50 (m, =CH, 6H), 7.43 (br t, J=7.3 Hz, =CH, 1H), 7.33 (br t, J=7.3 Hz, =CH, 1H), 7.16 (br t, J=7.3 Hz, =CH, 1H), 6.72 (d, J=1.5 Hz, =CH, 1H), 3.28–3.15 (m, CH_2, 2H), 2.50–2.48 (m, CH_2, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 208.9, 163.5, 152.0, 146.1, 136.4, 130.6, 130.3, 130.2, 129.5, 128.3, 127.5, 126.9, 125.7, 125.2 121.5, 119.7, 113.1, 35.1, 28.6. IR (KBr, cm^{-1}) 3225, 2901, 2847, 1752, 1603, 1558, 1468, 1392, 1258, 1048, 987. Anal. Calcd for $C_{21}H_{16}N_4O_3$: C, 67.73; H, 4.33; N, 15.05. Found: C, 67.95; H, 4.30; N, 14.93.

*4.1.13. 1-(2-(3-Oxocyclohex-1-enyl)-1H-indol-3-yl)-4-phenyl-1,2,4-triazolidine-3,5-dione (**37**).* The Michael adduct **37** was prepared as described for **36**. For **37** (90 mg, 50%, pale yellow crystals from acetone, mp 225–226 °C): ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.95 (m, NH, 1H), 7.56–7.41 (m, =CH, 7H), 7.28 (dd, J=8.2, 7.2 Hz, =CH, 1H), 7.12 (t, J=7.2 Hz, =CH, 1H), 6.51 (d, J=0.8 Hz, =CH, 1H), 2.87 (t, J=5.7 Hz, CH_2, 2H), 2.41 (t, J=6.4 Hz, CH_2, 2H), 2.07–2.06 (m, CH_2, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 199.1, 152.5, 152.0, 149.9, 135.8, 133.9, 132.5, 129.6, 128.8, 127.1, 125.6, 125.4, 125.2, 121.5, 119.1, 113.0, 112.4, 37.6, 26.5, 22.9. IR (KBr, cm^{-1}) 3338, 2918, 2857, 1776, 1700, 1619, 1577, 1488, 1412, 1258, 1127. Anal. Calcd for $C_{22}H_{18}N_4O_3$: C, 68.38; H, 4.70; N, 14.50. Found: C, 68.63; H, 4.68; N, 14.56.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2010.02.080.

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