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New Reactions of Contraction of the *o*-Quinone Ring with the Formation of Derivatives of 2-(2-Indolyl)-cyclopenta[b]pyrrole-3,4-diones and Pyrindino[1,2-a]indoles: A Combined Experimental and Density Functional Theory Investigation

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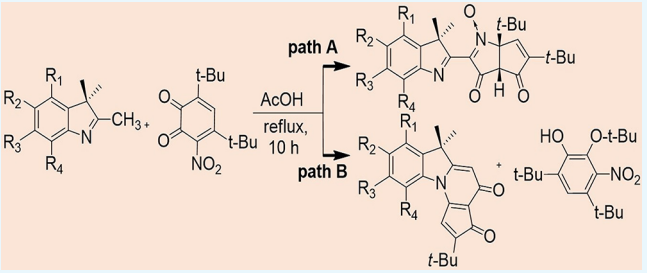
ABSTRACT: Derivatives of 2-(2-indolyl)-cyclopenta[b]pyrrole-3,4-diones and pyrindino[1,2-a]indoles were synthesized by a new reaction of contraction of the *o*-quinone ring, and their structures were investigated by X-ray crystallography and nuclear magnetic resonance spectroscopy. The mechanisms of the reactions were suggested based on density functional theory calculations of the critical parts of the potential energy surfaces.



INTRODUCTION

Due to their diverse biological (antibacterial, antimicrobial, anticancer, antidiabetic, and others) activities, derivatives of indole including those with fused aromatic and alicyclic rings attract considerable interest.[1−9] The compounds obtained in this work contain skeletal fragments of pyrido[1,2]indoles, HIV-1 inhibitors, and the alkaloid cantinone, known for its antibacterial and antimalarial properties.[10−12] The thoroughly studied approaches to the synthesis of polycyclic indole systems are based on catalytic intramolecular cyclization reactions of 2-(2-bromobenzyl) indoles, *N*-bromobenzylindoles (cat. Cu(I and II)), *N*-alkylindoles (cat. Co(II)), and indolyl-1,6-enins (indolyl-1,6-enynes) (cat. Au(I)).[13−15] An efficient method for the synthesis of polycyclic indoles is presented by the acid-catalyzed reactions of *o*-(tosylamino)benzyl alcohols with furans (cat. TfOH).[16] Cascade reactions of bromophenyl and iodobenzyl indolines with alkynes in the presence of Pd(II) salts afford indolines with condensed six- or seven-membered rings.[17]

In recent times, some scientists have demonstrated that the product structure made up from the reactions of 4,5,6,7-tetrachloro-1,2-benzoquinone (*o*-chloranil) and 3,5-di(*tert*-butyl)-1,2-benzoquinone depends on the substituents on the 1,2-benzoquinone ring.[18] The results of the reaction of 2,3,3-trimethylindoline **1a** with *o*-chloranil **2** perform the process of opening 1,2-benzoquinone to create the product 2-(2-indolyl)-1,3-tropolones **3**, while the reaction of **1a** with 3,5-di(*tert*-butyl)-1,2-benzoquinone **4** forms derivatives of indolo[1,2-a]indolines **5** (Scheme 1).[19]

In this paper, we report the synthesis of two new polycyclic indole systems **7** and **8** obtained in the course of the *o*-quinone ring contraction reaction by refluxing of 2,3,3-trimethylindoline derivatives **1** with 4,6-di(*tert*-butyl)-3-nitro-1,2-benzoquinone **6** in glacial acetic acid for 10 h. 2-*tert*-Butoxy-4,6-di(*tert*-butyl)-3-nitrophenol **9** was also isolated as a by/side product of this reaction (Scheme 2). Specific details of the reaction procedures are given in the Supporting Information.

RESULTS AND DISCUSSION

Experimental Results. Total yields (40−50%) of final products **7** and **8** were achieved with a double excess of quinone **6**. The relatively low yields of the desired products are caused by resinification of the reaction mixture and the formation of difficult-to-isolate byproducts with unidentified structures. Lower yields (16%) of polycyclic indole systems **8c** are probably due to the steric effect of the condensed benzene ring being in the same plane as the pyridine fragment.

The structure of compounds **7**−**9** obtained by us was confirmed by ^{1}H and ^{13}C NMR data, IR spectroscopy, and mass spectrometry. In the ^{1}H NMR spectra of compounds **7**, the

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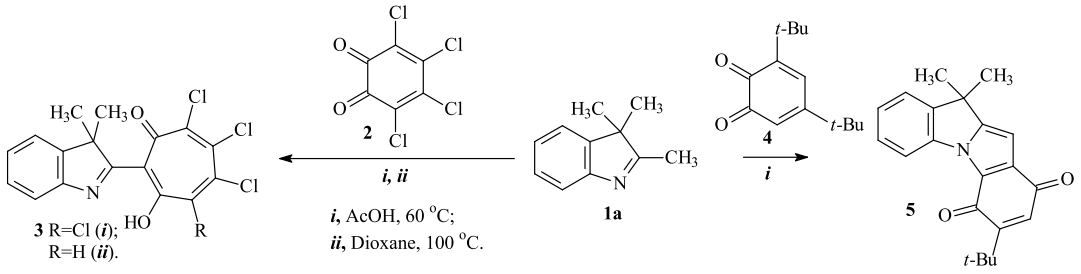
Scheme 1. General Scheme of the Synthesis of Indolo[1,2-a]indolines



signal of the bridging proton of the bicyclic product is observed in the range of δH 3.74−3.78 ppm in the form of a narrow singlet peak. The ^{1}H NMR spectrum of polycyclic indoles **8** is characterized by the presence of signals from the protons of the pyridine ring at δH 6.6 and 7.4 ppm in the form of narrow singlet peaks. The IR spectra of products **7** and **8** are characterized by the presence of absorption bands of vibrations of carbonyl groups in the regions of 1730 and 1690 cm^{-1} for **7** and 1700 and 1645 cm^{-1} for **8**.

In contrast to the known approaches to the synthesis of polycyclic indoles, the new reaction of narrowing the *o*-quinone ring is not optimized. Despite the relatively low yield of target products **7** and **8** caused by the severe conditions of the synthesis, the advantage of the proposed process is the availability and low cost of the initial reagents.

Molecular structures of 5,6a-di(*tert*-butyl)-2-(3,3-dimethylindol-2-yl)-1-*N*-oxy-3a,6a-dihydro-cyclopenta[b]pyrrole-3,4-dione **7a**, 13,13-dimethyl-9-*tert*-butyl-13*H*-pyrindino[1,2-a]-benzo[e]indole-10,11-dione **8b**, and 2-*tert*-butoxy-4,6-di(*tert*-butyl)-3-nitrophenol **9** have been determined by X-ray structural analysis (Figures 1−3).

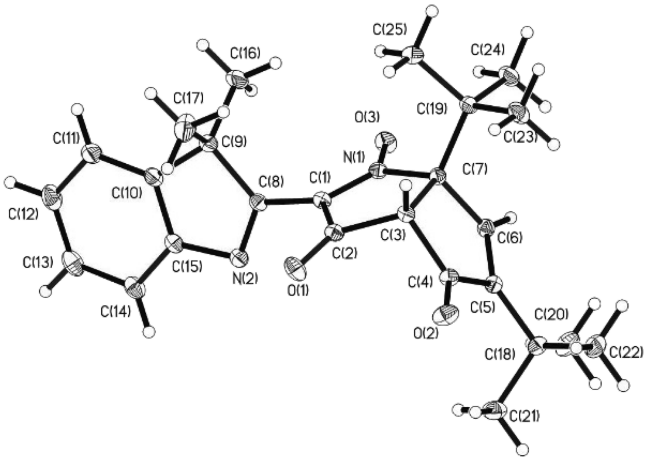


Figure 1. Molecular structure of 5,6a-di(*tert*-butyl)-2-(3,3-dimethylindol-2-yl)-1-*N*-oxy-3a,6a-dihydro-cyclopenta[b]pyrrole-3,4-dione **7a**. Thermal ellipsoids are drawn on the 50% probability level.

The main structural parameters of these compounds are given in the Supporting Information.

Theoretical Calculations. The reaction mechanism for the formation of 5,6a-di(*tert*-butyl)-2-(3,3-dimethylindol-2-yl)-1-*N*-oxy-3a,6a-dihydro-cyclopenta[b]pyrrole-3,4-dione **7a**, pyrindino[1,2-a]indole **8a**, and 2-*tert*-butoxy-4,6-di(*tert*-butyl)-3-nitrophenol **9** has been elucidated by means of calculations using the density functional theory (DFT) method with the PBE0 functional. The 6-311G(d,p) basis set was used to optimize geometries, and their single point energies were calculated at the PBE0/6-311++G(d,p) level. Results of the calculations are given in Figures 4−7, principal reaction stages are portrayed in Schemes 2−7, and the optimized structures of all transition states are shown in Figure S1 (SI).

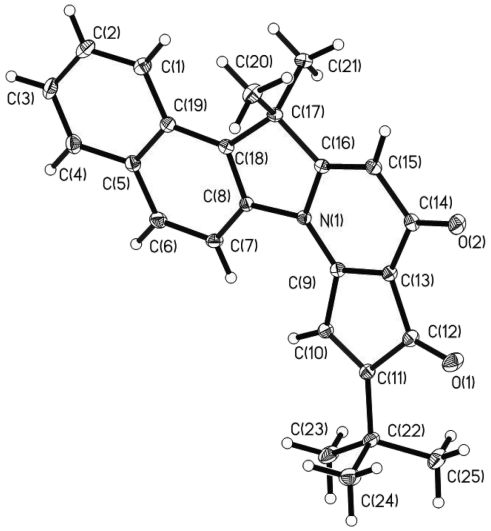


Figure 2. Molecular structure of 13,13-dimethyl-9-*tert*-butyl-13*H*-pyrindino[1,2-a]benzo[e]indole-10,11-dione **8b**. Thermal ellipsoids are drawn on the 50% probability level.

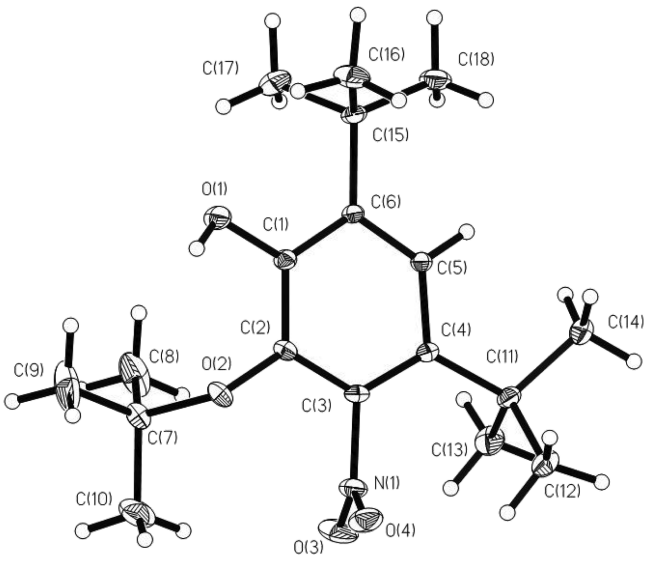


Figure 3. Molecular structure of 2-*tert*-butoxy-4,6-di(*tert*-butyl)-3-nitrophenol **9**. Thermal ellipsoids are drawn on the 50% probability level.

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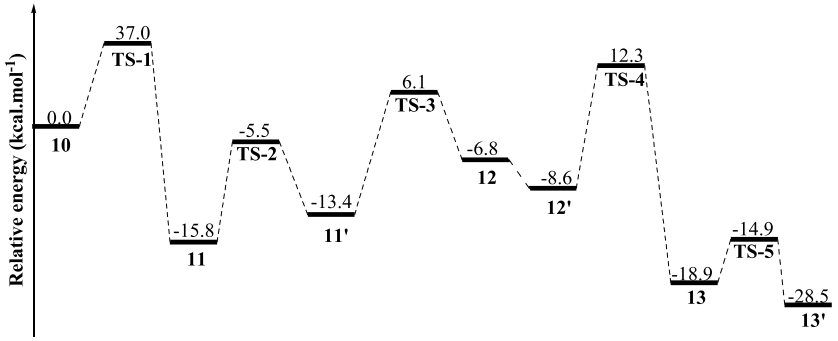

Figure 4. PES of the reactions of Scheme 3.

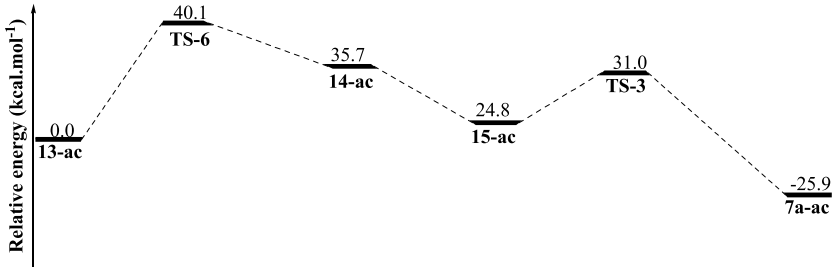

Figure 5. PES of the reactions of Scheme 4.

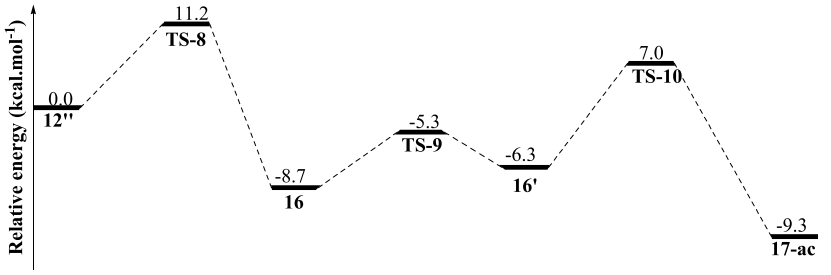

Figure 6. PES of the reactions of Scheme 5.

The presence of 2-*tert*-butoxy-4,6-di(*tert*-butyl)-3-nitrophenol **9** as a byproduct may be evidence of participation of 4,6-di(*tert*-butyl)-3-nitro-1,2-benzoquinone **6** in the oxidative dealkylation of the intermediate products in the course of the formation of pyrindino[1,2-a]indoles **8a−c**. The 2-*tert*-butylcyclopenta-2-enone fragment can be formed by the contraction of the *o*-quinone cycle of quinone **6**. A similar type of structural transformation of the *o*-quinone cycle occurs during photodecarbonylation of 1,2-benzoquinones and is also a result of the interaction of 3,5-di(*tert*-butyl)-1,2-benzoquinone or 3,4,5,6-tetrachloro-1,2-benzoquinone with hydrogen peroxide in the presence of catalytic amounts of iodine giving rise to 2,4-di(*tert*-butyl)-cyclopentadienone and 2,3,4,5-tetrachloro-cyclopentadienone, respectively.[20,21]

The intermediate **10** (Scheme 3), formed as a result of aldol condensation of **1** with **6**, was taken as a starting structure for the subsequent series of transformations leading to **7** and **8**.[22]

The first stage of the reaction, i.e., contraction of the *o*-quinone cycle with an activation barrier of 37.0 kcal/mol, leads to cyclopentadiene derivative **11**. This process is accompanied by the proton transfer from the hydroxyl group to the carbonyl oxygen. The heterocyclic fragment of **11** at the subsequent reaction step almost freely (the energy barrier is 10.2 kcal/mol) rotates around the C−C bond, in such a way that its carbonyl group becomes located above the five-membered ring (structure **11′**). The subsequent [1,2]-sigmatropic shift of the heterocyclic group (with an activation barrier of 19.5 kcal/mol) leads to the formation of the intermediate **12**. At this point, the reaction path is divided into the two channels leading to products **7** and **8**.

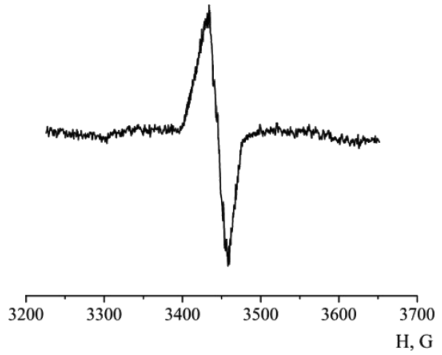

Figure 7. EPR spectrum of the solution of 2,3,3-trimethylindoline **1a** (0.03 mL, 0.2 mmol) and 4,6-di(*tert*-butyl)-3-nitro-1,2-benzoquinone **6** (0.106 g, 0.4 mmol) in glacial acetic acid (0.5 mL) recorded after boiling of the reaction mixture in a sealed ampoule for 1 h.

The reason for this branching is a possibility of the sigmatropic shifts of a nitro group into two adjacent positions of the five-membered ring to form two isoenergy intermediates.

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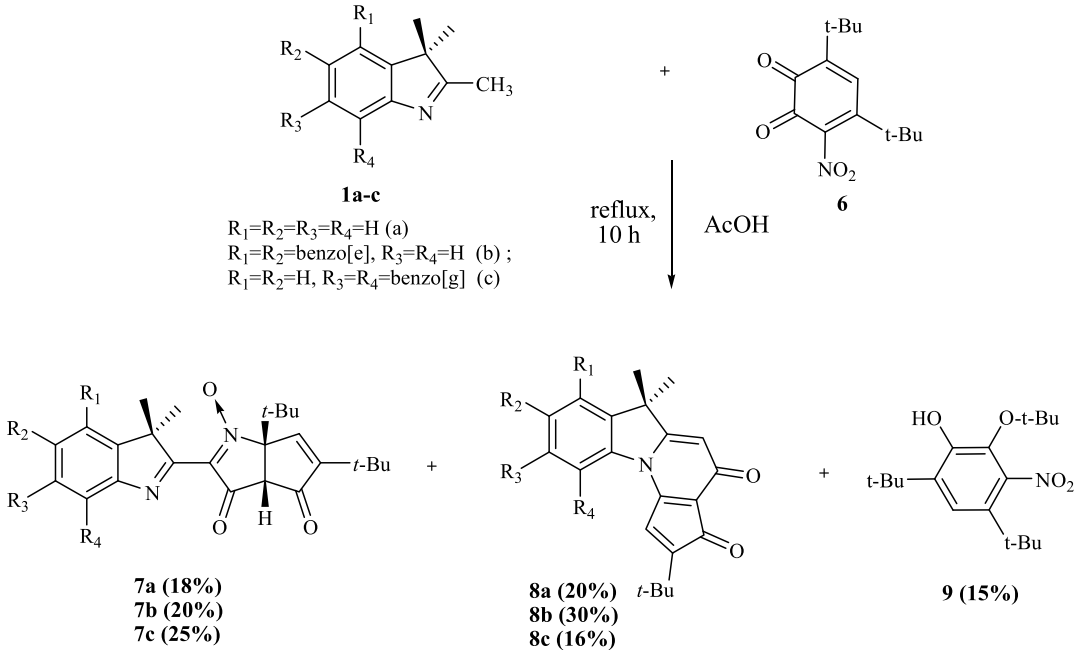
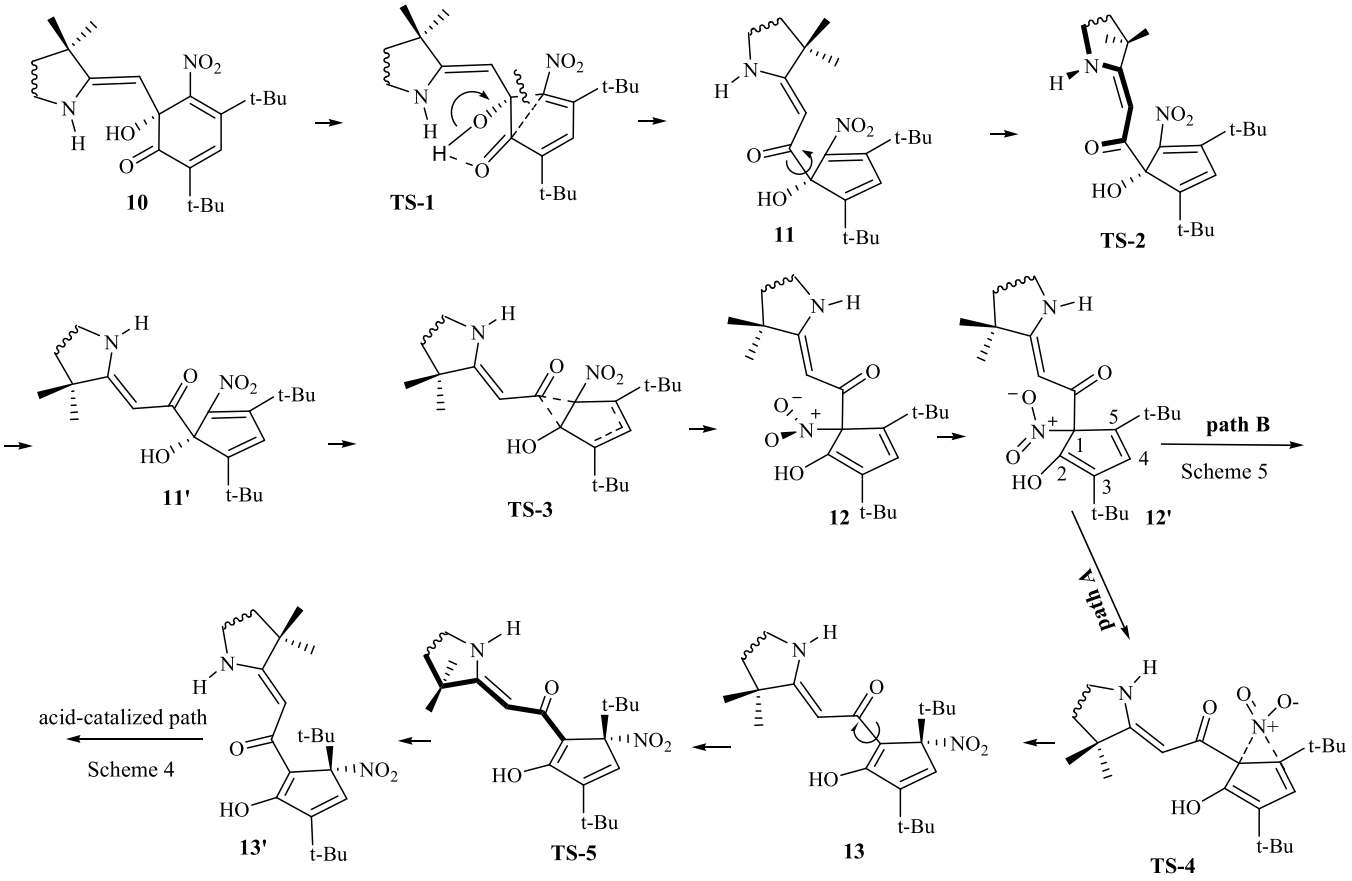
Scheme 2. General Scheme of the Synthesis of New Polycyclic Indoles



Scheme 3. The Mechanism for the Formation of Product 7 Part 1



The reaction path starting with a displacement of the nitro group of intermediate **12′** to the fifth position with a *tert*-butyl substituent (part A) leads to product **7**. The competitive shift to the second position with a hydroxyl group (part B) ultimately leads to the formation of **8** and **9**. Thus, the formation of product **7** from the bifurcation point of the reaction paths begins with a [1,5]-sigmatropic shift of the nitro group. The calculated activation barrier of this process was found to be 20.9 kcal/mol. The resulting intermediate **13** transforms to a more stable structure **13′**. The further course of the reaction includes the formation of a bicyclic structure **14** initiated by a proton transfer from the CH group of the intermediate **13′** to the nitro group

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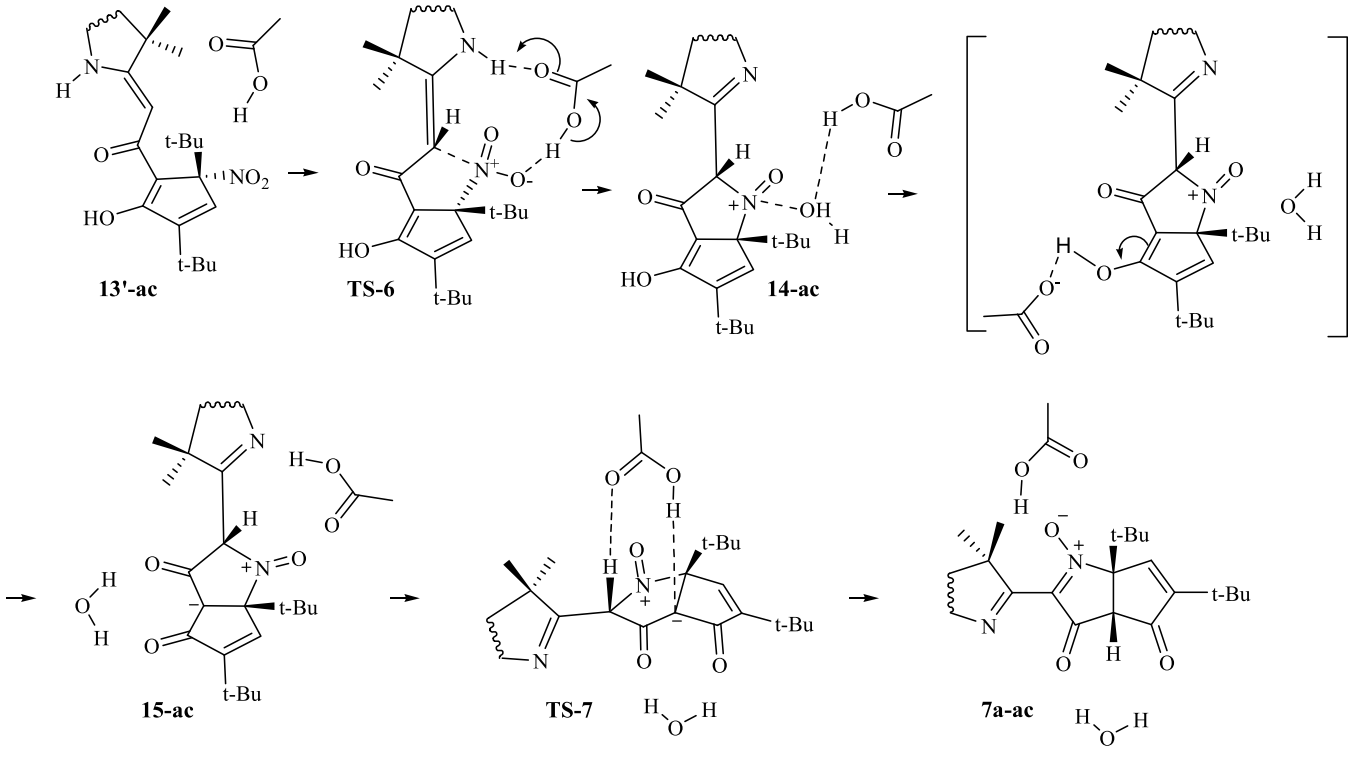
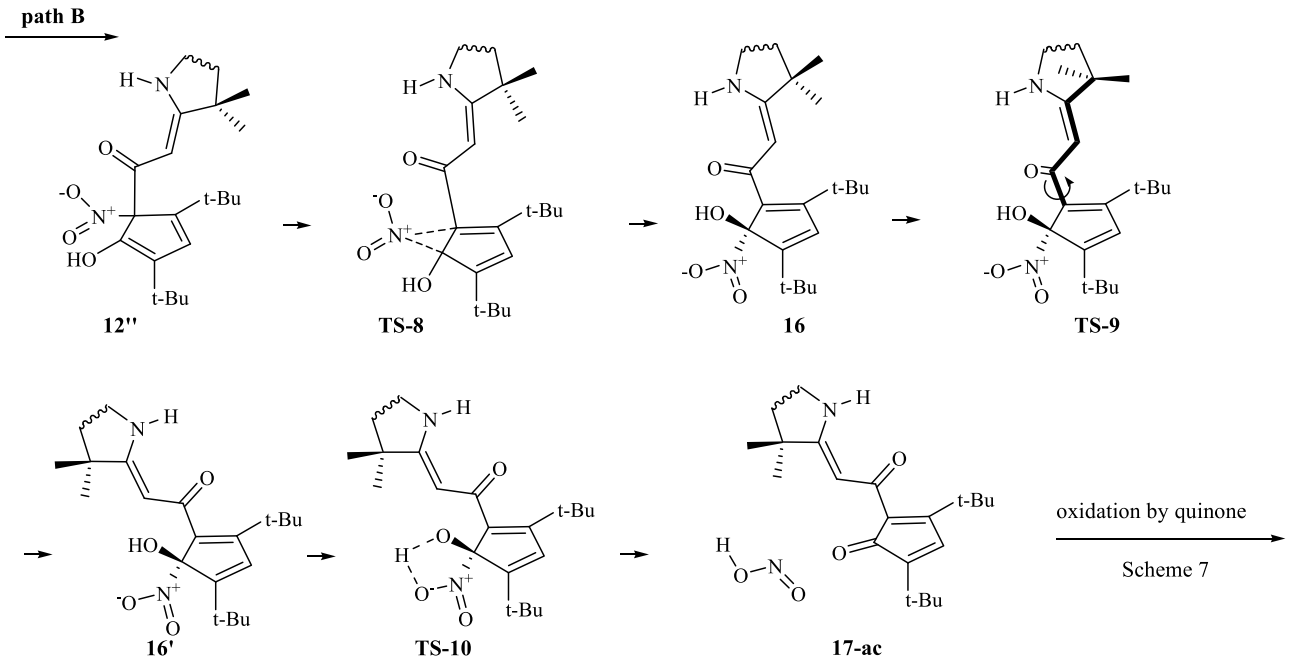
Scheme 4. The Mechanism for the Formation of Product 7 Part 2



Scheme 5. The Mechanism for the Formation of Products 8 and 9 Part 1



with an activation barrier of ~60 kcal/mol, which cannot be overcome in the course of the thermally initiated reaction.

Therefore, we have considered alternative variants of the reaction mechanism and found out that the most energy-favorable way to the formation of the bicyclic framework of the final product is given by the concerted double proton transfer from a nitrogen atom of the indoline fragment of **13′-ac** to an oxygen atom of the nitro group with acetic acid molecules as a mediator of the reaction (Scheme 4 and Figure 5). The activation barrier of this process was found to be 40.1 kcal/mol.

The structure of the final reaction product **7** suggests that the intermediate **14-ac** should be subjected to dehydration with the subsequent proton transfer to the carbon atom of the bridge of the bicyclic fragment. The OH group at the nitrogen atom in **14-ac** is protonated by an acid to eliminate a molecule of water, the carboxylate anion removes a proton from the hydroxyl group of the bicyclic fragment, and the energy of the system (complex **15-ac**) is lowered by 10.9 kcal/mol.

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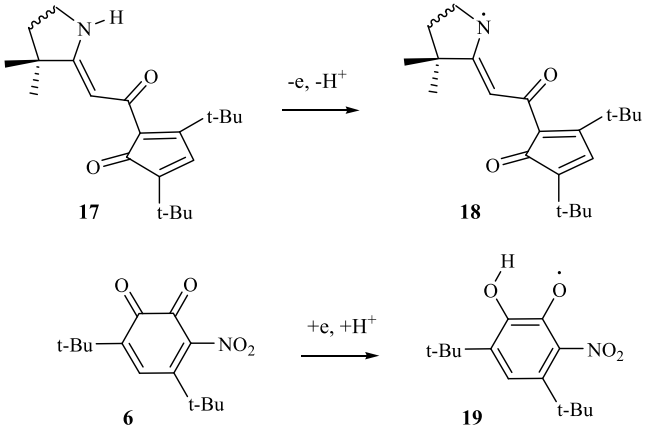
Scheme 6. One-Electron Oxidation Progress of the Intermediate 17 by Quinone 6



The final stage of the formation of **7a** is a low-energy barrier (6.2 kcal/mol) acid-assisted proton transfer from the CH group to the bridge fragment of the bicycle.

As mentioned above, the reaction path to product **8** starts from a [1,2]-sigmatropic shift of the nitro group of the intermediate **12′**. The calculated activation barrier of this reaction stage is equal to 11.2 kcal/mol and the resulting product **16** is thermodynamically more stable than the initial structure by 8.7 kcal/mol (Scheme 5 and Figure 6). The subsequent stages of the reaction include rotation of the heteroaryl fragment with a barrier of 3.4 kcal/mol and proton transfer from the hydroxyl group to an oxygen of the nitro group with a barrier of 13.3 kcal/mol that finally leads to elimination of a molecule of nitrous acid (structure **17-ac**).

The structures of products **8** and **9** clearly indicate that in the process of their formation, intermediate product **17** should undergo cyclization along with the elimination of a *tert*-Bu group and deprotonation of the nitrogen atom.

On the one hand, it has been reported that oxidative dealkylation of 2,4,6-tri-*tert*-butylphenol catalyzed by mononuclear copper(II) complexes occurred with the formation of radical species.[23]

On the other hand, quinones are well-known to act as a one-electron oxidant in single-electron transfer (SET) reactions with the formation of semiquinone radicals.[24]

To qualitatively confirm the formation of radicals in the course of the reaction under study, an EPR spectroscopy method was employed. The resulting spectrum of the reaction mixture of **1a** and **6** consists of a broad unresolved singlet with g = 2.0, which undoubtedly indicates the presence of radical centers (Figure 7).

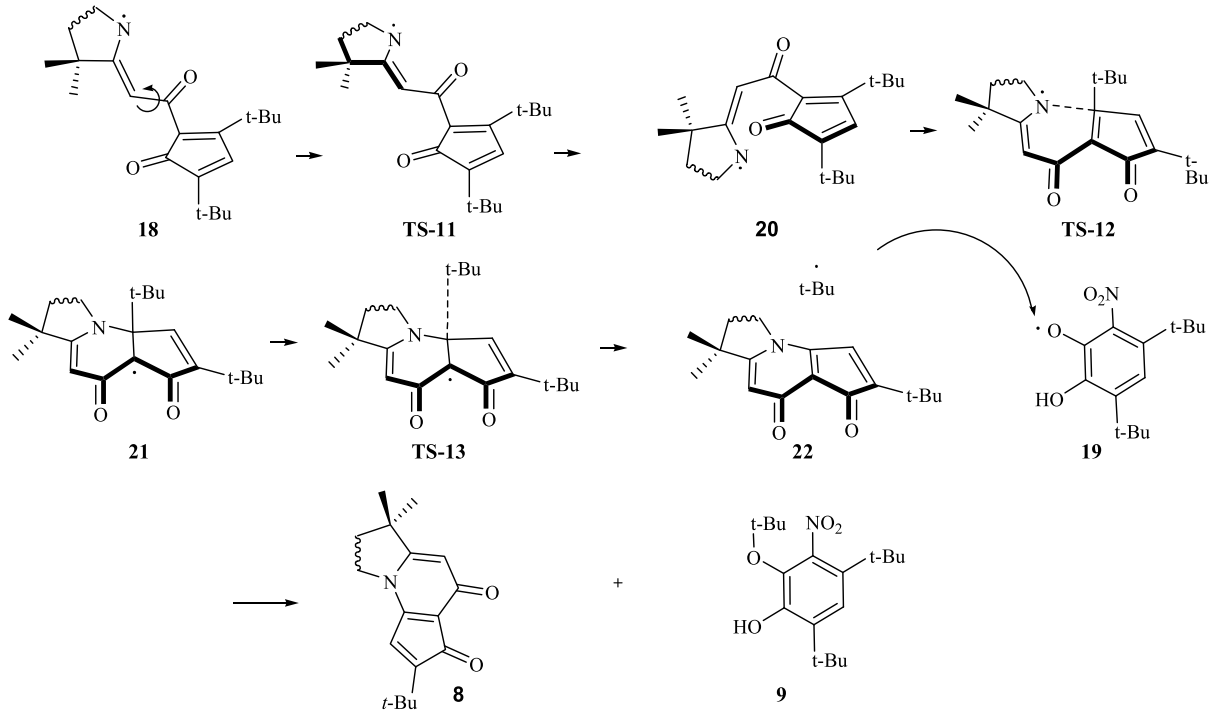
Hence, it is reasonable to suggest that the formation of products **8** and **9** proceeded by one-electron oxidation of the intermediate **17** by quinone **6** followed by further deprotonation of the nitrogen atom of **17** giving rise to radicals **18** and **19** (Scheme 6).

The radical **18** readily (with a barrier of 1.8 kcal/mol) isomerizes into the thermodynamically more stable structure **20**, which then cyclizes to form the intermediate **21** (Scheme 7 and Figure 8). The activation barrier for this reaction stage was found to be 20.8 kcal/mol. A further reaction pathway involves the elimination of a *tert*-butyl radical from **21** with an activation barrier of 14.4 kcal/mol to give the final product **8**. Another reaction product **9** is formed as a result of combining a *tert*-butyl radical with radical **19**.

CONCLUSIONS

To sum up, we have reported a new facile approach to synthesize two novel types of condensed indole systems and based on the DFT/PBE0/6-311G(d,p)//6-311++G(d,p) calculations suggested the most probable mechanisms for their formation.

Scheme 7. The Mechanism for the Formation of Products 8 and 9 Part 2



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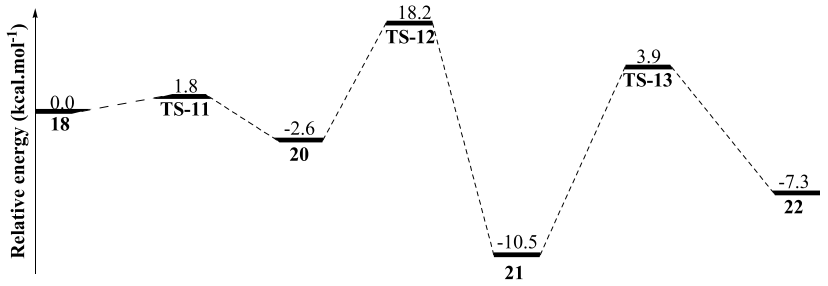

Figure 8. PES of the reactions of Scheme 7.

EXPERIMENTAL SECTION

General Information. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance 600 spectrometer. The chemical shifts are given with respect to the signal of $SiMe_4$ as the internal standard. Attenuated total internal reflectance IR (ATR-IR) spectra were measured on a Varian 3100 FT-IR Excalibur Series spectrometer. HRMS spectra were registered on a Bruker UHR-TOF Maxis Impact instrument. Chromatography was performed on columns packed with Al_2O_3 (Brockmann activity II-III). The melting point was measured on a Fisher–Johns apparatus. The IR and NMR spectra were recorded using equipment of the Shared Use Center "Molecular spectroscopy" of the Southern Federal University.

X-ray Crystal Data. The elementary cell parameters of crystals and the three-dimensional intensity sets for compounds **7a**, **8b**, and **9** were obtained using an auto diffractometer indicated in Table S1, in which information was collected on the main experimental and crystallographic data. The structures were identified using the direct method and refined by the least-squares matrix method with respect to F2 using the SHELXTL program and anisotropic approximation for nonhydrogen atoms.[25] The hydrogen atoms in the crystal structures were localized in the Fourier syntheses of the difference electron density. The coordinates and the isotropic thermal parameters were subsequently refined using the rider method (where it was possible).[26]

Atomic coordinates, full tables of bond lengths, bond angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Center (CCDC 1855413 (**7a**), CCDC 1855400 (**8b**), and CCDC 1855399 (**9**)).

Synthesis. 2,3,3-Trimethylindolenine, 98% (**1a**), 1,1,2-trimethyl-1*H*-benzo[e]indole (**1b**), 97%, and 2,3,3-trimethyl-3*H*-benzo[g]indole, 96% (**1c**) were obtained from Alfa Aesar. 4,6-Di(*tert*-butyl)-3-nitro-1,2-benzoquinone **6** was prepared by the method from ref 26.

Synthesis of 5,6a-Di(*tert*-butyl)-2-(3,3-dimethyl-3*H*-indol-2-yl)-1-*N*-oxy-3a,6a-dihydrocyclopenta[b]pyrrole-3,4-dione (7a), 2-*tert*-Butyl-6,6-dimethyl-6*H*-pyrindino-[1,2-a]indole-3,4-dione (8a), and 2-*tert*-Butoxy-4,6-di-*tert*-butyl-3-nitrophenol (9). A solution of 2,3,3-trimethylindoline **1a** (1.59 g, 0.01 mol) and of 4,6-di(*tert*-butyl)-3-nitro-1,2-benzoquinone **6** (7.3 g, 0.02 mol) in glacial acetic acid (20 mL) was refluxed for 10 h. After cooling, the reaction mixture was diluted with water and extracted with dichloromethane (2 × 50 mL). The combined organic layers were dried with anhydrous sodium sulfate, and the solvent was removed in vacuo. The residue was subjected to column chromatography (alumina, elution with 1:1 methylene chloride:ethyl acetate), and the first two yellow fractions and the third orange fraction were collected. The first fraction is compound **9** ($R_f \sim 0.9$), the second fraction is compound **7a** ($R_f \sim 0.65$), and the third fraction is compound **8a** ($R_f \sim 0.15$). After removal of the solvent in vacuo, the residues were recrystallized from propane-2-ol.

*5,6a-Di(tert-butyl)-2-(3,3-dimethyl-3H-indol-2-yl)-1-N-oxy-3a,6a-dihydrocyclopenta[b]pyrrole-3,4-dione (**7a**).* Yellow crystals; yield, 18%; mp, 173–174 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.17 (s, 9H, Bu^t(5)), 1.19 (s, 9H, Bu^t(6a)), 1.41 (s, 3H, Me(3)), 1.44 (s, 3H, Me(3)), 3.74 (s, 1H, H(3a)), 7.24–7.32 (m, 3H, H_{Ar}), 7.53 (s, 1H, H(6)), 7.74 (d, 1H, H_{Ar}). ^{13}C NMR (151 MHz, $CDCl_3$): δ 22.0, 22.2, 25.8, 28.0, 32.8, 36.5, 56.3, 60.8, 88.9, 120.8, 122.4, 127.6, 127.8, 136.3, 146.3, 149.5, 152.7, 158.2, 172.8, 185.1, 192.1. IR, ν/cm^{-1}: 1731, 1692, 1532, 1393, 1181, 1032, 983, 944, 856, 758, 637. HRMS (ESI): m/z calcd for $C_{25}H_{30}N_2O_3$, 406.2256; found, 407.2337 $[M + H]^+$ and 429.2153 $[M + Na]^+$. Crystals suitable for X-ray crystallographic analysis were obtained from a propane-2-ol solution.

*2-tert-Butyl-6,6-dimethyl-6H-pyrindino[1,2-a]indole-3,4-dione (**8a**).* Red crystals; yield, 20%; mp, >300 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.32 (s, 9H, Bu^t(2)), 1.52 (s, 6H, Me(6,6)), 6.55 (s, 1H, H(5)), 7.31 (s, 1H, H(1)), 7.36 (t, 1H, J = 6.0, H_{Ar}) 7.43–7.46 (m, 2H, H_{Ar}), 7.58 (d, 1H, J = 12.0, H(10)). ^{13}C NMR (151 MHz, $CDCl_3$): δ 28.8, 29.0, 33.0, 44.3, 109.9, 114.2, 119.2, 124.0, 124.4, 127.3, 128.9, 139.1, 141.2, 153.6, 157.7, 160.2, 172.0, 191.9. IR, ν/cm^{-1}: 1706, 1647, 1610, 1609, 1594, 1576, 1505, 1469, 1456, 1362, 1264, 1061, 872, 857, 758. HRMS (ESI): m/z calcd for $C_{21}H_{21}NO_2$, 319.1572; found, 342.1464 $[M + Na]^+$.

*2-tert-Butoxy-4,6-di-tert-butyl-3-nitrophenol (**9**).* Light yellow crystals; yield, 15%; mp, 163–165 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.33 (s, 9H, Bu^t(6)), 1.36 (s, 9H, Bu^t(4)), 1.37 (s, 9H, OBu^t(2)), 5.70 (s, 1H, H(5)), 7.11 (s, 1H, OH). ^{13}C NMR (151 MHz, $CDCl_3$): δ 29.1, 29.2, 30.9, 35.1, 35.5, 84.8, 120.8, 130.8, 135.7, 137.1, 144.6, 147.8. IR, ν/cm^{-1}: 3503, 2361, 2339, 1528, 1369, 1295, 1219, 1150, 1039, 987, 878, 835, 818, 809, 730. HRMS (ESI): m/z calcd for $C_{18}H_{29}NO_4$, 323.2096; found, 346.1954 $[M + Na]^+$. Crystals suitable for X-ray crystallographic analysis were obtained from a propane-2-ol solution.

Synthesis of 5,6a-Di(*tert*-butyl)-2-(1′,1′-dimethyl-1′*H*-benzo[e]indole-2-yl)-1-*N*-oxy-3a,6a-dihydrocyclopenta-[b]pyrrole-3,4-dione (7b) and 13,13-Dimethyl-9-*tert*-butyl-13*H*-pyrindino[1,2-a]benzo[e]indole-10,11-dione (8b). A solution of 1,1,2-trimethyl-1*H*-benzo[e]indoline **1b** (2.09 g, 0.01 mol) and of 4,6-di(*tert*-butyl)-3-nitro-1,2-benzoquinone **6** (7.3 g, 0.02 mol) in glacial acetic acid (20 mL) was refluxed for 10 h. After cooling, the reaction mixture was diluted with water and extracted with dichloromethane (2 × 100 mL). The combined organic layers were dried with anhydrous sodium sulfate, and the solvent was removed in

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vacuo. The residue was subjected to column chromatography (alumina, elution with 1:1 methylene chloride:ethyl acetate) collecting the first yellow and the second orange fractions. The first fraction is compound **7b** ($R_f \sim 0.65$), and the second fraction is compound **8b** ($R_f \sim 0.15$). After removal of the solvent in vacuo, the residues were recrystallized from propane-2-ol.

*5,6a-Di(tert-butyl)-2-(1′,1′-dimethyl-1′H-benzo[e]indole-2-yl)-1-N-oxy-3a,6a-dihydrocyclopenta[b]pyrrole-3,4-dione (**7b**).* Yellow crystals; yield, 19%; mp, 204−205 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.20 (s, 9H, Bu^t), 1.21 (s, 9H, Bu^t), 1.66 (s, 3H, Me), 1.69 (s, 3H, Me), 3.78 (s, 1H, H(3a)), 7.48 (m, 1H, H_{Ar}), 7.55 (m, 1H, H_{Ar}), 7.57 (s, 1H, H(7)), 7.84 (d, 1H, H_{Ar}, J = 8.5), 7.92 (m, 2H, H_{Ar}), 8.00 (d, 1H, H_{Ar}, J = 8.3). ^{13}C NMR (151 MHz, $CDCl_3$): δ 21.0, 21.2, 25.8, 28.0, 32.8, 36.5, 58.0, 60.9, 88.9, 121.2, 123.4, 125.4, 126.5, 127.7, 129.3, 129.7, 133.6, 140.0, 149.6, 150.0, 158.2, 174.6, 185.3, 192.2. IR, ν/cm^{-1}: 1732, 1693, 1569, 1535, 1463, 1410, 1399, 1365, 1314, 1243, 1187, 1041, 985, 856, 826. HRMS (ESI): m/z calcd for $C_{29}H_{32}N_2O_3$, 456.2412; found, 457.2490 $[M + H]^+$ and 479.2313 $[M + Na]^+$.

*13,13-Dimethyl-9-tert-butyl-13H-pyrindino[1,2-a]benzo-[e]indole-10,11-dione (**8b**).* Red crystals; yield, 19%; mp, >300 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.33 (s, 9H, Bu^t), 1.80 (s, 6H, Me), 6.64 (s, 1H, H(12)), 7.40 (s, 1H, H(8)), 7.54 (m, 1H, H_{Ar}), 7.63 (m, 1H, H_{Ar}), 7.78 (d, 1H, H_{Ar}, J = 9.0), 7.96 (m, 2H, H_{Ar}), 8.11 (d, 1H, H_{Ar}, J = 8.5). ^{13}C NMR (151 MHz, $CDCl_3$): δ 28.8, 29.0, 33.0, 46.0, 110.0, 112.8, 119.0, 123.3, 124.7, 126.4, 128.0, 129.1, 129.7, 130.8, 132.5, 134.7, 136.3, 153.6, 157.1, 161.7, 171.9, 191.9. IR, ν/cm^{-1}: 1702, 1643, 1593, 1579, 1510, 1493, 1459, 1377, 1366, 1335, 1276, 1210, 1048, 905, 865, 832, 800, 787, 749. HRMS (ESI): m/z calcd for $C_{25}H_{23}NO_2$, 369.1728; found, 392.1623 $[M + Na]^+$. Crystals suitable for X-ray crystallographic analysis were obtained from a propane-2-ol solution.

Synthesis of 5,6a-Di(*tert*-butyl)-2-(3′,3′-dimethyl-3′*H*-benzo[g]indole-2-yl)-1-*N*-oxy-3a,6a-dihydrocyclopenta-[b]pyrrole-3,4-dione (7c) and 7,7-Dimethyl-11-*tert*-butyl-7*H*-pyrindino[1,2-a]benzo[g]indole-9,10-dione (8c). A solution of 2,3,3-trimethyl-3*H*-benzo[g]indoline **1c** (2.09 g, 0.01 mol) and of 4,6-di(*tert*-butyl)-3-nitro-1,2-benzoquinone **6** (7.3 g, 0.02 mol) in glacial acetic acid (20 mL) was refluxed for 10 h. After cooling, the reaction mixture was diluted with water and extracted with dichloromethane (2 × 100 mL). The combined organic layers were dried with anhydrous sodium sulfate, and the solvent was removed in vacuo. The residue was subjected to column chromatography (alumina, elution with 1:1 methylene chloride:ethyl acetate) collecting the first yellow and the second orange fractions. The first fraction is compound **7c** ($R_f \sim 0.65$), and the second fraction is compound **8c** ($R_f \sim 0.15$). After removal of the solvent in vacuo, the residues were recrystallized from propane-2-ol.

*5,6a-Di(tert-butyl)-2-(3′,3′-dimethyl-3′H-benzo[g]indole-2-yl)-1-N-oxy-3a,6a-dihydrocyclopenta[b]pyrrole-3,4-dione (**7c**).* Yellow crystals; yield, 25%; mp, 221−222 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.20 (s, 9H, Bu^t), 1.22 (s, 9H, Bu^t), 1.52 (s, 3H, Me), 1.54 (s, 3H, Me), 3.76 (s, 1H, H(3a)), 7.40 (d, 1H, H_{Ar}, J = 8.2), 7.48 (m, 1H, H_{Ar}), 7.57 (s, 1H, H(7)), 7.58 (m, 1H, H_{Ar}), 7.81 (d, 1H, H_{Ar}, J = 8.2), 7.85 (d, 1H, H_{Ar}, J = 8.2), 8.62 (d, 1H, H_{Ar}, J = 8.0). ^{13}C NMR (151 MHz, $CDCl_3$): δ 21.3, 21.4, 25.9, 28.1, 32.8, 36.6, 57.5, 61.0, 88.6, 118.7, 123.7, 126.0, 126.8, 127.6, 128.0, 128.5, 133.7, 143.4, 148.3, 149.6, 158.2, 172.6, 185.1, 192.3. IR, ν/cm^{-1}: 1734, 1697, 1501, 1462, 1377, 1313, 1185, 1077, 1042, 980, 821, 750. HRMS (ESI): m/z calcd for $C_{29}H_{32}N_2O_3$, 456.2412; found, 457.2491 $[M + H]^+$ and 479.2314 $[M + Na]^+$.

*7,7-Dimethyl-11-tert-butyl-7H-pyrindino[1,2-a]benzo[g]-indole-9,10-dione (**8c**).* Red crystals; yield, 11%; mp, >300 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.28 (s, 9H, Bu^t), 1.58 (s, 6H, Me), 6.61 (s, 1H, H(13)), 7.18 (s, 1H, H(4)), 7.50 (d, 1H, H_{Ar}, J = 8.3), 7.57 (m, 1H, H_{Ar}), 7.62 (m, 1H, H_{Ar}), 7.89 (d, 1H, H_{Ar}, J = 8.3), 7.97 (d, 1H, H_{Ar}, J = 8.2), 8.12 (d, 1H, H_{Ar}, J = 8.5). ^{13}C NMR (151 MHz, $CDCl_3$): δ 28.2, 29.0, 32.9, 45.3, 110.9, 118.8, 120.0, 121.6, 122.2, 126.6, 126.9, 128.3, 129.2, 129.3, 133.5, 134.7, 139.4, 150.8, 158.3, 161.4, 172.4, 192.3. IR, ν/cm^{-1}: 1706, 1650, 1601, 1514, 1488, 1464, 1377, 1361, 1336, 1266, 1163, 1046, 954, 887, 816, 755. HRMS (ESI): m/z calcd for $C_{25}H_{23}NO_2$, 369.1728; found, 392.1633 $[M + Na]^+$.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.1c02033.

(Figures S1−S14) NMR spectra of some small molecules; (Figures S15−S17 and Tables S1−S6) X-ray crystal structures, crystal packing diagram and the main bond lengths, and valence angles of some small molecules (**7a**, **8b**, and **9**); (Figure S18) optimized structures of all transition states (PDF)

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Notes

The authors declare no competing financial interest.

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