Reactions of N-Acylated Indoles with Singlet Oxygen

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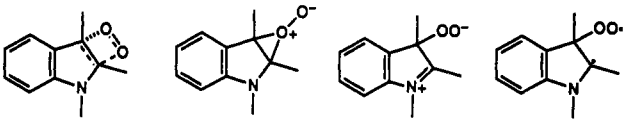
Reactions of seven *N*-acyl indole derivatives with singlet oxygen have been investigated. 1-Acetyl- (**1a**) and 1-(chloroacetyl)-2,3-dimethylindole (**1b**) gave exclusively 1-acetyl- (**2a**) and 1-(chloroacetyl)-2-hydroperoxy-3-methyleneindoline (**2b**), respectively, in high yields via ene reaction on irradiation with oxygen in the presence of TPP sensitizer. 1-Acetyl-3-methylindole (**1c**) gave only 1-acetyl-2-hydroperoxy-3-methyleneindoline (**2c**) in low yield under the same conditions. In contrast, 1-acetyl-2-methyl-3-ethylindole (**3a**) and 1-acetyl-2-methyl-3-isopropylindole (**3b**) gave a mixture of ene products, 2-hydroperoxy- and 3-hydroperoxyindolines (**4a** and **b** and **5a** and **b**), in addition to 2,3-bond cleavage products **6a** and **6b**, respectively. In the case of 1-acetyl-2-methyl-3-*tert*-butylindole (**7**), only the product of 2,3-bond cleavage (**8**) was obtained. A 1,2-dioxetane is intermediate in the cleavage and could be observed after photooxygenation of **7** at −5 °C by NMR and was reduced by trimethylphosphite and dimethyl sulfide. The decomposition rate constant of 1,2-dioxetane **10** was measured by NMR; E_a is 24.6 kcal/mol.

Introduction

Dye-sensitized photooxygenation of indole derivatives has been studied because of the important role that these heterocyclic compounds play in photodynamic damage to biological systems.[1-3] Electron-rich N-alkylated indoles react readily with singlet oxygen to give carbonyl and amide fragments via oxidative 2,3-bond cleavage.[4,5] On the other hand, 2,3-disubstituted indoles give ene reaction products, 3-hydroperoxyindolenines, with triplet and singlet oxygen (Scheme I).[1,3] However, ene reaction has rarely been observed on photooxygenation of other indoles, even where there are allylic hydrogens on both sides of the double bond.[6]

The mechanism of cleavage of the 2,3-bond is the subject of controversy, the main question being whether the reaction is a concerted [$\pi_{2s} + \pi_{2a}$] reaction[7-9] or stepwise, involving short-lived species such as a perepoxide,[10-13] a zwitterion,[13,14] or 1,4-diradicals.[13-16] 1,2-Dioxetane[17] and zwitterion[4,18] intermediates were proposed in the 2,3-bond cleavage of electron-rich indoles, based on spectroscopic and chemical trapping studies.



Few singlet oxygen reactions of electron-deficient indoles have been reported. The present paper describes the photooxygenation of seven *N*-acyl derivatives. In this series, ene reaction predominates over cleavage in the less sterically-hindered compounds. Cleavage increases with increasing steric bulk of the 3-substituent or the electron density of the ring. The electron-withdrawing properties of the acetyl group make the N-substituted 1,2-dioxetane derived from **7** stable enough to be characterized by spectroscopic and chemical methods.

Results

TPP-sensitized photooxygenation of 1-acetyl-2,3-dimethylindole (**1a**), 1-(chloroacetyl)-2,3-dimethylindole (**1b**), and 1-acetyl-3-methylindole (**1c**) in methylene chloride at 0 °C for 3 h produced exclusively 2-hydroperoxy indolines **2a** (85%), **2b** (79%), and **2c** (25%), respectively, in addition to unreacted starting material (Scheme II). No cleavage products were found by ^{1}H-NMR. Similar results were obtained when photooxygenation was carried out in acetone at −78 or 0 °C and chloroform at 0 °C.

Compounds **2a-c** were isolated by crystallization from pentane–methylene chloride (10:1). The structures were assigned on the basis of ^{1}H, ^{13}C, DEPT, and ^{1}H–^{13}C HETCOR 2D NMR and mass spectroscopy (see Experimental Section). Observation of ^{13}C-NMR singlets in **2a** and **2b** and a doublet in **2c** for C-2, which is attached to two heteroatoms (100.48 ppm for **2a**, 100.58 ppm for **2b**, 94.10 ppm for **2c**), and triplets for methylene carbons (negative DEPT peaks at 135°, 105.14 ppm for **2a**, 105.36 ppm for **2b** and 109.13 ppm for **2c**) establish the structure of the 2-hydroperoxyindolines **2**. The X-ray crystal structure of **2a** at −117 °C is shown in Figure 1.

The chemical shift of the hydroperoxy proton is strongly dependent on solvent. It appears as a sharp peak at ca. 11.0 ppm in deuterated acetone, indicative of hydrogen bonding with solvent. In deuterated chloroform and methylene chloride, it ranges from 8.2 to 10.0 ppm,

† Author from whom X-ray data can be obtained.

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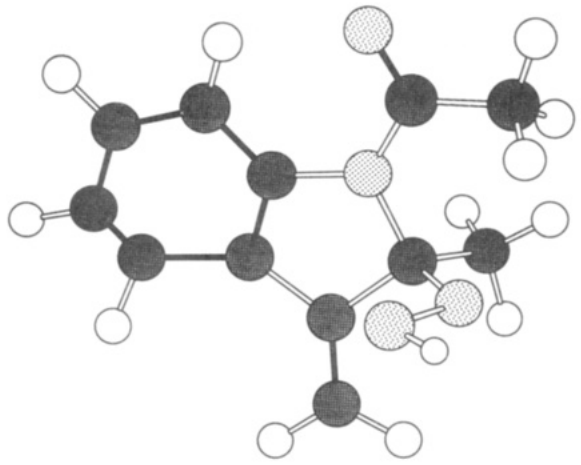
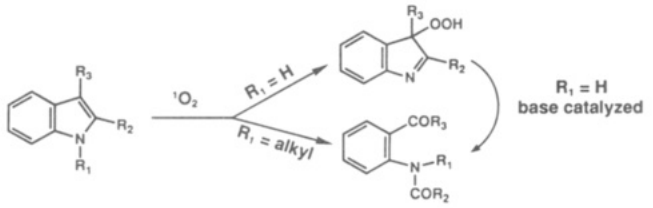
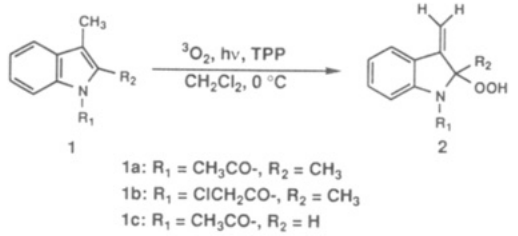


Figure 1. X-ray crystal structure of **2a**.

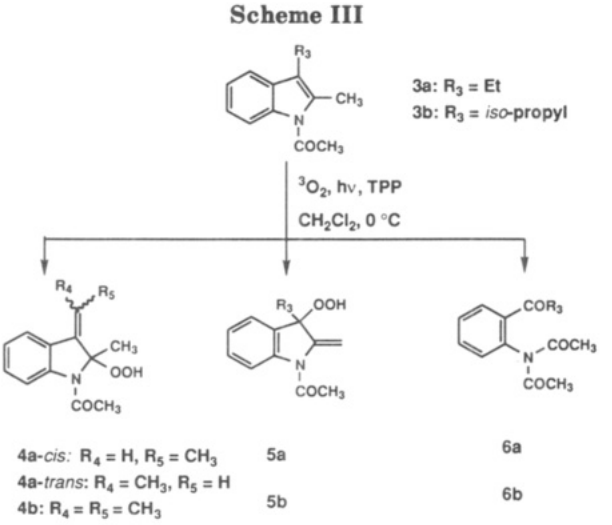
Scheme I



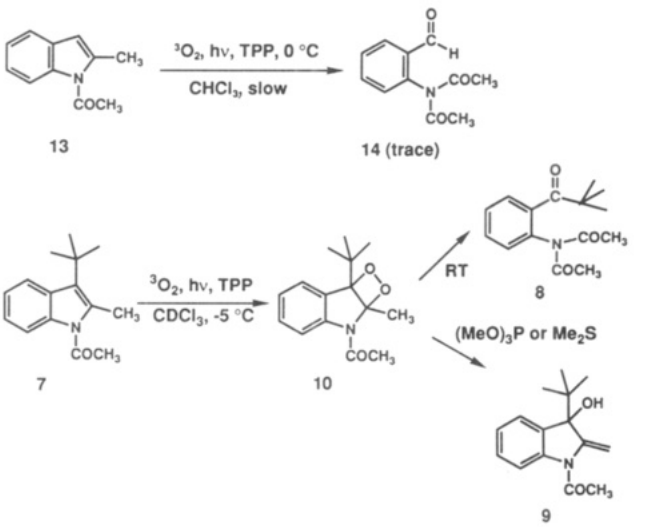
Scheme II



Scheme III



Scheme IV



depending on the concentration, and is usually broad. The clean doublets for the 7-protons (ortho to the N on the benzene ring) in **2a–c** shift downfield (ca. 0.3 ppm) and coalesce to a broad doublet on lowering the temperature to −10 °C. The X-ray crystal structure shows that the 7-H and carbonyl oxygen are separated by 2.2 Å in **2a**. These shifts undoubtedly are caused by rotation of the carbonyl group which is frozen out at low temperature.

Photooxygenation of 1-acetyl-3-ethyl-2-methylindole **3a** in methylene chloride at 0 °C for 4 h gave three products, including two regioisomeric indolines (ene products **4a** (15%), **5a** (1.4%)) and cleavage product **6a** (1.7%). The remaining material was unreacted **3a**, retrieved after isolation of the products. Under the same conditions 1-acetyl-2-methyl-3-isopropylindole (**3b**) gave the corresponding products **4b** (5%), **5b** (6%), and **6b** (5%) in addition to unreacted **3b** (Scheme III). **4a** and **4b** were crystallized from pentane–methylene chloride (7:3). **5a** and **5b** were separated from **6a** and **6b**, respectively, by flash column chromatography. **4a** is 87.5% cis and 12.5% trans by NMR. The stereochemistry was confirmed by an NOE experiment.[19] No obvious Hock rearrangement of **5ab** caused by silica gel, which would be expected to give 2,3-dihydro-1,4-benzoxazine[20–22] was observed. The most notable difference in the ^{1}H-NMR spectra of all compounds **2** and **5** is the fact that the methylene hydrogens in **2** appear as two one-proton singlets, whereas the methylene hydrogens in **5** appear as two-proton doublets (J = 2 Hz). This phenomenon was observed in similar compounds by Vice.[23]

To study the reaction further, photooxygenations of 1-acetyl-2-methylindole (**13**) and 1-acetyl-2-methyl-3-*tert*-butylindole (**7**) were performed (Scheme IV). In both cases, the ene pathway leading to 2-hydroperoxyindoline is prohibited due to lack of abstractable protons at the 3-position. Actually, reaction of **13** with singlet oxygen in chloroform (or methylene chloride, acetone) was so slow that a 2-h irradiation did not cause an observable spectroscopic change. Prolonged irradiation produced a trace of cleavage product, *N*-acetyl-*N*-(2-formylphenyl)-acetamide **14** by comparison with the authentic sample prepared from photooxygenation of **13** in methanol.[24] The sluggish reaction is obviously due to the decreased electron

(19) Saturation of the proton at 6.32 ppm in **4a**-*cis* produced a 16.8% enhancement for the 4-H (δ = 7.44 ppm) proton on the aromatic ring, while saturation of the proton at 5.95 ppm in **4a**-*trans* did not give a positive NOE.

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density on the 2,3-double bond. In contrast, photooxygenation of 7 at −5 °C in deuterated chloroform produced 10% of cleavage product 8 and 90% of 1,2-dioxetane 10, which was converted exclusively to 8 on warming to 50 °C. The ^{13}C-NMR chemical shifts of C-2 (107.46 ppm) and C-3 (100.14 ppm) are extremely useful in establishing the strained 1,2-dioxetane structure because C-2 is attached to two heteroatoms and C-3 is benzylic with one heteroatom attached.[17] 10 could be kept at −5 °C for several hours without obvious spectroscopic change. Warming 10 to 50 °C for 40 min resulted in disappearance of the peaks at 107.46 and 100.14 ppm. A new set of peaks grew in; those at 210.55 and 173.00 ppm were assigned to the carbonyl and amide carbon, respectively, of the cleavage product 8.

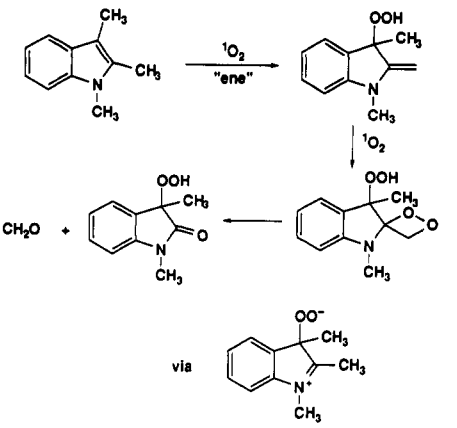
Irradiation of 7 in methanol-d_4 with methylene blue as sensitizer at −5 °C gave essentially the same result as in deuterated chloroform and deuterated methylene chloride. No trapping product from a zwitterionic intermediate was observed in the presence of methanol. Even though alkylated 1,2-dioxetanes are well documented[25] and some are stable at relatively high temperatures, only a limited number of 1,2-dioxetanes with nitrogen attached to the ring have been reported.[17,26,27] The kinetics of decomposition of 10 to 8 were investigated by NMR spectroscopy. The activation energy (E_a) is 24.6 kcal/mol. Decomposition of 10 at 35 °C is six times faster than 2,3-diphenylindene-1,2-dioxetane.[28] To our knowledge, 10 is the most stable nitrogen-substituted 1,2-dioxetane yet prepared. It liberates iodine from potassium iodide/ethanol solution.[25,29] Trimethyl phosphite[29,30] and dimethyl sulfide reduced 10 to give the same product, 9, the reduced ene product.

Discussion

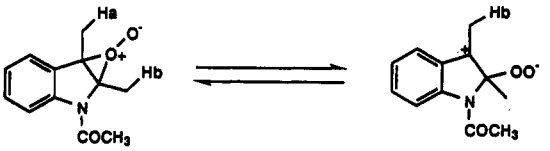
While alkenes bearing allylic hydrogens are well-known to react with singlet oxygen via an ene reaction, almost no ene reactions have been reported in enamine systems[26,27] and few in indole systems.[4] Saito reported that 1,2,3-trimethylindole underwent 2,3-bond cleavage with an ene side reaction giving the 3-hydroperoxy-2-indolinone via an indoline precursor in aprotic solvent at 0 °C[4] (Scheme V). In contrast, we obtained only 2-hydroperoxyindolines from **1a–1c**. The regioselectivity is completely reversed, and the reaction stops at the indoline stage when the N-alkyl group is replaced by *N*-acetyl. This profound effect is unprecedented and must reside in the fact that the nitrogen in the N-alkyl compounds is electron donating enough to stabilize a zwitterion intermediate (Saito et al. trapped this zwitterion with methanol[4]); N-acetylation decreases the donating ability to the point that a normal ene reaction takes over.

The remarkable difference in the product distribution from the indoles with 3-methyl substituents (Scheme II) and those with larger alkyl substituents (Scheme III) must be caused by steric effects of the 3-substituents. Two considerations rationalize the observed product distributions: (1) Oxidative 2,3-bond cleavage occurs where H abstraction in the ene pathway is made difficult by

Scheme V



Scheme VI



12a 12b

inaccessibility of the H atom. (2) Perepoxide or zwitterion intermediates have been proposed for the ene reaction, and the perepoxide has been widely accepted.[31,32] A zwitterionic intermediate of type **12b** (Scheme VI) was trapped by methanol in the reaction of indene with singlet oxygen.[33] In the transition state or intermediate **12**, the C_3–O bond is weaker than the C_2–O bond because the developing charge on C-3 can be stabilized by the benzene ring. Therefore, 2-hydroperoxyindoline predominates over 3-hydroperoxyindoline if all the other factors are equal (in the case of **1a**, **1b** and to a lesser extent with **3a**). But in the case of **3b**, abstraction of the methine proton on the isopropyl is made difficult by the steric congestion so that 3-hydroperoxyindoline and cleavage products predominate.

The results of the photooxygenation of 7 confirm that 2,3-bond cleavage comes from a strained intermediate 1,2-dioxetane. The mechanisms of reaction of dioxetanes with phosphites and sulfides were suggested to proceed via phosphoranes and sulfuranes (Scheme VII).[34-36] Once one of the weak O–P bond breaks, there are three ways for the zwitterion **11b** to react: (1) to form epoxide[34-36] which is impossible here because backside intramolecular nucleophilic attack is restricted by the ring,[37] (2) pinacol rearrangement to form indolinone,[17] and (3) elimination to give allylic alcohol,[36,37] the reaction observed here. The fact that there is no pinacol rearrangement implies that the migrating and leaving groups are not coplanar.

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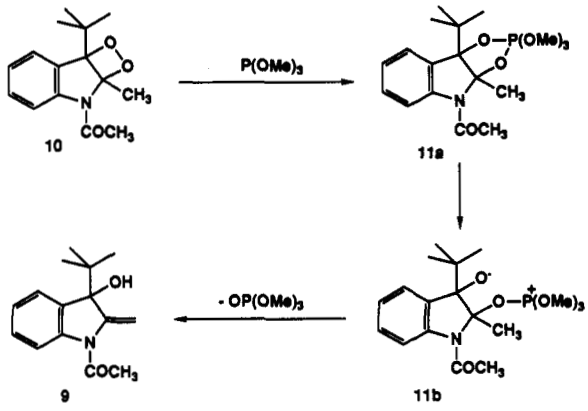
Scheme VII



Conclusions

N-Acetyl-2,3-disubstituted indoles undergo ene-type reaction unless steric hindrance at the 3 position is large and 2-hydroperoxyindoline is predominant over 3-hydroperoxyindoline. A 1,2-dioxetane is the precursor of the 1,2-bond cleavage product. The *N*-acetyl group stabilizes the 1,2-dioxetane, probably because the electron-withdrawing effect of the acetyl prevents the lone-pair electron of the nitrogen from participating in breaking the C–O bond of the 1,2-dioxetane.[38]

Experimental Section

General. All N-acetylated indoles were made from the corresponding indoles, prepared using Fischer indole synthesis,[39] followed by acetylation with acetyl chloride except for 1-acetyl-3-methylindole, which was acetylated with acetic anhydride in the presence of potassium acetate.[40] The acetyl indoles were isolated by column chromatography and recrystallized from 100% ethanol before use. Methanol was purified by distillation from magnesium/iodine and stored over 4-Å molecular sieves. All other commercially available reagents and solvents were used without further purification. Photooxygenations were performed with a Varian-Eimac Cermax 300-W Xenon lamp filtered with 0.0085 M $K_2Cr_2O_4$ solution (pathlength 3.5 cm) to remove light below 500 nm. Oxygen was passed through a drying tube containing activated 4-Å molecular sieves and bubbled through the reaction solution via a Teflon tube when a 5-mm NMR tube was used or a glass pipet when a flask was used. ^{1}H-NMR data were obtained at 360 and 500 MHz. ^{13}C-NMR data were taken at 90 and 125 MHz. Chemical shift values are reported in δ (ppm) relative to TMS.

Photooxygenation of 1-Acetyl-2,3-dimethylindole (1a). Compound **1a** (80 mg, 0.428 mmol) was combined with 20 mL of 2.5×10^{-4} M TPP/CH_2Cl_2 and photooxygenated at 0 °C. The reaction was monitored by ^{1}H-NMR. The starting material was completely consumed after 3 h of irradiation. The resulting mixture was concentrated under vacuum to yield the crude product as a reddish oil. A fine powder precipitated after the addition of 3 mL of 10:1 pentane–CH_2Cl_2 solution. The solution was filtered and the powder rinsed with 10 drops of 10:1 pentane–CH_2Cl_2 and then dried below 5 °C with a diffusion pump to give 79.8 mg (85%) of yellowish 1-acetyl-2-hydroperoxy-2-methyl-3-methyleneindoline (**2a**): ^{1}H-NMR (acetone-d_6) δ 11.08 (s, 1 H), 8.32 (d, J = 8.2 Hz, 1 H), 7.59 (d, J = 8.2 Hz, 1 H), 7.26 (t, J = 8.2 Hz, 1 H), 7.05 (t, J = 8.2 Hz, 1 H), 5.83 (s, 1 H), 5.34 (s, 1 H), 2.43 (s, 3 H), 1.75 (s, 3 H); ^{13}C-NMR (acetone-d_6) δ 169.97 (s), 147.41 (s), 144.93 (s), 130.42 (d), 126.79 (s), 123.99 (d), 120.76 (d), 117.76 (d), 105.14 (t), 100.48 (s), 25.50 (q), 24.15 (q); IR (cm^{-1}, KBr pellet) 3195 (br, s), 2880 (m), 1640 (s), 1460 (s), 1400 (s), 900 (m), 770 (s); EIMS m/z 219 (M, 7.3), 202 (M - 16, 44), 187 (M - 32, 5.3), 186 (M - 33, 100), 160 (M - 59, 49); M$^+$ calcd for $C_{12}H_{13}NO_3$ 219.0895, obsd 219.0918.

Photooxygenation of 1-(Chloroacetyl)-2,3-dimethylindole (1b). Compound **1b** (160.8 mg, 0.726 mmol) was combined with 20 mL of 2.0×10^{-4} TPP/CH_2Cl_2 in a flask. Photooxygenation was performed at 0 °C and monitored by ^{1}H-NMR. The starting material reacted completely after 3.5 h of irradiation. The resulting mixture was condensed under vacuum. A greenish powder precipitated upon adding ca. 2 mL of 10:1 of pentane–CH_2Cl_2. The solution was filtered and the powder rinsed with a few drops of 10:1 pentane–CH_2Cl_2. The product was dried below 5 °C with an oil pump to give 145.1 mg (79%) of 1-(chloroacetyl)-2-hydroperoxy-2-methyl-3-methyleneindoline (**2b**): ^{1}H-NMR (acetone-d_6) δ 11.46 (s, 1 H), 8.31 (d, J = 8.2 Hz, 1 H), 7.49 (d, J = 8.2 Hz, 1 H), 7.28 (t, J = 8.2 Hz, 1 H), 7.10 (t, J = 8.2 Hz, 1 H), 5.75 (s, 1 H), 5.34 (s, 1 H), 4.55 (AB, J = 13.5 Hz, 2 H), 1.77 (s, 3 H). ^{13}C-NMR (acetone-d_6) δ 166.02 (s), 144.94 (s), 142.53 (s), 130.41 (d), 125.85 (s), 124.71 (d), 120.26 (d), 117.67 (d), 105.36 (t), 100.58 (s), 42.57 (t), 25.51 (q); IR (cm^{-1}, KBr pellet) 3275.3 (s), 3086.7 (w), 2961.3 (m), 2820.8 (m), 1639.0 (s), 1465.4 (s), 1407.7 (s), 1283.7 (m), 895.3 (m), 746.6 (s); EIMS m/z 253 (M, 11), 237 (M - 16, 10), 220 (M - 33, 45), 168 (M - 85, 23), 144 (M - 109, 100); M$^+$ calcd for $C_{12}H_{12}NO_3Cl$ 253.0506, obsd 253.0444.

Photooxygenation of 1-Acetyl-3-methylindole (1c). Compound **1c** (34.4 mg, 0.197 mmol) was combined with 5 mL of 2.5×10^{-4} M TPP/CH_2Cl_2 in a test tube. Irradiation was carried out at 0 °C for 5 h. The resulting reaction mixture was condensed by blowing N_2 on it to remove the methylene chloride. A very fine powder appeared after adding three drops of 10:3 pentane–CH_2Cl_2 and was collected by filtration to give 10.3 mg (25%) of 1-acetyl-2-hydroperoxy-3-methyleneindoline (**2c**). The filtrate was identified by TLC and ^{1}H-NMR as unreacted starting material **1c**: ^{1}H-NMR (acetone-d_6) for **2c** δ 11.04 (s, 1 H), 8.17 (d, J = 7.92 Hz, 1 H), 7.57 (d, J = 7.92 Hz, 1 H), 7.24 (t, J = 7.92 Hz, 1 H), 7.04 (t, J = 7.92 Hz, 1 H), 6.39 (s, 1 H), 5.92 (d, J = 1.8 Hz, 1 H), 5.51 (d, J = 1.8 Hz, 1 H), 2.34 (s, 3 H); ^{13}C-NMR (acetone-d_6) δ 171.50 (s), 141.70 (s), 130.49 (d), 125.34 (s), 124.12 (d), 120.67 (d), 119.93 (s), 118.16 (d), 109.13 (t), 94.05 (d), 23.50 (q); IR (cm^{-1}, CD_2Cl_2) 3550 (br, m), 3430 (m), 1700 (s), 1410 (m); EIMS m/z 205 (M, 9), 189 (M - 16, 5), 173 (M - 32, 9), 172 (M - 33, 1), 145 (M - 60, 13), 130 (M - 75, 100); M$^+$ calcd for $C_{11}H_{11}NO_3$ 205.0739, obsd 205.0717.

Photooxygenation of 1-Acetyl-3-ethyl-2-methylindole (3a). Compound **3a** (0.5173 g, 2.57 mmol) was combined with 20 mL of 3.0×10^{-4} M of TPP/CH_2Cl_2 solution in a 25-mL flask and irradiated at 0 °C for 5 h. The resulting mixture was concentrated in vacuum. A yellowish powder **4a** precipitated upon adding 1.5 mL of 7:3 pentane–CH_2Cl_2. The powder was filtered and rinsed with 2 mL of 5:5 pentane–CH_2Cl_2 and dried below 5 °C by an oil pump to give 90.2 mg (15 %) of pure **4a**-*cis* and **4a**-*trans* in a ratio of 7:1. The filtrate was condensed and the residue separated by column chromatography (silica gel 60, 70–200 mesh) with 1:4 acetone–petroleum ether as eluent. Three fractions were obtained: the first was unreacted starting material **3a** (143.2 mg), the second was **6a** (9.8 mg, 2%), and the third was **5a** (8.2 mg, 1%): ^{1}H-NMR (acetone-d_6) for **4a**-*cis* δ 11.16 (s, 1 H), 8.28 (d, J = 8.17 Hz, 1 H), 7.44 (d, J = 8.17 Hz, 1 H), 7.16 (t, J = 8.17 Hz, 1 H), 7.00 (t, J = 8.17 Hz, 1 H), 6.32 (q, J = 7.56 Hz, 1 H), 2.42 (s, 3 H), 2.04 (d, J = 7.56 Hz, 3 H), 1.88 (s, 3 H); ^{1}H-NMR (acetone-d_6) for **4a**-*trans* δ 10.91 (s, 1 H), 8.42 (d, J = 8.17 Hz, 1 H), 7.62 (d, J = 8.17 Hz, 1 H), 7.18 (t, J = 8.17 Hz, 1 H), 7.07 (t, J = 8.17 Hz, 1 H), 5.94 (q, J = 7.55 Hz, 1 H), 2.45 (s, 3 H), 2.10 (d, J = 7.55 Hz, 3 H). ^{13}C-NMR (acetone-d_6) for **4a**-*cis* δ 169.04 (s), 142.87 (s), 137.36 (s), 128.87 (d), 127.36 (s), 123.25 (d), 118.60 (d), 118.16 (d), 116.94 (d), 100.44 (s), 23.57 (q), 23.19 (q), 12.43 (q); IR (cm^{-1}, KBr pellet) 3200 (br, m), 3040 (m), 1640 (s), 1590 (m), 1500 (s), 1450 (s), 780 (s); EIMS m/z 233 (M, 24), 217 (M - 16, 10), 201 (M - 32, 14), 200 (M - 33, 36), 158 (M - 75, 100); M$^+$ calcd for $C_{13}H_{15}NO_3$ 233.1052, obsd 233.1066.

^{1}H-NMR ($CDCl_3$) for **6a** δ 7.95 (d, J = 7.72 Hz, 1 H), 7.65 (t, J = 7.72 Hz, 1 H), 7.58 (t, J = 7.72 Hz, 1 H), 7.37 (d, J = 7.72 Hz, 1 H), 2.92 (q, J = 5.77 Hz, 2 H), 2.19 (s, 6 H), 1.04 (t, J = 5.77 Hz, 3 H); ^{13}C-NMR (methanol-d_4) δ 207.49 (s), 174.83 (s), 139.33 (s), 137.12 (s), 133.98 (d), 132.22 (d), 130.47 (d), 130.40 (d),

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39.14 (d), 26.89 (q), 19.14 (q); IR (cm^{-1}, CH_2Cl_2) 2920.5 (w), 1715.2 (s), 1580.5 (w), 1372.5 (m), 1260.2 (m), 1023.5 (w), 755.6 (m); EIMS *m/z* 233 (M, 12), 191 (M - 42, 69), 190 (M - 43, 12), 174 (M - 59, 14), 162 (M - 71, 100); M^+ calcd for $C_{13}H_{15}NO_3$ 233.1052, obsd 233.1076.

^{1}H-NMR (CD_2Cl_2) for **5a** δ 7.93 (s, br, 1 H), 7.94 (d, J = 8.23 Hz, 1 H), 7.41 (d, J = 8.23 Hz, 1 H), 7.37 (t, J = 8.23 Hz, 1 H), 7.20 (t, J = 8.23 Hz, 1 H), 5.54 (d, J = 1.66 Hz, 1 H), 5.15 (d, J = 1.66 Hz, 1 H), 2.56 (s, 3 H), 2.01 (m, 1 H), 1.88 (m, 1 H), 0.68 (t, J = 7.43 Hz, 3 H); irradiation at 0.68 ppm simplified the multiplicity at 2.01 ppm and 1.88 ppm, resulting in an AB system; EIMS *m/z* 233 (M, 35), 217 (M - 16, 49), 201 (M - 32, 26) 200 (M - 33, 100), 188 (M - 45, 41); M^+ calcd for $C_{13}H_{15}NO_3$ 233.1052, obsd 233.1057.

Photooxygenation of 1-Acetyl-3-isopropyl-2-methylindole (3b). Compound **3b** (170 mg, 0.791 mmol) was combined with 20 mL of 2.0×10^{-4} M TPP/CH_2Cl_2 solution. Photooxygenation was performed at 0 °C for 5 h. The reaction mixture was concentrated in vacuum. Adding 1 mL of 7:3 pentane–CH_2Cl_2 produced a yellowish powder **4b** which was filtered and rinsed with 1 mL of 5:5 pentane–CH_2Cl_2 to give 9.7 mg (5%) of pure **4b**. The filtrate was concentrated and separated by flash column chromatography using 1:4 acetone–petroleum ether as eluent. The first eluate was unreacted starting material **3b** (40 mg), the second was **6b** (10.2 mg, 5%), and the third was **5b** (11.5 mg, 6%): ^{1}H-NMR (acetone-d_6) for **4b** δ 10.96 (s, 1 H), 8.38 (d, J = 8.15 Hz, 1 H), 7.57 (d, J = 8.15 Hz, 1 H), 7.17 (t, J = 8.15 Hz, 1 H), 7.01 (t, J = 8.15 Hz, 1 H), 2.42 (s, 3 H), 2.19 (s, 3 H), 2.14 (s, 3 H), 1.84 (s, 3 H); ^{13}C-NMR (DMSO-d_6) δ 169.13 (s), 142.65 (s), 131.47 (s), 130.29 (s), 127.64 (s), 127.19 (d), 123.50 (d), 116.03 (d), 100.40 (s), 24.38 (q), 24.30 (q), 23.54 (q), 22.24 (q); IR (cm^{-1}, CD_2Cl_2) 3416.0 (br, s), 1663.3 (s), 1293.7 (m), 1156.2 (m), 821.1 (m), 752.3 (m); EIMS *m/z* 247 (M, 31), 231 (M - 16, 18), 229 (M - 18, 23), 215 (M - 32, 16), 214 (M - 33, 40), 172 (M - 75, 100); M^+ calcd for $C_{14}H_{17}NO_3$ 247.1208, obsd 247.1211.

^{1}H-NMR (acetone-d_6) for **5b** δ 10.46 (s, 1 H), 8.01 (d, J = 8.05 Hz, 1 H), 7.42 (d, J = 8.05 Hz, 1 H), 7.33 (t, J = 8.05 Hz, 1 H), 7.15 (t, J = 8.05 Hz, 1 H), 5.43 (d, J = 2 Hz, 1 H), 5.13 (d, J = 2 Hz, 1 H), 2.50 (s, 3 H), 2.14 (m, 1 H), 0.86 (d, J = 6.96 Hz, 3 H), 0.79 (d, J = 6.96 Hz, 3 H); ^{13}C-NMR ($CDCl_3$) δ 169.17 (s), 148.32 (s), 143.00 (s), 129.71 (d), 128.82 (s), 124.32 (d), 123.87 (d), 116.77 (d), 97.64 (t), 93.87 (s), 37.45 (d), 26.04 (q), 16.62 (q), 16.65 (q); IR (cm^{-1}, $CDCl_3$) 3326.1 (br, s), 3086.3 (w), 2974.5 (s), 2934.5 (m), 2878.5 (m), 1671.6 (s), 1455.8 (m), 912.3 (m), 728.4 (m); EIMS *m/z* 247 (M, 35), 231 (M - 16, 33), 215 (M - 32, 12), 214 (M - 33, 87), 204 (M - 43, 14), 188 (M - 59, 100); M^+ calcd for $C_{14}H_{17}NO_3$ 247.1208, obsd 247.1232.

^{1}H-NMR ($CDCl_3$) for **6b** δ 7.96 (d, J = 7.67 Hz, 1 H), 7.66 (t, J = 7.67 Hz, 1 H), 7.60 (t, J = 7.67 Hz, 1 H), 7.39 (d, J = 7.67 Hz, 1 H), 3.46 (septet, J = 6.8 Hz, 1 H), 2.15 (s, 6 H) 1.05 (d, J = 6.78 Hz); ^{13}C-NMR ($CDCl_3$) δ 205.83 (s), 173.01 (s), 138.05 (s), 135.96 (s), 132.58 (d), 130.81 (d), 128.96 (d), 128.90 (d), 38.08 (d), 26.65 (q), 18.65 (q); IR (cm^{-1}, $CDCl_3$) 3070.3 (w), 2974.4 (w), 2926.5 (m), 2870.5 (m), 1727.5 (s), 1599.6 (m), 1359.9 (m); EIMS *m/z* 247 (M, 4), 204 (M - 43, 76), 188 (M - 59, 22), 162 (M - 85, 100); M^+ calcd for $C_{14}H_{17}NO_3$ 247.1208, obsd 247.1197.

Photooxygenation of 1-Acetyl-2-methyl-3-*tert*-butylindole (7) at −5 °C. Compound **7** (10 mg, 0.044 mmol) was dissolved in ca. 0.4 mL of deuterated chloroform in a 5-mm NMR tube. Photooxygenation was performed at −5 °C (salt/ice bath) for 2 h. The resulting reaction mixture was immediately monitored by NMR at −5 °C and contained 10% of cleavage product **8** and 90% of 1,2-dioxetane **10**. Starting material had reacted completely. Warming **10** to 50 °C for 40 min resulted in complete conversion to **8**.

^{1}H-NMR (−5 °C, $CDCl_3$) for **10** δ 8.20 (d, J = 8.27 Hz, 1 H), 7.56 (d, J = 8.27 Hz, 1 H), 7.38 (t, J = 8.27 Hz, 1 H), 7.07 (t, J = 8.27 Hz, 1 H), 2.34 (s, 3 H), 2.08 (s, 3 H), 1.45 (s, 9 H); ^{13}C-NMR (−5 °C, $CDCl_3$) δ 168.92, 147.31, 131.03, 126.52, 125.61 123.41, 117.01, 107.46, 100.14, 35.59, 26.31, 25.45, 22.62.

^{1}H-NMR ($CDCl_3$) for **8** δ 7.54–7.40 (m, 3 H), 7.15 (d, J = 7.57 Hz, 1 H), 2.26 (s, 6 H), 1.23 (s, 9 H); ^{13}C-NMR ($CDCl_3$) δ 210.89 (s), 173.30 (s), 138.36 (s), 136.50 (s), 130.73 (d), 130.35 (d), 127.91 (d), 126.65 (d), 44.56 (s), 28.02 (q), 26.71 (q); IR (cm^{-1}, $CDCl_3$) 2978.0 (s), 2871.8 (m), 1730.5 (s), 1598.0 (m), 1478.2 (m), 1368.0 (m), 973.9 (m), 754.9 (m); EIMS *m/z* 204 (M-57, 100), M^+ calcd for $C_{15}H_{19}NO_3$ 261.1365, obsd 204.0636 (M - *tert*-butyl). The molecular ion could not be found even with a 5 °C source temperature.

Reaction of 1-Acetyl-2-methyl-3-*tert*-butylindole-1,2-dioxetane (10) with Trimethyl Phosphite or Dimethyl Sulfide. Compound **7** (10 mg, 0.044 mmol) was dissovled in ca. 0.4 mL of $CDCl_3$ in a 5-mm NMR tube containing a tiny amount of TPP. Photooxygenation was done at −5 °C for 2 h. Either 5.5 μL (0.0046 mmol) of trimethyl phosphite or 3.4 μL (0.046 mmol) of dimethyl sulfide was added to the NMR tube, which was left at −5 °C for 3 h. ^{1}H-NMR showed that **10** was completely reduced to **9**; 6.8 mg (64%) of **9** was obtained after column chromatography (eluent: 0.2:2:4 acetone–CH_2Cl_2–petroleum ether) when trimethyl phosphite was used, 5.4 mg (51%) of **9** was obtained with dimethyl sulfide: mp for **9** 113–114 °C; ^{1}H-NMR ($CDCl_3$) δ 8.01 (d, J = 8.05 Hz, 1 H), 7.40 (d, J = 8.05 Hz, 1 H), 7.30 (t, J = 8.05 Hz, 1 H), 7.13 (t, J = 8.05 Hz, 1 H), 5.29 (d, J = 1.73 Hz, 1 H), 5.17 (d, J = 1.73 Hz, 1 H), 2.48 (s, 3 H), 1.83 (s, 1 H), 0.996 (s, 9 H); ^{13}C-NMR ($CDCl_3$) δ 168.05 (s), 154.80 (s), 141.95 (s), 133.70 (s), 129.10 (d), 124.82 (d), 124.02 (d), 116.95 (d), 101.09 (t), 83.75 (s), 38.35 (s), 24.85 (s), 24.09 (q); IR (cm^{-1} CCl_4) 3440.9 (br, s), 2973.5 (s), 2856.7 (m), 1680.6 (s), 1470.3 (m), 1369.0 (m), 770 (s); EIMS *m/z* 245 (M, 5), 188 (M - 57, 52), 146 (M - 99, 100); M^+ calcd for $C_{15}H_{19}NO_2$ 245.1416, obsd 245.1393.

Measurement of Decomposition Rate Constant k_d of 1-Acetyl-2-methyl-3-*tert*-butylindole-1,2-dioxetane (10). Six independent experiments at six temperature points (9.8, 22.8, 30.0, 35.0, 45.1, and 53.3 °C) were done in the following way: 2.1–3.0 mg of **7** was weighed into a 5-mm NMR tube and dissolved with 0.7 mL of $CDCl_3$. A tiny amount of TPP was used. Irradiation was carried out at −5 °C for 90 min. TLC showed that the starting material reacted completely. The resulting 1,2-dioxetane solution was observed in the ^{1}H NMR on a AM-500 NMR spectrometer. The ratio of 1,2-dioxetane and cleavage product was obtained by measuring the integrations of the correspond *tert*-butyl peaks. The first-order kinetics were followed. The rate constants are as follows: k_d (9.8 °C) = 4.93×10^{-6} s^{-1}; k_d(22.8 °C) = 3.32×10^{-5} s^{-1}; k_d (30 °C) = 8.38×10^{-5} s^{-1}; k_d (35.1 °C) = 1.87×10^{-4} s^{-1}; k_d (45.1 °C) = 5.99×10^{-4} s^{-1}; k_d (53.3 °C) = 1.71×10^{-3} s^{-1}.

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Supplementary Material Available: X-ray structures for **2a** and ^{1}H-NMR spectra for all compounds (16 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.