1,2-Dioxetane Formation in Photooxygenation of N-Acylated Indole Derivatives

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Eight *N*-acylated indole derivatives (**1a-h**) react with singlet oxygen at low temperature (-5 to -78 °C) in methanol-d_4 or methanol-d_4-methylene chloride-d_2 to afford 1,2-dioxetanes **2a-h**, whose structures are characterized by low-temperature ^{13}C NMR and ^1H NMR spectra and chemical transformations. These strained 1,2-dioxetanes decompose smoothly and exclusively to dicarbonyl cleavage products **3a-h** upon warming to room temperature.

Introduction

Singlet oxygen undergoes 1,2-cycloaddition with indoles. In most cases, cleavage of the 2,3-double bond to dicarbonyl fragments occurs when *N*-alkyl- or 2,3-dialkylindoles are involved.[1-3] Several intermediates have been suggested for the 2,3-bond cleavage;[4-14] 1,2-dioxetanes[15] and zwitterions[16-18] are widely accepted. Decomposition of dioxetanes is greatly facilitated by electron-donating substituents.[19-25] Many dioxetanes with electron-donating substituents are inherently unstable. For example, enamine dioxetanes[5,26-30] and those from thioketene acetals and tetrathioethylenes[31-37] are difficult to isolate and can be detected only spectroscopically at low temperature in most cases. Saito et al. reported the first characterization of an indole-1,2-dioxetane in the photooxygenation of 1,3-dimethyl-2-*tert*-butylindole in Freon-11 at -78 °C by NMR;[15] this is the only indole dioxetane so far observed. It was argued that the bulky 2-*tert*-butyl group stabilizes it.

Recently, we found that *N*-acyl substitution promotes ene reaction in the photooxygenation of indole derivatives in solvents such as CH_2Cl_2, $CHCl_3$, or acetone.[38] However, in the case of *N*-acetyl-2-methyl-3-*tert*-butylindole, where ene reaction at the 3-position is blocked and the 2-position is hindered, *N*-acetyl-2-methyl-3-*tert*-butylindole-1,2-dioxetane was produced almost quantitatively at -5 °C in $CHCl_3$. The surprising stability of this dioxetane ($\tau_{1/2}$ = 5.0 h at 25 °C in $CHCl_3$) is a result of electronic and steric effects.[38]

In reactions of many substrates such as dihydropyrans[7,39,40] and indenes,[41-43] methanol promotes the formation of dioxetanes relative to ene or [2 + 4] pathways. In this paper, we show that this is also true for *N*-acylated indole derivatives.

Results

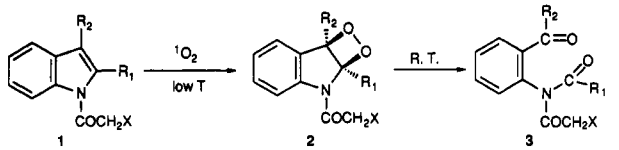
Methylene blue-sensitized photooxygenations of **1a-h** (Scheme I) in methanol-d_4 (methylene chloride-d_2 was added to increase solubility when necessary) were carried

• Abstract published in *Advance ACS Abstracts*, September 1, 1993.

(1) Schaap, A. P.; Zaklika, K. A. *Singlet Oxygen*; Wasserman, H. H., Murray, R. W., Eds.; Academic Press: New York, 1979; pp 174-243.
(2) Sundberg, R. J. *Chemistry of Indoles*; Academic Press: New York, 1970;
(3) Saito, I.; Imuta, M.; Matsugo, S.; Yamamoto, H.; Matsuura, T. *Synthesis* **1976**, *4*, 255-256.
(4) Foote, C. S. *Acc. Chem. Res.* **1968**, *1*, 104.
(5) Bartlett, P. D.; Schaap, A. P. *J. Am. Chem. Soc.* **1970**, *92*, 3223-3224.
(6) Foote, C. S. *Pure Appl. Chem.* **1971**, *27*, 635-645.
(7) Frimer, A. A.; Bartlett, P. D.; Boschung, A. F.; Jewett, J. G. *J. Am. Chem. Soc.* **1977**, *99*, 7977-7986.
(8) Kearns, D. R. *Chem. Rev.* **1971**, *71*, 395-426.
(9) Dewar, M. J. S.; Thiel, W. *J. Am. Chem. Soc.* **1975**, *97*, 3978-3986.
(10) Yamaguchi, K.; Fueno, T.; Fukutome, H. *Chem. Phys. Lett.* **1973**, *22*, 466-469.
(11) Yamaguchi, K.; Fueno, T.; Saito, I.; Matsuura, T.; Houk, K. N. *Tetrahedron Lett.* **1981**, *22*, 749-752.
(12) Yamaguchi, K.; Yabushita, S.; Fueno, T. *Chem. Phys. Lett.* **1981**, *78*, 566-571.
(13) Harding, L. B.; Goddard, W. A., III. *J. Am. Chem. Soc.* **1977**, *99*, 4520-4523.
(14) Harding, L. B.; Goddard, W. A., III. *Tetrahedron Lett.* **1978**, 747-750.
(15) Saito, I.; Matsugo, S.; Matsuura, T. *J. Am. Chem. Soc.* **1979**, *101*, 4757-4759.
(16) Jefford, C. W.; Jaggi, D.; Boukouvalas, J.; Kohmoto, S.; Bernadinelli, G. *Helv. Chim. Acta* **1984**, *67*, 1104-1111.
(17) Saito, I.; Matsugo, S.; Matsuura, T. *J. Am. Chem. Soc.* **1979**, *101*, 7332-7338.
(18) Saito, I.; Nakagawa, H.; Kuo, Y.-H.; Obata, K.; Matsuura, T. *J. Am. Chem. Soc.* **1985**, *107*, 5279-5280.
(19) Schuster, G. B. *Acc. Chem. Res.* **1979**, *12*, 366-373.
(20) Schaap, A.; Gagnon, S. D. *J. Am. Chem. Soc.* **1982**, *104*, 3504-3506.
(21) Schaap, A. P.; Gagnon, S. D.; Zaklika, K. A. *Tetrahedron Lett.* **1982**, *23*, 2943-2946.
(22) Zaklika, K. A.; Thayer, A. L.; Schaap, A. P. *J. Am. Chem. Soc.* **1978**, *100*, 4916-4918.
(23) McCapra, F.; Beheshti, I.; Burford, A.; Hahn, R. A.; Zaklika, K. A. *J. Chem. Soc., Chem. Commun.* **1977**, 944-946.
(24) Nakamura, H.; Goto, T. *Photochem. Photobiol.* **1979**, *30*, 27-30.
(25) Lee, C.; Singer, L. A. *J. Am. Chem. Soc.* **1980**, *102*, 3823-3829.
(26) Wasserman, H. H.; Terao, S. *Tetrahedron Lett.* **1975**, 1735-1739.
(27) Orito, K.; Manske, R. H.; Rodrigo, R. *J. Am. Chem. Soc.* **1974**, *96*, 1944-1945.
(28) Foote, C. S.; Dzakpasu, A. A.; Lin, J. W.-P. *Tetrahedron Lett.* **1975**, 1247-1250.
(29) Foote, C. S.; Lin, J. W.-P.; Wong, S.-Y. *Petroleum Preprints* **1970**, *15*, E89.
(30) Foote, C. S.; Lin, J. W.-P. *Tetrahedron Lett.* **1968**, 3267-3271.
(31) Ando, W.; Watanabe, K.; Suzuki, J.; Migita, T. *J. Am. Chem. Soc.* **1974**, *96*, 6766-6768.
(32) Ando, W.; Watanabe, K.; Migita, T. *J. Chem. Soc., Chem. Commun.* **1975**, 961-962.
(33) Ando, W.; Watanabe, K.; Migita, T. *Tetrahedron Lett.* **1975**, 4127.
(34) Ando, W.; Suzuki, J.; Arai, T.; Migita, T. *Tetrahedron* **1973**, *29*, 1507-1513.
(35) Adam, W.; Liu, J.-C. *J. Am. Chem. Soc.* **1972**, *94*, 1206.
(36) Adam, W.; Arias, L. A.; Scheutzow, D. *Tetrahedron Lett.* **1982**, *23*, 2835-2836.
(37) Geller, G. G.; Foote, C. S.; Pechman, D. B. *Tetrahedron Lett.* **1983**, *24*, 673-676.
(38) Zhang, X.; Foote, C. S.; Khan, S. I. *J. Org. Chem.* **1993**, *58*, 47-51.
(39) Bartlett, P. D.; Mendenhall, G. D.; Schaap, A. P. *Ann. N. Y. Acad. Sci.* **1970**, *171*, 79.
(40) Gollnick, K.; Knutzen-Mies, K. *J. Org. Chem.* **1991**, *56*, 4017-4027.
(41) Ando, W.; Watanabe, K.; Suzuki, J.; Migita, T. *J. Am. Chem. Soc.* **1974**, *96*, 6766-6768.
(42) Burns, P. A.; Foote, C. S. *J. Am. Chem. Soc.* **1974**, *95*, 4339-4340.
(43) Manring, L. E.; Foote, C. S. *J. Am. Chem. Soc.* **1983**, *105*, 4710-4717.
(44) Calvert, J. G.; Pitts, J. N. *Photochemistry*; Wiley: New York, 1966; pp 739.

0022-3263/93/1958-5524$04.00/0

Scheme I



a: X = H, R_1 = CH_3, R_2 = *tert*-butyl b: X = H, R_1 = CH_3, R_2 = *iso*-propyl
c: X = H, R_1 = CH_3, R_2 = Et d: X = H, R_1 = R_2 = CH_3
e: X = Cl, R_1 = R_2 = CH_3 f: X = R_1 = H, R_2 = CH_3
g: X = R_2 = H, R_1 = CH_3 h: X = H, R_2, R_3 = -$(CH_2)_4$-

Table I. 1,2-Dioxetane Formation in Photooxygenation of *N*-Acylated Indole Derivatives[a]

compd	concn, M	*T*, °C	irrad. time, h	products[d] (yield, %)
1a[b]	0.082	−30	1.0	**2a** (89), **3a** (11)
1b[c]	0.330	−5	4.0	**2b** (84), **3b** (16)
1c[c]	0.080	−78	2.5	**2c** (86), **3c** (14)
1d[c]	0.110	−78	2.0	**2d** (53), **3d** (10), ene (37)[e]
1e[c]	0.090	−30	2.0	**2e** (52), **3e** (1), ene (46)
1f[c]	0.185	−78	5.5	**2f** (33), **3f** (62%),[f] ene (5)
1g[c]	0.196	−78	6.0	**2g** (32), **3g** (20), sm (48)[e]
1h[c]	0.178	−78	7.0	**2h** (48), **38** (52)

[a] In methanol-d_4, except as noted; to avoid photolysis of dioxetane by UV, the output of the xenon lamp (Varian-Eimac, 300 W) was filtered with 3-cm aqueous 0.008 M $K_2Cr_2O_7$ solution.[44] [b] $CDCl_3$.[c] A few drops of methylene chloride-d_2 was added. [d] Determined by ^1H NMR at low temperature. [e] "Ene" stands for the ene products (2-hydroperoxy-3-methyleneindolines[38]); "sm" stands for unreacted **1g**. [f] **3f** contains two rotamers in a ratio of 73:27 at −78 °C.

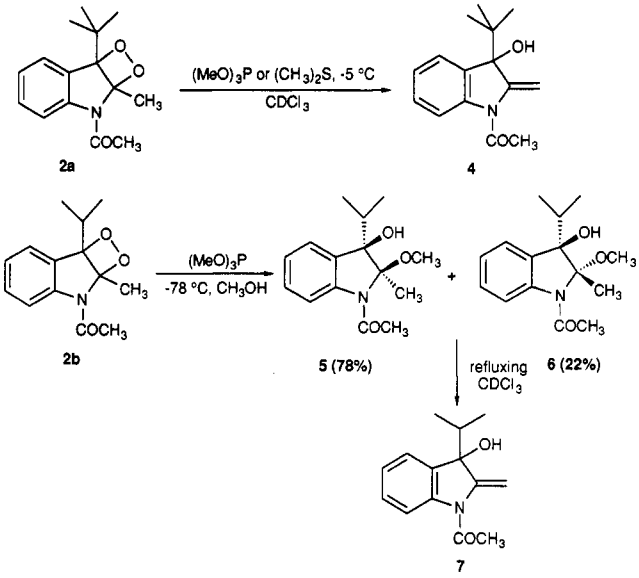
out in a 5-mm NMR tube at temperatures from −5 to −78 °C. Irradiation was stopped after starting material was consumed except in the case of **1g**, which reacts with singlet oxygen very slowly because of its low electron density. The NMR spectra of the resulting solutions (−40 to −78 °C) were measured immediately after photooxygenation. The results are shown in Table I, and ^{13}C NMR and ^1H NMR spectra of the 1,2-dioxetanes **2a–h** are summarized in Tables II and III.

The chemical shifts of C-2 and C-3 are particularly important for establishing the structures of the strained 1,2-dioxetanes since C-2 is attached to two heteroatoms and C-3 is at a benzylic position with one oxygen attached. With a methyl on C-2 and an alkyl on C-3 (**2a–e**), the shifts of C-2 range from 106.1 to 107.5 ppm and that of C-3 ranges from 93.6 ppm to 100.1 ppm, depending on the alkyl groups. Substitution of a proton for an alkyl at C-3 shifts C-3 upfield to 89.1 ppm (**2g**) and decreases the reaction rate dramatically, as expected, while replacement at C-2 shifts C-2 upfield to 97.7 ppm (**2f**). Compound **2h** is a 1,2-dioxetane with a novel propellane structure.

The chemical shifts of methyl protons at C-2 are also useful for characterizing the dioxetanes because they usually appear between 2.03 and 2.08 ppm as singlets (**2a–e**) but at ca. 2.20 ppm in the cleavage products. The AB pattern (J_{AB} = 20.0 Hz) for the methylene protons (at 2.80, 2.38 ppm, respectively) in **2e** and two doublet isopropyl methyls (at 1.30, 1.03 ppm) in **2b** provide further spectroscopic evidence for the structures of the 1,2-dioxetanes. Comparisons of results in Table I lead to the conclusion that (1) alkyl substitution at both the 2 and 3 positions facilitates the formation of the 1,2-dioxetane, with substitution at the 3 position more sensitive and (2) 1,2-dioxetanes with bulky alkyl groups at the 3-position have higher thermal stability than those without. This is in agreement with Saito's steric arguments.[15]

Warming the 1,2-dioxetane (**2c–2h**) solutions to room temperature resulted in clean conversion to the corresponding ketoamides (**3c–h**) as observed by variable-temperature NMR. However, *N*-acyl-2-methyl-3-*tert*-butylindole-1,2-dioxetane **2a** and *N*-acyl-2-methyl-3-isopropylindole-1,2-dioxetane **2b** are surprisingly stable at room temperature ($\tau_{1/2}$ = 5.0 h), and in both cases, gentle heating (50 °C in methanol-d_4) is needed to obtain rapid dioxetane ring cleavage. The products, ketoamides **3a–h**, were easily purified by column chromatography or preparative TLC and fully characterized by ^1H NMR, ^{13}C NMR, FT-IR, and exact mass measurement.

Scheme II



The structures of the 1,2-dioxetanes were further proved by chemical transformations. Reaction of **2a** with trimethyl phosphite or dimethyl sulfide in chloroform gave indoline **4**,[45,46] while reaction of **2b** with trimethyl phosphite in methanol afforded stereoisomeric methanol adducts **5** and **6** (78:22). Both **5** and **6** were transformed to indoline **7** on reflux in chloroform. Isolation of **7** unequivocally established the regiochemistry of the methanol adduct **5** and **6** as occuring at the 2-position. The *cis* relationship between the C-2 methyl and C-3 isopropyl group in **5** was confirmed by NOE. Saturation of the C-2 methyl (δ = 1.81 ppm) produced 15.3% enhancement of the methine proton (δ = 2.15 ppm) and 1.6% enhancement of one methyl (δ = 0.56 ppm) of the isopropyl group. Saturation of the methyl at 0.56 ppm produced 1.0% enhancement of the C-2 methyl.

Discussion

We expected that electron-withdrawing substituents on the 1-position on the indole ring would decrease the nucleophilicity of the nitrogen so that the 1,2-dioxetane should be stabilized to some extent. This idea was successful, and a number of labile indole-1,2-dioxetanes could be prepared and characterized spectroscopically. All the 1,2-dioxetanes decomposed to the ketoamides at room temperature. In methanol, products **5** and **6** incorporate solvent regiospecifically at C-2 position, strongly indicating carbocation formation at C-2 when the phosphorane intermediate opens, as shown in Scheme III.

The reason methanol favors 1,2-dioxetane formation over ene reaction is still obscure. This effect is not due

(45) Wasserman, H. H.; Saito, I. *J. Am. Chem. Soc.* **1975**, *97*, 905–906.
(46) Nahm, K.; Foote, C. S. *J. Am. Chem. Soc.* **1989**, *111*, 1909–1910.

Table II. ^{13}C NMR Chemical Shift Values of 1,2-Dioxetanes (δ, ppm Relative to TMS)[a]

entry	C-2	C-3	C-3a	C-4	C-5	C-6	C-7	C-7a	CO	$COCH_2X$	$R_1C(2)$	$R_2C(3)$
2a	107.5	100.1	126.5	125.6	123.4	131.0	117.0	147.3	168.9	26.3	25.5	35.6, 22.6
2b	107.1	97.7	125.9	132.2	125.2	137.0	118.9	148.2	171.5	27.1	17.9	31.1, 15.6
2c[b]	106.1	96.5	127.6	125.3	124.6	132.2	118.4	147.7	171.1	25.5	20.8	23.8, 9.0
2d	106.6	93.6	126.8	129.5	124.8	132.4	118.1	146.8	172.3	25.4	20.6	16.9
2e	106.9	93.8	127.1	129.7	124.0	132.6	118.3	146.5	167.3	41.7	20.7	16.8
2f	97.7	92.3	*c*	*c*	*c*	*c*	117.9	*c*	*c*	*c*		*c*
2g	104.4	89.1	127.7	128.3	124.2	136.2	118.1	148.1	170.6	25.8	23.4	
2h[b]	105.0	91.2	128.6	125.1	124.1	132.4	117.9	147.5	170.9	25.1	35.6, 20.9	31.0, 19.9

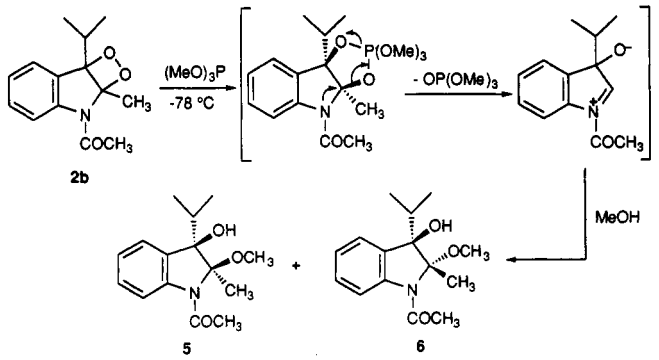
[a] On a Bruker AM 360 at 90 MHz for ^{13}C except for **2d**, which was done on an AM 500 at 125 MHz for ^{13}C. [b] DEPT was performed at low temperature. [c] Cannot be assigned because of rotamers.

Table III. ^1H NMR Chemical Shift Values of 1,2-Dioxetanes (δ, ppm Relative to TMS)[a]

dioxetanes	aromatic protons	$COCH_2X$	$R_1C(2)$	$R_2C(3)$
2a	7.56 (d), 7.38 (t), 7.07 (t), 8.20 (d), J = 7.57 Hz	2.34 (s)	2.08 (s)	1.45 (s)
2b	7.45 (d), 7.43 (t), 7.13 (t), 8.00 (d), J = 7.53 Hz	2.32 (s)	2.03 (s)	1.30 (d), 1.03 (d), 3.08 (m)
2c	7.32 (d), 7.47 (t), 7.22 (t), 8.33 (d), J = 8.03 Hz	2.31 (s)	2.07 (s)	2.45 (q), 0.91 (t)
2d	7.35 (d), 7.44 (t), 7.17 (t), 8.25 (d), J = 8.00 Hz	2.28 (s)	2.03 (s)	1.95 (s)
2e	7.36–7.33 (m), 7.48 (t), 8.27 (d), J = 7.94 Hz	4.29 (AB)	2.04 (s)	1.96 (s)
2f	7.39 (d), 7.46 (t), 7.20 (t), 8.24 (d), J = 8.09 Hz	2.19 (s)	2.97 (s)	2.00 (s)
2g	7.35 (d), 7.44 (t), 7.20 (t), 8.26 (d), J = 8.13 Hz	2.23 (s)	2.10 (s)	6.51 (s)
2h	7.34 (d), 7.44 (t), 7.17 (t), 8.26 (d), J = 8.05 Hz	2.24 (s)	2.47 (1 H), 2.06 (1 H)	1.85 (6 H)

[a] From −5 to −78 °C on a Bruker AM 360 or AM 500 spectrometer.

Scheme III



to polarity alone since ene reaction was practically the only reaction (>95%) when photooxygenations of *N*-acetyl-2,3-dimethylindole (**1d**) and *N*-acetyl-3-ethyl-2-methylindole (**1c**) were carried out in acetonitrile-d_3 and DMSO-d_6.[47] We suspect that the proticity plays a major role in stabilizing the transition state leading to 1,2-dioxetane, as it does in the indene series.[48–50]

Conclusions

Cleavage of the indole 2,3-double bond in substituted indoles involves an unstable intermediate 1,2-dioxetane. Spectroscopic detection of these intermediates was made possible by stabilization by an *N*-acetyl group and by alkyl substitution at C-2 and C-3 positions. Methanol is a particularly favorable solvent for dioxetane formation. The effect of solvent on the photooxygenation is under study.

Experimental Section

General. FT-IR was performed on a Nicolet-205 FT-IR spectrometer using NaCl plate–$CDCl_3$ film sampling unless otherwise stated. HRMS were done on a VG Analytical Autospec instrument. Methanol was distilled from magnesium–iodine and stored over 4-Å molecular sieves. Trimethyl phosphite was distilled from sodium before use. All other commercially available reagents and solvents were used without further purification. Photooxygenations were carried out at the desired temperature with a Cermax 300-W xenon lamp, filtered with a 0.0085 M $K_2Cr_2O_7$ solution (path length 3.5 cm) to remove light below 490 nm. Oxygen was dried by passing through activated 4-Å molecular sieves and bubbled through the solution via a Teflon tube when a 5-mm NMR tube was used or a glass pipet when a flask was used. The specific photooxygenation conditions for each substrate are given in Table I. The cleaved ketoamides **3a–h** were obtained by warming the low-temperature photooxidation reaction mixtures to room temperature, evaporating the solvent in vacuo, and purifying with flash column chromatography (silica gel, >230 mesh) or preparative TLC (Merck, silica gel 60F, 254) using ethyl acetate–hexane as eluent. The yields are usually in the range of 60–89%, except for **3g**, which was obtained in 30% yield. Attempts to separate **5** and **6** by column chromatography failed.

All ^1H and ^{13}C NMR data were taken on Bruker AM 360 or AM 500 machines equipped with a variable-temperature probe. Low-temperature NMR experiments were done in the following manner. The probe was cooled to the desired temperature, and then the sample, precooled in dry ice–acetone, was immediately placed in it. Usually 15 min or longer was needed before the probe temperature stabilized and good shimming could be achieved. The probe temperature fluctuation could be as small as 0.1–0.2 °C. Chemical shift values are in δ (ppm) relative to TMS. Carbon multiplicities were obtained by DEPT experiments. The ^{13}C NMR and ^1H NMR data of the *N*-acylindole-1,2-dioxetanes **2a–h** were summarized in Tables II and III, respectively.

***o*-(*N*,*N*-Diacylamino)neopentanophenone (3a):** ^1H NMR ($CDCl_3$) δ 7.53 (d, J = 7.57 Hz, 1 H), 7.48 (t, J = 7.57 Hz, 1 H), 7.42 (t, J = 7.57 Hz, 1 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} 2978.0 (m), 1730.5 (s), 1598.0 (m), 1478.2 (m), 1368.2 (m), 1239.3 (m), 973.9 (m), 754.9 (m); MS m/z 204 (M − 57, 100), 169 (M − 92, 36), 155 (M − 106, 11); HRMS calcd for $C_{15}H_{19}NO_3$ 261.1360, obsd 204.0636 (M − *tert*-butyl).

o-(*N*,*N*-Diacylamino)isobutyrophenone (3b): ^1H NMR ($CDCl_3$) 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 = 6.8 Hz, 6 H); ^{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} 2974.4 (m), 1727.5 (s), 1599.6 (m), 1359.9 (m), 745.5 (m);

(47) Unpublished results. The low solubility of *N*-acetyl-2,3-disubstituted indoles in DMSO makes the reaction preparatively useless.
(48) Zhang, J.; Foote, C. S. *Tetrahedron Lett.* **1986**, *27*, 6153–6156.
(49) Burns, P. A.; Foote, C. S.; Mazur, S. *J. Org. Chem.* **1976**, *41*, 899–907.
(50) Boyd, J. D.; Foote, C. S. *J. Am. Chem. Soc.* **1979**, *101*, 6758–6759.

MS *m/z* 247 (M, 4), 205 (M - 42, 22), 203 (M - 44, 100), 188 (M - 59, 66); HRMS calcd for $C_{14}H_{17}NO_3$ 247.1209, obsd 247.1197.

***o*-(*N,N*-Diacylamino)propiophenone (3c)**: ^{1}H NMR ($CDCl_3$) 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 ($CDCl_3$) δ 202.19 (s), 172.95 (s), 137.30 (s), 136.21 (s), 132.58 (d), 130.46 (d), 129.04 (d), 129.01 (d), 33.84 (t), 26.61 (q), 7.88 (q); IR cm^{-1} 2950.5 (m), 1720.6 (s), 1588.6 (m), 1370.4 (m), 970.4 (m), 745.6 (m); MS *m/z* 233 (M, 3), 191 (M - 42, 10), 161 (M - 72, 100), 146 (M - 87, 45), 134 (M - 99, 13); HRMS calcd for $C_{13}H_{15}NO_3$ 233.1048, obsd 233.1076.

***o*-(*N,N*-Diacylamino)acetophenone (3d)**: ^{1}H NMR ($CDCl_3$) δ 7.84 (d, J = 7.61 Hz, 1 H), 7.60 (t, J = 7.61 Hz, 1 H), 7.53 (t, J = 7.61 Hz, 1 H),7.18 (d, J = 7.61 Hz, 1 H), 2.54 (s, 3 H), 2.25 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 199.11 (s), 173.06 (s), 137.53 (s), 135.97 (s), 133.05 (d), 130.69 (d), 129.93 (d), 129.15 (d), 28.72 (q), 26.76 (q); IR cm^{-1} 1705.1 (s), 1656.0 (s), 1584.0 (s), 1525.0 (s), 1248.0 (s); MS *m/z* 219 (m, 12), 177 (M - 42, 50), 162 (M - 57, 11), 135 (M - 84, 62), 120 (M - 99, 100); HRMS calcd for $C_{12}H_{13}NO_3$ 219.0892, obsd 219.0898.

***o*-[*N*-Acyl-*N*-(chloroacyl)amino]acetophenone (3e)**: ^{1}H NMR ($CDCl_3$) δ 7.87 (d, J = 7.57 Hz, 1 H), 7.64 (t, J = 7.57 Hz, 1 H), 7.58 (t, J = 7.57 Hz, 1 H), 7.22 (d, J = 7.57 Hz, 1 H), 4.60 (d, AB, J = 16.1 Hz, 2 H), 2.55 (s, 3 H), 2.10 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 199.12 (s), 172.79 (s), 169.30 (s), 136.32 (s), 135.70 (s), 133.38 (d), 130.77 (d), 130.23 (d), 129.77 (d), 46.71 (t), 28.66 (q), 26.09 (q); IR cm^{-1} 2930.0 (w), 1711.8 (s), 1689.3 (s), 1364.9 (m), 1252.9 (s); MS *m/z* (M, 3), 211 (M - 42, 98), 196 (M - 57, 54), 177 (M - 76, 23), 135 (M - 118, 61), 120 (M - 133, 100); HRMS calcd for $C_{12}H_{12}NO_3Cl$ 253.0503, obsd 253.0492.

***o*-(*N*-Acyl-*N*-formylamino)acetophenone (3f)**: ^{1}H NMR ($CDCl_3$) δ 9.42 (s, 1 H), 7.87 (d, J = 7.62 Hz, 1 H), 7.64 (t, J = 7.62 Hz, 1 H), 7.57 (t, J = 7.62 Hz, 1 H), 7.20 (d, J = 7.62 Hz, 1 H), 2.55 (s, 3 H), 2.11 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 198.77 (s), 172.55 (s), 162.72 (d), 135.82 (s), 133.60 (s), 133.18 (d), 130.71 (d), 130.10 (d), 129.69 (d), 28.64 (q), 24.02 (q); IR (KBr pellet) cm^{-1} 3076.2 (w), 2960.9 (w), 2853.4 (w), 1721.6 (s), 1691.5 (s), 1685.5 (s), 1354.4 (s), 776.5 (m); MS *m/z* 205 (M, 4), 177 (M - 28, 16), 163 (M - 42, 47), 148 (M - 57, 23), 135 (M - 70, 57), 120 (M - 85, 100); HRMS calcd for $C_{11}H_{11}NO_3$ 205.0736, obsd 205.0752.

***o*-(*N,N*-Diacylamino)benzaldehyde (3g)**: ^{1}H NMR ($CDCl_3$) δ 9.94 (s, 1 H), 7.88 (d, J = 7.51 Hz, 1 H), 7.66 (t, J = 7.51 Hz, 1 H), 7.58 (t, J = 7.51 Hz, 1 H), 7.58 (d, J = 7.51 Hz, 1 H), 2.21 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 190.02 (d), 172.63 (s), 139.40 (s), 135.11 (d), 133.76 (d), 132.46 (s), 130.74 (d), 129.71 (d), 26.45 (q); IR cm^{-1} 1707.9 (s), 1600.0 (m), 1242.2 (s), 950.0 (m); HRMS calcd for $C_{11}H_{11}NO_3$ 205.0736, obsd 205.0739.

***N*-Acyl-1-aza-8,9-benzcyclononene-2,7-dione (3h)**:[51,52] ^{1}H NMR ($CDCl_3$) δ 7.60–7.53 (m, 3 H), 7.34 (d, J = 7.53 Hz, 1 H), 3.04 (m, 1 H), 2.51 (m, 2 H), 2.43 (s, 3 H), 2.00 (m, 2 H), 1.98–1.5 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 208.59 (s), 178.52 (s), 174.96 (s), 142.90 (s), 137.10 (s), 132.57 (d), 131.48 (d), 130.12 (d), 128.00 (d), 44.22 (t), 38.68 (t), 26.85 (q), 26.83 (t), 26.68 (t); IR cm^{-1} 2935.4 (m), 2861.9 (w), 1723.4–1698.9 (br, s), 1448.0 (m), 1209.3 (m), 1013.4 (m); MS *m/z* 245 (M, 15), 203 (M - 42, 92), 173 (M - 72, 38), 162 (M - 83, 88), 120 (M - 125, 100).

***cis*-2,3-Dihydro-*N*-acyl-3-hydroxy-3-isopropyl-2-methoxy-2-methylindole (5)**: ^{1}H NMR ($CDCl_3$) δ 7.37–7.11 (m, 4 H), 3.48 (s, 3 H), 2.96 (s, 1 H), 2.81 (m, 1 H), 2.38 (s, 3 H), 1.55 (s, 3 H), 0.93 (d, J = 6.4 Hz, 3 H), 0.71 (d, J = 6.4 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 169.59 (s), 137.77 (s), 129.12 (s), 128.69 (d), 126.51 (d), 123.94 (d), 113.99 (d), 100.60 (s), 88.34 (s), 51.92 (q), 28.09 (d), 25.39 (q), 23.06 (q), 17.65 (q), 16.15 (q).

***trans*-2,3-Dihydro-*N*-acyl-3-hydroxy-3-isopropyl-2-methoxy-2-methylindole (6)**: ^{1}H NMR ($CDCl_3$) δ 7.37 (d, J = 7.82 Hz, 1 H), 7.25 (t, J = 7.82 Hz, 1 H), 7.15–7.11 (m, 2 H), 3.43 (s, 1 H), 3.30 (s, 3 H), 2.38 (s, 3 H), 2.15 (m, 1 H), 1.83 (s, 3 H), 1.07 (d, J = 6.4 Hz, 3 H), 0.58 (d, J = 6.4 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 169.85 (s), 141.24 (s), 134.89 (s), 128.24 (d), 125.87 (d), 124.04 (d), 116.34 (d), 99.46 (s), 85.07 (s), 50.97 (q), 33.31 (d), 24.96 (q), 17.26 (q), 16.63 (q), 14.70 (q).

For **5** and **6**: MS *m/z* 263 (M, 4), 245 (M - 18, 2), 231 (M - 32, 12), 220 (M - 43, 13), 204 (M - 59, 17), 187 (M - 76, 81), 144 (M - 119, 100), 130 (M - 133, 37); HRMS calcd for $C_{15}H_{21}NO_3$ 262.1516, obsd 263.1561.

***N*-Acyl-3-hydroxy-3-*tert*-butyl-2-methyleneindoline (4)**:[38] mp 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} 3440.9 (br, s), 2973.5 (s), 2856.7 (m), 1680.6 (s), 1470.3 (m), 1369.0 (m), 770 (s); MS *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.

***N*-Acyl-3-hydroxy-3-isopropyl-2-methyleneindoline (7)**: mp 72–73 °C; ^{1}H NMR ($CDCl_3$) δ 8.02 (d, J = 7.88 Hz, 1 H), 7.38 (d, J = 7.88 Hz, 1 H), 7.31 (t, J = 7.88 Hz, 1 H), 7.16 (t, J = 7.88 Hz, 1 H), 5.24 (d, J = 1.87 Hz, 1 H), 5.19 (d, J = 1.87 Hz, 1 H), 2.50 (s, 3 H), 2.09 (septet, J = 6.96 Hz, 1 H), 1.98 (s, 1 H), 0.87 (d, J = 6.96 Hz, 3 H), 0.86 (d, J = 6.96 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 168.68 (s), 154.54 (s), 141.96 (s), 133.38 (s), 129.32 (d), 124.50 (d), 123.69 (d), 116.86 (d), 98.50 (t), 82.14 (s), 39.18 (d), 25.47 (q), 16.68 (q), 16.10 (q); IR (KBr pellet) cm^{-1} 3462.0 (s), 2950.0 (m), 2930.0 (m), 1657.0 (s), 1469.0 (s), 1372.0 (s), 1000.0 (m), 820.2 (m), 720.5 (m); MS *m/z* 231 (M, 33), 214 (M - 17, 2), 188 (M - 23, 100), 169 (M - 62, 15), 146 (M - 85, 18); HRMS calcd for $C_{14}H_{17}NO_2$ 231.1255, obsd 231.1203.

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Supplementary Material Available: Low-temperature ^{1}H NMR spectra for dioxetanes **2a–h**, cleavage products (ketoamides) **3a–h**, and *N*-acetyl-3-hydroxy-2-methyleneindolines **4** and **7** (18 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.

(51) Saito, I.; Imuta, M.; Matsuura, T. *Chem. Lett.* **1972**, 1173–1176.
(52) Saito, I.; Imuta, M.; Matsuura, T. *Chem. Lett.* **1972**, 1197–1200.