Indole Dioxetanes and Epoxides by Oxidation of *N*-Acylated Indoles with Singlet Oxygen and Dimethyldioxirane: Kinetics and Chemiluminescence Yields of the Thermal Dioxetane Decomposition and Fluoride Ion-induced CIEEL Emission

Waldemar Adam * and Dirk Reinhardt
Institut für Organische Chemie, Universität Würzburg, Am Hubland, D-97074 Würzburg, Germany

Photooxygenation of the *N*-acylated indoles **2** afforded the corresponding labile indole dioxetanes **3**, the allylic hydroperoxides **4** and the carbamates **5**. The dioxetanes were sufficiently stable for isolation and spectral characterization. Additionally, they were characterized by their chemiluminescence properties and chemical transformations, *i.e.* thermolysis to the fragmentation products **5** and dimethyl sulfide deoxygenation to the epoxides **7**. The latter were independently prepared by dimethyldioxirane oxidation. The activation parameters (E_a, log A, $\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$) and the excitation yields (Φ^S, Φ^T) of the direct chemiluminescence for the indole dioxetanes **3** were determined by standard isothermal kinetic methods. The fluoride ion-induced decomposition of the silyl-substituted dioxetane **3b** released intramolecular CIEEL emission.

The chemistry of 1,2-dioxetanes[1] has been intensively studied since their first synthesis[2] nearly 25 years ago. Besides chemical transformations, their chemiluminescence properties are of particular interest. It was established[3] that these high-energy molecules generate mainly triplet-excited carbonyl compounds on thermal decomposition, except when the dioxetane ring bears electron-donating substituents. In the latter case, such labile dioxetanes display chemically initiated electron exchange luminescence (CIEEL),[4] an electron-transfer mechanism originally discovered by Schuster for the diphenoyl peroxide.[5] An efficient intramolecular example represents the firefly bioluminescence, in which an α-peroxy lactone **A** intervenes.[6] It is the phenolate moiety which serves as internal electron donor to afford by electron transfer and decarboxylation the singlet-excited oxyluciferin as emitter in over 90% efficiency.[7] As an extension of this phenomenon figures the base- or enzyme-catalysed release of the phenolate site in the spiroadamantyl dioxetanes **B**.[8]

The interesting biochemical aspects of such triggerable dioxetanes, especially their applications in immunoessays, have recently been reviewed.[9] In this context, we have prepared[10] the novel CIEEL-active benzofuran dioxetanes **C**, which undergo base- or fluoride ion-triggered decomposition with appreciable chemiluminescence. Unfortunately, their efficiency of light emission was inferior to that of the spiroadamantyl dioxetanes **B**. Consequently, it was of interest to search for more effective, triggerable CIEEL-active dioxetanes.

Recently,[11] relatively persistent *N*-acylated indole dioxetanes were either detected by low-temperature NMR spectroscopy or even isolated by low-temperature column chromatography. In contrast, the unprotected indole dioxetanes (free NH group) are very labile and have been postulated as precursors for the C_2–C_3 ring cleavage products, which are obtained in many chemical[12] and biological[13] oxygenations of indoles. Our aim of the present study was to prepare persistent indole dioxetanes with triggering functionalities and investigate their CIEEL activity. The electron-rich indolyl anion, released through deacylation from the protected indole dioxetanes, should serve as an effective internal electron donor to afford enhanced chemiluminescence.

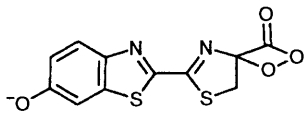
Results

The alkoxycarbonylated indoles **2a**, **b** were prepared according to literature procedure[14] (Scheme 1, i, ii). The tetraphenylporphine (TPP)-sensitized photooxygenation of these indoles in dichloromethane or deuteriochloroform at −30 °C (Scheme 1, iii) gave the corresponding indole dioxetanes **3a**, **b** as major products (45–59%), besides the allylic hydroperoxides **4a**, **b** (27–37%) and the carbamates **5a**, **b** (14–18%). The latter resulted from *in situ* decomposition of the dioxetanes by C_2–C_3 bond cleavage.

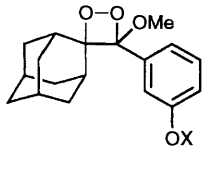
The dioxetanes **3a**, **b** were isolated by low-temperature silica gel chromatography at −20 °C and unequivocally characterized on the basis of their spectral data and by their chemiluminescence. The ^{13}C NMR chemical shifts of the C-2 (δ 105) and C-3 (δ 93) ring carbon atoms are characteristic for the 1,2-dioxetane structure.

The thermal decomposition of the indole dioxetanes **3a**, **b** gave quantitatively the expected, hitherto unknown carbonyl compounds **5a**, **b** (Scheme 1, iv). These were isolated and characterized on the basis of their spectral and analytical data.

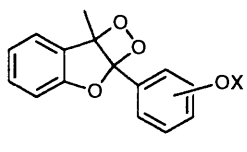
Reduction of the indole dioxetanes **3a**, **b** by Me_2S at −30 °C gave the corresponding epoxides **7a**, **b** (Scheme 1, vi), which were observed by NMR spectroscopy at this temperature. The latter were independently prepared in excellent yields by dimethyldioxirane oxidation of the indoles **2a**, **b** (Scheme 1, vii). The epoxides **7a**, **b** were sufficiently persistent at −20 °C for spectral acquisition. However, these epoxides are quite labile and decompose readily above 0 °C, which precluded their isolation and rigorous purification for elemental analyses. Thus, the structure assignment rests exclusively on NMR spectral data.



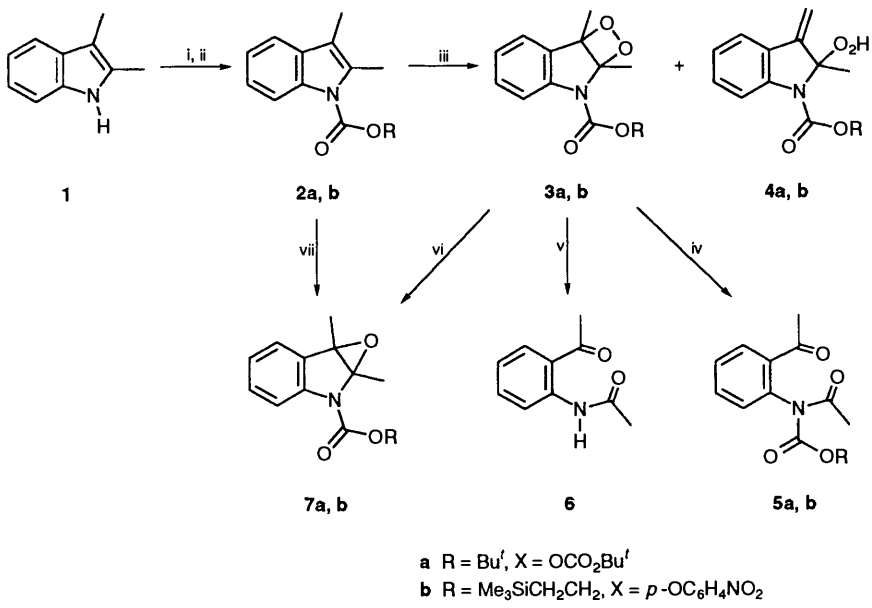
A



B X = $SiMe_2Bu^t$, PO_3^{2-}



C X = $SiMe_2Bu^t$, Ac



Scheme 1 *Reagents and conditions:* i, NaH, THF, 25 °C, 1 h, N_2; ii, ROCOX, THF, 25 °C, 6–15 h, N_2; iii, O_2, TPP, *hv*, $CDCl_3$, −30 °C, 6 h; iv, CH_2Cl_2, 25 °C, 24 h; v, only for **3b**: Bu_4NF, CH_3CN–H_2O, 25 °C, within 20 s; vi, Me_2S, $CDCl_3$, −30 °C, 1 h; vii, dimethyldioxirane, CH_2Cl_2–CH_3COCH_3, −78 to −20 °C, 4 h

Table 1 Rate constants,[a] activation parameters[b] and chemiluminescence efficiencies[c] for the thermal decomposition of the indole dioxetanes **3a**, **b** in toluene

Dioxetane	T/°C[d]	k/10^{-4} s^{-1}	E_a/kcal mol^{-1}	log A	$\Delta H^{\ddagger}$/kcal mol^{-1}	$\Delta S^{\ddagger}$/cal mol^{-1} K^{-1}	Φ^S/10^{-6} E mol^{-1}	Φ^T/10^{-4} E mol^{-1}
3a[e]	40	1.1 ± 0.1						
	50	2.7 ± 0.1						
	60	7.2 ± 0.1	20.5 ± 0.4	10.3 ± 0.3	19.5 ± 0.1	−15 ± 2	6 ± 3	2.2 ± 0.1
	70	18.3 ± 0.3						
	80	41.5 ± 1.3						
3b[f]	40	1.2 ± 0.1						
	50	3.0 ± 0.2						
	60	9.0 ± 0.5	20.1 ± 0.5	10.1 ± 0.3	19.3 ± 0.6	−15 ± 2	5 ± 2	2.0 ± 0.1
	70	20.1 ± 0.2						
	80	46.9 ± 0.2						

[a] Determined by first-order kinetics. [b] Determined by isothermal kinetics. [c] Determined by Stern–Volmer kinetics. [d] Temperature control within ± 0.1 °C. [e] [**3a**] = 1.03 × 10^{-4} mol dm^{-3}. [f] [**3b**] = 1.76 × 10^{-4} mol dm^{-3}.

Particularly characteristic are the ^{13}C NMR signals of the epoxide carbon atoms C-2 and -3 at δ 79–82 and 66.

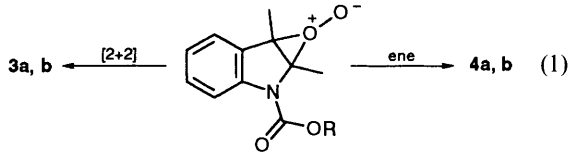
The activation parameters were determined by standard isothermal kinetic methods in toluene,[15] by monitoring the direct chemiluminescence decay of the dioxetanes **3a**, **b** photometrically. First-order semilogarithmic plots of the emitted light intensity *vs.* time were perfectly linear. Arrhenius and Eyring treatments of the rate data gave the activation parameters E_a, log A, and $\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$. The results together with the k values are given in Table 1.

The excitation yields of the direct chemiluminescence for the indole dioxetanes **3a**, **b** were determined by the well-established methods,[15] in which 9,10-diphenylanthracene (DPA) was employed for singlet and 9,10-dibromoanthracene (DBA) for triplet state counting.[16] Stern–Volmer treatment of the chemiluminescence data led to the singlet (Φ^S) and triplet (Φ^T) excitation yields, which are summarized in Table 1.

The fluoride ion-induced decomposition of the silyl-substituted dioxetane **3b** was performed by treatment with Bu_4NF in aqueous acetonitrile (Scheme 1, v) to set free the corresponding indolyl anion, the species responsible for the CIEEL decomposition. In contrast to the direct chemiluminescence, which affords a continuous signal over many minutes, a very short light flash of a few seconds was observed, with complete decomposition of dioxetane **3b**. The intensity–time profiles were evaluated by first-order kinetics and the chemiluminescence yield estimated, as described previously,[17] to be Φ^{CIEEL} = (3.3 ± 0.6) × 10^{-9} E mol^{-1}.

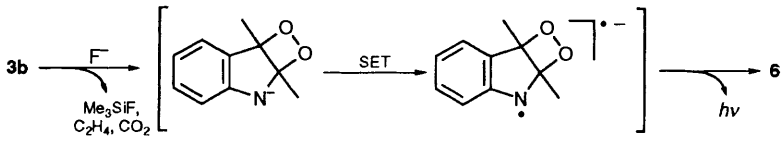
Discussion

The photooxygenation of the indoles **2a**, **b** afforded the corresponding dioxetanes **3a**, **b** by [2 + 2] cycloaddition and the 2-hydroperoxyindoles **4a**, **b** by ene reaction; a perepoxide is proposed as an intermediate[18] [eqn. (1)]. The regioselectivity in



(1)

the ene reaction of singlet oxygen (Schenck reaction[19]) with acylated indoles was recently[11] reported and the structure of such hydroperoxides established unequivocally by X-ray analysis.[11a] Thus, an electron-withdrawing group on the indole nitrogen atom favours formation of 2-hydroperoxyindolines (stabilization of the C-3 cation by phenyl conjugation), while *N*-alkylation (+I effect) leads exclusively to the 3-hydroperoxy



(2)

regioisomer (stabilization of the C-2 cation by pyrrole conjugation).[20]

N-Alkoxycarbonylation stabilizes sufficiently the labile indole dioxetanes **3** by reducing the electron density of the indole nitrogen atom to permit their isolation and spectral characterization. Among the chemical transformations, of particular significance is the Me_2S deoxygenation to the novel persistent epoxides **7a**, **b** (Scheme 1, vi), which were independently prepared in high yields by dimethyldioxirane oxidation (Scheme 1, vii). The labile dioxetanes **3a**, **b** and epoxides **7a**, **b** constitute some of the few known members of the rare class of persistent oxygenated indole derivatives of this type.[11,20,21]

The activation enthalpies for thermal decomposition of the indole dioxetanes **3a**, **b** (Table 1) are about 4 kcal mol^{-1} * lower than those of simple dioxetanes, *e.g.* tetramethyl-1,2-dioxetane or 3-hydroxymethyl-3,4,4-trimethyl-1,2-dioxetane.[22] This trend emphasizes the low thermal stability of indole dioxetanes despite acylation. The rather negative activation entropies obtained in the isothermal kinetic method suggest participation of dark catalytic decomposition,[23] a problem which is difficult to avoid for such labile dioxetanes.

As expected, the triplet yields (Φ^T) are much higher than the singlet yields (Φ^S) for the dioxetanes **3a**, **b** (Table 1); $\Phi^T:\Phi^S$ ratios are typically *ca.* 40. Moreover, the absolute values are very low, presumably owing to unfavourable energy transfer from the excited fragmentation products **5a**, **b** to the DPA and DBA fluorophors. This is analogous to the low excitation yields observed for benzofuran dioxetanes.[22]

The silyl-substituted indole dioxetane **3b** served the purpose of chemically triggering CIEEL emission. Treatment with fluoride ions induced rapid decomposition of dioxetane **3b** with appreciable chemiluminescence, which was considerably higher than the light emission derived from its direct thermal decomposition. This speaks for an intramolecular electron transfer mechanism of the CIEEL type,[4,5] which yields a higher proportion of singlet-excited carbonyl products and hence the more intense fluorescence.

The proposed mechanism [eqn. (2)] involves first removal of the *N*-silyl protection group through fluoride ion-promoted E-2 type elimination to generate the free indolyl anion, which subsequently acts as intramolecular electron donor to the dioxetane moiety. After single-electron transfer (SET), breakage of the O–O bond with formation of a ketyl radical, and electron back-transfer (BET), an electronically excited singlet state is generated, which emits fluorescence.[4-7]

Unfortunately, the CIEEL quantum yield is very low, *i.e.* Φ^{CIEEL} *ca.* 3×10^{-9} E mol^{-1} (Table 1), which is orders of magnitudes lower than we have recently reported for the benzofuran dioxetanes **C**[10b] and which has been established for the spiroadamantyl-substituted dioxetanes **B**.[8b] Therefore, in view of the very low Φ^{CIEEL} value and the inherent low thermal stability of the acylated indole dioxetanes, these compounds appear to be of limited use for chemiluminescence immunoassay applications.

Experimental

General Aspects.—^1H and ^{13}C NMR spectra were measured on a Bruker AC 200 spectrometer (^1H: 200 MHz, ^{13}C: 50 MHz) with TMS, [$^2H_6$]acetone or deuteriochloroform as internal standards. *J* values are given in Hz. IR spectra were recorded on a Perkin-Elmer 1420 Ratio Recording IR Spectrophotometer. Elemental analyses were carried out by the Microanalytic Division of the Institute of Inorganic Chemistry, University of Würzburg or by the Institute of Organic Chemistry, University of Gießen. Melting points were taken on a Büchi apparatus 535 and are not corrected. TLC analysis was conducted on precoated silica gel foils Polygram SIL G/UV_{254} (40 × 80 mm) from Machery and Nagel. Spots were identified under an UV lamp and peroxides additionally by aqueous KI–HOAc solution. Silica gel (63–200 μm; Woelm) was used for column chromatography, the adsorbance : substrate ratio was *ca.* 100 : 1. Low-temperature chromatography was performed on columns equipped with a vacuum-jacketed cooling mantle through which refrigerant was circulated from a RK 20 Lauda Cryomat.

All kinetic measurements were performed on a Mitchell–Hastings photometer[24] equipped with a RCA 926 B photomultiplier and a Lauda thermostat K 20 for temperature control of the cell compartment. Beckmann scintillation vials were used as reaction vessels. A Servogor 210 recorder registered the output signal of the kinetic run.

Starting Materials.—The preparation of a solution of dimethyldioxirane in acetone followed the recently improved method.[25] The indoles **1**[26] and **2a**[14] as well as 2-(trimethylsilyl)ethanol[27] and 4-nitrophenyl 2-(trimethylsilyl)ethyl carbonate[14] were prepared according to literature procedures. The physical and spectral data of these compounds were consistent with those reported.[14,26,27] 2,3-Dimethyl-1-[2-(trimethylsilyl)-ethoxycarbonyl]indole **2b** was obtained in 58% yield analogous to the literature procedure[14] by carbonylation of the indole **1** with 4-nitrophenyl 2-(trimethylsilyl)ethyl carbonate as colourless needles, m.p. 54–55 °C (Found: C, 66.59; H, 8.27; N, 4.67. $C_{16}H_{23}NO_2Si$ requires C, 66.39; H, 8.01; N, 4.84%); ν_{max}-(CCl_4)/cm^{-1} 1675 (CO); δ_H($CDCl_3$) 0.11 (9 H, s, $SiMe_3$), 1.26 (2 H, m, CH_2), 2.20 (3 H, s, CH_3), 2.56 (3 H, s, CH_3), 4.52 (2 H, m, CH_2), 7.25 (2 H, m, arom. H), 7.42 (1 H, m, arom. H) and 8.12 (1 H, m, arom. H); δ_C($CDCl_3$) −1.5 (q, $SiMe_3$), 8.7 (q), 13.7 (q), 17.7 (t), 65.2 (t), 114.1 (s), 115.4 (d), 117.8 (d), 122.5 (d), 123.3 (d), 125.1 (s), 130.9 (s), 132.9 (s) and 158.4 (s).

General Procedure for the Photooxygenation of the Indoles **2a**, **b**.—Into a 10 cm^3 test tube, equipped with gas inlet and outlet tubes, was placed a solution of the corresponding indole **2** (0.97–1.22 mmol) and 1–2 mg tetraphenylporphine (TPP) in metal-free (distilled from EDTA) dichloromethane (5 cm^3). The solution was cooled to −30 °C by means of a methanol bath with the help of a KT 290 S Cryomat (Colora Meßtechnik GmbH). A gentle stream of dry oxygen gas was bubbled through the solution while irradiating with two 250 W sodium lamps (Philips G/98/2-SON). The reaction progress was monitored by TLC. After complete consumption of the starting material, the solution was concentrated at −20 °C 0.01/Torr and the residue chromatographed on silica gel at −20 °C. The relative product distribution was determined by NMR analysis directly of the crude mixture obtained from the photooxygenation in $CDCl_3$ under the same conditions mentioned above.

3-(tert-*Butoxycarbonyl*)-2*a*,7*b*-*dimethyl*-2*a*,7*b*-*dihydro*-1,2-*dioxeto*[3,4-b]*indole* **3a**, [1-(tert-*butoxycarbonyl*)-2-*methyl*-3-*methylene*-2,3-*dihydroindol*-2-*yl*]*hydroperoxide* **4a** *and* tert-*butyl*

* 1 kcal mol^{-1} = 4.184 kJ mol^{-1}.

N-*acetyl*-N-(2-*acetylphenyl*)*carbamate* **5a** *by photooxygenation of* 1-(tert-*butoxycarbonyl*)-2,3-*dimethylindole* **2a**. Photooxygenation of indole **2a** (300 mg, 1.22 mmol) in dichloromethane (5 cm^3) at −30 °C for 6 h gave, after column chromatography at −20 °C with CH_2Cl_2 as eluent, dioxetane **3a** as a yellow amorphous powder (122 mg, 36%), which contained *ca.* 15% decomposition product **5a** according to ^1H NMR spectroscopy. In view of its thermal lability, it was not possible to obtain satisfactory elemental analyses; $R_f(CH_2Cl_2)$ 0.60; $\delta_H(CDCl_3$, −20 °C) 1.55 (9 H, s, Bu^t), 1.92 (3 H, s, CH_3), 2.01 (3 H, s, CH_3), 7.05 (1 H, t, *J* 7.2, arom. H), 7.22 (1 H, d, *J* 7.2, arom. H), 7.39 (1 H, t, *J* 7.2, arom. H) and 7.86 (1 H, d, *J* 7.2, arom. H); $\delta_C(CDCl_3$, −20 °C) 17.5 (q), 19.6 (q), 28.1 (q), 82.6 (s), 92.5 (s), 104.7 (s), 115.4 (d), 123.2 (d), 128.4 (d), 130.4 (s), 131.7 (d), 133.2 (s) and 150.9 (s).

A solution of the dioxetane **3a** (50.0 mg, 180 μmol) in dichloromethane (1 cm^3) was stirred at room temp. for 24 h. Evaporation of the solvent and recrystallization of the residue from hexane yielded carbamate **5a** as yellow plates (44.0 mg, 90%), m.p. 59–60 °C (Found: C, 64.49; H, 6.41; N, 5.03. $C_{15}H_{19}NO_4$ requires C, 64.97; H, 6.91; N, 5.05%); $\nu_{max}(CCl_4)/cm^{-1}$ 1715 (CO), 1680 (CO) and 1660 (CO); $\delta_H(CDCl_3)$ 1.35 (9 H, s, Bu^t), 2.53 (3 H, s, $COCH_3$), 2.63 (3 H, s, $COCH_3$), 7.14 (1 H, dd, *J* 7.5 and 1.6, arom. H), 7.44 (1 H, dt, *J* 7.5 and 1.6, arom. H), 7.56 (1 H, dt, *J* 7.5 and 1.6, arom. H) and 7.83 (1 H, dd, *J* 7.5 and 1.6, arom. H); $\delta_C(CDCl_3)$ 26.6 (q), 27.8 (q), 28.6 (q), 83.1 (s), 128.1 (d), 129.8 (d), 130.4 (d), 132.6 (d), 134.7 (s), 137.4 (s), 152.2 (s), 173.6 (s) and 198.4 (s).

Photooxygenation of the indole **2a** (177 mg, 722 μmol) at −30 °C for 6 h resulted in the products **3a, 4a** and **5a** in a ratio of 59:27:14 (by ^1H NMR analysis). Hydroperoxide **4a**: $R_f(CH_2Cl_2)$ 0.26; $\delta_H(CDCl_3$, −30 °C) 1.62 (9 H, s, Bu^t), 1.80 (3 H, s, CH_3), 5.38 (1 H, s, CH_2), 5.76 (1 H, s, CH_2), 6.96–7.50 (4 H, m, arom. H), 8.60 (1 H, br s, OOH); $\delta_C(CDCl_3$, −30 °C) 28.0 (t), 30.8 (q), 82.4 (s), 106.0 (t), 115.6 (d), 120.4 (s), 123.8 (d), 131.8 (d), 133.2 (d), 135.3 (s), 136.8 (s), 144.8 (s) and 151.6 (s).

2*a*,7*b*-*Dimethyl*-3-[2-(*trimethylsilyl*)*ethoxycarbonyl*]-2*a*,7*b*-*dihydro*-1,2-*dioxeto*[3,4-b]*indole* **3b**, {2-*methyl*-3-*methylene*-1-[2-(*trimethylsilyl*)*ethoxycarbonyl*]-2,3-*dihydroindol*-2-*yl*}-*hydroperoxide* **4b** *and* N-2-(*trimethylsilyl*)*ethyl* N-*acetyl*-N-(2-*acetylphenyl*)*carbamate* **5b** *by photooxygenation of* 2,3-*dimethyl*-1-[2-(*trimethylsilyl*)*ethoxycarbonyl*]*indole* **2b**. Photooxygenation of indole **2b** (280 mg, 968 μmol) in dichloromethane (5 cm^3) at −30 °C for 6 h gave, after column chromatography at −20 °C with CH_2Cl_2 as eluent, dioxetane **3b** as a yellow amorphous powder (93.0 mg, 30%), which contained *ca.* 20% decomposition product **5b** according to ^1H NMR spectroscopy. In view of its thermal lability, it was not possible to obtain satisfactory elemental analyses; $R_f(CH_2Cl_2)$ 0.64; $\delta_H(CDCl_3$, − 20 °C) 0.03 (9 H, s, $SiMe_3$), 1.24 (2 H, m, CH_2), 1.98 (3 H, s, CH_3), 2.02 (3 H, s, CH_3), 4.39 (2 H, m, CH_2) and 7.08–8.36 (4 H, m, arom. H); $\delta_C(CDCl_3$, −20 °C) −1.3 (q), 17.1 (q), 17.6 (q), 19.8 (q), 65.2 (t), 93.0 (s), 105.1 (s), 115.7 (d), 122.5 (d), 123.4 (d), 123.7 (d), 125.8 (s), 132.1 (s) and 145.5 (s).

A solution of the dioxetane **3b** (50.0 mg, 156 μmol) in dichloromethane (1 cm^3) was stirred at room temp. for 24 h. Evaporation of the solvent and recrystallization of the residue from hexane yielded carbamate **5b** as yellow plates (43.0 mg, 86%), m.p. 56–57 °C (Found: C, 59.99; H, 7.36; N, 4.16. $C_{16}H_{23}NO_4Si$ requires C, 59.79; H, 7.21; N, 4.36%); $\nu_{max}(CCl_4)/cm^{-1}$ 1715 (CO), 1680 (CO) and 1660 (CO); $\delta_H(CDCl_3)$ 0.07 (9 H, s, $SiMe_3$), 1.16 (2 H, m, CH_2), 2.54 (3 H, s, $COCH_3$), 2.66 (3 H, s, $COCH_3$), 4.18 (2 H, m, CH_2), 7.15 (1 H, dd, *J* 7.6 and 1.7, arom. H), 7.47 (1 H, dt, *J* 7.6 and 1.7, arom. H), 7.57 (1 H, dt, *J* 7.6 and 1.7, arom. H) and 7.85 (1 H, dd, *J* 7.6 and 1.7, arom. H); $\delta_C(CDCl_3)$ 1.0 (q), 26.5 (q), 28.6 (q), 29.7 (t), 65.5(t), 128.4 (d), 130.1 (d), 130.7 (d), 132.8 (d), 134.4 (s), 137.1 (s), 150.8 (s), 172.3 (s) and 196.9 (s).

Photooxygenation of the indole **2b** (198 mg, 684 μmol) at −30 °C for 6 h resulted in the products **3b, 4b** and **5b** in a ratio of 45:37:18 (by ^1H NMR analysis). Hydroperoxide **4b**: $R_f(CH_2Cl_2)$ 0.29; $\delta_H(CDCl_3$, −30 °C) 0.04 (9 H, s, $SiMe_3$), 1.10 (2 H, m, CH_2), 1.82 (3 H, s, CH_3), 4.17 (2 H, m, CH_2), 5.44 (1 H, s, CH_2), 5.79 (1 H, s, CH_2) 7.12–7.78 (4 H, m, arom. H) and 8.32 (1 H, br s, OOH).

General Procedure for the Epoxidation of the Indoles **2a, b** *by Dimethyldioxirane*.—A cooled solution of dimethyldioxirane (100–150% molar excess) in acetone (*ca.* 0.08 mol dm^{-3}), dried over molecular sieves, 4 Å at −20 °C, was rapidly added to a cooled (−78 °C), stirred solution of the indoles **2a, b** in dry CH_2Cl_2 (3.0 cm^3) under N_2. The stirring was continued until complete consumption of the indole (monitored by TLC), while the reaction temperature was allowed to increase to −20 °C. The solvent was removed at −20 °C/0.01 Torr to afford nearly quantitatively the epoxides **7a, b**. At 0 °C both epoxides decomposed rapidly.

2-(tert-*Butoxycarbonyl*)-1*a*,6*b*-*dimethyl*-1*a*,6*b*-*dihydrooxireno*[b]*indole* **7a**. By following the above procedure (3 h reaction time), from 8.0 cm^3 dioxirane solution (0.08 mol dm^{-3}, 640 μmol) and indole **2a** (149 mg, 607 μmol) the epoxide **7a** (150 mg, 95%) was obtained as a colourless amorphous powder; $\delta_H([^2H_6]$acetone, −30 °C) 1.56 (9 H, s, Bu^t), 1.72 (3 H, s, CH_3), 1.91 (3 H, s, CH_3), 7.05 (1 H, t, *J* 7.6, arom. H), 7.31 (1 H, t, *J* 7.6, arom. H), 7.53 (1 H, d, *J* 7.6, arom. H) and 7.88 (1 H, d, *J* 7.6, arom. H); $\delta_C([^2H_6]$acetone, −30 °C) 11.7 (q), 16.1 (q), 27.4 (q), 66.2 (s), 82.1 (s), 82.4 (s), 115.5 (d), 122.2 (d), 123.9 (d), 129.5 (d), 130.1 (s), 143.8 (s) and 151.6 (s).

1*a*,6*b*-*Dimethyl*-2-[2-(*trimethylsilyl*)*ethoxycarbonyl*-1*a*,6*b*-*dihydrooxireno*[b]*indole* **7b**. By following the above procedure (3 h reaction time), from 4.0 cm^3 dioxirane solution (0.08 mol dm^{-3}, 320 μmol) and indole **2b** (61.0 mg, 211 μmol) the epoxide **7b** (60.0 mg, 93%) was obtained as a colourless, amorphous powder; $\delta_H([^2H_6]$acetone, −30 °C) 0.09 (9 H, s, $SiMe_3$), 1.20 (2 H, m, CH_2), 1.79 (3 H, s, CH_3), 2.03 (3 H, s, CH_3), 4.40 (2 H, m, CH_2), 7.10 (1 H, t, *J* 7.5, arom. H), 7.36 (1 H, t, *J* 7.5, arom. H), 7.48 (1 H, d, *J* 7.5, arom. H) and 7.86 (1 H, d, *J* 7.5, arom. H); $\delta_C([^2H_6]$acetone, −30 °C), −1.6 (q), 12.3 (q), 17.4 (q), 31.1 (t), 64.8 (t), 66.4 (s), 78.6 (s), 116.1 (d), 122.4 (d), 123.7 (d), 129.6 (d), 129.7 (s), 143.3 (s) and 153.5 (s).

General Procedure for the Deoxygenation of Dioxetanes **3a,b**.—Dioxetane **3** (*ca.* 40 μmol) was dissolved in deuteriochloroform (0.5 cm^3) at −30 °C. One equivalent of Me_2S in $CDCl_3$ (0.5 cm^3) was added, and after 1 h the solution was submitted to NMR analysis.

Epoxide **7a**. Deoxygenation of the dioxetane **3a** (12.0 mg, 43.4 μmol) by Me_2S (1.88 cm^3, 43.5 μmol) converted it to the epoxide **7a** (by NMR analysis). The spectral data matched those reported above.

Epoxide **7b**. Deoxygenation of the dioxetane **3b** (12.0 mg, 37.3 μmol) by Me_2S (1.60 cm^3, 37.0 μmol) converted it to the epoxide **7b** (by NMR analysis). The spectral data matched those reported above.

Chemiluminescence Measurements.—A glass vial was charged with 3.0 cm^3 of toluene or the fluorescer solution, placed into the cell compartment of the Mitchell–Hastings photometer,[24] and allowed to equilibrate thermally for *ca.* 10 min. A 300 μl aliquot of the dioxetane solution (conc. determined by weighing) was introduced by means of a calibrated plastic pipette and the emitted light intensity continuously recorded.

For the determination of activation parameters, runs at several temperatures were carried out by direct chemiluminescence measurements under isothermal conditions.[15] The rate data were processed according to first-order kinetics and from

the set of k values the activation parameters were calculated by the Arrhenius and Eyring methods. The data are collected in Table 1.

The measurements of the excitation yields were performed at 333 K. The light intensity was calibrated by means of the scintillation cocktail of Hastings and Weber[28] as light standard. The excitation yields were determined from these data by using the Stern–Volmer treatment.[15] The data are collected in Table 1.

The fluoride ion-induced chemiluminescence of dioxetane **3b** was achieved by placing 3.0 cm^3 of the dioxetane solution (5×10^{-4} mol dm^{-3} in CH_2Cl_2) into a glass vial, which was transferred to the Mitchell–Hastings photometer. After 5 min of thermal equilibration at 25 °C, an appropriate amount of tetrabutylammonium fluoride (0.1 mol dm^{-3} in 50:1 CH_3CN–H_2O) was added by means of a syringe through the rubber septum into the above glass vial under rigorous exclusion of external light, with the photomultiplier open for immediate measurement of the light emission.

Acknowledgements

We thank the Deutsche Forschungsgemeinschaft (SFB 172 '*Molekulare Mechanismen kanzerogener Primärveränderungen*') and the *Fonds der Chemischen Industrie* for generous financial support.

References

1 W. Adam, M. Heil, T. Mosandl and C. R. Saha-Möller, in *Organic Peroxides*, ed. W. Ando, John Wiley, New York, 1992, ch. 5; A. L. Baumstark, in *Advances in Oxygenated Processes*, ed. A. L. Baumstark, JAI Press, Greenwich, 1988, vol. 1, ch. 2.
2 K. R. Kopecky and C. Mumford, *Can. J. Chem.*, 1969, **47**, 709.
3 W. H. Richardson, F. C. Montgomery, M. B. Yelvington and H. E. O'Neal, *J. Am. Chem. Soc.*, 1974, **96**, 7525.
4 G. B. Schuster, *Acc. Chem. Res.*, 1979, **12**, 366.
5 J.-Y. Koo and G. B. Schuster, *J. Am. Chem. Soc.*, 1977, **99**, 6107.
6 W. Adam and O. Cueto, *J. Am. Chem. Soc.*, 1979, **101**, 6511; S. P. Schmidt and G. B. Schuster, *J. Am. Chem. Soc.*, 1980, **102**, 306.
7 J.-Y. Koo, S. P. Schmidt and G. B. Schuster, *Proc. Natl. Acad. Sci.*, 1978, **75**, 30.
8 (*a*) A. P. Schaap, R. S. Handley and B. P. Giri, *Tetrahedron Lett.*, 1987, **28**, 935; (*b*) A. P. Schaap, T.-S. Chen, R. S. Handley, R. DeSilva and B. P. Giri, *Tetrahedron Lett.*, 1987, **28**, 1155; (*c*) A. P. Schaap, M. D. Sandison and R. S. Handley, *Tetrahedron Lett.*, 1987, **28**, 1159; (*d*) I. Bronstein, J. V. Voyta and B. Edwards, *J. Biolumin. Chemilumin.*, 1988, **2**, 186; (*e*) I. Bronstein, B. Edwards and J. V. Voyta, *J. Biolumin. Chemilumin.*, 1989, **4**, 99.
9 S. Beck and H. Köster, *Anal. Chem.*, 1990, **62**, 2258; S. Albrecht, H. Brandl and W. Adam, *Chem. Unserer Zeit*, 1990, 227.
10 (*a*) W. Adam and M. H. Schulz, *Chem. Ber.*, 1992, **125**, 2455; (*b*) W. Adam, R. Fell and M. H. Schulz, *Tetrahedron*, 1993, **49**, 2227.
11 (*a*) X. Zhang, C. S. Foote and S. I. Khan, *J. Org. Chem.*, 1993, **58**, 47; (*b*) X. Zhang and C. S. Foote, *J. Org. Chem.*, 1993, **58**, 5524; (*c*) W. Adam, M. Ahrweiler, M. Sauter and B. Schmiedeskamp, *Tetrahedron Lett.*, 1993, 5247; (*d*) W. Adam, M. Ahrweiler, K. Peters and B. Schmiedeskamp, *J. Org. Chem.*, in the press.
12 I. Saito, T. Matsuura, M. Nakagawa and T. Hino, *Acc. Chem. Res.*, 1977, **10**, 346; R. J. Sundberg, *Chemistry of Indoles*, Academic Press, New York, 1970; W. J. Houlihan, *Indoles*, part 1, John Wiley, New York, 1972.
13 P. Feigelson and F. O. Brady, *Molecular Mechanism of Oxygen Activation*, ed. O. Hayaishi, Academic Press, New York, 1974, p. 87; F. Hirata and O. Hayaishi, *J. Biol. Chem.*, 1975, **250**, 5960.
14 D. Dhanak and C. B. Reese, *J. Chem. Soc., Perkin Trans. 1*, 1986, 2181.
15 W. Adam and F. Yany, in *Small Ring Heterocycles*, ed. A. Hassner, part 3, John Wiley, New York, 1985, ch. 4; A. Beinhauer, Ph.D. Thesis, University of Würzburg, 1989.
16 T. Wilson and A. P. Schaap, *J. Am. Chem. Soc.*, 1971, **93**, 4126; N. J. Turro, P. Lechtken, G. Schuster, J. Orell, H.-C. Steinmetzer and W. Adam, *J. Am. Chem. Soc.*, 1974, **96**, 1627.
17 W. Adam, in *Chemical and Biological Generation of Excited States*, eds. W. Adam and G. Cilento, Academic Press, New York, 1982, ch. 4.
18 E. L. Clennan and K. Nagraba, *J. Am. Chem. Soc.*, 1988, **110**, 4312.
19 G. O. Schenck, H. Eggert and W. Denk, *Liebigs Ann. Chem.*, 1953, **584**, 177.
20 I. Saito, S. Matsugo and T. Matsuura, *J. Am. Chem. Soc.*, 1979, **101**, 4757.
21 X. Zhang and C. S. Foote, *J. Am. Chem. Soc.*, 1993, **115**, 8867.
22 W. Adam, A. Beinhauer and H. Hauer, in *Handbook of Organic Photochemistry*, ed. J. C. Scaiano, CRC Press, Boca Raton, 1989, vol. II, ch. 12.
23 T. Wilson, M. E. Landis, A. L. Baumstark and P. D. Bartlett, *J. Am. Chem. Soc.*, 1973, **95**, 4765.
24 J. W. Hastings and G. Weber, *J. Opt Am. Soc.*, 1963, **53**, 1410; G. W. Mitchell and J. W. Hastings, *Anal. Biochem.*, 1971, **39**, 243.
25 W. Adam, J. Bialas and L. Hadjiarapoglou, *Chem Ber.*, 1991, **124**, 2377.
26 V. Dave, *Org. Prep. Proced. Int.*, 1976, **8**, 41.
27 H. Gerlach, *Helv. Chim. Acta*, 1977, **60**, 3039.
28 J. W. Hastings and G. Weber, *Photochem. Photobiol.*, 1965, **4**, 1049.

Paper 4/00875H
Received 14*th February* 1994
Accepted 16*th March* 1994