

## 124. The Reaction of Singlet Oxygen with 1,3-Dimethylindole in the Presence of Aldehydes. Formation of 1,2,4-Trioxanes

by Charles W. Jefford\*, Danielle Jaggi, John Boukouvalas and Shigeo Kohmoto

Department of Organic Chemistry, University of Geneva

and Gérard Bernardinelli

Laboratory of Crystallography, University of Geneva, CH-1211 Geneva 4

Dedicated to Dr. Arnold Bossi on the occasion of his 60th birthday

(16. III. 84)

---

### Summary

The dye-sensitized photo-oxygenation of 1,3-dimethylindole in the presence of aldehydes initially generates a zwitterionic peroxide which condenses with the carbonyl function to give the corresponding *cis*-fused 1,2,4-trioxanes. Acetaldehyde gives a pair of diastereomers, one of whose structures was determined by X-ray analysis (*cis,cis* isomer), whereas pivalaldehyde gives only the *cis,cis* diastereomer.

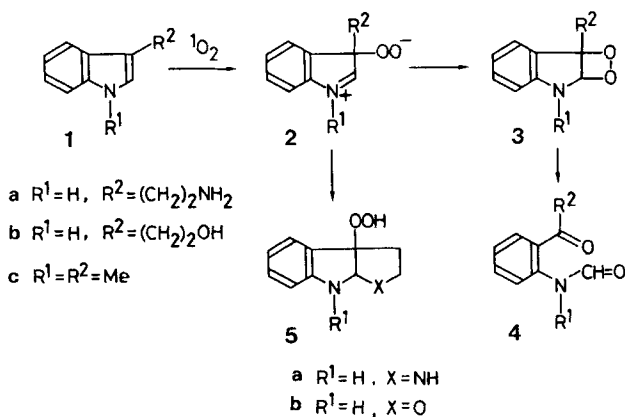
---

**Introduction.** – The dye-sensitized photo-oxygenation of indole and its derivatives has been the subject of numerous studies [1]. The reaction has been taken as a model for the biological oxygenation of certain indole amino acids. In particular, information has been sought on the mode of action of dioxygenases [2] and on the mechanism of photo-dynamic action [3] involving in both cases tryptophane and structurally related molecules.

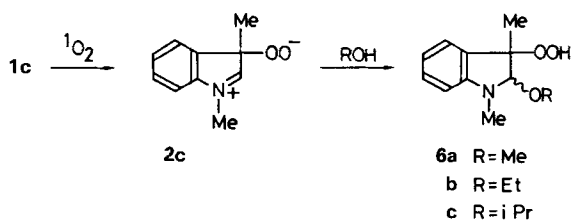
It is now understood that the ready, regioselective addition of triplet and singlet oxygen, implicated respectively in the enzymic and photogenic processes, to the C(2)–C(3) bond of the indole nucleus (**1**) may be ascribed to the ‘soft’ nucleophilic character located at the C(3) position [4]. Typically, the first chemical event is the formation of the zwitterionic peroxide **2**, which depending on the nature of the substituents, can either close to the 1,2-dioxetane **3** and then undergo scission to **4** or be captured by an internal nucleophile such as the amino [5], hydroxy [6], or carbonyl [7] groups to afford tricyclic hydroperoxides illustrated by the transformations **2a**→**5a** and **2b**→**5b** (Scheme 1).

Trapping by external nucleophiles has been achieved when 1,3-dimethylindole (**1c**) is photo-oxygenated in the presence of alcohols [8]. However, the resulting hydroperoxides **6**, explicable as arising from the intermediate zwitterionic peroxide **2c**, are short-lived (Scheme 2). We now describe experiments which not only confirm the existence of the zwitterionic indole peroxide, but demonstrate that the peroxide

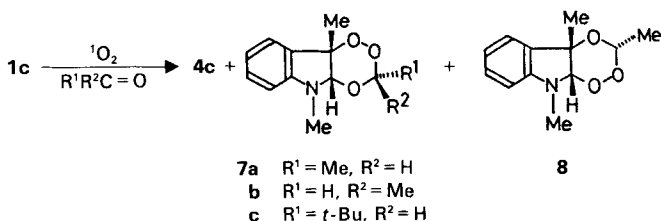
Scheme 1



Scheme 2



Scheme 3



function can react with electrophiles, exemplified by aldehydes, to give *cis*-fused 1,2,4-trioxanes (Scheme 3).

**Results.** – 1,3-Dimethylindole (**1c**) was photo-oxygenated using tetraphenylporphin as sensitizer in a solution of  $CCl_4$  containing a molar excess of acetaldehyde. Apart from the expected, normal cleavage product, the *N*-formyl ketone **4c** formed in 10% yield, the 1,2,4-trioxanes **7a**, **7b** and **8** were isolated in 50–60% yield in varying amounts depending on the chromatographic conditions. By conventional column chro-

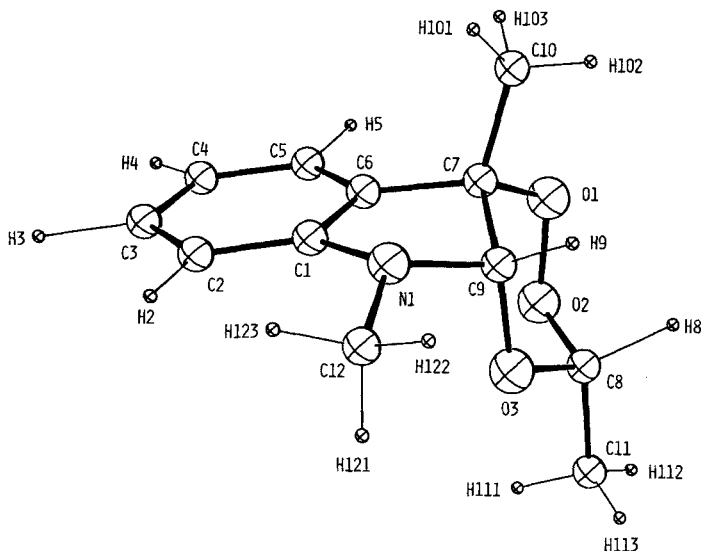


Figure. Computer-generated perspective drawing of the structure of trioxane **7a**

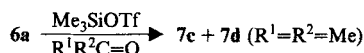
matography over silica gel, the major isomer **7a** was isolated and its structure determined by X-ray analysis (see *Exper. Part* for details). The trioxane ring, which is *cis*-fused to the indole nucleus, adopts a chair conformation with its acetaldehyde-derived methyl group (C(11)) disposed *cis* to the indole moiety and therefore occupying an equatorial position (*Fig.*). The second minor isomer **8** was separated and characterized by its NMR spectrum. It turned out to be a 1,2,4-trioxane, but with the sequence of O-atoms reversed with respect to the indole ring. It is inferred that **8** possesses the same configuration and conformation as **7a**.

The third, minor isomer **7b**, which proved to be unstable under the above-mentioned acidic chromatographic conditions, was only detected when chromatography was performed over silica gel pre-treated with gaseous  $\text{NH}_3$ . However, it could not be separated from the major isomer **7a**. Nonetheless, the structure of **7b** was deduced from the  $^1\text{H-NMR}$  spectra and the elemental analysis of the mixture. It has the same skeleton as **7a**, except that the methyl substituent on the trioxane ring has the *trans* configuration (*Scheme 3*). Control experiments confirmed that trioxane formation did not occur when the sensitizer was omitted from the reaction mixture. Furthermore, the indole was left intact.

Photo-oxygenation of **1c** in the presence of pivalaldehyde gave in addition to **4c** the corresponding *cis*-1,2,4-trioxane **7c** in poor yield (7%). No other isomers were detected.

To confirm these findings, we decided to exploit trimethylsilyl triflate (TMSOTf) [9] as a catalyst for the condensation of the indole hydroperoxide **6a** with aldehydes to furnish the 1,2,4-trioxanes [10]. When acetaldehyde and a molar equivalent of TMSOTf in  $\text{CH}_2\text{Cl}_2$  was added to **6a**, chromatography over  $\text{NH}_3$ -treated silica gel afforded the pair of diastereomeric trioxanes **7a** and **7b** in a ratio of 63:37 and in 60% yield accompanied by the cleavage product **4c** (10%). None of the odd trioxane **8** was

Scheme 4



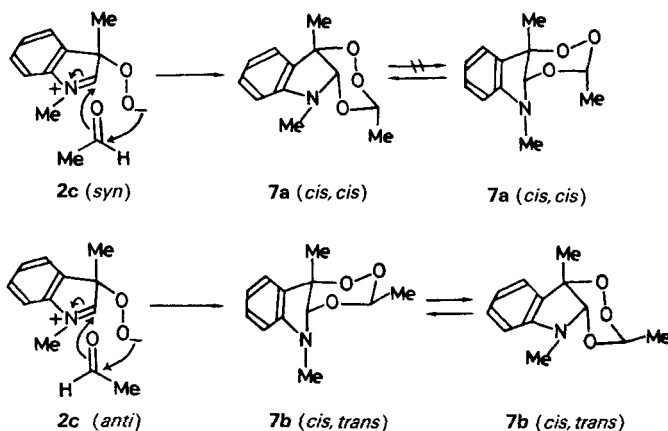
discernable. The TMSOTf-catalyzed reaction of **6a** with pivalaldehyde and acetone also gave the trioxanes **7c** and **7d** in yields of 22 and 46%, both of which were formed as single isomers, **7c** having the *t*-butyl group disposed *cis* (Scheme 4).

**Discussion.** – The present results parallel those obtained with enol ethers [11] and can be rationalized in terms of the same mechanism. Singlet oxygen attacks the C(3) position of **1c** to give the zwitterionic peroxide **2c** which can then be intercepted by aldehyde in two ways. The *syn* orientation leads to the *cis,cis* configuration. Ring formation necessarily generates the *cis*-fusion of the trioxane ring and selects the best chair conformation which places the new methyl substituent in the least hindered environment (**7a**; *cis,cis*). The other chair conformation of the trioxane ring is avoided as it would put the methyl group in steric conflict with an axial nitrogen substituent. The *anti* orientation still gives the *cis*-fused trioxane ring, but as the newly incorporated methyl substituent is *trans*, it can adopt either an axial or equatorial position in one of the two alternative chair conformations (**7b**; *cis,trans*). It is likely that the transition state is probably sensitive to steric forces or is product-like as pivalaldehyde with its bulky substituent gives only the *cis,cis* isomer **7c**.

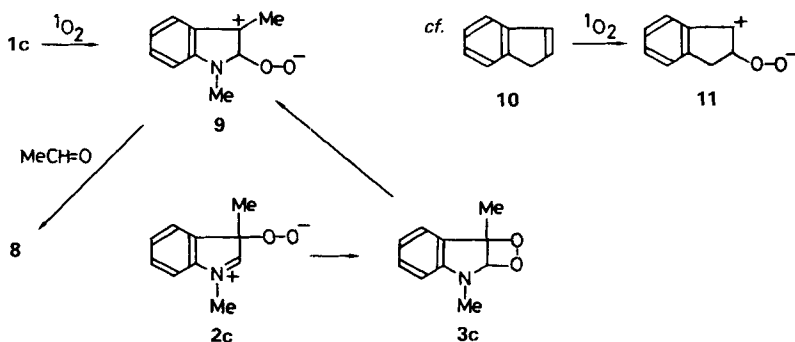
Similar arguments prevail for the trimethylsilyl triflate (TMSOTf) catalyzed condensation of the indole hydroperoxide **6a**. TMSOTf probably activates the carbonyl group of the aldehyde or ketone partner, thereby facilitating attack by the hydroperoxide grouping of **6a** which leads to the expulsion of the methoxy substituent. The high yields experienced may be attributed to the greater life expectancy of neutral or even cationic species over the self-annihilating zwitterion formed photochemically.

The other difference between the two reactions is the odd trioxane **8**, whose origin is hard to explain. Two more or less plausible mechanisms may be envisaged. The first is that a second additional zwitterionic peroxide **9** is also formed as a first event. Its

Scheme 5



Scheme 6



structure is similar to that of **11** which is now known to arise from indene **10** on photo-oxygenation [12]. The capture of **9** by acetaldehyde should give both *cis* and *trans* trioxane isomers, however, only the *cis* **8** is seen, probably on account of the much lower concentration expected for the *trans* isomer. The second possibility is that the first peroxide **2c** closes to the dioxetane **3c** which then promptly opens to **9** before scission occurs (Scheme 6).

**Conclusions.** – We have demonstrated that the first species derived from 1,3-dimethylindole and singlet oxygen is a zwitterionic peroxide which is intercepted by an electrophile, here exemplified by the carboxaldehyde function. The low yields may be due to the difficulty of capture which in turn may be a reflection of the fleeting nature of the zwitterion or perhaps the absence of any particular nucleophilic character [13]. More importantly, these results may be of biological significance as formylkynurenine, the metabolic product obtained from tryptophan, could itself react further with the initially formed peroxide to give the corresponding trioxane. It is also to be expected that other substrates which are specific for intramolecular dioxygenases, such as catechols, would similarly condense with aldehydes when photo-oxygenated. Further mechanistic and synthetic studies are in progress and will be reported elsewhere.

We are indebted to the Swiss National Science Foundation (grant No. 2.201-0.81) for the support of this work. We thank Messrs. J. P. Saulnier and A. Pinto for performing the NMR experiments and Ms. A. D'Ascoli for the MS measurements.

#### Experimental Part

**General.** Thin layer chromatography (TLC): silica gel 60 F254 Merck. Preparative layer chromatography: silica gel 60 F<sub>254</sub> (thickness 2 mm). Physical constants and spectra were determined as follows. Melting points (m.p.): Reichert hot-stage microscope (uncorrected). IR spectra: Perkin-Elmer 681 spectrometer. <sup>1</sup>H- and <sup>13</sup>C-NMR spectra (chemical shifts in ppm relative to internal TMS (= 0 ppm), coupling constants *J* in Hz: Bruker WH 360 spectrometer. Mass spectra: CH-4 MAT and Finnigan GC/MS 4023 using the INCOS data system. Elemental analyses were carried out by Drs. H. and K. Eder, Service de Microchimie, Institut de Chimie Pharmaceutique, University of Geneva.

**Procedure for Photo-oxygenation.** The solution to be photo-oxygenated was placed in a vessel cooled either by a cryostat maintained at  $-15^\circ$  or by a dry ice/acetone bath. Irradiation was provided by a 500-W Sylvania FFX halogen-tungsten filament lamp screened with a UV cut-off filter ( $> 418$  nm) while  $O_2$  was passed through

the solution. The progress of the reaction was monitored by TLC. Oxygenation was continued until complete disappearance of 1,3-dimethylindole (**1c**).

*Photo-oxygenation of 1,3-Dimethylindole (1c). – A) In the Presence of Acetaldehyde.* A solution of **1c** (180 mg, 1.24 mmol) in  $\text{CCl}_4$  (6 ml) and acetaldehyde (1 ml) containing *meso*-tetraphenylporphyrin (TPP, 4 mg) as sensitizer was photo-oxygenated for 10 h. TLC revealed the formation of a product which gradually decomposed. On evaporation of solvent, the residue was purified by flash chromatography over silica gel ( $\text{CH}_2\text{Cl}_2$ ) giving trioxanes **7a** (41 mg; 17%) and **8** (21 mg; 9%). In another experiment, **1c** (150 mg, 1.03 mmol) in  $\text{CCl}_4$  (4 ml), acetaldehyde (1 ml) and TPP (4 mg) was photo-oxygenated for 9 h. Products were isolated by column chromatography over silica gel pretreated with gaseous  $\text{NH}_3$  ( $\text{CH}_2\text{Cl}_2$ ). Trioxane **8** (10 mg; 4%), the cleavage product **4c** (18 mg; 10%), and trioxanes **7a** and **7b** as an inseparable mixture (109 mg, 48%, ratio 4:1) were obtained. In the crude mixture, the ratios of **7a/8/7b/4c** were found by  $^1\text{H-NMR}$  spectroscopy to be 48:8:22:22.

*3,5,9b-Trimethyl-4a,9b-dihydro-3 H,5 H-[1,2,4]trioxino[5,6-b]indole (7a).* M.p. 47–48° (recrystallized from pentane), b.p. 45°/0.01 Torr.  $R_f = 0.52$  (silica gel,  $\text{CH}_2\text{Cl}_2$ ).  $^1\text{H-NMR}$  (360 MHz,  $\text{CDCl}_3$ ): 1.22 (*d*,  $J = 5$ , 3 H); 1.41 (*s*, 3 H); 2.92 (*s*, 3 H); 4.73 (*s*, 1 H); 5.49 (*q*,  $J = 5$ , 1 H); 6.58 (*d*,  $J = 8$ , 1 H); 6.88 (*t*,  $J = 8$ , 1 H); 7.25 (*t*,  $J = 8$ , 1 H); 7.30 (*d*,  $J = 8$ , 1 H).  $^{13}\text{C-NMR}$  (90.6 MHz,  $\text{CDCl}_3$ ): 18.1 (*q*); 22.1 (*q*); 30.8 (*q*); 84.8 (*s*); 93.0 (*d*); 97.9 (*d*); 107.6 (*d*); 119.1 (*d*); 122.5 (*d*); 129.5 (*d*); 130.3 (*s*); 149.9 (*s*). MS: 221 (1,  $M^+$ ), 177 (12), 161 (29), 149 (36), 146 (15), 134 (100), 132 (25), 118 (18), 106 (20). Anal. calc. for  $\text{C}_{12}\text{H}_{15}\text{NO}_3$  (221.26): C 65.14, H 6.83, N 6.33; found: C 65.36, H 6.59, N 6.15.

*Crystallographic Data:* monoclinic  $a = 7.687$  (2),  $b = 10.574$  (2),  $c = 14.908$  (3) Å,  $\beta = 104.26$  (2)°, space group  $P2_1/c$ ,  $Z = 4$ ,  $d_c = 1.251$  g ·  $\text{cm}^{-3}$ . The lattice parameters and intensities were measured at r.t. on an automatic four-circle Philips PW 1100 diffractometer equipment with a graphite monochromator and using  $\text{MoK}_\alpha$  radiation. 1639 independent reflections were recorded ( $\omega - 2\theta$  scan) of which 924 had  $|F_o| > 3\sigma(F_o)$  and  $|F_{\text{int}}| > 6.0$ . The structure was solved by direct methods using the MULTAN-80 program [14] and refined by full-matrix least-squares analysis using the X-ray system [15], anisotropic temperature factors were employed for the non-hydrogen atoms. The hydrogen atoms were located from a difference electron density map and refined with U fixed. The final  $R$  factor, based on the 924 reflections observed, was 0.042 ( $R_w = 0.029$  with  $w = (F_o/32)^2$  for  $|F_o| < 32$  and  $w = (32/F_o)^2$  for  $|F_o| > 32$ ). The positional and vibrational parameters (Table 1) together with the bond lengths and principal torsional angles were determined (Table 2) <sup>1)</sup>.

*3,4a,9-Trimethyl-4a,9a-dihydro-3 H,9 H-[1,2,4]trioxino[6,5-b]indole (8).*  $R_f = 0.48$  (silica gel,  $\text{CH}_2\text{Cl}_2$ ).  $^1\text{H-NMR}$  (360 MHz,  $\text{CDCl}_3$ ): 1.27 (*d*,  $J = 5$ , 3 H); 1.78 (*s*, 3 H); 3.02 (*s*, 3 H); 5.08 (*s*, 1 H); 5.23 (*q*,  $J = 5$ , 1 H); 6.74 (*d*,  $J = 8$ , 1 H); 6.80 (*t*,  $J = 8$ , 1 H); 6.91 (*d*,  $J = 8$ , 1 H); 6.95 (*t*,  $J = 8$ , 1 H). MS: 221 (19,  $M^+$ ), 134 (100). Anal. calc. for  $\text{C}_{12}\text{H}_{15}\text{NO}_3$  (221.26): C 65.14, H 6.83, N 6.33; found: C 65.41, H 7.07, N 6.10.

**7b:**  $^1\text{H-NMR}$  (360 MHz,  $\text{CDCl}_3$ ); data extracted from that of the mixture with **7a**): 1.38 (*d*,  $J = 5$ , 3 H); 1.88 (*s*, 3 H); 2.83 (*s*, 3 H); 4.52 (*s*, 1 H); 5.79 (*q*,  $J = 5$ , 1 H); 6.64 (*d*,  $J = 8$ , 1 H); 6.80 (*t*,  $J = 8$ , 1 H); the two other phenyl ring protons overlapped with those of **7a**. Anal. calc. for  $\text{C}_{12}\text{H}_{15}\text{NO}_3$  (221.26) (for the mixture with **7a**:**7b** = 4:1): C 65.14, H 6.83, N 6.33; found C 64.94, H 7.09, N 6.44%.

*B) In the Presence of Pivalaldehyde.* A solution of **1c** (150 mg, 1.03 mmol) in  $\text{CCl}_4$  (1.5 ml) and pivalaldehyde (2.5 ml) with TPP (4 mg) was photo-oxygenated for 12 h. The solvent was evaporated and the residue was purified by chromatography over silica gel pre-treated with gaseous  $\text{NH}_3$  ( $\text{CH}_2\text{Cl}_2$ ) to give crude material (62 mg). Distillation in the Kugelrohr apparatus at 130°/0.001 Torr gave 3-(*t*-butyl)-5,9b-dimethyl-4a,9b-dihydro-3 H,5 H-[1,2,4]trioxino[5,6-b]indole (**7c**) (20 mg, 7%): m.p. 76–88° (recrystallized from pentane at –78°).  $^1\text{H-NMR}$  (360 MHz,  $\text{CDCl}_3$ ): 0.80 (*s*, 9 H); 1.39 (*s*, 3 H); 2.90 (*s*, 3 H); 4.74 (*s*, 1 H); 4.96 (*s*, 1 H); 6.55 (*d*,  $J = 8$ , 1 H); 6.85 (*t*,  $J = 8$ , 1 H); 7.22 (*t*,  $J = 8$ , 1 H); 7.28 (*d*,  $J = 8$ , 1 H). MS: 263 (34,  $M^+$ ), 206 (9), 161 (100), 146 (56), 134 (74), 132 (39), 118 (41). Anal. calc. for  $\text{C}_{15}\text{H}_{21}\text{NO}_3$  (263.34): C 68.42, H 8.04, N 5.32; found: C 68.27, H 7.95, N 5.10.

*Procedure for Condensing  $\beta$ -Methoxy Hydroperoxide 6a with Carbonyl Compounds Using Trimethylsilyl Trifluoromethanesulfonate (TMSOTf).* A solution of **1c** (160 mg, 1.1 mmol) in MeOH (8 ml) with rose bengal (RB, 4 mg) was photo-oxygenated for 10 h at –78°. All MeOH was evaporated at –10° *in vacuo*. To the residue was added  $\text{CH}_2\text{Cl}_2$  (2 ml) and the carbonyl compound (0.5 ml). The resulting solution was cooled to –78° while TMSOTf (1 equiv.) was added. Stirring was maintained at 1 h at –78°. Next,  $\text{Et}_3\text{N}$  (70  $\mu\text{l}$ ) and  $\text{CH}_2\text{Cl}_2$  (20 ml)

<sup>1)</sup> Observed and calculated structure factors may be obtained on request from G. B. Crystallographic data has been deposited with the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, England.

Table 1. Crystallographic Coordinates for **7a** and Equivalent Isotropic Temperature Factors,  $U_{eq}$  ( $\times 10^3 \text{\AA}^2$ ) with *e.s.d.*'s in Parentheses<sup>a)</sup>

	X	Y	Z	$U_{eq}$
O(1)	0.4183(5)	0.1354(3)	0.04375(20)	56.4(17)
O(2)	0.2623(5)	0.0516(4)	0.03208(21)	59.9(17)
O(3)	0.3306(5)	0.0010(3)	0.18794(20)	53.6(16)
N(1)	0.4236(6)	0.1743(4)	0.28505(25)	47.5(20)
C(1)	0.3007(7)	0.2678(6)	0.2419(3)	50(3)
C(2)	0.1872(7)	0.3412(6)	0.2802(3)	57(3)
C(3)	0.0801(8)	0.4299(6)	0.2235(4)	67(3)
C(4)	0.0858(8)	0.4449(6)	0.1316(4)	74(3)
C(5)	0.2012(8)	0.3698(6)	0.0946(4)	63(3)
C(6)	0.3078(7)	0.2824(5)	0.1493(3)	47.9(24)
C(7)	0.4524(7)	0.1947(5)	0.1340(3)	52(3)
C(8)	0.3193(7)	-0.0484(6)	0.0974(3)	53(3)
C(9)	0.4680(7)	0.0970(5)	0.2130(3)	46.9(24)
C(10)	0.6311(7)	0.2601(5)	0.1411(3)	62(3)
C(11)	0.1730(8)	-0.1467(6)	0.0771(3)	68(3)
C(12)	0.4103(8)	0.1160(5)	0.3710(3)	63(3)
H(2)	0.184(7)	0.325(5)	0.353(3)	63
H(3)	-0.032(7)	0.500(5)	0.257(4)	63
H(4)	-0.007(7)	0.513(5)	0.095(3)	63
H(5)	0.223(7)	0.384(5)	0.023(3)	63
H(8)	0.475(7)	-0.085(5)	0.089(3)	63
H(9)	0.613(7)	0.053(5)	0.242(3)	63
H(101)	0.689(7)	0.310(5)	0.200(3)	63
H(102)	0.737(7)	0.199(5)	0.145(3)	63
H(103)	0.622(7)	0.327(5)	0.088(4)	63
H(111)	0.046(7)	-0.101(5)	0.070(4)	63
H(112)	0.155(7)	-0.181(5)	0.015(4)	63
H(113)	0.211(7)	-0.212(5)	0.121(4)	63
H(121)	0.317(7)	0.047(5)	0.374(4)	63
H(122)	0.531(7)	0.067(5)	0.401(3)	63
H(123)	0.386(7)	0.188(5)	0.417(3)	63

<sup>a)</sup> The numbering of atoms is that shown in the *Figure*.

Table 2. Bond Lengths ( $\text{\AA}$ ) and Torsional Angles ( $^\circ$ ) with *e.s.d.*'s in Parentheses for **7a**<sup>a)</sup>

O(1)–O(2)	1.466(5)	C(1)–C(6)	1.403(7)	O(1)–C(7)–C(9)–O(3)	-42.9(6)
O(1)–C(7)	1.450(6)	C(2)–C(3)	1.389(8)	C(7)–C(9)–O(3)–C(8)	47.9(6)
O(2)–C(8)	1.431(7)	C(3)–C(4)	1.391(9)	C(9)–O(3)–C(8)–O(2)	-64.8(5)
O(3)–C(8)	1.429(6)	C(4)–C(5)	1.401(9)	O(3)–C(8)–O(2)–O(1)	72.8(5)
O(3)–C(9)	1.446(6)	C(5)–C(6)	1.364(8)	C(8)–O(2)–O(1)–C(7)	-67.3(5)
N(1)–C(1)	1.409(7)	C(6)–C(7)	1.507(8)	O(2)–O(1)–C(7)–C(9)	52.8(5)
N(1)–C(9)	1.455(7)	C(7)–C(9)	1.548(7)	N(1)–C(1)–C(6)–C(7)	- 2.5(6)
N(1)–C(12)	1.447(6)	C(7)–C(10)	1.518(8)	C(1)–C(6)–C(7)–C(9)	21.4(5)
C(1)–C(2)	1.392(8)	C(8)–C(11)	1.507(8)	C(6)–C(7)–C(9)–N(1)	-31.5(5)
				C(7)–C(9)–N(1)–C(1)	31.5(5)
				C(9)–N(1)–C(1)–C(6)	-19.3(6)

<sup>a)</sup> The numbering of atoms is that shown in the *Figure*.

were added. The solution was then washed with  $\text{H}_2\text{O}$  ( $3 \times$ ). Evaporation of the solvent gave a residue which was purified by column chromatography over silica gel treated with  $\text{NH}_3$ , so giving the corresponding trioxanes.

Acetaldehyde gave **7a** and **7b** (60% yield, **7a/7b** = 2:1), identical to those obtained by photo-oxygenation.

Pivalaldehyde gave **7c** (22% yield), identical with the photo-chemical product.

Acetone gave *3,3,5,9b-tetramethyl-4a,9b-dihydro-3H,5H-[1,2,4]trioxino[5,6-b]indole (7d)* (46% yield): m.p. 62–67° (recrystallized from pentane at –78°). <sup>1</sup>H-NMR (360 MHz, CDCl<sub>3</sub>): 1.50 (s, 3 H); 1.52 (br. s, 3 H); 1.70 (br. s, 3 H); 2.85 (s, 3 H); 4.67 (br. s, 1 H); 6.51 (d, *J* = 8, 1 H); 6.77 (t, *J* = 8, 1 H); 7.23 (m, 2 H). MS: 235 (26, *M*<sup>+</sup>), 220 (13), 178 (16), 161 (32), 149 (26), 134 (100). Anal. calc. for C<sub>13</sub>H<sub>17</sub>NO<sub>3</sub> (235.28): C 66.36, H 7.28, N 5.95; found: C 66.14, H 7.10, N 6.02.

## REFERENCES

- [1] Review: *I. Saito, T. Matsuura, M. Nakagawa & T. Hino*, Acc. Chem. Res. 10, 346 (1977).
- [2] *J. M. Wood*, in 'Metal Ion Activation of Dioxygen', ed. T. G. Spiro, J. Wiley & Sons, New York, 1980, pp. 163–180; 'Molecular Mechanisms of Oxygen Activation', ed. O. Hayaishi, Academic Press, New York, 1974.
- [3] *U. Gallo & L. Santamaria*, ed. 'Research Progress in Organic, Biological, and Medicinal Chemistry', Vol. II, Elsevier, New York, 1972; *J. D. Spikes & R. Livingston*, Adv. Rad. Biol. 3, 29 (1969).
- [4] Review: *C. W. Jefford & P. A. Cadby*, Prog. Chem. Org. Nat. Prod. 40, 191 (1981).
- [5] *M. Nakagawa, H. Okajima & T. Hino*, J. Am. Chem. Soc. 99, 4424 (1977); *M. Nakagawa & T. Hino*, Heterocycles 6, 1675 (1977); *M. Nakagawa, J. Chiba & T. Hino*, Heterocycles 9, 385 (1978); *M. Nakagawa, S. Kato, S. Kataoka & T. Hino*, J. Am. Chem. Soc. 101, 3136 (1979).
- [6] *I. Saito, M. Imuta, A. Nakada, S. Matsugo & T. Matsuura*, Photochem. Photobiol. 28, 531 (1978); *T. Hino, H. Miura, R. Murata & M. Nakagawa*, Chem. Pharm. Bull. 26, 3695 (1978).
- [7] *M. Ihara, K. Noguchi, K. Fukumoto & T. Kametani*, Heterocycles 20, 421 (1983).
- [8] *I. Saito, M. Imuta, Y. Takahashi, S. Matsugo & T. Matsuura*, J. Am. Chem. Soc. 99, 2005 (1979).
- [9] *R. Noyori, S. Murata & M. Suzuki*, Tetrahedron 37, 3899 (1981).
- [10] *C. W. Jefford, J. Boukouvalas & S. Kohmoto*, J. Chem. Soc., Chem. Commun. 1984, 523.
- [11] *C. W. Jefford, S. Kohmoto, J. Boukouvalas & U. Burger*, J. Am. Chem. Soc. 105, 6498 (1983).
- [12] *T. Hatsui & H. Takeshita*, Bull. Chem. Soc. Jpn. 53, 2655 (1980).
- [13] *I. Saito, S. Matsugo & T. Matsuura*, J. Am. Chem. Soc. 101, 7332 (1979).
- [14] *P. Main, S. J. Fiske, S. E. Hull, L. Lessinger, G. Germain, J. P. Declercq & M. M. Woolfson* (1980). MULTAN-80, A System for Computer Programms for the Automatic Solution of Crystal Structure from X-Ray Diffraction Data, University of York.
- [15] *J. M. Stewart, P. A. Machin, C. W. Dickinson, H. L. Ammon, H. Heck & H. D. Flack* (1976). The X-Ray System. Version of March 1976. Tech. Rep. TR-446. Computer Science Center, University of Maryland, College Park, Maryland.