SYNTHESIS OF 2-(1-METHYL-3-INDOLYL)-3-ALKYL OR ARYL-1,4-DIOXENES

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The title dioxenes were synthesized by short steps from indole.

Recent studies[1] on the mechanism of chemi-and bio-luminescence suggested that the high efficiency of singlet excited state production and the instability of the intermediate dioxetanes in bioluminescence and efficient chemiluminescence may be explained in terms of the conjugation of an electon-donating and highly fluorescent chromophore with the excited state carbonyl group to be formed by decomposition of an intermediate dioxetane.

β-Indolyl group may be one of the simplest chromophores to fulfil the above requirements, i.e., electoron-donating and strongly fluorescent abilities. Matsumoto and Kondo reported[2] that 3-vinylindole reacts with singlet oxygen to give 1,4-endoperoxide which on warming decomposes with very weak chemiluminescence; a transient dioxetane is assumed in this case. We synthesized from 2-(1-methyl-3-indolyl)-3-alkyl or aryl-dioxenes by sensitized photooxygenation at a low temperature 1-(1-methyl-3-indolyl)-6-alkyl or aryl-2,5,7,8-tetraoxabicyclo[4,2,0]octanes, which resulted in highly efficient chemiluminescence as reported elsewhere.[3]

2,3-Disubstituted 1,4-dioxenes have usually prepared[4,5] by acid-catalyzed condensation of the corresponding benzoins and ethylene glycol, but this method could not be applied to the synthesis of the 3-indolyldioxenes since benzoins having 3-indolyl group instead of a phenyl were obtainable with difficulty and since the attempted acid-catalyzed condensation failed.
We wish to report herewith a convenient new synthesis of the 3-indolyldioxenes; the method would be widely applicable to the synthesis of other 2,3-disubstituted 1,4-dioxenes.

The starting materials, 1-methyl-3-(α-haloacyl)indoles (**1**), were prepared from indole and α-halo acid halide by two steps.[6] Dioxene **4c** was synthesized as follows: the haloacylindole **1c** was treated with two molar equivalents of sodium ethylene glycoxide in ethylene glycol and dioxane (1:1 v/v) at 100°C for 2hr to give a mixture of β-hydroxyethyl ether **2c** and ketal **3c**, which were separated by a silica gel column or thin-layer chromatography using CH_2Cl_2-MeOH (95:5) as the eluant. PMR of **2c**: $\delta(CDCl_3)$ 3.74 (br,s, 7H), 5.32 (s, 1H), 7.1-7.6 (m, 8H), 7.94 (s, 1H), 8.36 (m, 1H); PMR of **3c**: $\delta(CDCl_3)$ 3.65 (s, 3H), 3.91 (m, 4H), 5.07 (s, 1H), 6.75 (s, 1H), 7.0-7.7 (m, 9H). The β-hydroxyethyl ether (**2c**) was refluxed in toluene under azeotropic condition in the presence of a catalytic amount of DL-camphorsulfonic acid for 2 hr to yield dioxene **4c**, colorless prisms, mp 134.5-135.5°C, in 94% yield; PMR $\delta(CDCl_3)$ 3.65 (s, 3H), 4.34 (3, 4H), 6.87 (s, 1H), 6.9-7.3 (m, 9H). Yields for the several β-hydroxyethyl ethers (**2**), ethylene ketals (**3**), and dioxenes (**4**) prepared by this method are summerized in Table 1. The condensation product **3** may be formed *via* an epoxide intermediate (A), and the ratio (**2**)/(**3**) is dependent on the substitutions, X and R. Attempted conversion of **3** to **4** failed although benzoin ethylene ketal could be transformed into the corresponding dioxene with acid.[4]

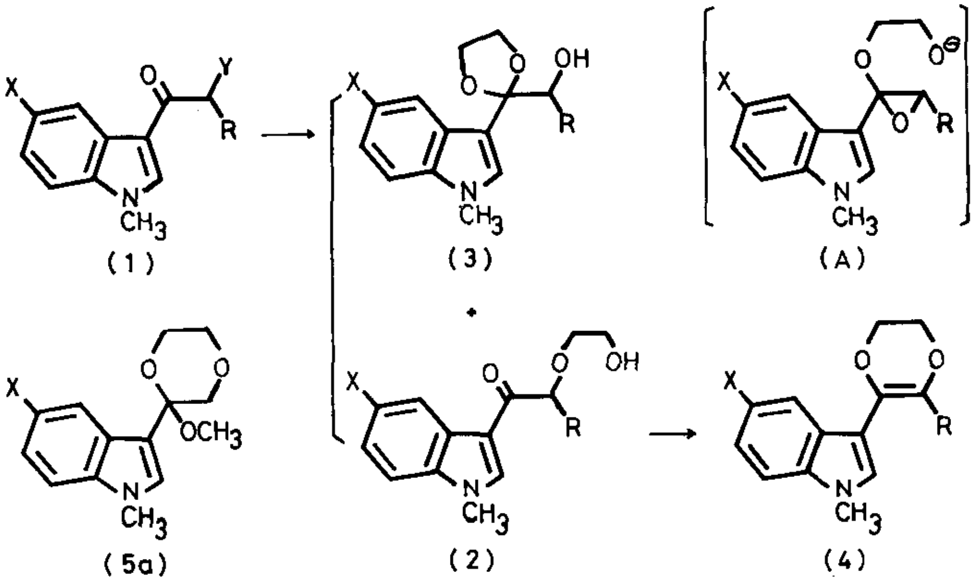

TABLE 1

Starting Material				Isolated Yield (%)			mp of 4 (°C)*
	X	Y	R	2	3	4	
1a	H	I	H	52	–	93	syrup**†
1b	H	Br	CH_3	67	32	18	98-99†
1c	H	Cl	C_6H_5	48	23	94	134.5-135.5
1d	H	Cl	C_6H_4Br-p	53	16	89	156.5-157.5
1e	Br	Cl	C_6H_5	35	38	82	159-160
1f	OMe	Cl	C_6H_5	49	28	52	133-134

* 4b-4f were crystallized from methanol and satisfactory elemental analyses and spectral data were obtained.

** Distilled at 215°/1-2 Torr.

† Decomposed on standing at room temp.

1-Methyl-3-iodoacetylindole (**1a**) gave exclusively β-hydroxyethyl ether **2a**, but it could not be converted to the dioxene **4a** by the acid-catalyzed cyclization. The hydroxyethyl ether **2a** was therefore treated with trimethyl orthoformate and a catalytic amount of DL-camphorsulfonic acid in methanol at room temp. for 0.5 hr to give methyl ketal **5a** (m/e 247 M^+), which without purification was pyrolyzed at 210°C/1-2 Torr for 1 hr to afford dioxene **4a** in 93% yield; PMR δ($CDCl_3$) 3.77 (s, 3H), 4.28 (m, A_2B_2, 4H), 6.63 (s, 1H), 7.18 (s, 1H), 7.0-7.4 (m, 3H), 7.59 (m, 1H).

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