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CHEMILUMINESCENCE OF MONOCYCLIC 3,6-DISUBSTITUTED PYRIDAZINES: A MODEL FOR LUMINOL CHEMILUMINESCENCE

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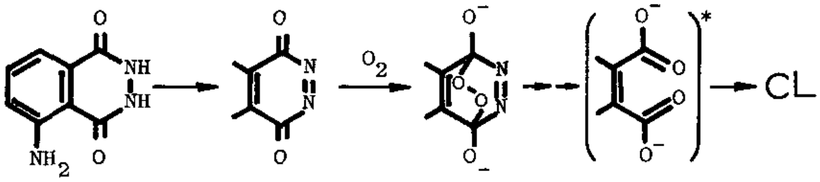
Abstract —— Several monocyclic 3,6-disubstituted pyridazines (**1-5**) were oxidized by molecular oxygen under the basic conditions in dimethyl sulfoxide to yield corresponding maleic acids and/or its derivatives with chemiluminescent light emission.

Luminol (I), the famous chemiluminescent compound, gives strong light emission when oxidized either by hydrogen peroxide in an aqueous solution in the presence of a catalyst (such as hemoglobin)[1] or by molecular oxygen in dimethyl sulfoxide (DMSO) under the basic condition (such as t-BuOK).[2] Many mechanisms have been proposed for the reaction.[1-3] Aminophthalate anion (V) is believed to be the emitter.



Luminol (I) Diazaquinone (II) III V*

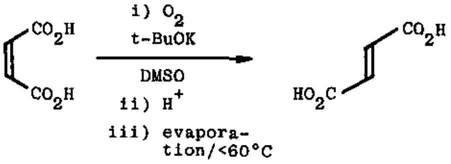
(1)

On the course of studies of luminol chemiluminescence, we found a chemiluminescent (CL) reaction of monocyclic 3,6-substituted pyridazines which have no condensed aromatic moieties like luminols studied formerly.[4,5] We now describe the CL reaction of the monocyclic pyridazines induced by the oxygenation with molecular oxygen in DMSO in the presence of t-BuOK. Although the chemiluminescent reaction of the 3,6-dihydroxy derivatives (**4a** and **b**) seems to proceed through a similar mechanism to that of luminol, different mechanisms are to be plausible for the other pyridazines employed.

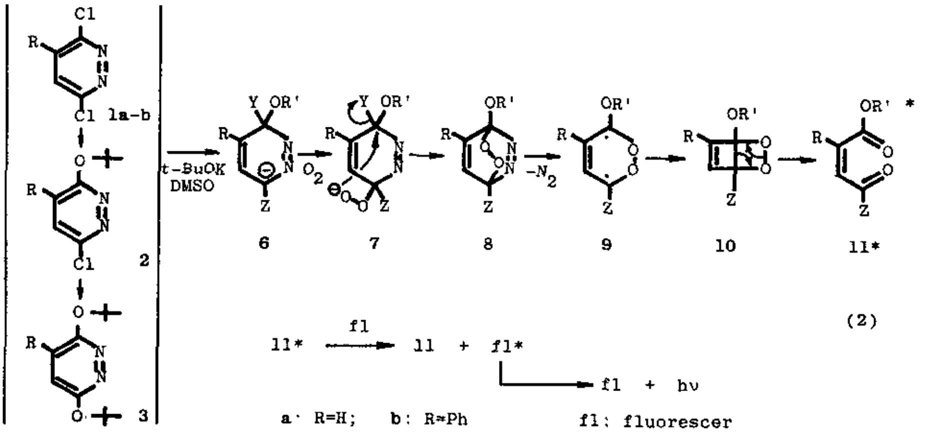
Into a solution of the dichloropyridazine (1a)[6] (10^{-2} M) in DMSO (2 ml; dried over and distilled from CaH_2 and then saturated by O_2 before use) being flushed with O_2 gas, was added t-BuOK (10^{-1} M) in DMSO (2 ml) at room temperature. Light emission coming out; the CL and fluorescence (FL) spectra were measured on a Hitachi Fluorescence/Phosphorescence Photometer Model MPF-2A. Quantum yields were measured by using a photomultiplier tube exposed to the CL reacting solution (Hamamatsu R-105 UH) and are relative to the Seliger's standard (luminol).[10] The values obtained were corrected for the phototube spectral response.

The resulted mixture was evaporated in vacuo at the temperature below 40°C after acidification with aqueous 1N HCl to pH 2, washed with ether, and then extracted with $CHCl_3$. The residue from the extracts was identified to be fumaric acid (12a) with comparison of mp, IR, and NMR with those of authentic sample. Formation of fumaric acid (**12a**) may be explained either by the thermal isomerization of maleic acid (**11a**) under the isolation conditions or by the isomerization in the excited state. Treatment of maleic acid (**11a**) with t-BuOK/O_2/DMSO gave fumaric acid (**12a**) after the similar work-up. This seems to prefer to the possibility that fumaric acid was not produced directly from the excited state of maleic acid.

3,6-Di-t-butoxy-, 3-chloro-6-t-butoxy- and 3,6-dimethoxy-pyridazines (**3a**,[6] **2a**,[6] and **5a**[6]) reacted as above and gave the same product **11a** almost as the sole product with light emission; the facts suggest that **2a** and **3a** could be the intermediates in the CL reaction of **1a** or, at least, the reactions of **1a**-**3a** go through a common intermediate. The CL gave similar spectra to the corresponding FL spectra of the solution and also of the basic solutions of **1a**-**3a** in the absence of O_2 (in vacuo).[11] This suggests that the each emitter of these CL reactions is **1a**-**3a** themselves, respectively. The basic mixtures in vacuo gave no light but they gave light when O_2 gas was added through the solutions.

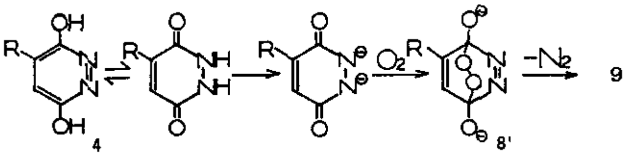


The reaction path is best described as scheme 2: namely, the pyridazines **1**-**3** gave an anion **6**, which took a molecular oxygen to give endo peroxide **8**, through **7**. Spontaneous extrusion of N_2 molecule from **8** gave biradical peroxide **9**, or its recyclized dioxetane **10**, one of which yielded **11** as an excited state (**11***), whose energy could be transfered to the starting material **1**-**3**.



(2)

3,6-Dihydroxy derivative **4a**[6] gave rather strong CL under the similar conditions. However, successive addition of the base revealed that the mechanism was different from that of the other pyridazines: The compounds (**4a** and b) needed more than 2 moles of the base and the higher reaction temperature decreased the quantum yields, while the others reacted by a trace of the base to give the light emission and the higher reaction temperature increased the quantum yields. We propose for **4a** and b a different mechanism which is similar to the case of luminol.



Large amount of dimethyl sulfone was also isolated from the reaction mixtures, resulting from base catalysed oxidation of DMSO.[12]

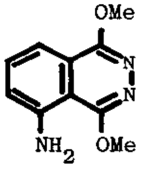
Table 1. Quantum Yields of CL of 1,4-Pyridazines

	R	Y	Z	Φ_{CL}[a] × 10^5		λ_{max} (nm)	
				t-BuOK/O_2	t-BuOK/vac → O_2	CL	FL
1a	H	Cl	Cl	9.8	11.2	540±10	540±5[b]
2a	H	Cl	O-t-Bu	9.8	9.8	510±10	510±5[b]
3a	H	O-t-Bu	O-t-Bu	5.4	2.5	480±10	475±5[b]
4a	H	OH	OH	298	235	445±10	445±5
5a	H	OMe	OMe	6.3	7.0	—	440±5 465±5 500±5
1b	Ph	Cl	Cl	2.6	2.5	510±10	510±5
4b	Ph	OH	OH	80	116	500±10	510±5

a) relative to luminol (ref. 10). b) FL in vacuo.

For the ease of isolation of the final product, 4-phenyl-3,6-pyridazines[13] (1b and 4b) were employed. The phenyl derivatives gave the similar CL under the similar conditions used as above. The CL spectra were identical with the FL spectra of the compound used. Phenylmaleic anhydride was isolated and identified as the final product after the isolation procedure as above with comparison of mp, GLC, IR, and NMR with the authentic sample.[15] Phenylmaleic acid (11b), the supposed product, was known to be unstable and to give the anhydride easily.[17] Therefore, the compound directly generated from the CL reaction as the excited state could be the compound 11b*.

Goto et al.[18] had examined a photochemical oxidation of the similar system, dimethyl ether of luminol (VI), with O_2 at the dry ice temperature. However, no CL was detected when the solution was warmed up to room temperature.



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6) **1a**: mp 68-69°C (lit.$^{7)}$ 69°C); ν_{max} (KBr) 1545, 1380, 1145, 830, 780 cm^{-1}; δ_{ppm} ($CDCl_3$) 7.56 (2H, s) (lit.$^{8)}$ 7.57); m/z 148 (M^+).

2a: mp 93.5-94°C (lit.$^{9)}$ 90-92°C); ν_{max} (KBr) 1580, 1130, 840 cm^{-1}; δ_{ppm} ($CDCl_3$) 1.60 (9H, s), 6.76 (1H, d, J = 9 Hz), 7.26 (1H, d, J = 9 Hz); m/z 171 $(M\text{-}Me)^+$; 131 $(M\text{-}t\text{-}Bu)^+$.

3a: mp 77-78°C (lit.$^{9)}$ 76-78°C); ν_{max} (KBr) 1425, 1265, 1160 cm^{-1}; δ_{ppm} ($CDCl_3$) 1.60 (18H, s), 6.72 (2H, s); m/z 209 $(M\text{-}Me)^+$.

4a: purchased from Wako Chem. Co. (Kyoto).

5a: mp 106-108°C (lit.$^{8)}$ 106-107°C); ν_{max} (KBr) 1470, 1400, 1260, 1000 cm^{-1}; δ_{ppm} ($CDCl_3$) 4.02 (6H, s), 6.84 (2H, s); m/z 140 (M^+).

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12) W. Ando, H. Miyazaki, K. Ito, and D. Auchi, *Tetrahedron Lett.*, 1982, **23**, 555.

13) **1b**: mp 97-98°C (lit.$^{14)}$ 92°C); ν_{max} (KBr) 1540, 1480, 1320, 1120, 750, 680 cm^{-1}; δ_{ppm} ($CDCl_3$) 7.38 (1H, s), 7.46 (5H, s); m/z 224 (M^+).

4b: mp 267-272°C (lit.$^{14)}$ 273°C); ν_{max} (KBr) 3000 br, 1640, 1560 cm^{-1}; δ_{ppm} (DMSO-d_6) 7.08 (1H, s), 7.40 (3H, m), 7.70 (2H, m); m/z 188 (M^+).

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15) **12**: mp 117-120°C (lit.$^{16)}$ 119-120°C); ν_{max} (KBr) 3100, 1810, 1760, 1220 cm^{-1}; δ_{ppm} ($CDCl_3$) 6.91 (1H, s), 7.20 (1H, d), 7.48 (2H, m), 7.90 (2H, m).

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18) T. Goto, M. Isobe, and K. Ienaga, in ref. 1b, p. 492.

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