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PHOTOOXYGENATION OF PYRAZIN-2(1H)-ONES

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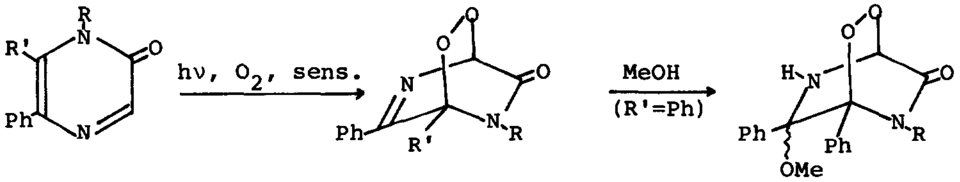
Summary: 1-Alkyl-5,6-diphenylpyrazin-2(1H)-ones (1a-b) reacted with singlet oxygen in dichloromethane to afford the stable endoperoxide (1a-b), while in methanol to afford the 1:1-adduct (3a-b) of the endoperoxide (2a-b) and methanol.

Photooxygenation of organic substrates have been extensively studied in recent years. Singlet oxygen, for example, is known to react with different types of organic compounds, giving rise to a variety of products.$^{1)}$ However, the reactions of singlet oxygen with heterocyclic substrates containing nitrogen atom are largely limited to five-membered ring systems such as the pyrroles and indoles,$^{2)}$ except that Markham and Sammes$^{3)}$ recently reported six-membered heterocycles containing nitrogen atom such as pyrazines and pyrimidines reacted with singlet oxygen to form endoperoxides. We report here the reaction of pyrazin-2(1H)-ones (1) with singlet oxygen and the isolation of stable endoperoxides (2).

Irradiation of an oxygenated solution of 1-methyl-5,6-diphenylpyrazin-2(1H)-one (1a) in dichloromethane in the presence of methylene blue as a sensitizer with visible light at room temperature for 2 h afforded a stable endoperoxide (2a) (positive starch iodide test); m.p.(decomp.) 103-105°C (from dichloromethane-hexane); IR(KBr) 1705, 1605, 1570, 1450, 1380, 760, and 700 cm^{-1}; NMR(δ in $CDCl_3$) 2.60(s, 3H, $NC\underline{H}_3$), 6.08(s, 1H, bridgehead -C$\underline{H}$), and 7.0-7.5(m, 10H, aromatic); m/e 295(QM + 1) (Found: C, 69.03; H, 4.76; N, 9.46. $C_{17}H_{14}N_2O_3$ requires C, 69.37; H, 4.97, N, 9.51%), in 60% yield. Similarly, irradiation of 1-ethyl-5,6-diphenylpyrazin-2(1H)-one (1b) in dichloromethane under the same conditions gave the endoperoxide (2b)$^{4)}$ in 22% yield. The photooxygenation of (1a) was quenched by the addition of DABCO. A slow oxidation of the pyrazin-2(1H)-one (1a) also occurred in the absence of methylene blue, producing low yield of the endoperoxide (2a) and suggesting that the pyrazin-2(1H)-one (1a) can act as its own sensitizer.

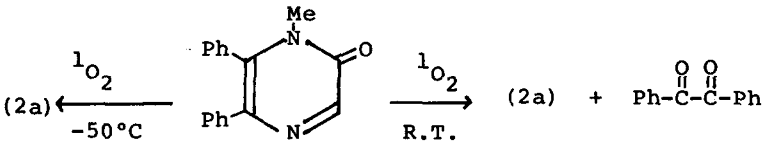


(1)
a; R=Me R'=Ph
b; R=Et R'=Ph
c; R=Me R'=H

(2)
a; R=Me R'=Ph
b; R=Et R'=Ph

(3)
a; R=Me
b; R=Et

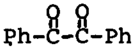
A photochemical process is required since the endoperoxide (2a) could not be obtained on exposure of (1a) to oxygen in the dark[5)] and (1a) was recovered quantitatively. The endoperoxide (2a-b) was stable at room temperature but decomposed when (2a-b) was warmed in benzene or heated at higher temperature (>m.p). Irradiation of an oxygenated solution of (1a-b) in methanol in the presence of methylene blue with visible light gave the 1:1-adduct (3a-b) of the endoperoxide (2a-b) and methanol.[6)] The 1:1-adduct (3a) was also obtained in almost quantitatively when (2a) was stirred in methanol in the dark at room temperature. When eosin or tetraphenylporphin was used as sensitizer instead of methylene blue on photooxygenation of (1a), the endoperoxide (2a) was also obtained. (Table 1)
On the other hand, irradiation of an oxygenated solution of (1a) in dichloromethane in the presence of rose bengal as sensitizer at room temperature gave the endoperoxide (2a) and benzil in 28 and 15% yield, respectively and at low temperature (-50°C) gave a single product, the endoperoxide (2a) in 52% yield.



(1a)

The formation of benzil is presumed to arise by radical fragmentation of dioxetane intermediate.[7)] 1-Methyl-5-phenylpyrazin-2(1H)-one (1c) also rapidly reacted with singlet oxygen and gave a positive peoxide test (starch iodide). However, reaction products decomposed in explosive after the evaporation of the solvent. Although the endoperoxide (2c) was not isolated, evidence for its formation was obtained by NMR spectrum. Photooxygenation of the pyrazin-2(1H)-one (1c) in deuteriodichloromethane using methylene blue as sensitizer for 20 min at -50°C gave a new compound (2c), of which NMR spectrum showed a singlet at δ 3.11, two doublets at δ 5.91(J=1.4 Hz) and 6.23(J=1.4 Hz), and the multiplet at δ 7.3-8.1 in the ratio of 3:1:1:5 assignable to methyl, bridgehead methine, and aromatic protons, respectively, in addition to the peaks of the starting pyrazin-2(1H)-one (1c).[10)]

Table 1. Yield of the endoperoxide (2a)[a]

Solvent	Sensitizer	Yield of (2a) (%)	
CH_2Cl_2	MB[b]	60	
CH_2Cl_2	Eosin	18	
CH_2Cl_2	TPP[c]	67	
CH_2Cl_2	RB[d] (r.t.)	28	 $Ph-\overset{O}{\overset{\|}{C}}-\overset{O}{\overset{\|}{C}}-Ph$ (15%)
CH_2Cl_2	RB (-50°C)	52	
MeOH	MB	(49)[e]	
MeOH	RB	76	
Acetone	MB	40	
Acetone	RB	68	

[a] Isolated yield. [b] Methylene blue. [c] Tetraphenylporphin.
[d] Rose bengal. [e] The yield of the 1:1-adduct of (2a) and methanol.

In conclusion proceding experiments are the first example of the isolation of endoperoxides from six-membered conjugated carbonyl compounds containing nitrogen.

References and notes

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ibid., 79, 447 (1979).

2) H.H. Wasserman and B.H. Lipshtz, "Singlet Oxygen", ed. H.H. Wasserman and R.W. Murray, Academic Press, New York, 1979, p. 429.

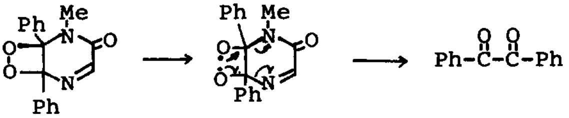
3) J.L. Markham and P.G. Sammes, J. Chem. Soc.(Chem. Comm.), 1976, 417.

4) Compound (2b); positive starch iodide test; m.p.(decomp.) 112°C; IR(KBr) 1710, 1600, 1580, 1450, 1380, 760, and 700 cm^{-1}; NMR(δ in $CDCl_3$) 0.88(t, 3H, $CH_2C\underline{H}_3$), 2.88-3.77(m, 2H, $C\underline{H}_2CH_3$), 6.08(s, 1H, bridgehead -C$\underline{H}$), and 6.9-7.7(m, 10H, aromatic) (Found: C, 70.50; H, 5.24; N, 8.76. $C_{18}H_{16}N_2O_3$ requires C, 70.11; H, 5.23; N, 9.08%).

5) Sammes et al. reported that 5-ethoxy-1,3-dimethylpyrazin-2(1H)-one rapidly reacted with oxygen on exposure to air to give 5-ethoxy-3-hydroxy-1,3-dimethylpyrazin-2(3H),6(1H)-dione via endoperoxide intermediate, however, in case of (1a), the endoperoxide (2a) could not be detected. (P.J. Marchin, A.E.A. Porter, and P.G. Sammes, J. Chem. Soc.(Perkin I), 1973, 404).

6) Irradiation of (1a) under these conditions using rose bengal as sensitizer instead of methylene blue for 2 h gave the endoperoxide (2a) in 76% yield. Compound (3a); positive starch iodide test; yield 49%; m.p.(decomp.) 117-118°C; IR (KBr) 3320, 1710, 1600, 1495, 760, and 700 cm^{-1}; NMR(δ in $CDCl_3$) 2.76(s, 3H, $NC\underline{H}_3$), 3.30(s, 3H, $OC\underline{H}_3$), 3.8(br s, 1H, N$\underline{H}$, exchangeable with D_2O), 5.40(d, 1H, J=3.4 Hz, bridgehead -C$\underline{H}$), and 7.05(m, 10H, aromatic); m/e 307(QM + 1). Compound (3b); positive starch iodide test; yield 7%; oil; IR(film) 3320, 1690, 1600, 1490, 760, and 695 cm^{-1}; NMR(δ in $CDCl_3$) 0.92(t, 3H, $CH_2C\underline{H}_3$), 3.30(s, 3H, $OC\underline{H}_3$), 3.41(q, 2H, $C\underline{H}_2CH_3$), 3.73(br s, 1H, N$\underline{H}$), 5.40(d, 1H, J=3.6 Hz, bridgehead -C$\underline{H}$), and 7.1-7.75(m, 10H, aromatic); m/e 339(QM + 1).

7) The formation of α-diketone from the photooxygenation of tetrathioethylenes[8] and enamines[9] is reported.



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9) H.H. Wasserman and S. Terao, Tetrahedron Lett., 1975, 1735. W. Ando, T. Saeki, and T. Migita, J. Am. Chem. Soc., 97, 5028 (1975).

10) Compound (1c); NMR(δ in CD_2Cl_2) 3.55(s, 3H, $NC\underline{H}_3$), 7.3-7.7(m, 6H, =C$\underline{H}$ and aromatic), and 8.16(s, 1H, =C$\underline{H}$).

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