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OXIDATIVE CYCLIZATION OF 2-UNSATURATED 1,4-DIOXIMES

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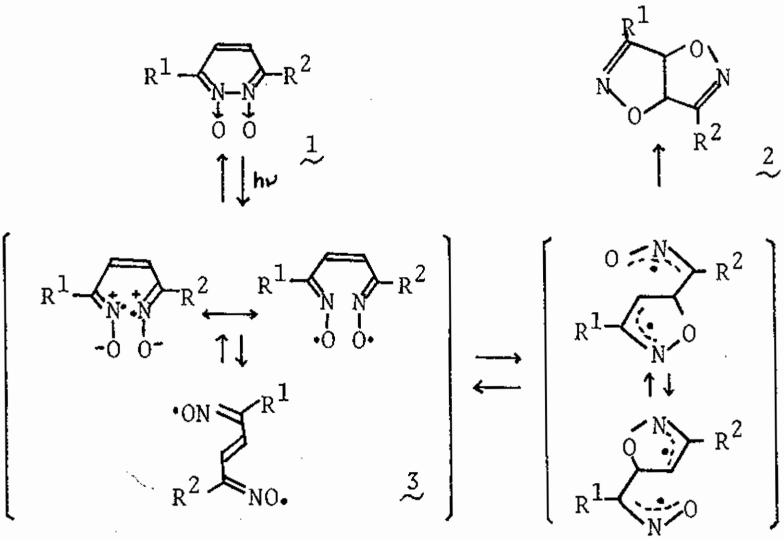
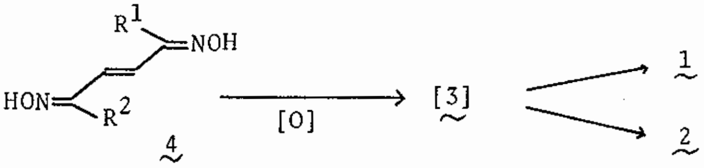
The major product of the oxidation of 1,4-diphenyl-2-butene-1,4-dioxime(4c) with phenyliodoso bis-trifluoroacetate(PITFA) was 3,6-diphenyl-dihydro-isoxazoloisoxazole(2c) which had been incorrectly assigned to the 3,6-diphenylpyridazine dioxide(1c) by other authors. Lead tetraacetate was found to be more applicable reagent than PITFA for the preparation of dioxides(1) from 2-unsaturated 1,4-dioximes.

In the previous paper,[1] we have reported that the photoisomerization of pyridazine 1,2-dioxides(1) afforded 3a,6a-dihydroisoxazolo[5,4-d]isoxazoles(2) of a novel ring system, and bis-iminoxyl radicals(3) were posturated as the intermediates in the reaction.

If radicals(3) are the intermediate of the compounds(2), dioximes(4) might be transformed into 2 by the oxidation under appropriate conditions, because oximes are known to generate iminoxyl radicals by oxidation.[2-4]



In this respect, Spyroudis *et al.*[5] have reported that the oxidation of dioximes of hexa-3-ene-2,5-dione(4a, $R^1=R^2=Me$) and 1,4-diaryl-2-butene-1,4-diones(4, $R^1=Ar$, $R^2=Ar'$) with phenyliodoso bis-trifluoroacetate(PITFA) afforded the pyridazine dioxides(1).



This paper describes the novel results of the oxidation of 4 with PITFA. The results are shown in the table on the next page.

When 4a was treated with ceric ammonium nitrate(CAN, 1.2 molar eq.), small amounts of 3-methyl-5-acetylisoxazole[6] [5a, mp.73-75°(75-76°),[7] NMR(δ): 2.42(3H,s), 2.63(3H,s), and 6.77(1H,s), IR(KBr): 1580 and 1690 cm^{-1}], 2,5-dinitrohexa-2,4-

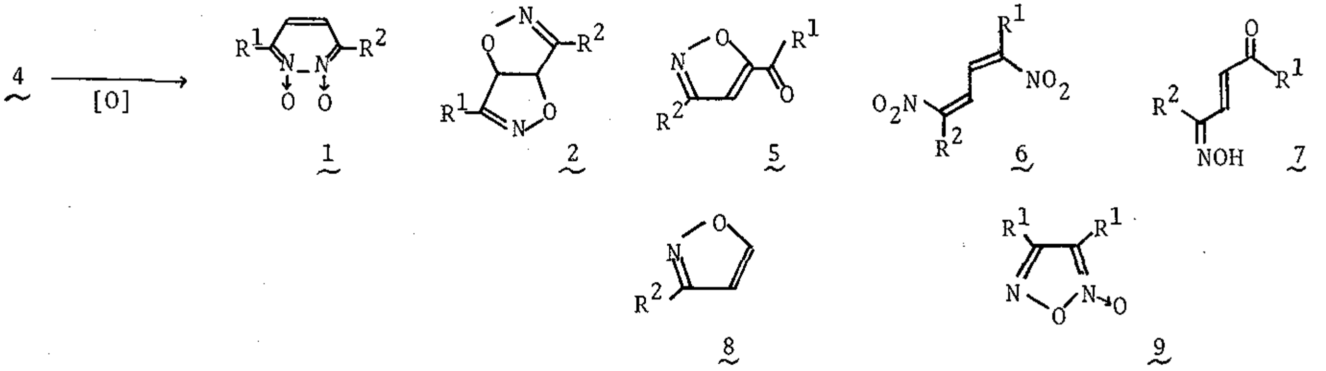


Table (The yields are shown in %.) $^{a)}$

Dioximes	Oxidation	1	2	5	6	7	8	9	4(recov.)
4a, $R^1=R^2=Me$	CAN/aq.AcOH	0	0	3	10	6	---$^{c)}$	---$^{c)}$	0
	LTA/CH_2Cl_2	33	8	trace	11	0	---$^{c)}$	---$^{c)}$	0
	PITFA/CH_2Cl_2	15(10)$^{b)}$	5	0	2	0	---$^{c)}$	---$^{c)}$	0
4b, $R^1=Me, R^2=Ph$	LTA/CH_2Cl_2	19	10	3	---$^{c)}$	---$^{c)}$	trace	---$^{c)}$	0
4c, $R^1=R^2=Ph$	CAN/aq.AcOH	0	8	---$^{c)}$	trace	---$^{c)}$	trace	trace	50
	LTA/CH_2Cl_2	15	60	---$^{c)}$	2	---$^{c)}$	trace	trace	0
	PITFA/CH_2Cl_2	0	51(55)$^{b)}$	---$^{c)}$	6	----$^{c)}$	3	trace	0

a) at room temperature for 1-2 hr, for all runs

b) Spyroudis et al., see footnote 5

c) All attempts to isolate these compounds have been failed although the formation of these compounds can not be denied.

diene[**6a**, mp.160-161°(165-166°),[8] NMR(δ): 2.45(6H,s) and 7.70 (2H,s), IR(KBr); 1330 and 1520cm^{-1}], and monooxime[9][**7a**,mp.109-111°, NMR(δ): 2.05(3H,s), 2.33(3H,s), 6.42(1H,d,J=17Hz), and 7.21(1H,d,J=17Hz), IR(KBr): 1620 and 1675cm^{-1}] were isolated from the reaction mixture(silica gel chromatography).

When lead tetraacetate(LTA, 1.5 molar eq.) was used as an oxidizing reagent, **4a** was transformed into **2a**[10][mp.95-96°, NMR(δ): 2.10(6H,s) and 5.75(2H,s), IR(KBr): 900, 1040,1325, 1400 and 1440cm^{-1}], together with **1a**[11][mp.215-216°, NMR(δ):2.53 (6H,s) and 6.95(2H,s), IR(KBr): 840, 1395 and 1480cm^{-1}, MS(*m/e*): 140(M$^+$), 124(M$^+$-O), 110(M$^+$-NO), 82 and 79], **5a** and **6a**.

The oxidation of **4a** with PITFA(1.3 molar eq.) also yielded **2a**, besides **1a** and **6a**. Similarly, **2b**[10][mp.102-103°, NMR(δ): 2.10(3H,s), 5.88(1H,d,J=9.8Hz), 6.23(1H,d,J=9.8Hz), 7.35-7.55 (3H,m) and 7.70-7.90(2H,m), IR(KBr): 900, 1030, 1325, 1360 and 1440cm^{-1}] was obtained by the oxidation of **4b** with LTA.

Moreover, **1b**[mp.181-182°, NMR(δ): 2.55(3H,s), 7.10(2H,br,s), 7.40-7.60(3H,m) and 7.70-7.95(2H,m), IR(KBr): 840, 1400 and 1480cm^{-1}, MS(*m/e*): 202(M$^+$), 186(M$^+$-O), 172(M$^+$-NO), 144 and 115], **5b**[13][mp.95-96°, NMR(δ): 2.64(3H,s), 7.28(1H,s), 7.40-7.60(3H,m) and 7.73-7.95(2H,m), IR(KBr): 1700cm^{-1}], and trace of **8b**[14][bp. *ca*.70°/1mmHg, NMR(δ): 6.67(1H,d,J=1.8Hz), 7.40-7.65(3H,m), 7.78-7.95(2H,m), 8.48(1H,d,J=1.8Hz), IR(KBr): 765, 880 and 1440cm^{-1}] were isolated from the reaction mixture.[15]

Further, the oxidation of **4c** with LTA yielded a major product(60%)[**A**, mp.176-177°, NMR(δ): 6.45(2H,s), 7.30-7.65(6H, m) and 7.70-7.95(4H,m), IR(Nujor): 900, 1000 and 1343cm^{-1}] and a minor product(15%)[**B**, mp.258°(dec.), NMR(δ): 7.40-7.66(6H+2H,m), 7.85-8.00(4H,m), IR(KBr): 825, 1350, 1398 and 1460cm^{-1}, MS(*m/e*): 264(M$^+$), 248(M$^+$-O), 234(M$^+$-NO), 206, 128 and 102]. The melting point and the spectral data of the compound A are essentially identical with those of 3,6-diphenylpyridazine 1,2-dioxide(1c).[5]

However, the IR absorption of A at 900 and 1343cm^{-1} are not necessarily assigned to the N-oxide stretching because all 2 showed the absorptions of medium strength in the similar regions.

And, in the NMR spectra, the signal at δ 6.45(which had been assigned to the pyridazine ring protons of 1c) was observed in abnormally high field compared to those of the protons on the C-4 and C-5 of other pyridazine 1,2-dioxides, because those of 1a and 1b appeared at δ 6.95 and 7.10, respectively.

Moreover, the mass spectra of A showed strong ion peaks at *m/e* 264(M$^+$), 145(M$^+$-PhCNO) and 119(PhCNO$^+$).[5] This type of the fragmentation is characteristic of compounds 2,[1,17] and not common as for 1.[18] Thus, the data obtained from the compound A do not agree with the dioxide 1c.

On the other hand, the catalytic reduction(on Pd-C) of compound B yielded 3,6-diphenylpyridazine 1-oxide(major) and 3,6-diphenylpyridazine(minor).[22] This fact shows that the compound B must be the 1,2-dioxide(1c), and the spectral data for B well agree with this conclusion. Additionally, 6c[mp. 222-223°(219-221°),[19] NMR(δ): 7.30-7.68(m), IR(KBr): 1500 and 1320cm^{-1}], 8c(=8b), and 9c[mp.113°(115°),[20] NMR(δ): 7.55-7.70(m)] were obtained as the minor products by the LTA oxidation of 4c.[21] The oxidation of 4c with CAN or PITFA also gave 2c, 6c, 8c and 9c although 1c was not obtained.

Thus, present data show that the oxidation of **4** yields **2** as a result of the double cyclization together with the formation of **1**, and that the oxidation of **4** with PITFA is not a favourable method for the preparation of 3,6-diarylpyridazine 1,2-dioxides. Additionally, LTA could be better oxidizing reagent than PITFA for the preparation of pyridazine 1,2-dioxides from **4**.[22]

FOOTNOTES

1) H.Arai, A.Ohsawa, K.Saiki, H.Igeta, A.Tsuji, T.Akimoto, and Y.Iitaka, *J.C.S.Chem.Commun.*, 1977,856.

2) R.N.Butler,"*Synthetic Reagents*"(J.S.Pizey Ed.),Vol.**3**, pp277, J.Wiley & Sons, N.Y.(1977).

3) R.N.Butler, F.L.Scott, and T.A.F.O'Mahony, *Chem.Revs.*, **73**, 93(1973).

4) J.L.Brokenshire, J.R.Roberts, and K.U.Ingold, *J.Amer.Chem. Soc.*, **94**,7040(1972).

5) S.Spyroudis and A.Varvoglis, *Synthesis*, 1976, 837.

6) Acetylisoxazole(**5a**) may be produced from the oxidation of its oxime(but not from **7a**; **7a** gave diketone instead of **5a** by the oxidation under similar conditions) because it is known that oximes give ketones by the oxidation.[2,3]

7) A.Quilico, L.Panizzi, and C.Epifani, *Gazz.Chim.Ital.*, **69**, 536(1939),*C.A.* **34**,1316.

8) J.A.Durden Jr., D.L.Heywood, A.A.Sousa, and H.W.Spurr, *J.Agr.Food Chem.*, **18**,50(1970), *C.A.* **72**,63929s.

9) Ketooxime(**7a**) might be produced by the oxidative deiminoxylation of **4a**, see footnote 6.

10) Dihydroisoxazoloisoxazoles(**2a** and **2b**) were identified with the authentic samples which have been obtained from the photolyses of the corresponding pyridazine 1,2-dioxides.[1,17]

11) Dioxides(1a and 1b) were identified with the authentic samples which were obtained from the oxidation of corresponding pyridazines with 90% H_2O_2.[12]

12) M.Nakadate, S.Sueyoshi, and I.Suzuki, Chem.Pharm.Bull., 18, 1211(1970), Tetrahedron Letters, 1968,1855.

13) 3-Methyl-5-benzoylisoxazole(5, R^1=Ph, R^2=Me) has not been isolated despite of attempts, so far.

14) G.Bianchi and P.Grünanger, Tetrahedron, 21,817(1965).

15) 3-Methylisoxazole(8, R^2=Me) has not been isolated, see footnote c in the table.

16) Thus, the structures of 2 have been incorrectly assigned twice, once to 1,4,6,7-dioxadiazocin(R^1,R^2=H or Me) by the authors,[17] and once to pyridazine 1,2-dioxides(R^1,R^2=Ar) by Spyroudis et al.[5] because of the tricky spectral characters of these compounds.

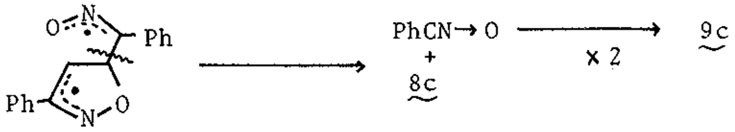
17) H.Arai, A.Ohsawa, K.Saiki, and H.Igeta, J.C.S.Chem.Commun., 1977, 133.

18) The common fragment ions of pyridazine 1,2-dioxides are M^+-16(O), M^+-30(NO) and M^+-58($C_2H_2O_2$?).

19) E.S.Lipina, V.V.Perekalin, and Y.S.Bobovich, Zh.Obshch. Khim., 34, 3640(1964), C.A.62,8989h.

20) J.H.Boyer and U.Toggweiler, J.Amer.Chem.Soc., 79,895(1957).

21) The compounds(8c and 9c) could be produced by the following mechanism:



22) The oxidation of 3,6-diarylpyridazines using 90% H_2O_2 did not yield the practical amounts of 1,2-dioxides.

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