OXIDATIVE CYCLIZATION OF 2-UNSATURATED 1,4-DIOXIMES

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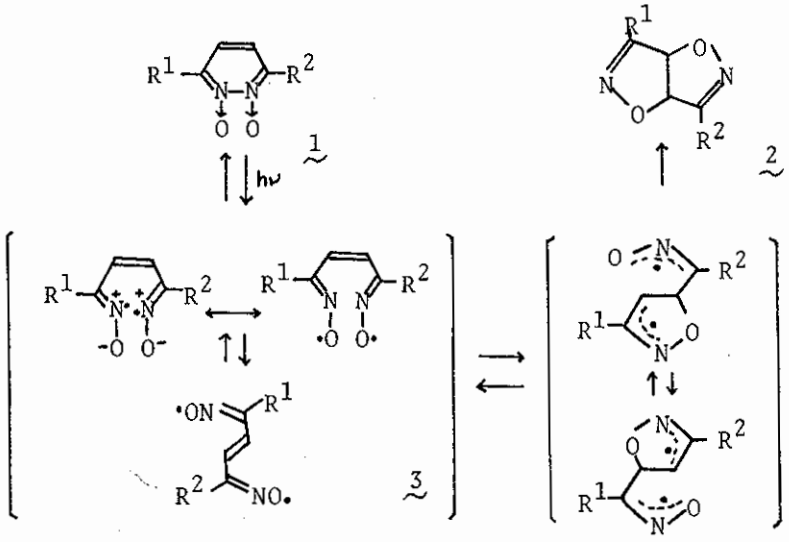
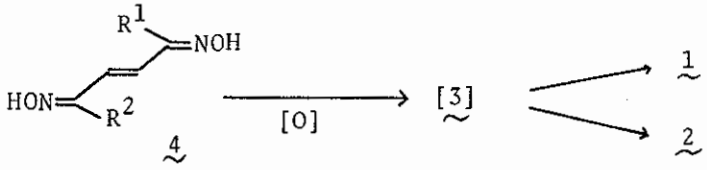
The major product of the oxidation of 1,4-diphenyl-2-butene-1,4-dioxime(4c) with phenyliodoso bistrifluoroacetate(PITFA) was 3,6-diphenyl-dihydroisoxazoloisoxazole(2c) which had been incorrectly assigned to the 3,6-diphenylpyridazine dioxide(1c) by other authors. Lead tetraacetate was found to be more 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-

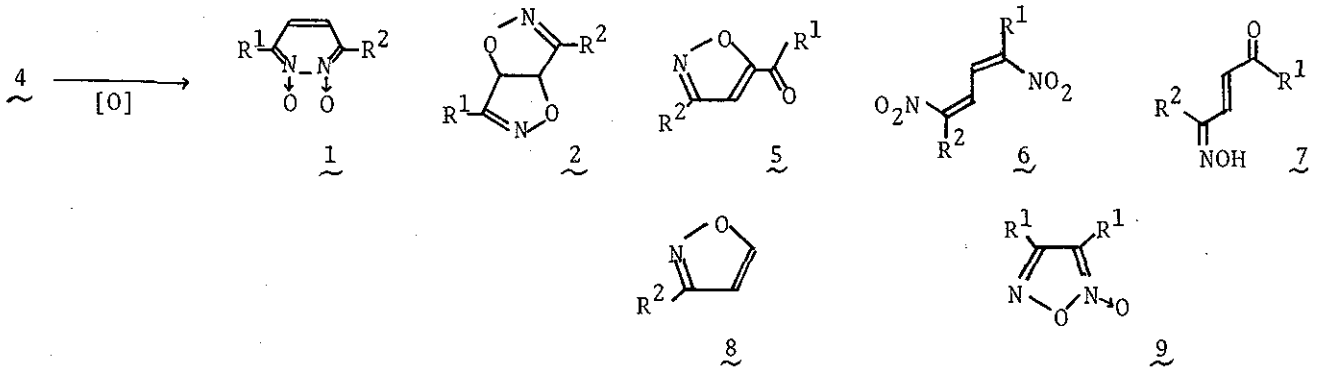


Table (The yields are shown in %.) [a]

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-diaryl-pyridazine 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]

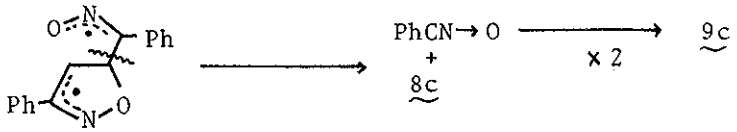
7) A.Quilico, L.Panizzi, and C.Epifani, Gazz.Chim.Ital., 69, 536(1939),C.A.34,1316.

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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