Tetrahedron Letters No.43, pp. 3797-3800, 1970. Pergamon Press. Printed in Great Britain.

THE OXIDATION OF 1,4-DIHYDROXYPYRAZOLES. 1,3,4-OXADIAZIN-6-ONE-4-OXIDES, A NEW HETEROCYCLIC SYSTEM

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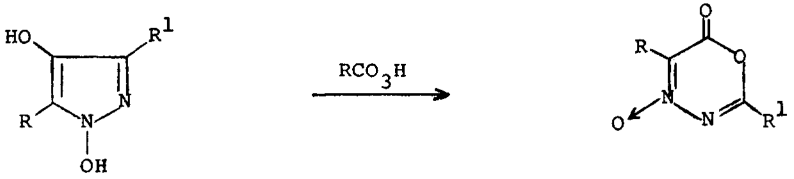
(Received in USA 16 July 1970; received in UK for publication 17 August 1970)

The reduction of 3,4-diazacyclopentadienone dioxides to the corresponding 1,4-dihydroxypyrazoles 1 was described recently.(1) While oxidation of these latter compounds with Fremy's salt and other mild oxidizing agents produced the corresponding 3,4-diazacyclopentadienone monoxides, it was observed that oxidation with peracids yielded an isomer of the dioxides. We propose that these new compounds (2) contain the 1,3,4-oxadiazin-6-one nucleus. No compounds containing this structural unit appear to have been reported.



1, a) $R=R^1=C_6H_5$
b) $R=CH_3$, $R^1=C_6H_5$
c) $R=C_2H_5$, $R^1=C_6H_5$

2, a) $R=R^1=C_6H_5$
b) $R=CH_3$, $R^1=C_6H_5$
c) $R=C_2H_5$, $R^1=C_6H_5$

Structure 2 is based upon spectral properties, reduction products, base-catalyzed rearrangement to 1,3,4-oxadiazoles, and analogies to oxidations in comparable systems.

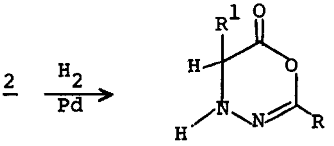
Spectral properties.

The infrared spectra of 2 show strong bands at 1750-1760 cm^{-1}, a region completely transparent in the spectra of the diazacyclopentadienone oxides, consistent with the lactone function. (The carbonyl band of 2-phenylbenzoxazinone(2) appears at 1764 cm^{-1}.) Bands at 1600 and 1560 cm^{-1} are probably associated with the doubly-bonded nitrogen functions. The chemical shift of the alkyl groups in the n.m.r. spectra of 2b and 2c are intermediate between those of the same groups in the mono- and di-oxides indicating that their magnetic environment is not drastically different from theirs.

The mass spectra are all characterized by a molecular ion, but the base peak and the highest in all was at m/e 105 ($C_6H_5CO^{\oplus}$). They are further characterized by major peaks at M^+-CO_2, and m/e 119 ($C_6H_5CNO^{\oplus}$) and m/e 103 ($C_6H_5CN^{\oplus}$).

Reduction.

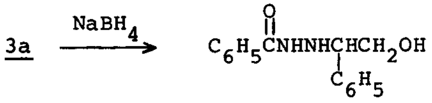
The oxadiazinones 2 could be reduced with zinc-acetic acid or catalytically to yield 4,5-dihydro-1,3,4-oxadiazin-6-ones, 3. Because of the sensitivity of these compounds to hydrolysis, the catalytic method was preferred. It was also more reliable and easier to control. The structure of 3 is based upon elemental analysis, infrared and n.m.r. spectra, and their further reduction products. The infrared spectra of 3 show bands at 1775-1800 cm^{-1} and 1640 cm^{-1} consistent with the imino-anhydride structure* and the absence of the strong 1560 cm^{-1} band associated with the nitrone function. The n.m.r. spectrum of 3b shows the methyl group as a doublet consistent with its original association with the nitrone function in 2.



3, a) $R=R^1=C_6H_5$

b) $R=C_6H_5$, $R^1=CH_3$

Sodium borohydride reduction of 3a occurred at the carbonyl group** to yield 2-(β-benzoylhydrazino)-2-phenylethanol, 5.



$$\text{3a} \xrightarrow{NaBH_4} C_6H_5\overset{O}{\overset{\|}{C}}NHNH\underset{C_6H_5}{\underset{|}{C}}HCH_2OH$$

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The structure of 5 was proven by its synthesis from styrene oxide and benzhydrazide in the presence of an acid catalyst.

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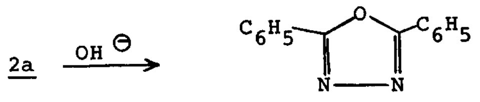
[*] The shift of the carbonyl band to higher frequency upon reduction supports removal of the nitrone function whose conjugation (through back donation) with the carbonyl in 2 tends to lower its normal frequency.

[**] This reduction stands in contrast to that of 2-phenylbenzoxazinone which produces N-benzylanthranilic acid.(2)

Basic Hydrolysis.

Attempts to hydrolyze the oxadiazinones 2 led in the case of 2b and 2c to intractable residues possibly due to base-catalyzed reaction of the alkyl nitrone function. Hydrolysis of 2a, however, was accompanied by a facile rearrangement to the corresponding 1,3,4-oxadiazole, 6, in high yield.



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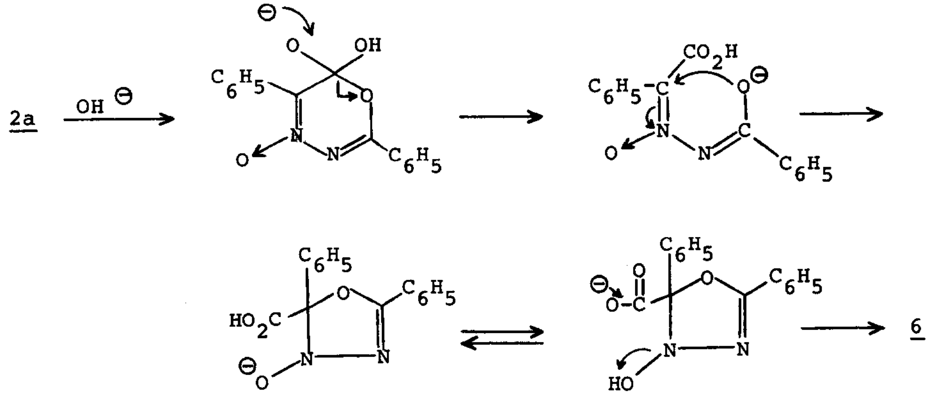
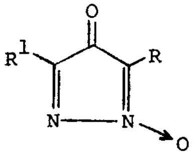
This reaction may be viewed in the following manner:



These base-catalyzed reactions were very rapid and thwarted attempts at hydride reductions of 2. Oxadiazoles could be obtained directly from all the 1,4-dihydroxypyrazoles 1 in yields of 50-60% by oxidation of the latter with alkaline hydrogen peroxide.

The oxidation of 1 probably proceeds by way of the 3,4-diazacyclopentadienone monoxides 7. Independently it was shown that 7 were oxidized to 2 under the reaction conditions. The oxidation of 7 to 2 has some analogy to the peracid oxidation of 3-oxo-2-phenylindolenine to 2-phenylbenzoxazinone.[2] That oxidation occurs on the imine rather than the nitrone side is suggested by the similarity of the chemical shift of the alkyl group in the dioxides and in 1 and 7, the structure of the reduction products 3 derived by reduction of the nitrone function in 2, and the inertness of the dioxides, which contain only ketonitrone functions, to further oxidation. That the alkyl group R in 7 is associated with the nitrone function has been established previously.(1,3)



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Acknowledgment.

We are indebted to the National Cancer Institute, National Institutes of Health for a grant (CA-10742) in support of this research. We are also grateful to the High Resolution Mass Spectrometry Center, Battelle Memorial Institute for mass spectral data and to the National Science Foundation for a grant from which the Varian A60A n.m.r. instrument used in this research was purchased.

References.

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