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ASYMMETRICALLY SUBSTITUTED FUROXANS. V.
DECOMPOSITION OF 4-METHYL-3-FUROXANCARBOXYLIC ACID.

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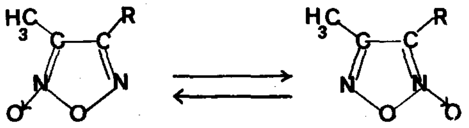
In the course of our study on the position of equilibrium of the isomerisation reaction a$\rightleftarrows$b(1) for some furoxans containing a methyl group as one of the substituents, we found that, in the case of the isomeric methylfuroxancarboxylic acids Ia and Ib it was impossible to reach their thermodynamic equilibrium concentrations, because the 4-methyl-3-furoxancarboxylic acid Ib, at the temperature of the experiment, (120-30°), readily decomposed.

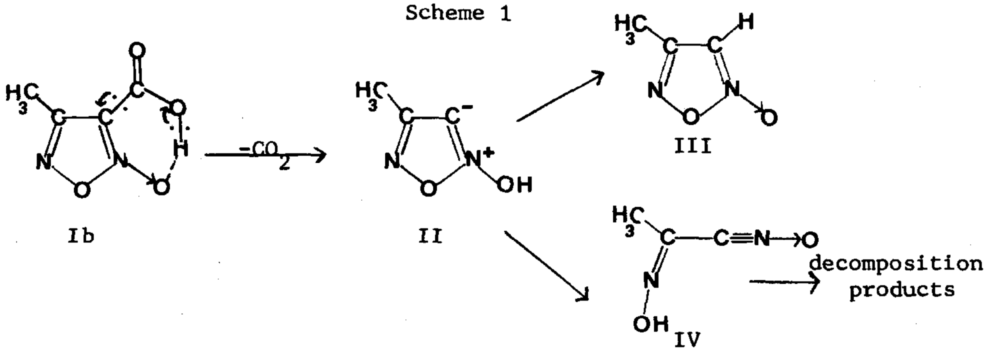


Ia$\rightleftarrows$Ib   R = COOH

In order to study this decomposition, we heated Ib(2) for about 2h at 120° in xylene. The heating was followed by development of gases in which CO$_2$ was identified, and a progressive darkening of the solution. TLC analysis showed that a complex mixture was formed.

The easy decarboxylation of Ib, analogous to the decarboxylation of α-carboxy-N-oxides(3), probably proceeds via zwitterion of type II. (See scheme 1).

Scheme 1



In this case, however, we feel that II would ring open to the α-hydroximino propionitrile oxide IV faster than it would undergo proton transfer to C (3) forming the 4-methylfuroxan III. This argument is supported, in our opinion, by the considerable ease with which the 4-phenylfuroxan ring opens, at room temperature, to give the α-hydroximino-phenylacetonitrile oxide(4). IV could also be obtained directly from Ib through a concerted mechanism.

In order to have some evidence of the existence of IV as a decarboxylation product of Ib, we have attempted to trap this compound with dipolarophiles. By reaction of Ib in xylene at 120° for 2h with phenylacetylene we obtained a white crystalline compound (m.p. 164-6° from benzene). The structure V (3-acetyl-5-phenylisoxazole oxime) was assigned to this compound because, by acid hydrolysis, it gave a substance VI identical (IR, mixed m.p.) to 3-acetyl-5-phenylisoxazole prepared as described by Quilico(5). (See scheme 2). The NMR spectrum of V [(DMSO-d_6), δ 2.23 (s,3,CH_3); 7.23 (s,1,CH); 7.50-8.10 (m,5 phenyl); 11.96 (s,1,OH)] confirmed the assigned structure.

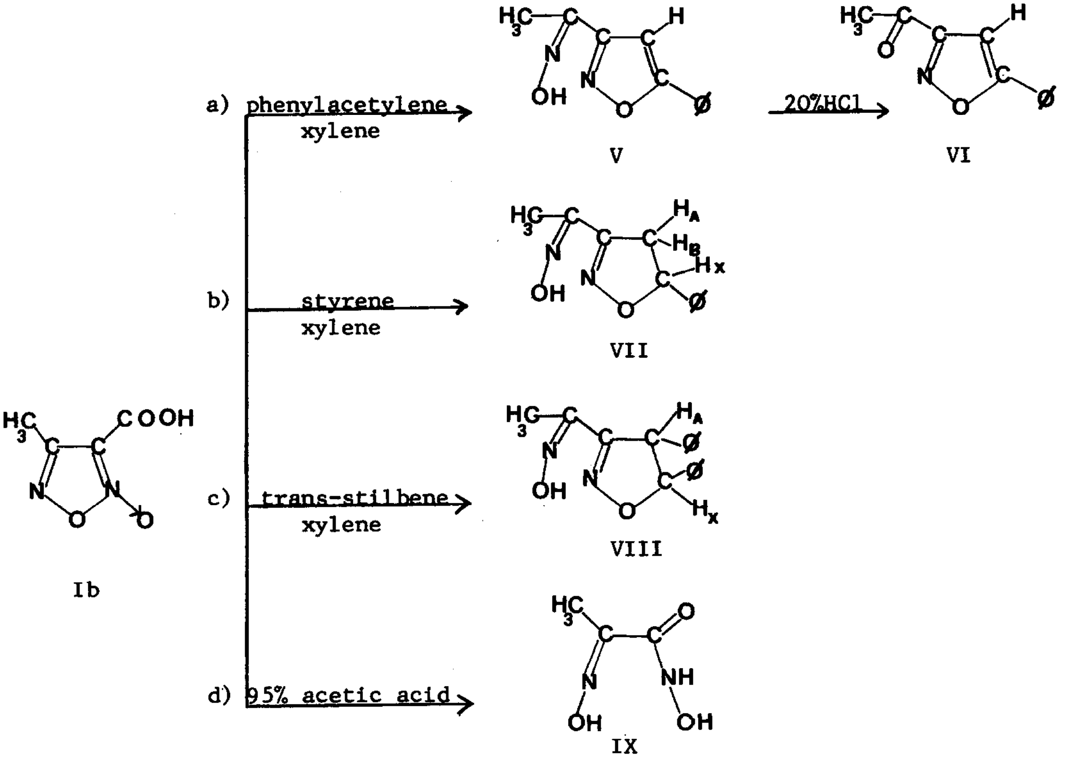
The reaction of Ib (see scheme 2) under similar conditions, with styrene (with added quinol) and trans-stilbene gave the 3-acetyl-5-phenyl-2-isoxazoline oxime VII(6) [m.p. 136-7° from benzene; NMR ($CDCl_3$) δ2.23 (s,3,CH_3); isoxazolinic protons at H_B 3.16, H_A 3.56, H_X 5.71; J_{AB} 17.5; J_{BX} 9; J_{AX} 11 Hz; 7.36 (s, 5, phenyl); 8.78 (s,1,OH)] and the 3-acetyl-4,5-diphenyl-2-isoxazoline oxime VIII(6) respectively [m.p. 127-8° from petr. ether 100-140°; NMR (DMSO-d_6), δ2.08 (s,3,CH_3); 4.60 (d,1,H_A); 5.50 (d,1,H_X); J_{AX} 5 Hz; 7.26-7.40 (m,10,phenyl); 11.76 (s,1,OH)].

3-Methyl-4-furoxancarboxylic acid Ia, under the some conditions, was largely unaltered. Traces of the compounds V, VII and VIII however, were found by TLC. These facts can be explained in terms of an equilibrium Ia $\rightleftharpoons$ Ib, occurring at the temperature of the experiment. Thus, under these conditions, Ib is slowly formed.

The existence of IV cannot be conclusively proved from these results, because an alternative,or, more probably, a competitive mechanism to form V, VII, VIII, could be a direct attack of Ib by the dipolarophiles. Boulton and coworkers(7), in fact, have found that the dibenzoylfuroxan can react, as a nitrone, with a number of dipolarophiles. However, as we have isolated a compound identified as the α-hydroximino-propiohydroxamic acid IX, (see scheme 2), by heating Ib in 95% acetic acid for 1.5h, we can support the proposal that the decarboxylation of Ib occurs via IV. In fact it is well known that the hydroxamic acids occur by hydration of nitrile oxides under acid catalysis. The violet colour that appears immediately on shaking IX with a $FeCl_3$ solution and its IR spectrum [(KBr) 3240 (s), 1675 (s), 1630 (s), 1535 (m), 1375 (m), 1315 (m), 1020 (s), 892 (m), 735 (m) cm^{-1}]

are consistent with the hydroxamic acid structure. IX (m.p. 154-7° from ethyl acetate) was found to be identical (IR, mixed m.p.) with a sample prepared as described by Ponzio(8).

Scheme 2



a) To isolate V, the reaction mixture was evaporated to dryness under reduced pressure and the residue, dissolved in $CHCl_3$, was filtered over a silica gel column. Yield 42%. b)To isolate VII, the reaction mixture was worked up as described for the preparation of V. Yield 78%. c) To isolate VIII, the reaction mixture was evaporated to dryness under reduced pressure and the residue was stirred with a 10% NaOH solution. The aqueous layer was filtered, acidified and extracted with $CHCl_3$. The chloroform extract was filtered over a silica gel column. Yield 40%. d) To isolate IX, the reaction mixture was added with $CHCl_3$. The solid which crystallized from the solution was collected by filtration. Yield 30%.

References and Footnotes.

1) A.Gasco and A.J.Boulton, J. Chem. Soc., Perkin II, 1612 (1973).

2) This compound was prepared as described by A.Gasco, V.Mortarini, G.Ruà, G.M. Nano and E.Menziani, J. Heterocyclic Chem., 9, 577 (1972), but recrystallized from benzene. Caution! The dried potassium salt explodes violently, not only on heating, but also on impact and friction.

3) A.R.Katritzky and J.M.Lagowski, "Chemistry of Heterocyclic N-Oxides", Academic Press, London and New York, 1971, pp.382.

4) J.V.Burakevich, R.S.Butler, and G.V.Volpp, J. Org. Chem., 37, 503 (1972).

5) A.Quilico and M.Simonetta, Gazz. Chim. Ital., 76, 200 (1946). The oxime derivative described in this paper melts at 161°. The same compound, described by T.Ajello and S.Cusmano, Gazz. Chim. Ital., 68, 792 (1938), melts at 170°.

6) Satisfactory analytical and mass spectral data were obtained for all new compounds.

7) M.Altaf-ur-Rahman, A.J.Boulton and D.Middleton, Tetrahedron Letters, 33, 3469 (1972).

8) G.Ponzio and G.Ruggeri, Gazz. Chim. Ital., 55, 453 (1925).

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