Photolysis of Phenyldisic Acids: Evidence for Unique Product Formation from Discrete Tautomers

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3-Hydroxy-2-methyl-4-phenylisoxazol-5(2*H*)-one exists as four tautomers, two of which are isolated and characterised; photolysis in methanol leads to formation of products identified as arising uniquely from three of the tautomers, and the 2-phenyl analogue and phenyldisic acid undergo similar photochemical reactions.

As part of our studies on the effect of substituents on the photochemical decomposition of isoxazol-5(2*H*)-ones,[1–3] we have synthesised 2-methyl- and 2-phenyl-3-hydroxy-4-phenylisoxazol-5(2*H*)-one, **1a** and **2**, and compared their photochemical behaviour with that of the 2-*H* parent, phenyldisic acid.[4,5] When **1** was prepared from *N*-methylhydroxylamine and diethyl phenylmalonate, followed by cyclisation under acidic conditions, the product isolated, mp 126–128 °C, was exclusively the enolic tautomer **1a**. However, if the hydroxylamine was treated with phenylmalonyl chloride in pyridine, with minimal contact with acid, the product was the 4-*H* tautomer **1b**, mp 99–101 °C. The latter was characterised by the C–H proton at δ 4.45, and the C–H carbon at δ 47 in the respective NMR spectra. Tautomer **1b** was rapidly converted to **1a** on addition of a polar solvent: **1a** could be converted to **1b** by mild acidification of the sodium salt.

Irradiation of **1a** in methanol at 254 nm at 20 °C gave a mixture of three compounds. The neutral fraction was identified as *N*-methyl-2-methoxy-2-phenylacetamide **3** (15%), independently synthesised from mandelic acid. The acidic fraction gave the amino acid **4** (40%) and the amido acid **5** (40%). The structure of the former was confirmed by acidic hydrolysis to *N*-methylphenylglycine, and the latter by decarboxylation to the mandelic amide **3**.

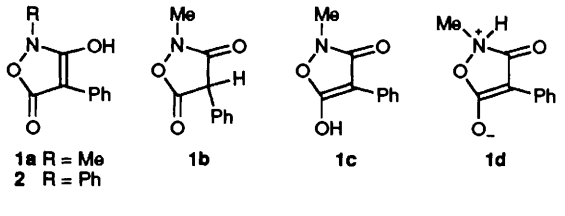
Zvilichovsky[5] has presented chemical[4] and X-ray[5] evidence that phenyldisic acid itself exists as a mixture of the enolic and betaine tautomers **6a** and **6b**. Accordingly, we have rationalised the formation of **3–5** as photolysis products of the three tautomers **1a**, **1c** and **1d** (Schemes 1–3).

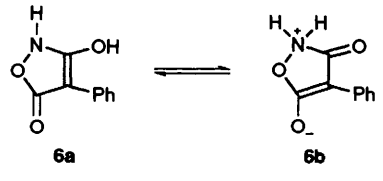
The formation of **3** is consistent with the observed facile loss of CO_2 from isoxazol-5(2*H*)-ones on irradiation[1–3,6] or heating[7] to form an iminocarbene. The amino acid **4** is suggested to arise from the tautomer **1c** (Scheme 2). Such products have not previously been observed as photolysis or pyrolysis products of isoxazol-5(2*H*)-ones, but are logical products from nucleophilic opening of aziridinones *e.g.* **7**, which are suggested intermediates in the photolysis of 5-iminoisoxazolines[8] or 3-hydroxyisoxazoles.[9]

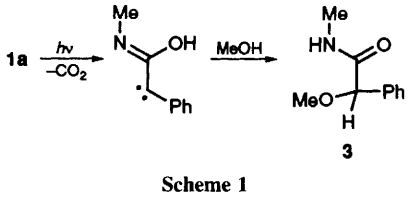
The amido acid **5** is suggested to arise from photochemically induced nucleophilic addition to C-4 of the betaine tautomer **1d** (Scheme 3). Methanol has no tendency to react with **1** in the absence of light.

In support of the above hypotheses, phenyldisic acid was methylated[4,5] to give 3-methoxy-4-phenylisoxazol-5(2*H*)-one **8**, 5-methoxy-4-phenylisoxazol-3(2*H*)-one **9**, and the betaine **10**. Each was separately photolysed in methanol. The isoxazol-5-one **8** gave only the product **11** expected from the iminocarbene, isolated as the methoxyamide **3** and the ester **12** (100%, 3 : 1) after hydrolysis. The isoxazol-3-one **9** gave the aminomalonic ester **13** (95%), while the betaine **10** gave a mixture of the iminocarbene derived product **14** (55%), and the methanol addition product **15** (45%).

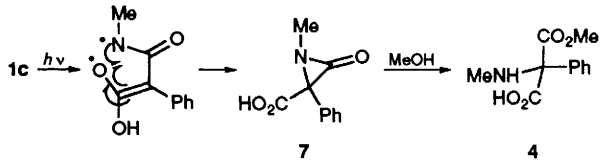
Photolysis of phenyldisic acid **6a** in methanol gave only the products expected from Schemes 1 and 3, whereas the



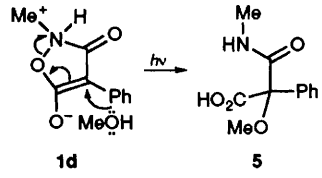




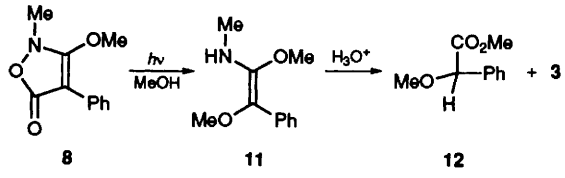
Scheme 1



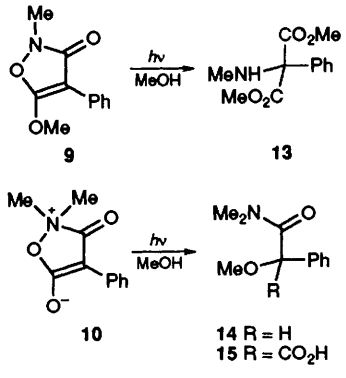
Scheme 2



Scheme 3



Scheme 4



N-phenyl analogue **2** gave a single product (70%) corresponding to methanol addition according to Scheme 3. The electronic effects of the nitrogen substituents clearly influence the contribution of each of the three pathways to the mode of photolysis. The separate pathway taken by each tautomer noted here suggests that solvent effects will be quite considerable.

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