Direct N.M.R. Detection of an Epoxyfuran Intermediate in Peracid Oxidation of the Fungicide Methfuroxam

Luis O. Ruzo,* John E. Casida, and Ian Holden

Pesticide Chemistry and Toxicology Laboratory, Department of Entomological Sciences, University of California, Berkeley, California 94720, U.S.A.

A 4,5-epoxyfuran intermediate has been detected by ^{1}H and ^{13}C n.m.r. spectroscopy in the oxidative conversion of 2,4,5-trimethyl-*N*-phenylfuran-3-carboxamide (the fungicide Methfuroxam) into 3-(*N*-phenylcarbamoyl)-4-methylhex-3-ene-2,5-dione.

Oxidation of substituted furans by peracids results in formation of formyl- and acyl-substituted ethylenes, but no direct evidence has been presented for the postulated epoxyfuran intermediates.[1—3] Certain furan derivatives are metabolized to unsaturated dialdehydes or ketoaldehydes which bind to tissue macromolecules. Thus, 2- and 3-methylfurans yield 3-acetylacrolein and 2-methylbut-2-ene-1,4-dial, respectively, which bind to components of hepatic and pulmonary microsomal systems.[4] The insecticide resmethrin (5-benzyl-3-furylmethyl chrysanthemate) and its analogues are also oxidized by rat liver microsomes to unsaturated ketoaldehydes which are probably responsible for persisting fragments in mammals.[5] These biologically formed ring-opened products are identical to those obtained on oxidation with *m*-chloroperbenzoic acid (MCPBA). We therefore used MCPBA oxidation as a model in seeking an epoxyfuran intermediate in the ring-opening and rearrangement reactions.[5] The fungicide Methfuroxam (**1**) was selected for study because it may yield a

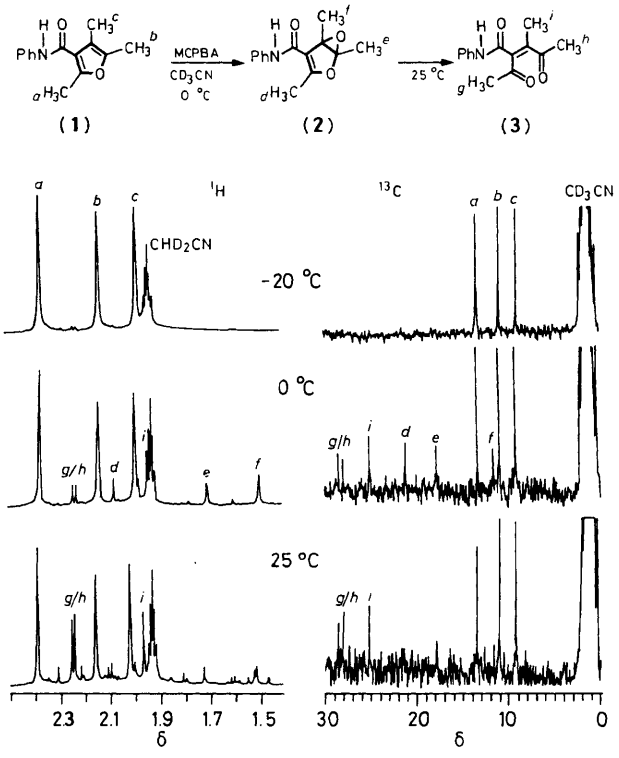

Figure 1. Reaction of (**1**) to give its epoxy (**2**) and diketo (**3**) oxidation products and ^1H and ^{13}C n.m.r. spectra of the relevant methyl groups as a function of temperature (−20 to 25 °C).

relatively stable 4,5-epoxyfuran (**2**) since the 2,3-double bond is deactivated towards epoxidation (Figure 1).

Compound (**1**) is readily oxidized by an equimolar amount of MCPBA in CD_3CN at 25 °C to yield one major product (**3**) (80% of product mixture) at 30% conversion. A larger amount of peracid or greater extent of conversion results in formation of many unidentified products. Compound (**3**) was characterized by chemical ionization–mass spectrometry (c.i.–m.s.) and n.m.r. spectroscopy (Figure 1).† Direct n.m.r. observation of the reaction at 0 °C indicates the presence of an additional compound (~50%) with both ^1H and ^{13}C resonances consistent with the structure of the proposed intermediate (**2**) (Figure 1). On warming to 25 °C (**2**) disappeared and (**3**) was the major product. The intermediacy of the epoxide (**2**) is also supported by reaction of the mixture obtained at 0 °C, but not at −20 or 25 °C, with 4-(*p*-nitrobenzyl)pyridine, which gave the blue-violet colour characteristic of epoxides.[6]

It may now be possible to evaluate the relative contribution of epoxide and diketo metabolites to the biological activities and reactions of substituted furans.

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† Mass spectra were recorded on a Hewlett Packard 5985B instrument interfaced with a gas chromatograph utilizing a high performance capillary methyl silicone column (10 m) operated at 80—240 °C, with temperature programming (20 °C/min). Important peaks for (**3**) are as follows: c.i.–m.s. (230 eV, methane) *m/z* 274 $[M + C_2H_5]^+$, 18%; 246 $[MH]^+$, 100%; 228 $[MH-H_2O]^+$, 56%. Retention times for (**1**) and (**3**) are 7.6 and 8.1 min, respectively, under these conditions. N.m.r. spectra were recorded on a Bruker 300 MHz instrument. Additional ^1H signals for (**3**) are at δ 7.1—7.4 (C_6H_5) and 8.8 (NH). Protons *g* and *h* (Figure 1) are not assigned.