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OXIDATIVE REARRANGEMENT OF N-(DIMETHOXYPHOSPHINOTHIOYL)CARBAMATE ESTERS

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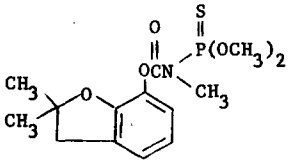
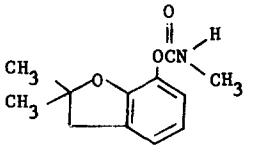
2,2-Dimethyl-2,3-dihydrobenzofuranyl-7-N-methyl-N-(dimethoxyphosphinothioyl)carbamate (I) is a highly effective selective insecticide, i.e., it is toxic to insects but is substantially less toxic to mammals.[1] The basis for its selective toxicity appears to reside in the ability of insects to metabolize I to the toxic carbamate (II) more efficiently than mammals by means of oxidative and hydrolytic processes.

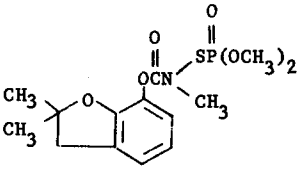


I

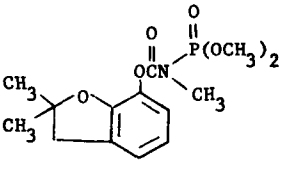


II

In our study of the oxidation of I by m-chloroperbenzoic acid, we have discovered that I oxidatively rearranges to the corresponding N-dimethoxyphosphinylthio derivative (III), in addition to direct desulfuration to the expected N-dimethoxyphosphinyl derivative (IV).



III

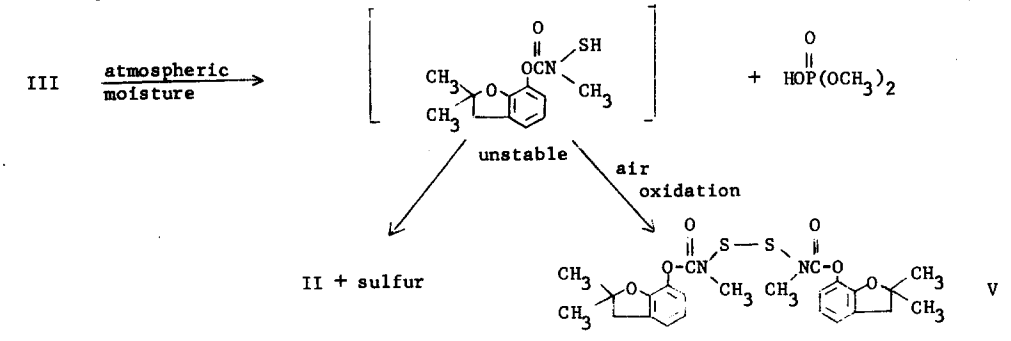


IV

Treatment of I with m-chloroperbenzoic acid afforded III and IV as the principal products along with lesser amounts of II and starting material (I). Sulfur also was isolated. II was

identical to material synthesized independently from methyl isocyanate and the corresponding phenol (mp 151-2°).[2] Attempts to synthesize IV by the method[1] described for I failed and its structure was established from the following spectral data: IR, 1725 cm^{-1} (C=O) and 1260 cm^{-1} (P=O); NMR (δ, 60 MHz, $CDCl_3$) 3.28 (doublet, J = 8 Hz, 3H, $-NC\underline{H}_3$), 3.9 (doublet, J = 12 Hz, 6H, $-OC\underline{H}_3$), 3.05 (singlet, 2H, $-C\underline{H}_2$), 1.25 (singlet, 6H, $-C\underline{H}_3$), and 6.8-7.2 (multiplet, 3H, aromatic protons); MS, m/e 329 (M^+, 8.8%), 166 (31.4%), 109 (100%), and 164 (10.8%). The structure of III was established from the following spectral data: IR, 1725 cm^{-1} (C=O) and 1260 cm^{-1} (P=O); NMR (δ, 60 MHz, $CDCl_3$), 3.45 (singlet, 3H, $-NC\underline{H}_3$), 3.95 (doublet, J = 13 Hz, 6H, $OC\underline{H}_3$) and relevant absorptions similar to IV; MS, m/e 361 (M^+, 10.6%), 198 (62.3%), 141 (100%) and 109 (34%). The downfield shift and the change to a singlet for N-$C\underline{H}_3$ absorption for III is consistent with the displacement of this moiety another atom away from phosphorus. The value of m/e 198 (62.3%) in the MS of III is consistent with $[O{=}\overset{+}{C}N(CH_3SP(O)(OCH_3)_2]$, m/e 166 (31.4%) for IV with $[O{=}\overset{+}{C}N(CH_3)P(O)(OCH_3)_2]$ and m/e 182 (29.4%) for I with $[O{=}\overset{+}{C}N(CH_3)P(S)(OCH_3)_2]$. Further fragmentation of each of these ions by the loss of methyl isocyanate produced: m/e 141 (100%) $[SP(O)(OCH_3)_2]^+$ for III which then lost sulfur to give m/e 109 (34%) $[OP(OCH_3)_2]^+$; m/e 109 (100%) $[OP(OCH_3)_2]^+$ for IV; and m/e 125 (100%) $[SP(OCH_3)_2]^+$ for I.

Further evidence for the structure of III was obtained from its decomposition on silica gel thin-layer plates. III evidently is unstable to prolonged atmospheric exposure on silica gel and decomposes mainly to a disulfide (V), the carbamate II, and sulfur, presumably by the following scheme.



V, mp 131-3°; S, 12.1%, $C_{24}H_{28}O_6N_2S_2$ requires S, 12.7%; NMR (δ, 60 MHz, $CDCl_3$), 3.45 (singlet, 6H, $-NC\underline{H}_3$), 3.05 (singlet, 4H, $-C\underline{H}_2$), 1.25 (singlet, 12H, $-C\underline{H}_3$), and 6.8-7.2 (multiplet, 6H,

aromatic protons); MS m/e 504 (M^+, 5.4%), 447 (2.1%), 390 (6.2%), 164 (27%), 163 (100%), 149 (10%), 135 (27%), and 107 (14.5%).

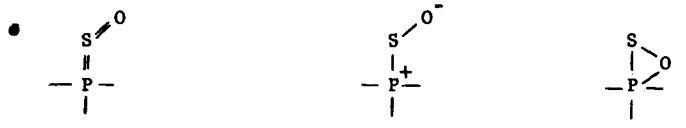
Oxidation of ^{14}C-labeled I ($N^{14}CH_3$) with m-chloroperbenzoic acid also was carried out for quantitative determination of the products by TLC. The results are presented in the table below.

Table 1

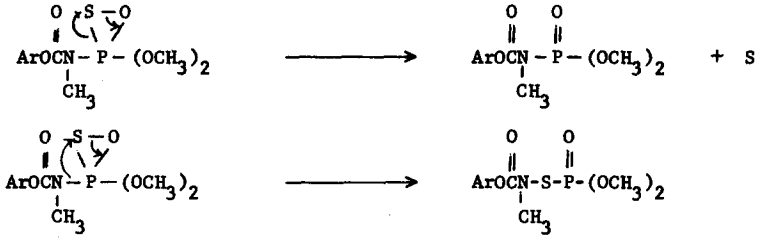
Oxidation products of I[a]			Decomposition products of III[b]		
Compound	R_f	% Radioactivity	Compound	R_f	% Radioactivity
I	0.56	11.5	II	0.34	31.4
II	0.34	13.7	IV[c]	0.08	6.4
III	0.15	35.0	V	0.60	62.2
IV	0.08	39.8			

a) based on 92% total recovery, b) based on 97% total recovery, c) it is uncertain whether IV is formed from III or whether this small amount was present as a contaminant in III prior to TLC exposure.

Our findings may be explained by assuming that oxidation of I proceeds through an unstable S-oxide intermediate[3] which may be written in the following resonance and tautomeric forms.



This intermediate explains the formation of III and IV as follows.



Recent studies on the m-chloroperbenzoic acid oxidation of O-ethyl S-phenyl ethylphosphonodithioate[4] has shown that one of the major products is phenyl ethoxy(ethyl)phosphinyl disulfide which undoubtedly is obtained by the same type of rearrangement. A similar rearrangement also has been reported for the peracid oxidation of C-sulfonylthioformamides.[5]

A typical oxidation procedure is as follows. To 250 mg of I dissolved in 25 ml methylene chloride at 0° was added with stirring 125 mg of purified m-chloroperbenzoic acid. After standing at room temperature for 15 minutes, the organic solvent was washed with 5% $NaHCO_3$, then

water, dried over anhydrous Na_2SO_4, concentrated, and the residue was chromatographed on 1.5 mm silica gel plates using a mixture of ether-hexane (3:1).

The radioactive sample of I was prepared using $H_2N^{14}CH_3 \cdot HCl$ (Amersham-Searle) according to a previously described procedure.[1]

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