Thermal Ring Contraction of Oxygenated Pyrazines to Imidazoles *via* Diazoxepins

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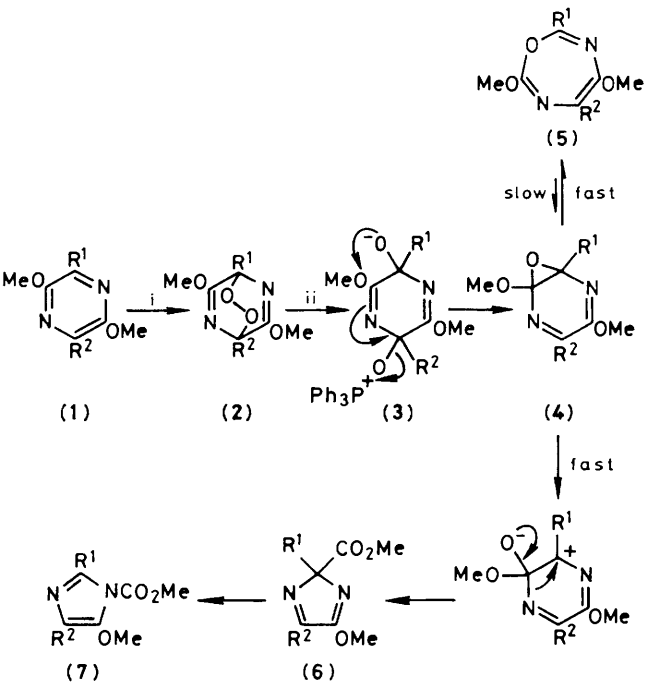
Deoxygenation of pyrazine endoperoxides with triphenylphosphine can result in ring contraction to imidazoles, a process involving the heterocyclic analogues of arene oxides, these being in equilibrium with the corresponding 3,6,1-diazoxepins.

Previous studies have shown that pyrazines derived from 2,5-dioxopiperazines can undergo cycloaddition reactions with oxygen.[1] It was further shown that such species can be deoxygenated with triphenylphosphine although only a tentative structural assignment of the product was made.[2] Because of the current interest in the extrusion of sulphur from the related 3,6-epidithia-2,5-dioxopiperazines by triphenylphosphine[3] we have investigated more fully the behaviour of the endoperoxides with this reagent.

The peroxides (**2a**—**d**) were readily prepared from the corresponding 2,5-dimethoxypyrazines (**1a**—**d**).† Use of the methoxy-substituted pyrazines rather than the hydroxy-derivatives was dictated by the accessibility of the former; the dihydroxypyrazines are only obtained with difficulty.[4] Oxygenation was effected with singlet oxygen, generated using methylene blue as sensitizer in dichloromethane solution.

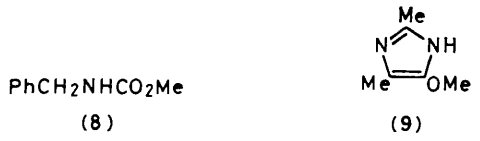
The peroxide (**2a**), obtained from the pyrazine (**1a**),[5] was treated with triphenylphosphine in aqueous tetrahydrofuran. The solution slowly turned yellow with liberation of triphenylphosphine oxide. After periods of up to 5 days, when virtually all the starting peroxide had reacted, one major product could be isolated by column chromatography through silica gel. The product (47%), a low melting solid (m.p. 12 °C), analysed as $C_8H_{12}N_2O_3$, indicating loss of one oxygen atom from the starting peroxide (**2a**), showed a carbonyl absorption at ν_{max} 1755 cm^{-1}, indicating the presence of an ester group, and ^1H n.m.r. signals corresponding to the retention of the two aromatic methyl signals and the two methoxy-groups. Treatment of the product with benzylamine in dichloromethane at



a; $R^1 = R^2 = Me$
b; $R^1 = CH_2{=}C(CH_2CH_2OTHP)$, $R^2 = H$
c; $R^1 = CH_2Ph$, $R^2 = H$
d; $R^1 = CH_2CHMe_2$, $R^2 = H$

Scheme 1. i, $^1O_2$; ii, PPh_3. THP = tetrahydropyran-2-yl.

† All new compounds gave satisfactory microanalytical and/or mass spectroscopic data.



room temperature liberated methyl *N*-benzylurethane (**8**), reflecting the presence of a methoxycarbonyl group, and an air-sensitive compound identified as the imidazole (**9**), λ_{max} 215, 266 nm. Thus this deoxygenation product is assigned structure (**7a**) or its *N'*-isomer.‡

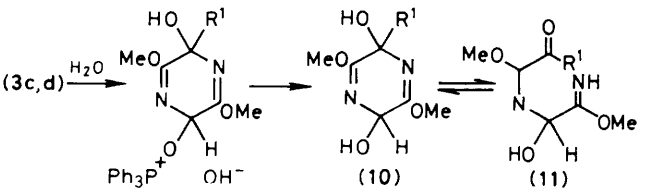
The reaction pathway illustrated in Scheme 1 is envisaged as explaining the deoxygenation–rearrangement process. The intermediate diazoxepine (**5a**) could be observed when the reaction was followed by ^{1}H n.m.r. spectroscopy; thus small signals formed at δ ($CDCl_3$) 1.93, 2.19, 3.60, and 3.82 during the course of the reaction but disappeared as the imidazole product peaks appeared at 2.23, 2.57, 3.87, and 3.95.

When the reaction was repeated with the endoperoxide (**2b**), obtained from the pyrazine (**1b**) and using triphenylphosphine in anhydrous tetrahydrofuran, a faster deoxygenation reaction took place which allowed isolation of the intermediate diazoxepine (**5b**). This yellow, viscous liquid showed λ_{max}(EtOH) 220 nm (ε 17 000) and 354 nm (ε 3 000), the latter extending to 450 nm with gross features comparable to those shown by 2,7-dimethyloxepin (λ_{max} 297 nm, ε 1 800, extending into the visible region).[6] Its ^{13}C n.m.r. spectrum showed the ring-carbon resonances at δ 107, 142, 144, and 151 p.p.m. below tetramethylsilane. The isolated material (**5b**) was unstable, the neat substance forming polymers on leaving it at room temperature, whilst, in solution, it mainly afforded the imidazole (**7b**) (48%) or its *N'*-isomer. It should be noted that the products correspond to attack of the triphenylphosphine at the least hindered oxygen atom of the starting peroxide, as is observed for its attack on other peroxides.[7]

None of the heteroaromatic oxide tautomers (**4**) (Scheme 1) could be detected spectroscopically. Presumably, once formed, these rapidly rearrange to the 2-substituted imidazole (**6**), which can undergo a 1,5-acyl shift to one of the adjacent nitrogen atoms to form the observed product.

The pyrazines (**1c**) and (**1d**) behaved in a similar fashion, their peroxides (**2c**) and (**2d**) yielding the corresponding

‡ Only one of the two possible *N*-methoxycarbonyl isomers was detected from each of the ring contractions reported in this work.



Scheme 2

imidazoles (**7c**) (11%)§ and (**7d**) (52%) or their *N'*-isomers. For these, however, the use of triphenylphosphine in aqueous tetrahydrofuran gave, besides the acylated imidazoles, quantities of polar materials assigned the hydrated structures (**10**) and (**11**), formed by interception of the intermediate (**3**) (see Scheme 2) by water.

Although the ring contraction of substituted pyrazine *N*-oxides to substituted imidazoles has been recorded previously,[8] these were effected under photochemical conditions. The reported ring contractions are the first in which a non-photochemical reaction is involved.

We thank the S.E.R.C. and G.D. Searle & Co., High Wycombe, for a CASE award (to A. J. O'C.) and the S.E.R.C. for financial support of this work.

Received, 6th December 1982; Com. 1401

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§ Yield after extensive t.l.c. purification.