Carbene and Radical Pathways in Pyrolysis
of Benzisoxazolones and Benzotriazoles

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A comparative study of the flash vacuum pyrolysis of a number of N-alkyl and N-acyl benzotriazoles and benzisoxazolones has confirmed that carbene derived pathways predominate at lower temperatures, and radical pathways at highter temperatures. Two new general unimolecular thermal reactions are also highlighted.

Subsequent to the initial report of Sasaki [1] that isoxazol-5(2H)-ones lose carbon dioxide on photolysis at 254 nm to give carbenes, we have carried out a detailed investigation of the synthetic potential of this reaction, as the carbene may undergo reactions both intramolecularly [2] and intermolecularly [3,4] with nucleophiles e.g., Scheme 1. Flash vacuum pyrolysis (fvp) has proved to be the preferred procedure when intramolecular reactions are desired [5].

The intermediate carbene is superficially the same as that arising from the decomposition of 1,2,3-triazoles (Scheme 2), which have been extensively studied, and for which mostly diradical structures have been suggested [6-9], although carbene structures have also been implicated [10,11].

Since isoxazolones can generally be decomposed under milder conditions than the corresponding aromatic triazoles, we have carried out a comparison of the product

Scheme 1

Scheme 2
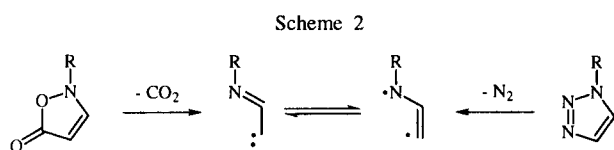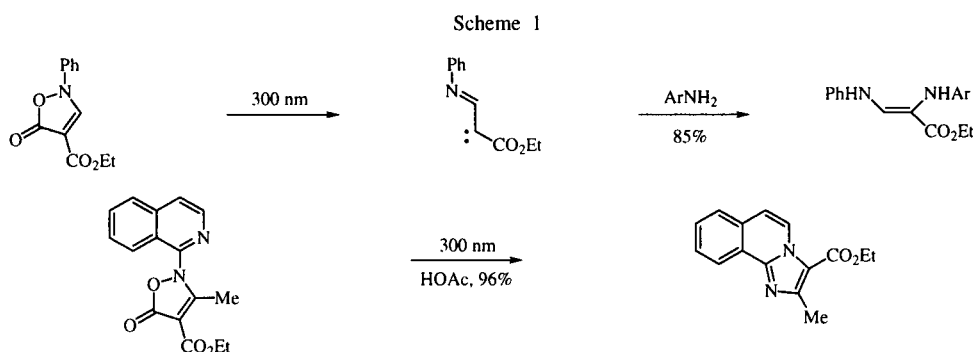
composition from the pyrolysis and photolysis of a number of N-alkyl and N-acyl benzisoxazolones and benzotriazoles in order to ascertain whether the differences in product composition reflected different mechanistic pathways or merely differently activated, but otherwise identical, intermediates. In choosing to investigate the benzo analogues, we hoped to find some evidence for the intramolecular capture of a carbene species as shown in Scheme 3, which would lead to intriguing tetracyclic systems.
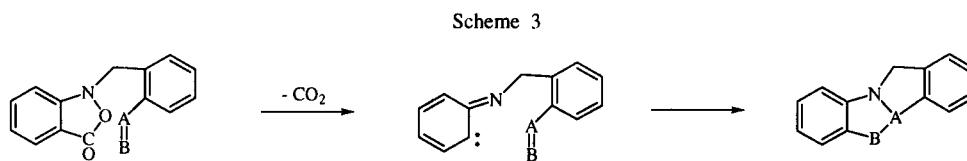
Results and Discussion.

1. Products from N-Alkylbenzotriazoles and N-Alkyl-benzisoxazolones.

Although the pyrolysis of some 1-alkylbenzotriazoles has been reported by Storr [12], that of the 1-methyl analogue has not. Both 1-methylbenzotriazole and N-methylbenzisoxazolone gave high yields of the trimer of formaldehyde phenylimine (Scheme 4), which could arise by either radical or carbene pathways.

phenanthridone (4, 9%), all of which are postulated to arise from the initial diradical intermediate (Scheme 6). An interesting feature of these pathways is that they involve initial elimination of formaldehyde by a process that involves hydrogen abstraction by the aryl radical rather than the amidyl radical, and the resulting diradical then forms the phthalimidine, 2.

The formation of phenanthridine and N-methylphenanthridone involves two further unusual reactions, of which the first involves a [2 + 2] cheletropic reaction of a novel
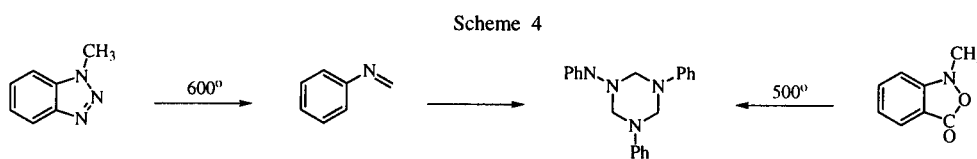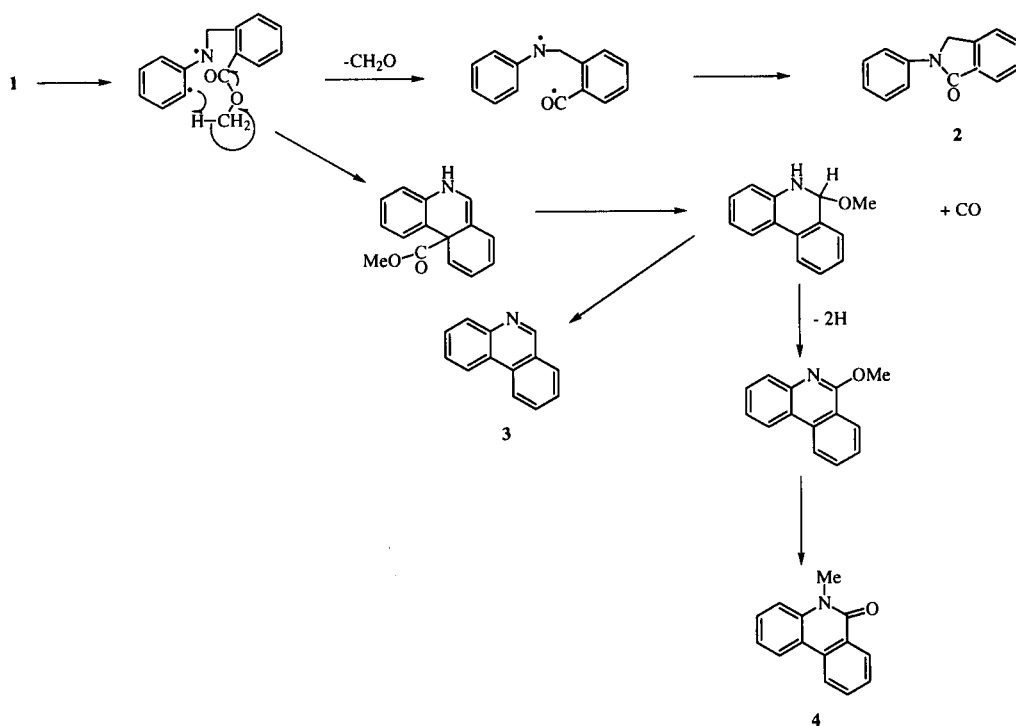
Scheme 4

The fvp of 1-benzyl and 1-(2-cyanobenzyl)benzotriazole gave largely the corresponding benzaldehyde N-phenylimine, rationalized [11,12] by 1,4-hydrogen transfer (Scheme 5). Strong support for a diradical process came from the nature of the products from the fvp of the 2-methoxycarbonyl compound 1, which gave N-phenylphthalimidine (2, 29%), phenanthridine (3, 36%) and N-methyl-

type, clearly driven by the energy of aromatization. We have independently shown that this is a general reaction, by the synthesis and fvp of the triene 5 (Scheme 7).

The second unusual reaction was the rearrangement of the presumed intermediate 6-methoxyphenanthridine to the observed N-methylphenanthridone, as shown in Scheme 6. While a few instances of such transformations were known [13], such reactions had usually been reported after high temperature bulk distillation, and not in the vapor state. We have subjected a considerable number of 2-alkoxyhetarenes and 4-alkoxyhetarenes to fvp, and have found that such reactions do occur in the vapor state, and by an intramolecular process , as no crossover was seen in the pair shown in Scheme 8.
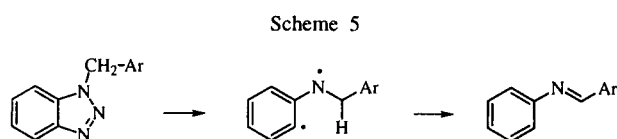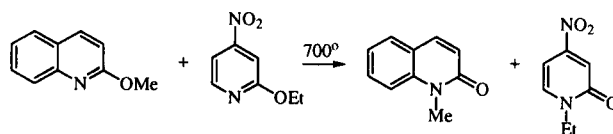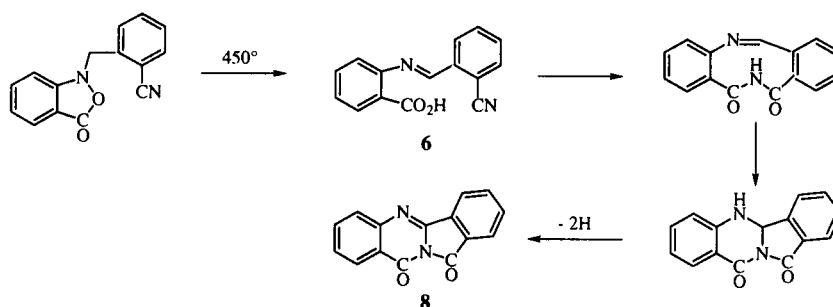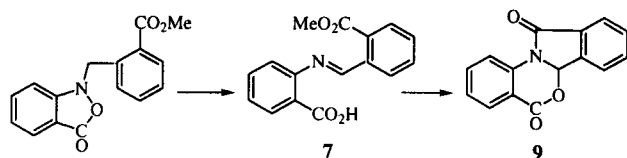
Scheme 5
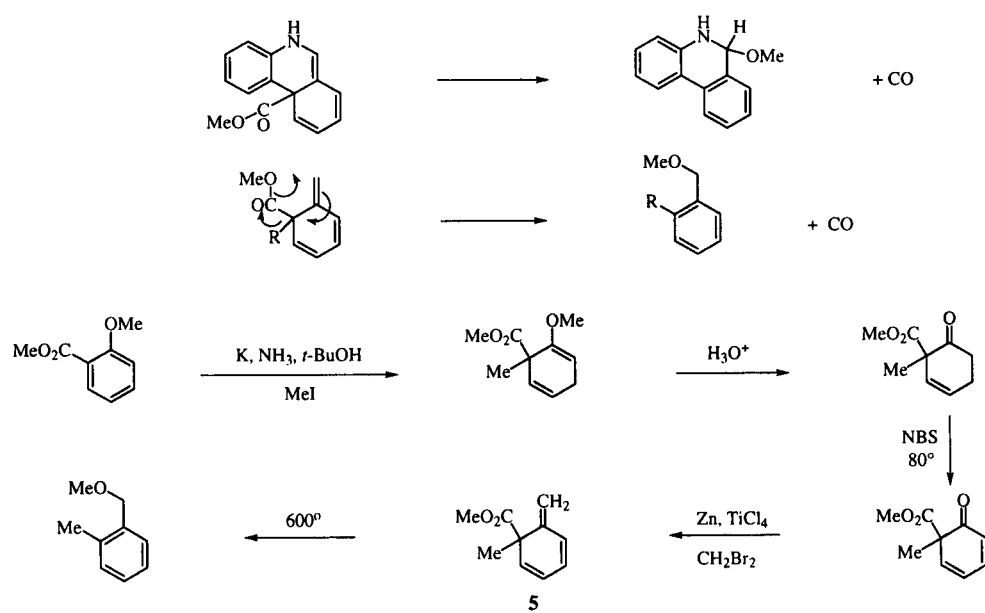
Scheme 6

Scheme 7

Scheme 8

The fvp of neither the cyanobenzyl nor the methoxycarbonylbenzylbenzisoxazolones proceeded by decarboxylation, the products **8** and **9** arising from subsequent reactions of the initial elimination products **6** and **7** (Schemes 9 and 10).
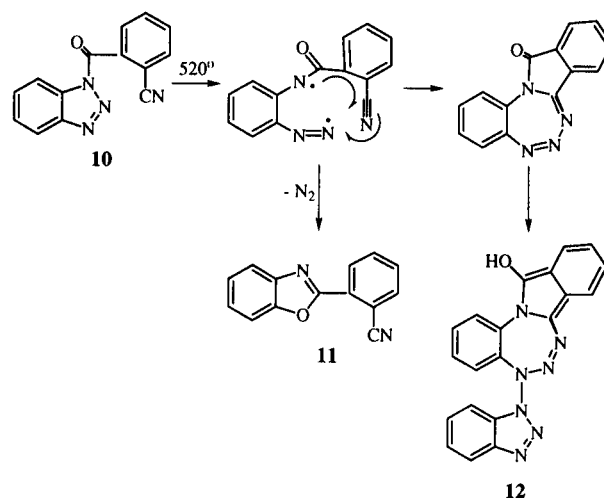
Scheme 9

Scheme 11

Scheme 10

2. Products from *N*-Acylbenzotriazoles and *N*-Acylbenzisoxazolones.

Previous work on the pyrolysis of acylated benzotriazoles has always given low yields of products [6,15,16]. We have synthesized a number of 2-substituted acyl derivatives [17], which we hoped would offer separate pathways for diradical and carbenoid intermediates. Thus, the 2-cyano analogue **10** at 520° was found to give the oxazole **11** (16%), and the novel benzotetraazepine **12** (33%), which we suggest arises as shown in Scheme 11, where benzotriazole itself is a decomposition product of **10**. As the temperature was raised, **12** disappeared, and the yield of the oxazole was raised to 32%.

The ester **13** gave the oxazole **14** as the only characterized product (42%), but the chloromethyl analogue **15** gave acridine hydrochloride as the major product (65%). We believe this is firm evidence for the presence of an intermediate triplet diradical **16** (Scheme 12), but were surprised that on this occasion hydrogen abstraction occurred only by the amidyl radical and not the aryl radical, which would have given the chlorophthalimidine **17**, which was totally absent.

13

14

compounds **23** and **24** were only minor products, the major being acridine hydrochloride. It thus appears clear that the singlet carbene is the low energy intermediate, but that the higher temperatures necessary to decompose the triazole gives rise to diradicals.

Scheme 12

15

16

17

The cyano- and methoxycarbonyl acylbenzisoxazolones **18** and **19** gave good yields of the benzoxazoles **20** and **21** at 550° (72% and 83%), and the chloromethylisoxazolone **22** at 520° gave the oxazole **23** as the minor product (11%); the major product was the isoindolo[2,1-*b*]benzoxazole **24** (59%), which had not previously been prepared, although the S, N, and Se analogues have been prepared sometime ago by Russian workers [18-20] (Scheme 13). When the pyrolysis temperature was raised to 650°, the

The photolysis of the chloromethyl benzisoxazolone **22** was also informative. At 300 nm in acetone, diradical pathways are followed, as might be expected, and phthalide (60%) and anthranilic acid (53%) were isolated, clearly involving homolysis of the N-O bond, and hydrogen abstraction from the solvent (Scheme 14). In acetonitrile, no hydrogen abstraction occurs, and the detection of 2-chloroaniline is most easily rationalized in terms of carbenoid intermediates (Scheme 14).

Scheme 13

18 R = CN
19 R = CO₂Me

20 R = CN
21 R = CO₂Me

22

23

24

Scheme 14

3. Products from N-Heterocyclylbenzotriazoles and Isoxazolones.

Benzotriazole readily reacts with activated chlorohete-rocycles to give N-heteroarylbenzotriazoles [8,21,22], and we have confirmed that fvp of such compounds proceeds in very high yield (Scheme 15).
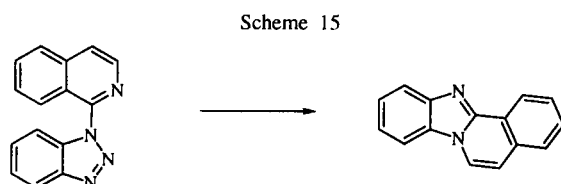
While isoxazolones readily react with chloroheterocy-cles [4,5], we have been unable to isolate the arylation products from benzisoxazolones. The product isolated from 1-chloroisoquinoline was the chlorinated quino-quinazoline **26** (Scheme 16), the structure of which was established independently.

In conclusion, this work supports the conclusion of Yonezawa [7] who suggested that both singlet and triplet pathways are involved in the decomposition of triazoles. The benzisoxazolones have the advantage that they can be decomposed under sufficiently mild conditions to give the lower energy singlet carbene.

Acknowledgements.

Scheme 15

Scheme 16
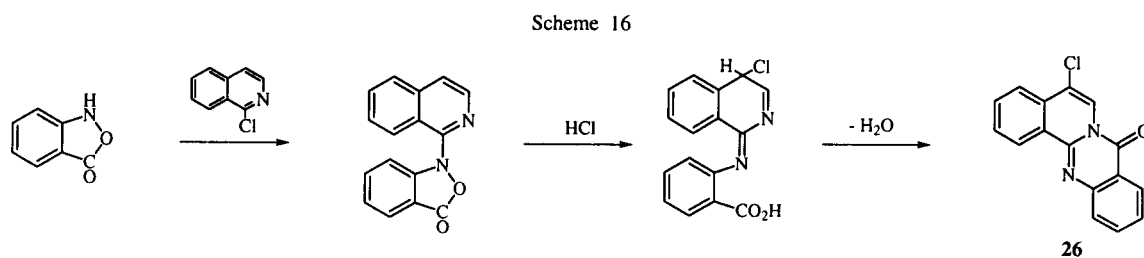
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