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A PHOTOCHEMICAL ROUTE TO THE UNSATURATED β-LACTAM, *N*-METHYL-AZETINONE: A THERMALLY LABILE RING-SYSTEM

Guy Kretschmer and Ronald N. Warrener*

Department of Chemistry, S.G.S., Australian National University, Canberra, A.C.T., Australia.

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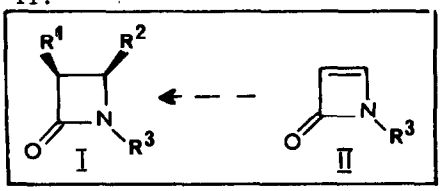
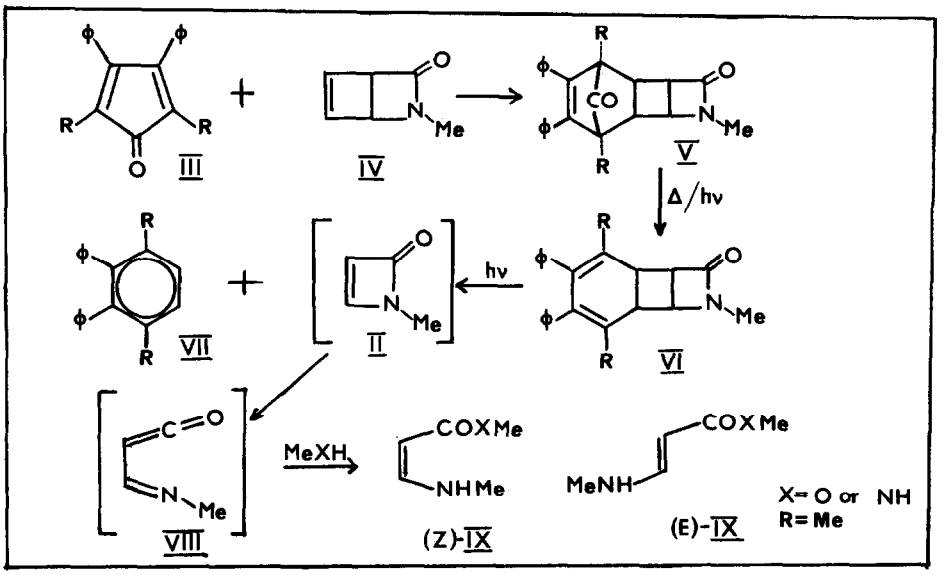
Much attention has been focused on the azetidinone (saturated β-lactam) ring system (1) since it was discovered in the naturally occurring β-lactam antibiotics. Numerous synthetic schemes and strategems have been employed, many of which start from a suitably substituted β-lactam moiety.[1] Functionalisation of the β-lactam *via* stereoselective addition to the α,β-unsaturated-β-lactam (II) is a stratagem towards cephalosporin and penicillin synthesis which has not been reported to date. This may well be due to the unavailability of the required synthon II.[2]



In this communication we report on the synthesis of II via our 1,2-photoaromatisation route[3], which suggests that it has limited synthetic utility due to its extremely limited thermal stability.

The reaction sequence outlined in the scheme was used to obtain the required precursor (V). Thus cycloaddition of the substituted cyclopentadienone (III) with the photoisomer (IV) derived from *N*-methyl-α-pyridone[4], gave a good yield of two 1:1 adducts (V). These are assigned the *endo*-anti (Va) and *exo*-anti (Vb) structures by analogy with those adducts derived from the similar addition of III to *cis*-3,4-dichlorocyclobutene, the stereochemistry of which was



reported earlier from our laboratory[5]. The major isomer, assigned the *exo*-anti stereochemistry (Vb)* could not be separated from the *endo*-anti isomer by chromatography but was readily purified by recrystallisation from benzene/light petroleum, m.p. 191-3°C (p.m.r. $CDCl_3$ 60 MHz δ ppm: 1.20, 1.24, s, $C_{1,8}$-Me; 2.74, 2.97, m, $C_{3,6}$-H; 2.82, s, *N*-Me; 3.31, 3.64, m, $C_{2,7}$-H; 7.14, brm, aromatics). This compound was used in the detailed photochemical experiments described hereafter. Irradiation of (V) in deuteriochloroform yielded the tricyclic diene (VI), which, on continued irradiation fragmented to form the aromatic hydrocarbon (VII) and (presumably) the azetinone (II). This reaction,

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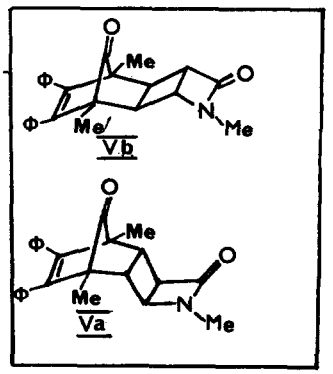
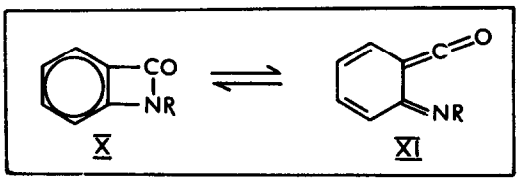
* The minor isomer (Va) is more readily decarbonylated thermally than the major isomer which is consistent with the known anchimeric assistance of an *endo*-cyclobutyl σ-bond in reactions involving chelotropic elimination.[6] Both isomers (Va,b) yielded the same product on photodecarbonylation, which confirmed the *anti* fusion about the cyclobutane ring. Attempts to utilise L.I.S. pmr spectroscopy to confirm these assignments was indecisive as complexation preferentially occurred on the β-lactam carbonyl group.



which was monitored by pmr spectroscopy at temperatures as low as -50°, gave quantitative yields of the aromatic hydrocarbon (VII) but no spectral evidence for the 4-membered olefin or any product derived therefrom (no *N*-methyl signals even!). Irradiation in d_8-tetrahydrofuran produced similar results, while irradiation in methanol (or THF/methanol mixtures) gave a mixture of (Z)- and (E)-methyl β-methylamino acrylates (IX; X=O) as well as (VII). Reaction in THF/methylamine yielded the related acrylamides (IX; X=NH).

The acrylates are logically derived from addition of methanol (or methylamine) to the imino ketene (VIII), which obviously derives from the desired β-lactam (II). The conversion of the β-lactam to the imino ketene is a reversal of the well documented [$_{\pi}2_s$ + $_{\pi}2_a$] cycloaddition of ketenes with imines, a reaction known to be thermally allowed.[7] The relief of ring-strain, together with the low activation energy likely associated with such a thermally-allowed transformation are sufficient to account for the ready conversion of (II) to (VIII). The related transformation of (X) to (XI) has previously been documented.[8]



X XI

The ratio of (E) to (Z) isomers [(E)-IX:(Z)-IX = 1:1.25] corresponds to neither the thermodynamic ratio (100% (E)-IX) or the photoequilibrium (1:2.4). This suggests that addition may occur initially to the ketene moeity to form an intermediate imino ester which rapidly isomerises (1,3-H shift, photochemical?) to the acrylic esters (IX). The conformational mobility of this intermediate is reflected in the observed mixture of (E)-IX and (Z)-IX. This ratio is inconsistent with a mechanism involving direct reaction of the methanol to the azetinone, which would be expected to yield the (Z)-isomer exclusively. The photochemical isomerisation (*vide supra*) was too slow to account for the observed ratio. Experiments designed to trap the azetinone (II) in adduct form, prior to ring-opening, are currently in progress as well as matrix photolysis experiments aimed at detecting the intact 4-membered heterocycle.

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