TANDEM 1,3-DIPOLARCYCLOADDITIONS OF CYCLOHEXANE FURAZAN-N-OXIDE WITH N-ARYLMALEIMIDES : NOVEL ENTRY TO SUBSTITUTED TETRAHYDRO-2H-ISOXAZOLO-[2,3-b]ISOXAZOLES (ISOXAZOLIZIDINES).

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Summary : The reaction of cyclohexane furazan-N-oxide with substituted N-phenylmaleimides involves successive 1,3-dipolar cycloadditions leading to isoxazolizidines.

Our studies of the cycloaddition of triazolium imides (1) have shown that these highnitrogen heterocyclic 1,3-dipoles undergo cycloaddition to give unstable adducts which display



a range of exciting rearrangements, fragmentations, or ring expansions leading to new monocyclic and fused polycyclic ring systems<sup>1-3</sup>. The remarkable versatility of the reaction prompted a replacement of nitrogen atoms by oxygen atoms. The triazolium oxide 1,3-dipole (2) proved to less reactive than (1) towards dipolarophiles but nevertheless gave an interesting reaction, leading to 1,2,3-triazine derivatives from dimethylacetylene dicarboxylate<sup>3</sup>. We now report cycloadditions of the furazan-N-oxide system (3) with substituted N-arylmaleimides. The sytem (3) might have been expected<sup>4-6</sup> to behave like a bis-nitrileoxide in thermal cycloadditions as do many furazan oxides but this did not occur.

When compound (3) was heated<sup>†</sup> with substituted N-phenylmaleimides in toluene the products formed in moderate yields were the substituted isoxazolizidines (4) (Table). Most of the known derivatives of this system have been obtained from reactions of nitro-alkanes with olefins<sup>7-10</sup>. The structures of compounds (4) were established by carbon and 270 MHz proton n.m.r. spectra (Scheme). An x-ray crystal structure of a derivative of this fused ring system, compound (4c), is shown (Figure)<sup>§</sup>. It confirmed the endo- and exo-structures at the adduct sites in (4) arising from successive cycloadditions.

We interpret this interesting reaction as involving an initial 1,3-dipolar cycloaddition (5). This may occur in an endo manner facilitated by secondary orbital interactions similar



Scheme. (some <sup>1</sup>H and <sup>13</sup>C shifts for compound (4c) shown) Ar =  $p-YC_6H_4$ . Y = (a), H; (b), Br; (c), NO<sub>2</sub>; (d), Cl; (e), Me.



Figure. X-ray crystal structure of (4c)

to that observed<sup>1-3</sup> with structures (1) and (2), but however the stereochemistry of the initial cycloaddition was lost in this case because the labile bond of the intermediate (6) proved to be the imino N-O bond of the dihydrofurazan ring. This cleaved to give a nitrile and the nitrone (7), the structure of which is independent of the stereochemistry of the first cycloaddition. The newly generated 1,3-dipole is now present in a saturated fused bicyclic ring which already has an endo-structure. Hence the second cycloaddition occurred in the sterically favourable exo-mode thereby giving the products (4) containing a useful pentano-nitrile chain at the bridgehead. The final stereochemistry of the products (4) was therefore controlled by the second cycloaddition only. From a detailed perusal of ref.4 and a literature survey we note that the cleavage of the furazan moiety in the intermediate (6) to a nitrile and "nitro" function appears to be a novel type of fragmentation which has not been reported previously.

Table	:	Isoxazolizidines	(4)	
Cpd.		М.р. °С	Conversion (%) <sup>a</sup>	Yield (%) <sup>b</sup>
(4a)		239-241	30	>75
(4b)		235-7	35	-
(4c)		178-180	28	>65
(4d)		220-222	47	>68
(4e)		211-213	12	>65

<sup>a</sup>Isolated yield of product, the remainder being unchanged starting substrates. <sup>b</sup>Minimum estimated reaction yield corrected for recovered starting materials. Losses during difficult chromatographic separation of the substrates precluded a precise value. No other products were present.

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<sup>+</sup>General Procedure : A solution of compound (3) (3.57 m.mol) in toluene (20 cm<sup>3</sup>) was treated with the substituted N-phenylmaleimide (7.14 m.mol) and stirred under reflux for 16-28h. during which the product (4) separated. On cooling the solution further crops were obtained. Fractional evaporation of the filtrate and treatment with diethyl ether resulted in recovery of unchanged starting materials. All compounds gave satisfactory CHN microanalysis. The products (4) showed nitrile stretching at 2246±1 cm<sup>-1</sup>. Related proton and carbon signals (Scheme) and coupled proton signals were identified by off-resonance and selective proton decoupling.

## $^{\$}$ Crystallographic Data for C<sub>26</sub>H<sub>20</sub>N<sub>6</sub>O<sub>10</sub>

A crystal with approximate dimensions of 0.32 x 0.38 x 0.22 mm was used for data collection : Crystal Type; Monoclinic, a = 27.524(6), b = 10.35(3), c = 20.745(5)  $A^{O}$ ,  $\alpha = \gamma = 90$ ,  $\beta = 91.958(4)$ , U = 5908  $A^{O}$  <sup>3</sup>,  $\mu = 0.65$  cm<sup>-1</sup>, FOOO = 2384. Space Group  $C_{2/c}$ , Z = 8, Radiation Mo-K<sub> $\alpha$ </sub> ( $\lambda = 0.71069$   $A^{O}$ ), Graphite Monochromator Range 2 <  $\theta$  < 24<sup>O</sup>. Final Full Matrix Least Squares Cycle : Reflections with I > 3  $\sigma$  I, 2716; No. of Variable Parameters, 379; Max.Shift/ESD < 0.001; Residuals R = 13.72%. Final Difference Fourier Map Max. Peak = 0.20 e/A<sup>O</sup> <sup>3</sup>, Min. Peak = -0.18 e/A<sup>O</sup> <sup>3</sup>. R = [[ $\Sigma(|F_O-F_C|)^2$ ]/[ $\Sigma(|F_O|)^2$ ]]<sup>1</sup> Unit Weights. The crystals of this compound were of poor quality and did not diffract strongly. The structure was solved by a combination of Patterson research and direct methods, SHELX86<sup>11</sup>, and refined by full matrix least squares using SHELX76<sup>12</sup>. Data were corrected for Lorentz and polarization effects but not for absorption.

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