

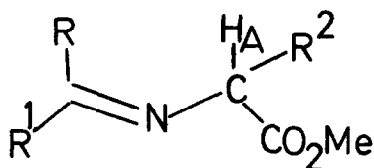
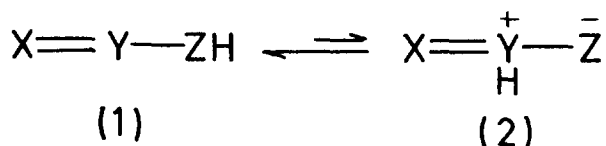
X=Y-ZH SYSTEMS AS POTENTIAL 1,3-DIPOLES. CYCLOADDITIONS OF  
 THIOIMINOETHERS AND THIOIMINOCARBONATES

by R. Grigg\*, L.D. Basanagoudar, D.A. Kennedy, J.F. Malone  
 and S. Thianpatanagul

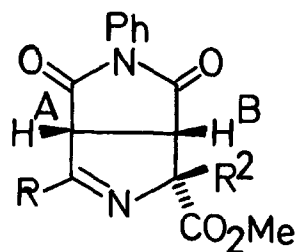
(Department of Chemistry, Queen's University, Belfast  
 BT9 5AG, Northern Ireland)

**Summary.** Thioiminoethers and thioiminocarbonates of  $\alpha$ -amino acid esters undergo acetic acid catalysed cycloaddition reactions with N-phenylmaleimide via their 1,3-dipolar tautomers.

We have recently described many examples, both inter- and intra-molecular, of cycloadditions of X=Y-ZH systems which we believe involve the thermal tautomeric equilibrium (1  $\rightleftharpoons$  2).<sup>1</sup> The cycloadditions of imines of  $\alpha$ -amino acid esters (3a) are dependent on the basicity of the imino nitrogen atom and the pKa of the H<sub>A</sub> proton<sup>2</sup>, and are subject to Bronsted and Lewis acid catalysis.<sup>3</sup>

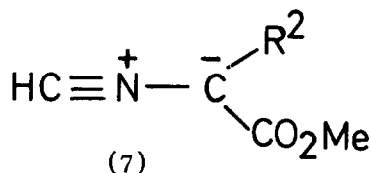
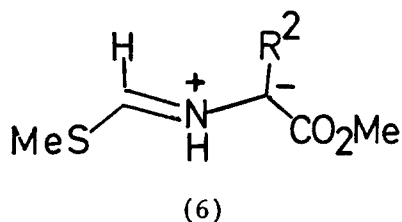
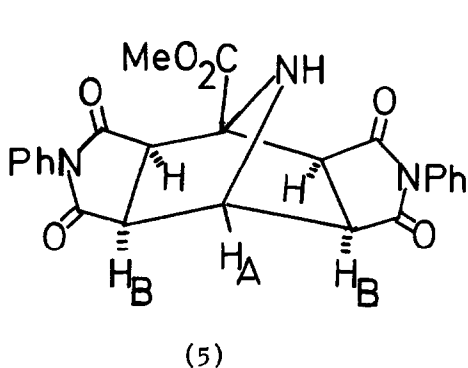


- (3) a. R=H, R<sup>1</sup>= Ar  
 b. R=H, R<sup>1</sup>= SMe  
 c. R=R<sup>1</sup>= SMe

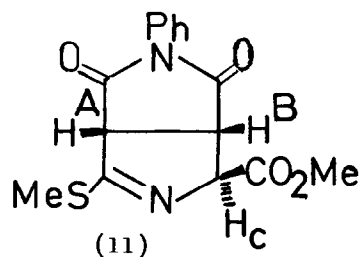
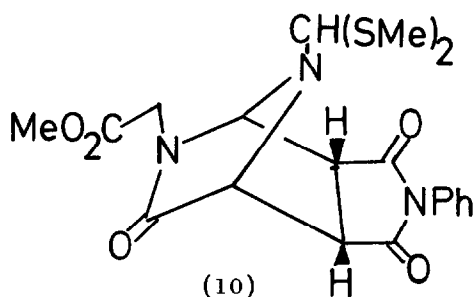
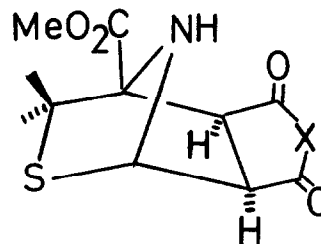
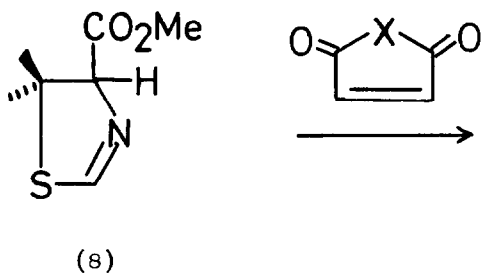


- (4) a. R=H  
 b. R=SMe, R<sup>2</sup>= H<sub>C</sub>

The relative rates of cycloaddition of (3a;  $R^2 = \text{Ph}$ ) to N-phenylmaleimide (NPM) in toluene (0.2M solutions;  $105^\circ$ ) are  $\text{Ar} = \text{p-Me}_2\text{NC}_6\text{H}_4$  (33)  $>$   $\text{C}_6\text{H}_5$  (5.5)  $>$   $\text{p-NO}_2\text{C}_6\text{H}_4$  (1).<sup>2</sup> This rate dependence on imine basicity prompted a study of thioiminoethers (3b). Thioiminoethers (3b;  $R^2 = \text{Ph}$  or  $\text{CH}_2\text{Ph}$ )<sup>4</sup> react with NPM in xylene ( $144^\circ$ ) in the presence of a mole equivalent of acetic acid to give (4a;  $R^2 = \text{Ph}$  or  $\text{CH}_2\text{Ph}$ ) in 69% and 46% yield respectively.<sup>5,6</sup> Cycloadducts (4a;  $R^2 = \text{H}$ ) should be capable of further cycloaddition via transfer of  $R^2 (=H)$  to the imino nitrogen atom. In accord with this a small yield (5%) of (5) was obtained when (3b;  $R^2 = \text{H}$ ) was reacted with 2 mole of NPM (toluene,  $110^\circ$ , 5h). Exo-exo stereochemistry is assigned to (5) on the basis of its  $^1\text{H}$  nmr spectrum which shows no coupling of the bridgehead proton  $\text{H}_A$  with the adjacent  $\text{H}_B$  protons.<sup>7</sup> These cycloadditions are believed to involve tautomeric generation of (6), followed by cycloaddition and then elimination of methane thiol from the initial cycloadduct.



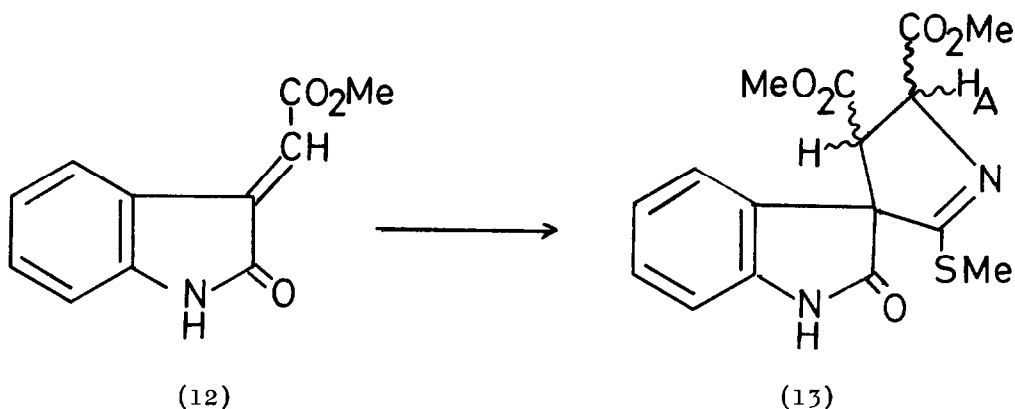
The possibility of prior thermal elimination of methane thiol from (3b) to give (7) as the active dipolar species, is rendered unlikely by the observation that (8)<sup>4</sup> gives (9a; 50%) and (9b; 50%) on heating with (144 $^\circ$ ; xylene) with NPM and maleic anhydride respectively. Acetic acid catalysis is not necessary in these cases. Exo stereochemistry is assigned to (9a,b) on the basis of  $^1\text{H}$  nmr coupling constants as for (5).



A novel bridged ring adduct (10) was obtained (50%) when two mole of (3b;  $R^2 = H$ ) were reacted with one mole of NPM (benzene,  $25^\circ$ , 14dy) in the presence of one mole of acetic acid. The structure of (10) was established by X-ray crystallography.<sup>8</sup>

The iminothiocarbonate (3c;  $R^2 = H$ )<sup>9</sup> reacts (xylene,  $144^\circ$ , 2dy) with NPM in the presence of 1 mole of acetic acid to give (4b; 60%;  $J_{AB} = 8.8\text{Hz}$ ,  $J_{BC} = 9.9\text{Hz}$ ). On further (1.5dy) heating (4b) isomerised to (11;  $J_{AB} = 8.45\text{Hz}$ ;  $J_{BC} = 2.57\text{Hz}$ ). Regiospecific cycloaddition of (3c;  $R^2 = H$ ) to (12) occurs (xylene; 1 mole acetic acid,  $144^\circ$ , 5dy) to give (13; 50%) as a 1:1 mixture of cis- and trans-isomers separable by fractional crystallisation. The separated isomers undergo epimerisation on heating under the cycloaddition conditions suggesting the cis/trans product mixture is a result of the lability of  $H_A$  in (13).

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### References

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