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## Brönsted and Lewis Acid Catalysis of X=Y–ZH Cycloadditions

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Cycloadditions of arylidene imines of methyl phenylglycinate show substantial rate enhancements in the presence of Brönsted and Lewis acids; for Brönsted acids the rate is related to the  $pK_a$  of the acid, whilst for the Lewis acids studied the rate acceleration decreased in the order  $Zn(OAc)_2 > AgOAc > LiOAc > Mg(OAc)_2$ .

Catalysis of  $6\pi$ -electron cycloadditions by complex formation between a Lewis acid and the dienophile (Diels-Alder)<sup>1</sup> or enophile (ene reaction)<sup>2</sup> is well known. Following our studies of both inter<sup>3</sup>- and intra<sup>4</sup>-molecular cycloadditions of X=Y-ZH systems, we report here a series of acidcatalysed cycloadditions in which Brönsted and Lewis acids

$$\begin{array}{c} \mathbf{X} = \mathbf{Y} - \mathbf{Z}\mathbf{H} \stackrel{\mathbf{L}}{\rightleftharpoons} \mathbf{X} = \stackrel{\mathbf{Y}}{\mathbf{Y}} - \mathbf{Z}\mathbf{H} \stackrel{\mathbf{B}:}{\rightleftharpoons} \mathbf{X} = \stackrel{\mathbf{F}}{\mathbf{Y}} - \stackrel{\mathbf{Z}}{\mathbf{Z}} \\ & | \\ \mathbf{L} \\ \mathbf{L} \\ \end{array}$$

Scheme 1.  $L = H^+$  or Lewis acid.



Table 1.<sup>a</sup> Effect of  $pK_a$  of acid catalyst on the half life for the cycloaddition of the Schiff's base (1) and N-phenylmaleimide in  $[{}^{2}H_{a}]$ toluene.

Schiff's base	Acid	pK <sub>a</sub> of acid	t <sub>1</sub> /min <sup>e</sup>	Temp./ °C⁵
<b>(1a)</b>			$120 \pm 4$	105
(1a)	2-Pyridone	11.99	$88 \pm 6$	105
(1a)	MeCO <sub>2</sub> H	4.75	6 <sup>d</sup>	105
(1a)	Meldrum's acide	5.1	5ª	105
(1a)	2,4-Dinitrophenol	4.0	3ª	105
(1b)			668 ± 8	105
(1b)	MeCO <sub>2</sub> H	4.75	56 $\pm$ 4	95
(1c)			583 $\pm$ 7	105

<sup>a</sup> Kinetics were measured in the probe of a Bruker WH90 spectrometer, spectral width 1000 Hz, 4K data points. <sup>b</sup> Temperature accurate to  $\pm 0.5$  °C. <sup>c</sup> Errors refer to statistical errors. <sup>d</sup> Approximate values of  $t_2$ . <sup>e</sup> 2,2-Dimethyl-1,3-dioxan-4,6-dione.

promote 1,3-dipole formation from imines (Scheme 1).† These processes differ from the above  $6\pi$ -cycloadditions, which involve complexation of  $2\pi$ -components, in that complexation of the  $4\pi$ -component is involved.

We have studied the effect of Brönsted acids on the cycloaddition  $(1) \rightarrow (2)$  (Table 1) and Lewis acids on the cycloaddition  $(1) \rightarrow (3)$ ; (Table 2). The reactions proceeded cleanly and in high yield with no evidence of decomposition apart from a little hydrolysis of the Schiff's base (1). The stereo-

Table 2.<sup>a</sup> Effect of Lewis acids on the half life for the cycloaddition of the Schiff's base (1a) and methyl propiolate in  $[{}^{2}H_{8}]$ toluene (80 °C).

Lewis acid <sup>b</sup>	$t_{\frac{1}{2}}/h$	Yield (%)°
	38	94
MeCO <sub>2</sub> H	1.8	
$Zn(OAc)_2.2H_2O$	3.0	88
AgOAc	3.25	95
LiOAc.2H <sub>2</sub> O	5.5	93
$Mg(OAc)_2$	8.75	

<sup>a</sup> Reactions were run in a thermostatted oil bath; temperature variation  $\pm 0.5$  °C. <sup>b</sup> The metal salts only partially dissolved in the hot solvent. <sup>c</sup> Estimated by n.m.r. spectroscopy using hexamethylbenzene as internal standard.

chemistry of (2) and (3) is assigned on the basis of our earlier studies.<sup>3</sup> The cycloaddition  $(1) \rightarrow (3)$  is regiospecific and the regiochemistry is assigned on the basis of the n.m.r. spectrum of (3) which shows only a small coupling constant between  $H_A$  and  $H_B$  (J 1.95 Hz).<sup>‡</sup>

The half life  $(t_1)$  for the cycloaddition  $(1) \rightarrow (2)$  was found to be dependent on the  $pK_a$  of added protonic acids (Table 1).§ Reactions were performed in sealed n.m.r. tubes with equimolar amounts of the Schiff's base (1) and the acid dissolved in [ ${}^{2}H_{8}$ ]toluene (0.4 M). The fastest rate was observed with 2,4-dinitrophenol, the strongest acid of those studied, whilst the slowest rate was observed with 2-pyridone, the weakest acid studied.¶

Enhanced rates of the cycloaddition  $(1) \rightarrow (2)$  in the absence of added acid were also observed when  $[{}^{2}H_{8}]$ -toluene was replaced by CD<sub>3</sub>NO<sub>2</sub> (pK<sub>a</sub> 10.6) as solvent.\*\* Thus, the  $t_{\frac{1}{2}}$  values for (1a) (59.8 min), (1b) (160 min), and (1c) (175 min) were substantially less in CD<sub>3</sub>NO<sub>2</sub> than in  $[{}^{2}H_{8}]$ toluene (Table 1).

Analogous rate enhancements were observed using metal salts as Lewis acid catalysts for the process  $(1a) \rightarrow (3)$  (Table 2).§ Use of AlCl<sub>3</sub> as Lewis acid catalyst tends to divert the reaction to pyrrole formation.<sup>5</sup>

The activity of lithium acetate (Table 2) is of particular interest in the light of Kauffmann's extensive studies on anionic cycloadditions of lithium salts of 2-aza-allyl anions.<sup>6</sup> These lithium aza-allyl species may thus be a further example of the general dipolar species depicted in Scheme 1 in which  $L = Li^+$ . In our examples dual co-ordination to the imine nitrogen and ester oxygen atoms [structure (4)] is thought to be important.

‡ Coupling constants for CH-CH= are 6.5—11.5 Hz. Fourbond 'W' coupling constants for CH-C=CH are 1.5—2.5 Hz and are dependent on the angle between the protons: A. J. Gordon and R. A. Ford, 'The Chemists Companion,' Wiley-Interscience, New York, 1972, p. 273.

§ Progress of the reaction was followed by plotting R/(R + P) against time where R = reactant Schiff's base and P = cyclo-adduct.

<sup>&</sup>lt;sup>†</sup> Other species, *e.g.*, X=Y-Z(H)-L, are also expected to be present and in certain cases may, depending on the nature of X, Y, and Z, retard the reaction.

<sup>¶</sup> Added in proof: We have recently found that the cycloaddition  $(1) \rightarrow (2)$  can be carried out at room temperature in acetic anhydride containing a little acetic acid [e.g.  $(1; R = OMe) \rightarrow (2; R = OMe; 79\%)$  in 2 h], or in acetonitrile containing 10% acetic acid.

<sup>\*\*</sup> This rate enhancement may be partly due to solvent polarity.

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