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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 6π -electron cycloadditions by complex formation between a Lewis acid and the dienophile (Diels-Alder)¹ or enophile (ene reaction)² is well known. Following our studies of both inter³- and intra⁴-molecular cycloadditions of X=Y-ZH systems, we report here a series of acidcatalysed cycloadditions in which Brönsted and Lewis acids

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

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



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

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

promote 1,3-dipole formation from imines (Scheme 1).† These processes differ from the above 6π -cycloadditions, which involve complexation of 2π -components, in that complexation of the 4π -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.^a 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 ^b	$t_{\frac{1}{2}}/h$	Yield (%)°
	38	94
MeCO ₂ H	1.8	
$Zn(OAc)_2.2H_2O$	3.0	88
AgOAc	3.25	95
LiOAc.2H ₂ O	5.5	93
$Mg(OAc)_2$	8.75	

^a Reactions were run in a thermostatted oil bath; temperature variation ± 0.5 °C. ^b The metal salts only partially dissolved in the hot solvent. ^c 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.³ 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).[‡]

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 CD₃NO₂ (pK_a 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 CD₃NO₂ 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 AlCl₃ as Lewis acid catalyst tends to divert the reaction to pyrrole formation.⁵

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.⁶ 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.

[†] 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.

[¶] 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.

^{**} This rate enhancement may be partly due to solvent polarity.

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