

THE ACTIVITY SCALE OF DIPOLAROPHILES VERSUS THIOBENZOPHENONE S-METHYLIDE

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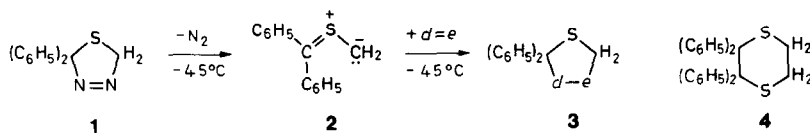
Summary Competition experiments of pairs of dipolarophiles for thiobenzophenone S-methylide (2) furnish relative rate constants which reveal an unusually high selectivity of the nucleophilic 1,3-dipole, in accordance with Sustmann's PMO concept.

Sustmann classified Diels-Alder reactions and 1,3-dipolar cycloadditions by their predominant HO-LU interaction.¹ Daring simplifications led to Eq.(1) for the second-order term of the perturbation equation; E refers to the MO energies of the dipolarophile and E' to those of the 1,3-dipole. On assuming that variation of the dipolarophile causes parallel shifts of its HO and LU energies by an amount x, one arrives at Eq.(2) for the energy gain in forming the MOs of the transition state; E_I and E_{II} are the MO separations of the 1,3-dipole with a standard dipolarophile, e.g., ethylene.

$$\Delta E = \text{Const} \frac{1}{E_{\text{HO}} - E'_{\text{LU}}} + \frac{1}{E'_{\text{HO}} - E_{\text{LU}}} \quad (1)$$

$$= \text{Const} \frac{1}{E_{\text{I}} + x} + \frac{1}{E_{\text{II}} - x} \quad (2)$$

E_I ~ E_{II} pertains to well-balanced nucleophilic-electrophilic 1,3-dipoles (Sustmann's type II), whereas E_I > E_{II} concerns nucleophilic 1,3-dipoles (type I), i.e., the first fraction of Eq.(2) becomes small. The function of ΔE versus x should be all the steeper, the more E_I > E_{II}. Thus, the most nucleophilic 1,3-dipole, i.e., the one with the highest MO energies, should display high selectivity; a phenomenon which is so far insufficiently documented in rate measurements.



Sulfur has the same electronegativity as carbon on the Pauling scale. Therefore, thiocarbonyl ylides should possess the highest MO energies amongst the known 1,3-dipoles. We have chosen thiobenzophenone S-methylide (2) and determined its specific reactivity scale of dipolarophiles. The N₂ extrusion from the 1,3,4-thiadiazoline 1 proceeds with t_{1/2} = 55 min in THF at -45°C;² the nonisolable 2 combines in situ with dipolarophiles d=e to give adducts 3.^{2,3} After the reaction of thiobenzophenone

with diazomethane at -78°C two dipolarophiles in known concentrations were added to the solution of 1. At -45°C the dipolarophiles compete for the thiocarbonyl ylide 2 and furnish cycloadducts. HPLC (Du Pont 830, Zorbax Sil, UV detector, mixtures of hexane and chloroform as mobile phase) allowed the quantitative analysis of the cycloadducts and the dimer 4 (formed in the presence of weak dipolarophiles) as well as their separation from the excess of the dipolarophiles. The competition constants were evaluated by Eq. (3), and a higher concentration of the less reactive dipolarophile contributed to the analytical precision. The sum of the adduct yields corresponded closely to the thiobenzophenone used for the preparation of 1, i.e., the yields were quantitative except for some weak dipolarophiles. The italic figures in Table 1 refer to the measured competition constants.

$$\kappa = \frac{k_A}{k_B} = \frac{\log A_o - \log (A_o - A\text{-adduct})}{\log B_o - \log (B_o - B\text{-adduct})} \quad (3)$$

The κ values can be tied into an entire string of relative rate constants by the arbitrary assignment of the value of 1 to methyl propiolate, a poor dipolarophile versus 2. Table 1 reveals that the relative rate constants stretch over eight powers of ten. All the listed dipolarophiles are electron-deficient. The activity scale of dipolarophiles would cover further powers of ten if the ability of thiobenzophenone S-methylide to dimerize with formation of 4 did not impose a lower limit.

Thione bonds are pre-eminent. With 78 million, thiofluorenone shows the highest dipolarophilic activity so far. Thiobenzophenone is 68 times less active, but even the resonance-stabilized 1-dithionaphthoic ester and diphenyl trithiocarbonate accept 2, albeit with smaller k_{rel} .

Tetracyanoethylene occupies the top position amongst CC double bonds with a k_{rel} of 33 million. In Diels-Alder reactions the dienophilic activity of N-phenyltriazolinedione exceeds that of tetracyanoethylene. In Table 1 the cyclic azo compound falls behind by a factor of 2.

The introduction of three more cyano groups into acrylonitrile gives rise to a millionfold rate increase versus 2 which reflects the successive lowering of the LU energy. The k_{rel} of 280 and 32 for methyl acrylate and acrylonitrile demonstrate that the ester group activates ethylene stronger than the cyano group. Why is k_{rel} of tetramethyl ethylenetetra-carboxylate as low as 40 instead of surpassing tetracyanoethylene? This is a picture-book test of steric hindrance. The four ester functions cannot achieve planarity with the ethylenic system; steric hindrance of resonance reduces the activating effect. In addition, the ester groups massively hinder the approach of the thiocarbonyl ylide.

The selectivity of thiobenzophenone S-methylide (2) as a 1,3-dipole is unusual indeed. $k(\text{TCNE})/k(\text{acrylonitrile}) = 1,000,000$ drops to 400 versus diphenyldiazomethane (5), which is still a nucleophilic 1,3-dipole with a similar substitution pattern (Table 2). The ratio of the rate constants of maleic anhydride, dimethyl fumarate and methyl acrylate is 1040 : 20 : 1 versus 2 and 10 : 3 : 1 towards 5.⁴ The loss of selectivity becomes greater for nucleophilic-electrophilic 1,3-dipoles; $k(\text{dimethyl fumarate})/k(\text{methyl acrylate})$, 20 for 2, amounts to 1.6 for N-methyl-C-phenylnitrene,⁵ 0.7 for methyl diazoacetate (7)⁶ (Table 2), 0.74 for benzonitrile oxide,⁷ and 0.21 for an azomethine imine⁸ of high

Table 1. Relative rate constants of dipolarophiles in 1,3-dipolar cycloadditions with thiobenzophenone S-methylide in THF at -45°C

$$k_{\text{rel}} = 78,000,000$$

33,000,000

18,100,000

6,800,000

1,780,000

1,150,000

320,000

290,000

71,000

57,000

34,000

5,300

1,350

1,300

1,230

840

340

280

82

40

32

 $\equiv 1$

		Thiofluorenone	
		Tetracyanoethylene	
		1.80	
		4-Phenyl-1,2,4-triazoline-3,5-dione	
		2.68	
		Thioxanthione	
	59		65
		5.87	
		Xanthione	
		1.5, 1.6	
		Thiobenzophenone	
		Dimethyl azodicarboxylate	
		1.11	
		Maleic anhydride	
	15.3, 16.5		
		3.93	
		4,4'-Dimethoxythiobenzophenone	
		5.27, 4.99	
		N-Phenylmaleimide	
		1.24, 1.25	
	52, 49		
		10.7	
		4,5-Dioxo-2-thioxo-1,3-dithiolane	
		Dimethyl fumarate	
			28
		Tetramethylcyclobutane-3-one-1-thione	
		4.06	
		Fumarodinitrile	
		1.10	1.6
	16.5		
		Methyl dithio-1-naphthoate	
		3.77	
		Diphenyl trithiocarbonate	
			3.61
		Dimethyl acetylenedicarboxylate	
		4.22	
		Methyl acrylate	
		3.34	
		Dimethyl maleate	
		2.73	
		Tetramethyl ethylenetetracarboxylate	
		1.24	
		Acrylonitrile	
		32	
		Methyl propiolate	
	9.3		
		2.46	

Table 2. Rate comparison of some 1,3-dipolar cycloaddition reactions

	$(C_6H_5)_2C=S^+-CH_2^-$	$(C_6H_5)_2C=N^+=N^-$	$C_6H_5-C\equiv N^+-CH-C_6H_5^-$	$CH_3O_2C-CH=N^+=N^-$
	<u>2</u>	<u>5</u>	<u>6</u>	<u>7</u>
	(THF, -45°C)	(DMF, 40°C)	(neat, 25°C)	(Toluene, 80°C)
Dipolarophile	<u>2</u> (k_{rel})	<u>5</u> ($10^4 k_2$)	<u>6</u> (k_{rel})	<u>7</u> ($10^4 k_2$)
Tetracyanoethylene	33,000,000	19,000		97
Fumaronitrile	1,300	40	33,000	7.2
Acrylonitrile	32	47	≅ 32	
Maleic anhydride	290,000	788		
Dimethyl fumarate	5,300	247	15,000	12.3
Dimethyl maleate	82	6.9	30	3.1
Methyl acrylate	280	83	28	17.7

steric requirements. Values < 1 suggest that the steric hindrance caused by the second ester group of fumaric ester takes precedence over the electronic activation.

It is only benzonitrilium N-benzylide (6) which appears to be still more selective than 2.⁹ Here dimethyl fumarate is 540 times more active than methyl acrylate, and fumaronitrile is 1000 times faster than acrylonitrile. Also $k(\text{fumaric ester})/k(\text{maleic ester})$ is a probe of selectivity: 500 for 6, 65 for 2, 35 for 5,⁴ 29 for benzonitrile oxide,⁷ 4 for 7,⁶ and 2.9 for N-methyl-C-phenylnitrene.⁵

The FMO energies of 6 are probably lower than those of 2. This indicates that other factors than MO energies influence selectivity. In general, 1,3-dipoles of the propargyl-allenyl type are more discriminating than those of the allyl type.¹⁰ The fact that 2 is a 1,3-dipole of the allyl type makes its selectivity all the more impressive.

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(Received in Germany 22 July 1983)