

1,3-Dipole: An Inverted V-Shaped Hammett Plot

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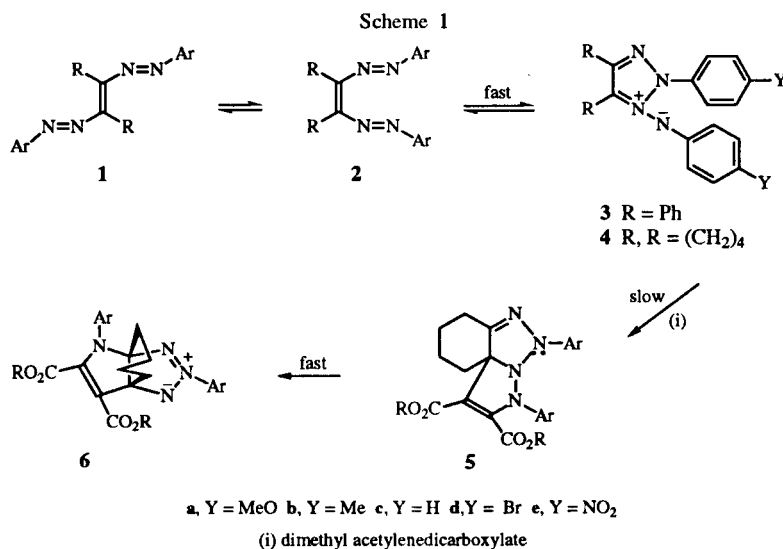
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An unusual inverted V-shaped Hammett plot has been observed for substituent effects at the *N*-terminus of 1,2,3-triazolium-1-imide 1,3-dipoles in cycloaddition reactions. Theoretical studies (3-21G and 6-31G) suggest strong resonance interactions separately stabilizing both ends of the dipole.

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Triazolium-1-imide 1,3-dipoles such as **3** display a wide synthetic scope [1-4] through sequential cycloaddition-rearrangement reactions with 2π -dipolarophiles Scheme 1. These dipoles display Sustmann type I behav-

stituents in the *C*-phenyl ring of the nitron to inhibit the reaction [7b,8]. Since dipoles such as **3** are obtained by generating the *trans*-bisaryldiazoethene structure **1** which rapidly equilibrates to the *cis*-structure **2** followed by



our [5-6] namely a dipole HOMO controlled cycloaddition transition state. For such a reaction substituent effects at the *N*-terminus of the dipole should display a linear Hammett relationship with a negative ρ value. However we have found that for the substituent *Y* both electron donating and withdrawing groups inhibited the reaction thereby giving an inverted V-shaped Hammett plot (Figure 1). U-Shaped Hammett plots are a feature of 1,3-dipolar cycloadditions of the Sustmann type II category where the energy gap in the transition state between the dipole-HOMO and dipolarophile-LUMO is about equal to that between the dipole-LUMO and dipolarophile-HOMO [7]. Inverted V-shaped plots where all substituents on the dipole inhibit the reaction are very rare.

One such case was the reaction of *C*-aryl-*N*-phenylnitrones with *N*-phenylmaleimide where conjugative stabilization of the ground state of the nitron, which was lost in the cycloaddition transition state, caused all sub-

electrocyclisation to the 1,3-dipole **3**, it is necessary to explore whether the unusual effect of the substituents in the aryl ring of the *N*-terminus of **3** could have arisen from the complexities of these pre-equilibria.

The equilibrium $\mathbf{1} \rightleftharpoons \mathbf{2}$ was removed from the kinetics of the dipole system by using the dipole **4** derived from cyclohexane-1,2-dione bisaryldiazoethene (Table 1). Here the structure **1** cannot arise. The $\mathbf{2} \rightleftharpoons \mathbf{3}$ equilibrium can be excluded because in a variable temperature nmr study [9] between -83° and 60° this cyclic $\rightleftharpoons$ acyclic equilibrium of compound **4e** was directly observed as a degenerate rearrangement and the rate of intramolecular exchange of the aryl rings between the two environments in **4e** at 40° in hexadeuteriodimethyl sulfoxide was found to be three orders of magnitude faster than the rates of the intermolecular reaction of the series **4** with dimethyl acetylenedicarboxylate. Variable temperature proton nmr spectra of compound **4a** also showed broadened signals due to rapid

Table 1

Kinetic Results ($k \times 10^3$, $\text{dm}^3 \cdot \text{mol}^{-1} \cdot \text{s}^{-1}$) for Substrates 4 with Dimethyl Acetylenedicarboxylate at 37°

No.	Y	MeO	Me	H	Br	NO ₂
1	$k_{\text{(acetone)}}$ [a]	1.7 [b]	19 [d]	42 [d]	36 [d]	18 [f]
2	$\Delta H^\ddagger$ (kJ·mol ⁻¹)	44 [c]	—	28 [e]	—	36 [9]
3	$\Delta S^\ddagger$ (J·mol ⁻¹ ·K ⁻¹)	-157	—	-182	—	-163
4	$k_{\text{(acetonitrile)}}$	8.7	—	133	—	27
5	$k_{\text{(toluene)}}$	0.55	—	10	—	11
6	$k_{\text{(ethyl acetate)}}$	0.58	—	14	—	13

[a] Solvent E_T values [11], acetone 42, acetonitrile 46, toluene 34, ethyl acetate, 38. [b] Wavelength for kinetics 440 nm. [c] $k_{\text{(acetone)}} \times 10^3$, (T°) 3.0 (50), 0.73 (25). [d] Wavelength for kinetics 400 nm. [e] $k_{\text{(acetone)}} \times 10^3$, (T°) 70 (50), 27 (25). [f] Wavelength for kinetics 460 nm. [g] $k_{\text{(acetone)}} \times 10^3$, (T°) 31 (50), 9.3 (25).

exchange of the *N*-aryl rings. In such kinetic systems the rapid pre-equilibrium does not influence the slower second order kinetics of the cycloaddition process [10]. The rates of reaction of the series 4 with dimethyl acetylenedicarboxylate at 37° in acetone are shown in the Table 1

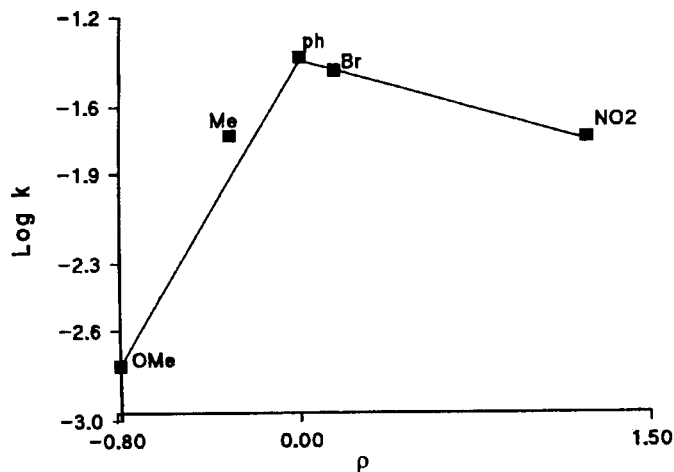


Figure 1. Hammett plot using resonance exalted σ_p^+ and σ_p^- values for substituents [11].

(row No. 1). The rates were second order being first order in *each* reactant thereby confirming no kinetic influence from any pre-equilibria. The Hammett plot (Figure 1) is an inverted V shape with both electron donating and withdrawing groups inhibiting the reaction. For a dipole HOMO controlled reaction electron donating substituents, which raise the energy of the HOMO, should lower the HOMO-LUMO gap in the transition state, and enhance the reaction. The observed behaviour is therefore surprising. To explore a possible change of mechanism the two extreme cases 4a and 4e were examined in detail. It was found that (i) synthetic reactions with dimethylmaleate and dimethylfumarate showed that the stereospecificity of the reaction was retained throughout the series; (ii) the thermodynamics of activation (Table 1, rows 2,3) showed

little change and in particular the high negative entropy which is characteristic of a cycloaddition was retained; (iii) the relative insensitivity of the rates to solvent polarity was retained throughout the series (Table 1, rows, 1, 4, 5, 6). For the compounds 4a, 4c and 4e there was no correlation of rates with the solvent polarity E_T values and a small positive solvent effect which appears to be present is not significant. For a change to a mechanism involving a two-step dipolar intermediate solvent factors of ca.1000 times would be expected in the magnitude of the rate constants for $k_{\text{(acetonitrile)}}/k_{\text{(toluene)}}$ [7a]. All of these results support a concerted cycloaddition with no change in mechanism through the series of substituents Y in the substrates 4.

We believe the substituent effects are due to separate strong resonance stabilizations of the 1,3-dipole. Most studies on planar 1,3 dipoles have envisaged an attack of the dipolarophile from above the terminal atoms of the dipole or, in certain cases, in plane with the dipole. Most theoretical studies have not used large substituents on the dipole such as phenyl groups. It is thus instructive to calculate conformational changes of the present dipole with a variety of phenyl and methyl substituents on the triazole. For the first theoretical study, a conformational energy map is calculated for the 1,2,3-triazolium-1-*N*-phenylimide 1,3-dipole, (3, H atoms at all triazole ring sites). An energy map over 180° is obtained for the rotation of the phenyl group around the unsubstituted triazole ring.

Using analytical second derivatives to calculate equilibrium and transition state points, slightly different results are obtained with the 3-21G and 6-31G basis sets. Each gave a minimum where the twist of the phenyl group is ca. 20° out of the plane of the triazole ring, on the C atom side (24.5°, 3-21G; 23.5°, 6-31G). Each set gave transition states where the phenyl C1 atom eclipses the triazole C-5 and N-2 atoms. The difference arose in that the 3-21g basis set finds a minimum at a twist angle of 43.1° from the triazole N-2 atom and a transition state at 89.3° from the triazole C-5 atom. These points are missing in the 6-31G case, which finds a fairly flat surface in this region. A very similar surface is found for the 6-31G(d) basis set (Table 2).

Table 2
Relative Energies (kJ) for Imide *N*-Phenyl Rotation in 3

twist	3-21G	6-31G	6-31G*
0°	5.52	6.44	4.06
25°	0.0	0.0	0.0
90°	7.59	—	—
135°	4.27	—	—
180°	12.43	17.99	14.23

In all cases two positive vibrational frequencies at less than 100 cm⁻¹ were found. These correspond to phenyl twist and ring breathing. Only in the transition states was

there a negative frequency which corresponds to the phenyl rotation.

In the next study an additional phenyl group was placed on the triazole N-2 atom. Using the geometric parameters found for the energetically lowest point in the above cases as a starting point, optimization at the 3-21G or 6-31G levels resulted in a minimum at ca. 90°. No negative frequencies were found and the low positive ones corresponded to those found in the monophenyl case. Similar findings were obtained for trisubstituted cases with N-2,C-5-diphenyl (Figure 2) and also N-2-phenyl, C-2-methyl and the N-2,C-5-dimethyl.

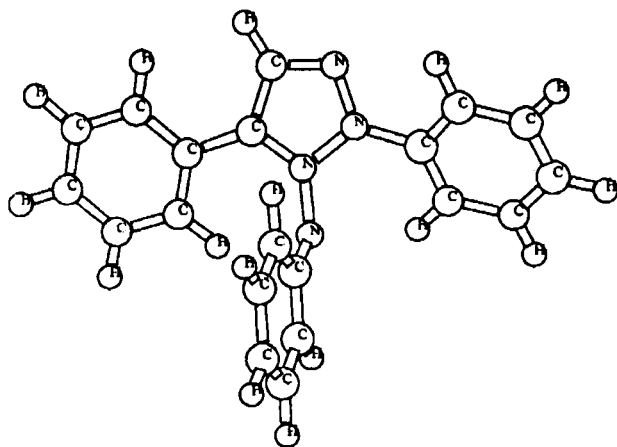
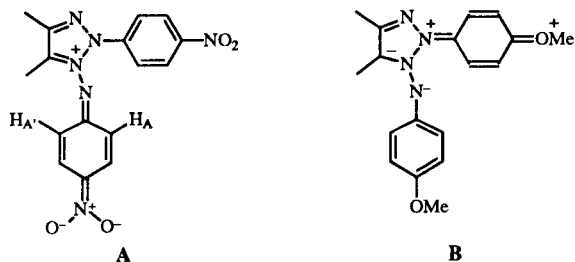


Figure 2. Optimised structure of the dipole 3, (4-C-R, R = H).

The calculations indicate that in the case of the exocyclic *N*-imidophenyl substituted, dipole 3 there is a zwitterionic structure with the positive charge in the triazole ring while the negative charge on the exo imido N atom lies *perpendicular* to the triazole ring and is stabilized by the bonded phenyl ring (Figure 2). The main influence of electron withdrawing Y-substituents in 3 and 4 is to stabilize the negative charge and make the imido N less reactive (Structure A). Electron donating Y-substituents exert



a major stabilizing influence on the positive triazolium end of the 1,3-dipole as in structure (B). The combination of these effects is that both electron-donating and electron-withdrawing substituents reduce the reactivity of the dipole thereby giving rise to the unusual Hammett plot.

EXPERIMENTAL

The substrates 4 and products were prepared as previously described [1-3,9]. The rate constants were measured by following the disappearance of the dipole at the wavelengths shown (Table) using a Philips PU8740 UV-VIS scanning spectrophotometer equipped with an interval timer and a constant temperature cell compartment. Temperatures were accurate to $\pm 0.5^\circ$. The accuracy of reproduction on the rate constants was $\pm 2.5\%$. Rates were measured under pseudo-first-order conditions with the dipolarophile present in a molar excess of at least 2500. The pseudo-first-order rate constants k_1 , were obtained from straight-line plots of $\ln(A_t - A_\infty)$ vs. t ; the slopes of which were $-k_1$. The k_1 values gave linear plots with the initial concentration of the dipolarophile (as expected for normal second order reactions) and the second order rate constants k (Table) were the slopes of these lines. The rate constants quoted are the mean values of at least 3 runs but in most cases rates were repeated from fresh substrates six times.

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