Triazolines V (1a). Dipolar Aprotic Solvents and Steric Acceleration Effects in 1,3-Cycloaddition Reactions. Electronic *vs* Steric Control

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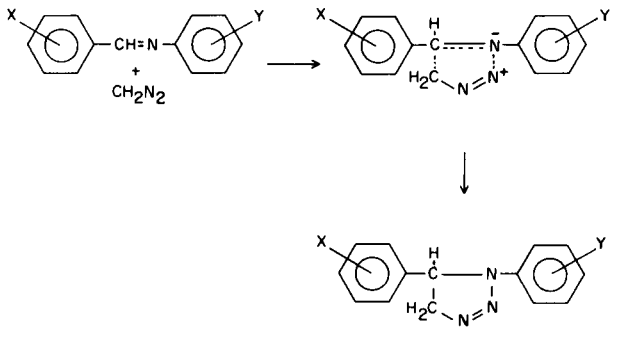
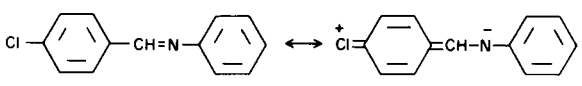
The various known steric factors in 1,3-cycloaddition reactions have a definite decelerating effect (2). However. in the cycloaddition of diazomethane to Schiff bases (3), we have found for the first time, that the *ortho* substituent groups on the C-phenyl of the Schiff bases, have an accelerating effect on the reaction (Table I). The rate enhancing factor appears to be one of steric origin; since a number of experimental results clearly indicate the existence of mesomeric effects in the *para* substituted compounds, it appears logical that the rate acceleration in the *ortho* isomers arises from steric inhibition of resonance. The *o*-substituents apparently twist the



phenyl out of resonance conjugation with the C=N bond, thereby raising the ground state energy of the Schiff base and as a result, the energy gap between the ground and activated states is diminished. All available experimental data support this hypothesis.

While resonance effects are generally known to be predominent in the nitro and methoxy groups, this is not usually the case with the chloro substituent. The existence



of mesomeric double bonding of the type in the *p*-chloro compound was first indicated by the low rate constant (lower than that for the benzalaniline itself) for the addition reaction (4) (Table I). This is further supported by our observations on solvation effects and the role of protic-dipolar aprotic solvents in 1,3-cycloaddition reactions (1). Though the cycloaddition of diazomethane to Schiff bases is essentially a concerted process, and is not generally dependent on solvent polarity, a fourfold increase in rate is obtained when the diazomethane-*p*-chlorobenzalaniline reaction is run in a dipolar aprotic solvent such as DMF (1) (Table I). This rate increase apparently results from better solvation of the negatively charged transition state, relative to the reactants; the ground state mesomerism, reflected to a certain degree in the transition state, would lead to a polarizable transition complex which is better solvated in DMF (1). The threefold increase in DMF relative to dioxane for the *p*-nitro and methoxy compounds, similarly, reveals resonance conjugation in these compounds.

In the *ortho*-substituted compounds steric inhibition of resonance would lead to a less polarizable transition state, and as a result the latter would be less solvated in DMF. And indeed, the failure to obtain rate increases for the *o*-compounds comparable to those found in the *p*-isomers, upon transfer from dioxane to DMF, clearly indicates steric inhibition of resonance in the former. In fact, when studying steric effects in cycloaddition reactions, it is important to use an inert solvent medium, as these effects become more apparent in an inert solvent where no solvation effects are involved (1).

Ultraviolet absorption data on the *p*- and *o*-substituted compounds (7) (Table II) also bear evidence for the proposed model. The absorption maxima corresponding to the π-π^* benzenoid band, clearly indicate a lengthening of the π system in the *p*-compounds and a shortening of the same in the *o*-compounds. The U.V. data are strikingly in accord with the kinetic results.

TABLE I

Second Order Rate Constants for the Addition of Diazomethane to *p*-, *m*- and *o*- Substituted Schiff bases at 24.9°

C-Phenyl Substituent X	$k_2 \times 10^2$ l. mole^{-1} hour^{-1} DMF			Dioxane	
	p-	*m*-	*o*-	*p*-	*o*-
H	2.0	—	—	3.5	—
NO_2	24.5	24.5	27.1	7.6	17.4
Cl	6.1	5.6	16.2	1.5	8.7
OCH_3	1.6	—	5.6	0.81	3.2

TABLE II

Comparison of Absorption Maxima Corresponding to the π-π^* Benzenoid Band for the *p*- and *o*- Substituted Schiff bases in Ethanol.

	λ max (mμ) in Ethanol.			
	H	NO_2	Cl	OCH_3
p-Compounds	263.5	289.5	269	284.5
o-Compounds	—	260	261	265

Chemical data also support the conclusions derived (3,4,5), the yields of the triazoline adducts from the *ortho* substituted anils being consistently higher than those obtained from the corresponding *p*-substituted compounds.

Our observations on these steric acceleration effects have led us to doubt the validity of steric factors claimed to override electronic control in certain cycloaddition reactions (2,6). Also, our results contradict the general thought, that conjugation always enhances dipolarophilic reactivity (6) in 1,3-cycloaddition reactions, in two ways; first, by stabilizing the partial charge formed in the transition state through resonance (1,3,6) and second, by increasing the polarizability of multiple bonds, thereby increasing the mobility of the bonding electrons and hence facilitating the cyclic addition process (6).

The results presented in Table I indicate, that, in the present case, increased conjugation in the dipolarophile (*p*-substituted compounds) does not contribute to increased reactivity. This means that the resonance stabilization of the ground state resulting from increased conjugation should not be neglected, when considering dipolarophilic reactivity. For example, in the cycloaddition reactions of styrenes and stilbenes, the lower reaction rate for the latter is usually attributed to an inhibiting steric effect of the second phenyl group that exceeds the activation resulting from extended conjugation (6). However, in view of our observations, it appears that the decrease in rate constant for stilbenes relative to styrenes is not solely the result of an inhibiting steric effect; it is, at least partly, due to resonance stabilization of the ground state.

Furthermore, increased electron mobility in itself in a conjugated system does not seem to contribute much to dipolarophilic activity, as evidenced by the examples of *p*-chloro and *p*-methoxy benzalanilines. The primary factor that determines dipolarophilic activity appears to rest largely on charge stabilization in the transition state and unless the direction of electron shift favours charge stabilization in the transition complex (as for example, in the transition complex from the reaction of *p*-chlorobenzalaniline, the mesomeric effects are unfavorable for negative charge stabilization in the transition state), it is hardly likely that dipolarophilic activity can be attained through electron mobility alone in conjugated systems.

EXPERIMENTAL

Rate Measurements.

The Schiff bases required for the kinetic studies were synthesized by known methods by reacting the appropriate aldehydes with the amines and were purified by distillation under reduced pressure or by crystallization from suitable solvents (3).

Rate constants for the addition of diazomethane to Schiff bases were determined by the pseudo first order technique described earlier (4). The solvents used for the kinetic runs were all of reagent grade quality. The diazomethane solutions were prepared in the solvent that was used for the reaction medium and in the case of DMF, blank experiments indicated no reaction between the solvent and diazomethane.

U.V. Data.

The absorption maxima for the *o*- and *p*-substituted Schiff bases were determined in ethanol solution, using a Beckman DB-G grating spectrophotometer.

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