(4+2)-CYCLOADDITIONS OF SUBSTITUTED ARENEDIAZOCYANIDES A KINETIC STUDY OF A NEW DIENOPHILE

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Abstract the rate constants of the (4+2)-cycloaddition reaction between substituted E-arenediazocyanides and 2,3-dimethyl-1,3-butadiene have been determined in several solvents. The reaction displays linear Hammett behavior, the data suggest a concerted reaction mechanism

Since the initial use of azoesters by Diels and Alder,¹ many different types of azo compounds have been successfully used as (4+2)-cycloaddition reaction partners ² However, this general reactivity toward conjugated dienes has not been realized for <u>aromatic</u> azo dienophiles ³ We have recently reported the successful utilization of <u>E</u>-arenediazocyanides <u>2</u> as cycloaddition reaction partners with a wide variety of dienes to form novel reduced pyridazine ring systems <u>3</u> ⁴ We further observed that the arenediazocyanides, when reacted with unsymmetrical dienes, exhibited a variable degree of regioselectivity, depending upon the particular phenyl substituent of the azo compound Thus, when <u>trans</u>-piperylene <u>1a</u> was reacted with parasubstituted arenediazocyanides, the major regionsomer <u>3</u> was obtained in ratios of <u>ca</u> 8 1 (2g), 4 1 (2c), and 2 1 (2f)



The variable regioselectivity of this system can be rationalized in terms of a two-step process involving a dipolar, or zwitterionic intermediate, (Scheme), whose orientation depends upon the relative ability of the nitrogen atoms to stabilize the developing negative charge. Such a model has been invoked for several unsymmetrical cycloadditions involving heteratomic dienophiles 5 In this particular reaction, the aryl-substituted nitrogen competes effectively with the cyano-nitrogen as the substituent \underline{X} becomes more electronegative

However, the observed regiochemistry is also consistent with a concerted, one-step mechanism based upon a frontier molecular orbital (FMO) approach, which considers the energies and terminal coefficients of the dominant interacting orbitals Following generalizations made by Houk, 6 the relative magnitudes of the HOMO(diene) and LUMO(dienophile) terminal coefficients is predicted to be that shown in the Scheme below, assuming that the cyano group has a greater inductive effect than the phenyl group Preferential bonding of the larger terminal coefficients leads to the observed regiochemistry Of course, as substituent \underline{X} becomes more electron-withdrawing, the difference between these coefficients in the LUMO(dienophile) becomes less pronounced, and the regioselectivity of the cycloaddition declines

Scheme



Since the arenediazocyanides represent a new family of dienophiles, we were interested in categorizing their cycloadditions within these two mechanistic extremes We therefore initiated some kinetic studies, selecting as a model reaction the cycloaddition of 2 with 2,3dimethyl-1,3-butadiene (DMBD, <u>1b</u>), (which affords a single product and proceeds readily under mild conditions) The second-order rate constants for the reaction of <u>2a-f</u> with <u>1b</u> were determined in deuterated chloroform at $35^{\circ}C^{-7,8}$ Additionally, the analogous rate constants for the reaction of <u>2c</u> were determined in several other solvents at the same temperature The data obtained are presented in the table below

Compound No	X (o-Value) ⁹	Solvent	$k_2 \times 10^5 (M^{-1} sec^{-1})$	Linear Corr Coeff
2a	н (о)	CDC13	4 2	0 948
2b	F (+0 06)	CDC1	79	0 999
2c	C1 (+0 23)	CDC1	23	0 999
2d	Br (+0 23)	CDC1	21	0 997
2e	COOEt (+0 45)	CDC1	65	0 994
2f	NO ₂ (+0 78)	CDCI	1100	0 991
2c	c1 ์	acetone-d ₆	22	0 999
2c	C1	CH ₃ CN-d ₃	30	0 998
2c	C1	DMSO-d6	84	0 999

Second-Order Rate Constants for Arenediazocyanide Cycloadditions with DMBD at 35⁰C

A Hammett-type plot of log (k_x/k_H) versus the σ_p -values⁹ of the arenediazocyanide substituents displayed excellent linear correlation, (r = 0 994), with a corresponding slope ρ = +2 97



The ρ -value obtained from this reaction series is unusually high for a (4+2)-cycloaddi-Comparable values (ca +2 5) have been reported only for some cycloadditions tion reaction of substituted nitrosoarenes 10 Classically, ρ -values of this magnitude have been interpreted as indicating a significant degree of charge-buildup in a rate-determining transition state However, as recently pointed out by Sauer and Sustmann¹¹, (2+2)-cycloadditions of cyanoethylenes, (which proceed via zwitterionic intermediates), are generally characterized by much higher absolute ho-values, (ca 6-7) Thus, a value of +2 97 is insufficient to justify a true ionic intermediate for the arenediazocyanide-DMBD reaction This conclusion is further supported by the relative insensitivity of the reaction rate toward changes in solvent polar-As shown in the table, the reaction rate of $\frac{2c}{2c}$ in acetone-d₆ is essentially identical ity to the rate in CDCl₃, and increases by only a factor of four in DMSO-d₆ Such solvent insensitivity is typical of concerted (4+2)-cycloadditions, while (2+2)-reactions involving ionic intermediates generally display rate accelerations of several powers of ten 11

Thus, the kinetic data for this reaction support a symmetry-allowed, concerted process, most likely involving an unsymmetrical transition state having some degree of partial charges 11,12 It is interesting to note that our previously-reported⁴ entropy of activation for the reaction of <u>2c</u> with DMBD, (-26 9 eu), is slightly less than the value (-33 eu) reported for the reaction of some nitrosoarenes with the same diene. This difference suggests a less highly-ordered transition state for the arenediazocyanide reaction, which is consistent with its higher ρ -value

Several workers¹³ have recently interpreted such non-zero p-values for cycloaddition reactions as indicative of the magnitude of the energy gap between the interacting frontier molecular orbitals. Accordingly, the positive p-value indicates that these cycloadditions are

of the "normal" type,¹¹ with the privileged, or dominant FMO interaction occuring between the HOMO(diene) and LUMO(azocyanide), the usual case for electron-deficient enes. Further, the relatively large ρ -value suggests that these interacting FMO's are separated by only a small mean energy gap. Further investigations are planned in order to determine the pertinent FMO energy levels of the arenediazocyanides, and relate these to the rate constants

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- 7 Arenediazocyanides were synthesized according to procedures reported in reference 4
- 8 Rate constants were determined via 60 MHz ¹H-nmr spectroscopy, using equimolar initial concentrations of diene and azocyanide, (<u>ca</u> 0 25M) in the appropriate solvent Repetitive integrations were performed to measure the concentration of diene (vinyl protons, δ <u>ca</u> 5 0 ppm) and concentration of cycloadduct (allylic protons, δ <u>ca</u> 3 8 ppm) versus time Plot of ratio [cycloadduct]/[diene] versus time yields straight line, with slope = k₂a, (a = initial concentration), and linear correlation coefficients as noted Temperature was maintained at 35 \pm 1° C via constant-temperature controller, and measured by ethylene glycol standard
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