Tetrahedron Letters No.10, pp. 703-706, 1970. Pergamon Press. Printed in Great Britain.

THE MECHANISM OF CYCLOADDITION OF DIPHENYLKETENE WITH AZO COMPOUNDS

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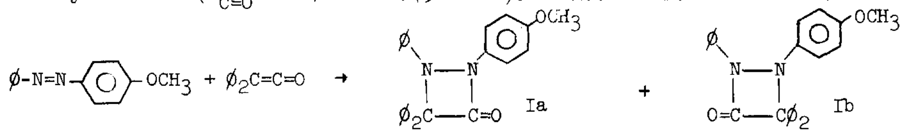
(Received in USA 29 December 1969; received in UK for publication 22 January 1970)

Although Staudinger reported in 1912[1] the cycloaddition of ketenes and azo compounds to give diazetidinones, little mechanistic work has been done on this [2+2] cycloaddition. In contrast, cycloadditions of ketenes with alkenes[2] and enol ethers[3] have been found to be largely concerted, based primarily on stereospecificity and small solvent effects on rates. Cycloadditions of ketenes with enamines[4] and imines[5] occur at least in part by a two-step ionic process, based upon trapping of dipolar intermediates and large solvent effects on reaction rates.

Since only cis-azobenzenes react with ketenes at room temperature,[6] the trans-isomers being inert, the cycloaddition reaction is usually run by irradiating mixtures of trans-azo compound and ketene, the ketene trapping photogenerated cis-azo compound in situ.[7] On allowing p-(phenylazo)anisole to react with diphenylketene in this manner, comparable amounts of the two isomeric diazetidinones Ia and Ib, which could not readily be separated, were indicated by infrared ($\nu_{C=O}$ at 1786 and 1752 cm^{-1}). Since the reaction did not seem to be very sensitive to substitution on the phenyl rings of azobenzene, we undertook to study azo compounds having different substituents on the azo group itself. The compounds investigated were of the type ϕN=N-R [R = $-CO_2Et$, $-\phi$, $-CH(CH_3)_2$, and $-N(CH_3)_2$].



Of the trans-azo compounds investigated, only ethyl phenylazocarboxylate undergoes cycloaddition with diphenylketene,[8] forming diazetidinone II, the structure based on chemical degradation results.[8b] These compounds react at 25° with a second-order rate constant of 3.9×10^{-3} M^{-1} sec^{-1} in cyclohexane, 11.7×10^{-3} M^{-1} sec^{-1} in acetonitrile. Irradiation of the reaction mixture* causes marked acceleration of the reaction by converting trans-azoester to cis, but does not change the product; II was isolated in 69% yield.[9]

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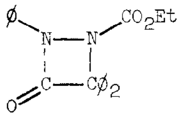
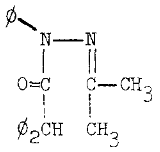
*All irradiations used light from a "Uviarc" 360-watt lamp, filtered through a 5% $CuSO_4$ soln. $\lambda > 310$ nm.

Irradiation of an otherwise stable mixture of trans-azobenzene and diphenylketene is accompanied by rapid loss of diphenylketene due to cycloaddition to form 1,2,4,4-tetraphenyldiazetidinone, isolated in 76% yield. We have found that cis-azobenzene, generated by irradiation of an azobenzene solution prior to addition of diphenylketene, reacts with the ketene at the rate of $2.1 \times 10^{+2}\ M^{-1}\ sec^{-1}$ in cyclohexane, $20 \times 10^{+2}\ M^{-1}\ sec^{-1}$ in acetonitrile, both at 25°. This is substantially faster than any other ketene cycloaddition reported to date.

Trans-phenylazoisopropane[10] ($n \rightarrow \pi^*$ band at 403 nm, ϵ 137) reacts with diphenylketene by an "ene" reaction[11] to give III, identical to the product of reaction of the ketene with acetone phenylhydrazone. No evidence of cycloaddition can be detected. Irradiation of the azo compound with light of wavelength >310 nm causes a shift of the $n \rightarrow \pi^*$ band to shorter wavelength and an increase in absorbance. Addition of diphenylketene causes rapid return of the maximum to its original wavelength, with absorbance falling to less than the original value, indicating conversion of trans-azo compound to cis, which then reacts rapidly with diphenylketene. Irradiation of a mixture of phenylazoisopropane and the ketene produces only one diazetidinone, IV, in 11% yield,[9] in addition to a large quantity of III. The structure of IV is assigned based on its analysis, infrared ($\nu_{C=O}$ 1770 cm^{-1}), nmr (isopropyl


II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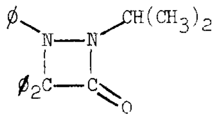
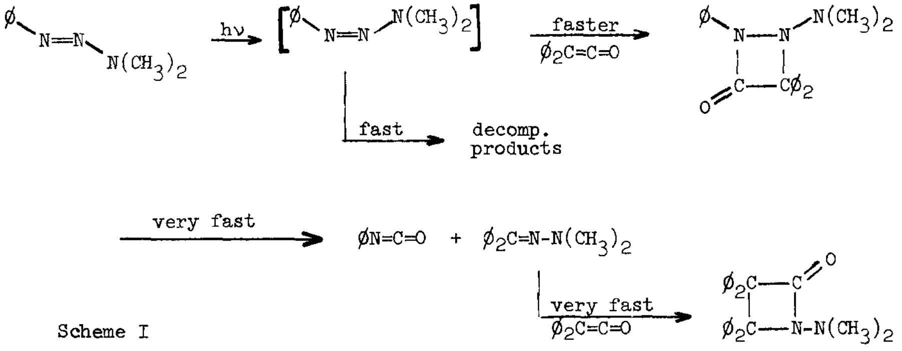

IV

CH septet at δ 3.72) and mass spectra [fragments at m/e 257 ($\phi_2C{=}N\phi^{+\cdot}$), and 180 $\phi C{\equiv}N\phi^{+}$)].

No reaction occurs when trans-1-phenyl-3,3-dimethyltriazene[12] is stirred with diphenylketene for four days in CCl_4. However, irradiation with light of wavelength >310 nm causes rapid reaction. After four hours, 55% of the starting triazene can be recovered, plus a 25% yield of phenyl isocyanate and a 35% yield of 1-(dimethylamino)-3,3,4,4-tetraphenylazetidinone, V. These results are interpreted as shown below. (Scheme 1). The azetidinone V was identical to the product which formed very quickly on reaction of benzophenone dimethylhydrazone with diphenylketene.

Reactions of a five-fold excess of diphenylketene with ethyl trans-phenylazocarboxylate, cis-azobenzene, and cis-1-phenyl-3,3-dimethyltriazene were conducted in order to trap possible dipolar intermediates as 2:1 adducts.[4,5]

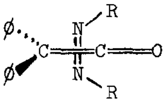


V

Scheme I

In all cases, only 1:1 adducts identical to those described above were obtained; no evidence of 2:1 adducts was obtained. Similarly, cis-azobenzene and diphenylketene gave essentially the same yield of 1,2,4,4-tetraphenyldiazetidinone in cumene as in benzene or carbon tetrachloride, arguing against a diradical intermediate.

These results (high reactivity of cis isomers, absence of trappable intermediates, very small solvent effect on reaction rates) are most consistent with a concerted cycloaddition of azo compound to ketene, analogous to that proposed by Woodward and Hoffmann[13] for alkene-ketene cycloadditions. In the scheme proposed, the reactants align themselves as pictured below, an orientation which is electrostatically most favorable, and which is stabilized by favorable overlap between the bonding π-orbital of the azo compound and the low-lying antibonding orbital of the ketene.[13] In support of this idea, we have found that isocyanates, which lack this low-lying antibonding orbital, do not undergo cycloaddition with azo compounds,



even under very stringent conditions (e.g. p-nitrophenyl isocyanate and azobenzene do not react during 22 hours heating at 205°).

The specific diazetidinone obtained from unsymmetrical azo compounds seems most readily understood in terms of attack by the more nucleophilic nitrogen in each case. This implies some dissymmetry in the rate of formation of the two new C-N bonds, with the bond to the carbonyl being more developed than the other bond in the transition state, and with some consequent charge separation. Such a process has also been established for cycloadditions of ketenes and enol ethers.[3]

Acknowledgements: This work has been supported by a grant from Rohm and Haas Company, to whom we express our appreciation. T.J.R. was supported in part as a NASA Trainee, for which we are also grateful.

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