Reactivity of Fulvenes. Nucleophilic Displacement by Piperidine in 6-*p*-Tolylsulphonyloxyfulvene

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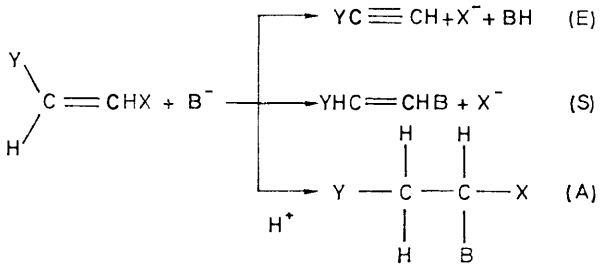
The reaction of 6-*p*-tolylsulphonyloxyfulvene with piperidine in several solvents has been followed kinetically by means of the stopped-flow technique. The high reactivity observed is attributed to the intervention of an intermediate which involves delocalization of the negative charge into the five-membered ring. The lack of catalysis by the reacting amine, the absence of an isotope effect when *N*-deuteriopiperidine is the reagent, and other observations lead to the conclusion that the formation of the intermediate is rate determining and its decomposition occurs in a fast step.

NUCLEOPHILIC substitution of olefins activated by electron-withdrawing groups generally occurs readily.[1] If a hydrogen atom is available β to the leaving group, elimination becomes an important competitor.[1] Occasionally a process is observed which, by means of nucleophilic addition, leads to a saturated adduct.[2] These paths are illustrated for a 1,2-disubstituted ethylene in the Scheme, where for the sake of simplicity the reactions which the products often undergo after their formation have not been shown.

Vinylic systems activated by such diverse groups as aryl,[3,4] sulphone,[2,5] sulphoxide,[5b,c] ketone,[6] alkoxycarbonyl,[6e,7] cyano,[7b,c,8] and trifluoromethyl[9] have been



SCHEME Y = Electron-withdrawing group, X = leaving group

investigated. A few reports have also suggested that an olefinic[10-12] or an aromatic[13] system could be activated by groups which can delocalize the negative charge through the formation of the cyclopentadienide system.

[1] For reviews see (*a*) G. Modena, *Accounts Chem. Res.*, 1971, **4**, 73; (*b*) Z. Rappoport, *Adv. Phys. Org. Chem.*, 1969, **7**, 1.

[2] G. Marchese and F. Naso, *Chimica e Industria*, 1971, **53**, 760; G. Marchese, F. Naso, L. Schenetti, and O. Sciacovelli, *ibid.*, p. 843.

[3] G. Marchese, G. Modena, F. Naso, and N. Tangari, *J. Chem. Soc.* (*B*), 1970, 1196; G. Marchese, G. Modena, and F. Naso, *ibid.*, 1968, 958; *Tetrahedron*, 1968, **24**, 663; A. Giametta, G. Marchese, and F. Naso, *Gazzetta*, 1971, **101**, 247; G. Marchese, F. Naso, and V. Sgherza, *ibid.*, p. 251.

[4] S. I. Miller and P. K. Yonan, *J. Amer. Chem. Soc.*, 1957, **79**, 5931; P. Beltrame, P. L. Beltrame, M. L. Cereda, and G. Lazzerini, *J. Chem. Soc.* (*B*), 1969, 1100 and previous papers in this series; M. D. Johnson and B. S. Meeks, *ibid.*, 1971, 185; M. Schlosser and M. Zimmermann, *Chem. Ber.*, 1971, **104**, 2885 and previous papers in this series.

[5] (*a*) L. Di Nunno, G. Modena, and G. Scorrano, *J. Chem. Soc.* (*B*), 1966, 1186; (*b*) F. Montanari, *Boll. sci. Fac. Chim. ind. Bologna*, 1958, **16**, 31 and earlier papers in this series; (*c*) G. Modena, *Ricerca sci.*, 1958, **28**, 341.

[6] (*a*) D. Landini, G. Modena, F. Montanari, and F. Naso, *J. Chem. Soc.* (*B*), 1969, 243; (*b*) D. Pitea and G. Favini, *J.C.S. Perkin II*, 1972, 291; (*c*) P. Beltrame, G. Favini, M. G. Cattania, and F. Guella, *Gazzetta*, 1968, **98**, 380; (*d*) M. I. Rybinskaya, A. N. Nesmeyanov, and N. K. Kochetkov, *Russ. Chem. Rev.*, 1969, **38**, 433; (*e*) W. E. Truce and M. L. Gorbaty, *J. Org. Chem.*, 1970, **35**, 2113.

[7] (*a*) D. E. Jones, R. O. Morris, C. A. Vernon, and R. F. M. White, *J. Chem. Soc.*, 1960, 2349; (*b*) G. Pattenden and B. J. Walker, *J. Chem. Soc.* (*C*), 1969, 531; (*c*) F. Théron, *Bull. Soc. chim. France*, 1969, 278.

[8] F. Scotti and E. J. Frazza, *J. Org. Chem.*, 1964, **29**, 1800.

[9] J. D. Park and E. W. Cook, *Tetrahedron Letters*, 1965, 4853; D. J. Burton and H. C. Krutzsch, *J. Org. Chem.*, 1971, **36**, 2351.

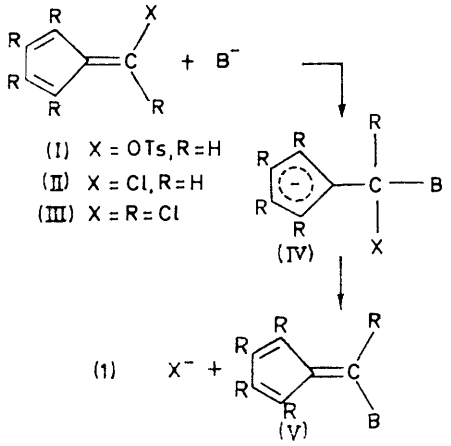
[10] K. Hafner, W. Bauer, and G. Schulz, *Angew. Chem. Internat. Edn.*, 1968, **7**, 806.

[11] E. T. McBee, E. P. Wesseler, R. Hurnaus, and T. Hodgins, *J. Org. Chem.*, 1972, **37**, 1100.

[12] M. B. D'Amore and R. G. Bergman, *Chem. Comm.*, 1971, 461.

[13] M. J. Perkins, *Chem. Comm.*, 1971, 231.

Accordingly, 6-*p*-tolylsulphonyloxy-, 6-chloro-, and hexachloro-fulvene [10-12] (I)—(III) react with nucleophiles giving substitution products probably through an intermediate of the type (IV).



Quantitative data and mechanistic information on this rather novel activation are lacking [14] and therefore a kinetic investigation appeared to deserve attention. The reaction of the readily accessible [10] 6-*p*-tolylsulphonyloxyfulvene (I) with piperidine was suitable for the fulfilment of this aim.

RESULTS

The reactions of (I) with piperidine in a variety of solvents led to the quantitative formation of 6-piperidinofulvene (V; B = NC_5H_{10}, R = H), m.p. 66—67° (from cyclohexane).[15] The rates of reactions were found to be very high and the use of a stopped-flow instrument was necessary. Pseudo-first-order conditions were obtained by employing piperidine in large excess over the substrate. By changing the initial concentration the reaction was shown to be first order in amine. The relevant data are in Table 1. Activation parameters for the various solvents are in Table 2.

TABLE 1

Rate coefficients [a] for the reaction of 6-*p*-tolylsulphonyloxyfulvene ($1{\cdot}2 \times 10^{-5}$M) with piperidine in various solvents

10[Piperidine]/M	Method [b]	k/l mol^{-1} s^{-1} 18°	25°	35°
Solvent : methanol				
0·2	A		3·42	5·51
0·2	D		3·43	5·52
0·5	A	2·51	3·38	5·67
0·5	D	2·45	3·57	5·78
1·0	A	2·53	3·45	5·66
1·0	D	2·43	3·40	
2·0	A		3·33	5·72
2·0	D		3·43	5·80
Solvent : ethanol				
0·1	A	3·17	4·32	
0·2	A	3·16	4·31	7·13
0·5	A	3·22	4·66	7·29
0·7	A	3·22	4·30	
1·1	A	3·26	4·57	7·44
Solvent : propan-2-ol				
0·1	A			9·53
0·1	D			9·12
0·2	A	4·49		9·29
0·2	D	4·48	6·20	9·41
0·5	A	4·43	6·01	9·87
0·5	D	4·48	5·99	
1·0	A	4·50		9·83
1·0	D	4·38	6·09	
2·0	A	4·58	5·75	
2·0	D	4·52	6·09	
Solvent : chloroform				
0·1	A	25·4		39·7
0·1	A		30·4 [c]	
0·2	A	25·8	30·0	38·9
0·2	A		29·0 [c]	
0·5	A	25·6		
0·5	A		29·8	
1·0	A	25·0	29·1	37·1
1·0	A		29·5 [c]	
Solvent : acetonitrile				
0·1	A	150	171	210
0·2	A	148	171	215
0·5	A	144	169	211
1·0	A	146	169	209

[a] Second-order rate coefficients obtained by dividing pseudo-first-order rate coefficients by the amine concentration. [b] A and D refer to reactions where the appearance of the substitution product and the disappearance of the starting material were followed, respectively. [c] The concentration of the substrate was $2{\cdot}5 \times 10^{-5}$M.

TABLE 2

Activation parameters for the reaction of 6-*p*-tolylsulphonyloxyfulvenes with piperidine in various solvents [a]

Solvent	E_a/ kcal mol^{-1}	$\Delta H^{\ddagger}$/ kcal mol^{-1} [b]	$\Delta S^{\ddagger}$/ cal mol^{-1} K^{-1} [b]
MeOH	8·7	8·1	−28·9
EtOH	8·6	8·0	−28·6
$(Me)_2CHOH$	7·9	7·3	−30·4
$CHCl_3$	4·4	3·8	−39·0
MeCN	3·8	3·2	−37·5

[a] Probable errors are ±0·5 kcal mol^{-1} for E_a and $\Delta H^{\ddagger}$, ±1·5 cal mol^{-1} K^{-1} for $\Delta S^{\ddagger}$. [b] At 25°.

TABLE 3

Deuterium isotope effect in the reaction of 6-*p*-tolylsulphonyloxyfulvene with piperidine in chloroform at 25° [a]

10[$C_5H_{10}ND$]/M	Method [b]	k/l mol^{-1} s^{-1}
0·1	A	27·9
0·2	A	28·4
0·3	A	28·1
1·0	A	27·5
	A	29·6 [c]

[a] [(I)] = $1{\cdot}3 \times 10^{-5}$M. [b] As in Table 1. [c] Average of the values reported in Table 1 for $C_5H_{10}NH$.

The rate of the reaction of the [1-^{2}H]piperidine was also measured in chloroform at 25°, giving a $k_H : k_D$ ratio of 1·06 (see Table 3). Within the limits of experimental error this value could be considered as unity. A correction for incomplete deuteriation of the amine would not change the result significantly. The product was shown to be (V; B = piperidino, R = H) by i.r. comparison with an authentic sample, thus suggesting the lack of any significant deuterium incorporation (*cf.* below).

[14] For a recent kinetic investigation on the related 9-(α-halogenoarylidene)fluorenes, see Z. Rappoport and A. Gal, *J. Org. Chem.*, 1972, **37**, 1174.

[15] K. Hafner, G. Schulz, and K. Wagner, *Annalen*, 1964, **678**, 39.

DISCUSSION

A relevant feature revealed by inspection of Tables 1 and 2 is the high reactivity of the system. Comparison with the rates of other reactions would illustrate this point, but it cannot be made in a straightforward manner since halide ions have usually been the leaving groups in activated vinylic substitution.[1] However, kinetic data concerning the reactivity of 1-*p*-nitrophenyl-1-*p*-tolylsulphonyloxy-2,2-diethoxycarbonylethylene have recently been reported.[16a] The rate coefficient for the reaction of this substrate with piperidine in acetonitrile at 30° was found to be $1{\cdot}85 \times 10^{-1}$ l mol^{-1} s^{-1} and, therefore, about three orders of magnitude lower than the value which can be extrapolated for our system from the data in Tables 1 and 2 (*e.g.* k at 30° in acetonitrile, 190 l mol^{-1} s^{-1}). Furthermore, if difference in the leaving group is neglected and comparison with the comprehensive series of kinetic data summarized by Rappoport[1b] is made, the unusually high reactivity of compound (I) is again shown. Indeed, among the rate coefficients reported for the reactions of piperidine with various substrates activated by one electron-withdrawing group only the data for 2-benzoyl-1-fluoropropene in ethanol[6c] are comparable with those reported here.

An intermediate of the type (VI) may be advocated to explain the high reactivity observed. The decomposition of this species should occur by equation (2) which also shows that one of the possible pathways, k_3, involves the intervention of a second molecule of the amine. These mechanistic possibilities together with their variations and implications are most frequently met in nucleophilic substitution by amines of vinylic[16,17] or aromatic[18,19] carbon atoms and have been thoroughly discussed. Without repeating the detailed kinetic treatment here, it will suffice to say that the results, *i.e.* the lack of base catalysis and the absence of a significant primary isotope effect, suggest that the formation of (VI) is rate determining and its decomposition occurs rapidly, *i.e.* $k_2 + k_3[C_5H_{10}NH] \gg k_{-1}$.

Within this framework the increase in reactivity observed on going from chloroform to the more polar acetonitrile may be interpreted as the result of the increased polar character of the transition state relative to the initial state.[18] However, an apparent departure from the above behaviour is observed in the series of protic solvents in which the reactivity increases on going from methanol to propan-2-ol. A similar trend has been observed also in the case of sulphonyl-activated systems[17] and it may be explained in terms of increased solvation of the nucleophile in the initial state by the more acidic methanol.[20]

In principle, besides the mechanism presented above, other competing or alternative routes may be operating.[1,16,18] First, a saturated adduct of type (VII) may intervene [equation (3)]. Neutralization of (VI) could occur internally or by abstraction of a proton from the solvent, depending on the nature of the latter. Clearly, the lack of amine catalysis argues against the intermediacy of species (VII). Compound (VII) would be expected to be relatively stable and its decomposition would be catalysed by base. An additional argument against intermediate (VII) is furnished by the equal rate coefficients obtained upon the disappearance of the substrate or appearance of the product. Finally, it seems reasonable to assume that if compounds of the types (VIIa and c) were generated from the deuteriated amine, they would retain the isotopic label partially or completely after decomposition. This was not observed when the reactions with [1-^{2}H]piperidine were performed in chloroform.

It could be argued that the rapid decomposition of intermediate (VI) and the lack of the saturated adduct along the reaction path is a consequence of the high mobility of the *p*-tolylsulphonyloxy-group. However, base catalysis in nucleophilic substitution has been observed for substrates involving groups considerably

[16] (*a*) Z. Rappoport and A. Topol, *J.C.S. Perkin II*, 1972, 1823; (*b*) Z. Rappoport and N. Ronen, *ibid.*, p. 955 and previous papers in this series.

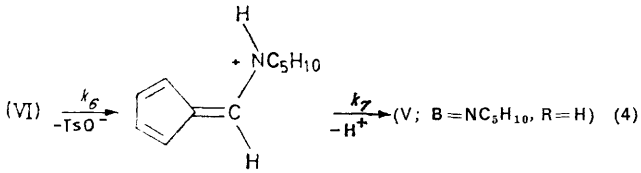
[17] S. Ghersetti, G. Lugli, G. Melloni, G. Modena, P. E. Todesco, and P. Vivarelli, *J. Chem. Soc.*, 1965, 2227.

[18] For reviews on S_NAr reactions see F. Pietra, *Quart. Rev.*, 1969, **23**, 504; J. Miller, 'Aromatic Nucleophilic Substitution,' eds. C. Eaborn and N. B. Chapman, Elsevier, Amsterdam, 1968; Th. J. De Boer and I. P. Dirkx in 'The Chemistry of the Nitro and Nitroso Groups,' eds. S. Patai and H. Feuer, Interscience, New York, 1969, ch. 8.

[19] J. A. Orvik and J. F. Bunnett, *J. Amer. Chem. Soc.*, 1970, **92**, 2417 and previous papers in this series.

[20] F. Naso and A. M. Piepoli, *Ricerca sci.*, 1968, **38**, 427; see also F. Pietra and F. Del Cima, *Tetrahedron Letters*, 1970, 1041.

more reluctant to depart from the carbon atom.[16,18,19] The leaving group effect is an open problem in the fulvene series and information on this aspect would help in clarifying the role of other mechanisms which, although less common than those discussed, cannot be dismissed solely on the basis of the results reported here. For instance, the possibility exists that in the slow step cleavage of the C–O bond only is involved with formation of (VIII) which rapidly loses a proton [16] [equation (4)].



(VIII)

It should be observed that in the foregoing discussion the possibility of a one-step process has been ignored. This approach is in harmony with current views on nucleophilic vinylic substitution.[1] However, rigorously speaking, one cannot rule out a mechanism in which C–N bond formation occurs to a greater extent than C–O cleavage.

EXPERIMENTAL

U.v. and i.r. measurements were taken with Zeiss M4QII and Perkin-Elmer spectrophotometers, respectively. N.m.r. spectra were recorded with a JEOL MH-60-II instrument.

Materials.—Solvents and piperidine were purified by standard procedures.[21] 6-*p*-Tolylsulphonyloxyfulvene, m.p. 47—48° (decomp.) (from ether), was prepared as reported,[10] except that toluene-*p*-sulphonyl chloride was dissolved in tetrahydrofuran and the crude product was purified over silica gel using n-hexane–ether (9 : 1) as eluant. [1-^{2}H]Piperidine was obtained by means of H–D exchange with D_2O according to the procedure of Hawthorne [22] and was *ca.* 90% deuteriated (by n.m.r. analysis).

Kinetic Experiments.—Experiments were performed with a thermostatted Gibson–Durrum stopped-flow apparatus, the appearance of 6-piperidinofulvene being followed at 330 nm in chloroform and at 325 nm in the other solvents. In methanol and propan-2-ol the disappearance of 6-*p*-tolylsulphonyloxyfulvene at 260 nm was also followed.

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[21] J. A. Riddick and W. B. Bunger, jun., in ' Techniques of Chemistry,' ed. A. Weissberger, Wiley–Interscience, New York, 1970, vol. 2.

[22] M. F. Hawthorne, *J. Amer. Chem., Soc.*, 1954, **76**, 6358.