ethyl penicillanate **1f** was added to a MeCN solution of $AgNO_3$ and DBN (1 mol equiv of each, 48 h, 0 °C in the dark, N_2) followed by [(*tert*-butyldiphenylsilyl)oxy]acetyl chloride (1 h, 20 °C), to yield thio ester **7f** (55%). Ozonolysis (CH_2Cl_2, −70 °C) and reductive workup (Me_2S) afforded the oxoamide **9** (92%); penem **10** was thence obtained by plain heating with triethyl phosphite (2 mol equiv, 9 h refluxing toluene, 80%),[15] thus completing a straightforward, three-step penam–penem conversion. Further manipulation of this key intermediate toward the target compound conformed to a well-established pattern.[16,17]

Supplementary Material Available: A listing of physical properties of new compounds **1–7**, **9**, and **10** (6 pages). Ordering information is given on any current masthead page.

(14) Franceschi, G.; Foglio, M.; Alpegiani, M.; Battistini, C.; Bedeschi, A.; Perrone, E.; Zarini, F.; Arcamone, F.; Della Bruna, C.; Sanfilippo, A. *J. Antibiot.* **1983**, *35*, 938–941.
(15) Battistini, C.; Scarafile, C.; Foglio, M.; Franceschi, G. *Tetrahedron Lett.* **1984**, *25*, 2395–2398.
(16) Alpegiani, M.; Bedeschi, A.; Perrone, E.; Franceschi, G. *Tetrahedron Lett.* **1984**, *25*, 4171–4174.
(17) FCE 22101 was obtained from its trichloroethyl ester by hydrolysis with activated Zn in THF–pH 4.2 phosphate buffer.

Effects of Molten Salts on Reactions. Nucleophilic Aromatic Substitution by Halide Ions in Molten Dodecyltributylphosphonium Salts[1]

Slaton E. Fry and Norbert J. Pienta*

Department of Chemistry, University of Arkansas
Fayetteville, Arkansas 72701

Received May 28, 1985

Organic molten salts have found limited use as solvents and reactants for organic reactions.[2–4] One should expect enhanced nucleophilicity in such media when the anionic portion is also a nucleophile[2,5,6] although the nature of the fused salts themselves could have a significant effect on relative reactivities.[7] A second potential advantage lies in the salts' apparent ability to stabilize charged intermediates or transition states by ion–ion interactions.[8] We report herein on studies of nucleophilic aromatic substitution reactions.

Table I (entries 1–4) contains rate constants measured for the reaction in eq 1.[9] The salts **2** were prepared from the commercially available tributyl phosphine and alkyl halides and were chosen simply because all of them melt below 40 °C.[10] Hammett plots give reasonable fits to straight lines and yield ρ values of +1.5 and 1.1 for σ and σ^-, respectively. Alternatively, one can postulate that the data represent a curved plot. Nonetheless, the small effects of the para groups G are substantially lower than those in the literature for reactions proceeding through the S_NAr mechanism.[11] These generally range from +3 to +5 with a few as high as +8 and are cases in which Meisenheimer complexes have been invoked. Our data suggest a transition state that is much earlier with respect to carbon–nucleophile bond formation in which only a small portion of the anionic charge can be interacting with the G group. If we assume a limiting ρ value of ~+4, our data suggest a transition state with about one-third C–X bond formation.

$$\text{G–Ph–OTs} + n\text{-dodecyl}(n\text{-Bu})\text{P}^+\text{X}^- \xrightarrow{100\ °C} \text{G–Ph–X} \quad (1)$$

1a, G = NO_2; **1b**, G = CO_2Et; **1c**, G = H; **1d**, G = OCH_3; **2a**, X = Cl; **2b**, X = Br; **2c**, X = I; **3**

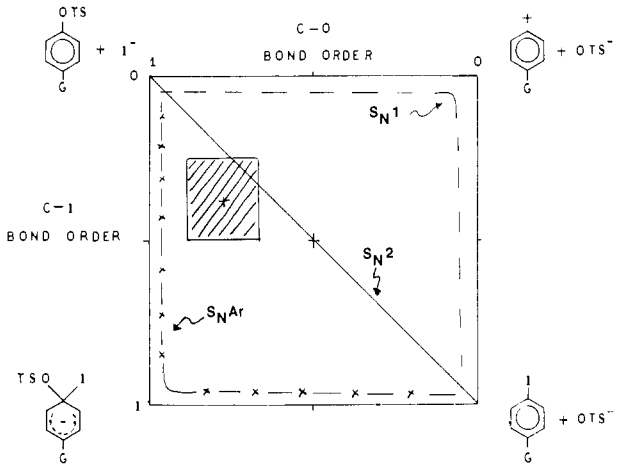


Figure 1. Projection of a three-dimensional potential energy surface for nucleophilic aromatic substitution. Limiting reaction pathways are indicated. The crosshatched rectangle represents the location of the transition state from this work.

Table I (entries 1, 5, 6) represent data from the reaction in eq 2 in which a substituent effect on the leaving group is probed.[9]

$$\text{NO}_2\text{–Ph–OSO}_2\text{–Ph–Y} + \mathbf{2c} \xrightarrow{100\ °C} \text{NO}_2\text{–Ph–I} \quad (2)$$

1a, Y = *p*-Me; **5**, Y = *p*-Br; **6**, Y = *m*-NO_2

The ρ value is +0.22 and thus implies that there is some sensitivity of the transition state to the substituent Y on the leaving group. We interpret it as the development of a partial negative charge on the leaving group that arises from some C–O bond breaking. The small magnitude of the ρ value makes its absolute certainty somewhat debatable because of the question of scatter in the rates, even though there is a good linear fit. Likewise, it is difficult to get unequivocal values for the limiting cases of ρ. We suggest $\rho \approx +1$ for the S_N1 equivalent (complete C–O bond scission) and $\rho \approx 0$ for the case of the addition complex in which we postulate

(1) Taken in part from the dissertation of S.E.F., 1985; preliminary results were reported at the National ACS Meeting: *Abstr. Pap.–Am. Chem. Soc.* **1985**, *189th*, ORGN 198.
(2) Gordon, J. E. In "Techniques and Methods of Organic and Organometallic Chemistry"; Denney, D. B., Ed.; Dekker: New York, 1969; pp 51–188.
(3) "Molten Salt Techniques"; Lovering, D. G., Gale, R. J., Eds.; Plenum Press: New York, 1983; Vol. 1.
(4) "Advances in Molten Salt Chemistry"; Braunstein, J., Mamantov, G., G. P. Smith, G. P., Eds.; Plenum Press: New York, 1971, 1973, 1975, 1981, 1984; Vols. 1–5.
(5) Gordon, J. E. "The Organic Chemistry of Electrolyte Solutions"; Wiley-Interscience: New York, 1975; pp 170–174, 440–441.
(6) Gordon, J. E.; Varughese, P. *J. Chem. Soc., Chem. Commun.* **1971**, 1160.
(7) Ford, W. T.; Hauri, R. J.; Smith, S. G. *J. Am. Chem. Soc.* **1974**, *96*, 4316.
(8) We saw little evidence for such an effect in a series of aliphatic substitution reactions conducted on neat oxyphosphonium salts where reactions, at primary and even at secondary carbons, occurred almost exclusively via a S_N2 pathway. Fry, S. E.; Pienta, N. J. *J. Org. Chem.* **1984**, *49*, 4877–4880.
(9) A 2-mL solution of 1–3 mol % of **1** in **2** was placed in a constant-temperature oil bath (100 ± 1 °C). Aliquots were removed by syringe and analyzed by liquid chromatography (C18 reversed-phase column, hexane–methanol–glyme mixtures as eluent) for the appearance of products. Detection was accomplished by absorption at 254 nm and converted to concentration using calibration samples. A single preparation of phosphonium salt generally served as solvent for three replicate runs each done for four different substrates (one substrate per vial). This was repeated 3 times for each entry, and, thus, the rate constants are an average of at least nine separate independent kinetics experiments. Rate constants were extracted as slopes from the linear regression analysis of the appropriate integrated rate expression using 5–8 samples at successive times.
(10) Beck, P. In "Organic Phosphorus Compounds"; Wiley: New York, 1972; Vol. 2, Chapter 4, p 189.
(11) Miller, J. "Aromatic Nucleophilic Substitutions"; American Elsevier: New York, 1968; (linear free energy relationships) p 65–75, (halide relative reactivity) pp 194–200, 316–8.
(12) "Advances in Linear Free Energy Relationships"; Chapman, N. B., Shorter, J., Eds.; Plenum Press: New York, 1972.

0002-7863/85/1507-6399$01.50/0 © 1985 American Chemical Society

Table I. Rate Constants for Reaction of p-G-Ph-OSO_2-Ph-Y with Halide Ion in Salt **2** at 100 °C

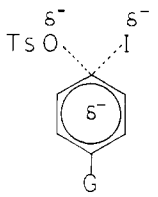
entry	substrate	G	Y	σ^a	σ^{-b}	salt	$k \times 10^7$, M^{-1} s^{-1} [c]	log k	ρ^d
1	**1a**	NO_2	p-CH_3	0.78	1.24	**2c**	18	-5.75	
2	**1b**	CO_2Et	p-CH_3	0.52	0.64	**2c**	1.8	-6.75	
3	**1c**	H	p-CH_3	0	0	**2c**	0.33	-7.27	
4	**1d**	OCH_3	p-CH_3	-0.27	-0.27	**2c**	0.41	-7.39	1.5 (1.1)[e]
5	**5**	NO_2	p-Br	+0.23		**2c**	20	-5.68	
6	**6**	NO_2	m-NO_2	0.71		**2c**	27	-5.52	0.22[f]
7	**1a**	NO_2	p-CH_3			**2a**	9 ± 1		
8	**1a**	NO_2	p-CH_3			**2b**	18 ± 3		

[a] Reference 12, p 28. [b] Reference 12, p 32. [c] Pseudo-first-order rate constant: $[\text{substrate}]_0 = 1\text{-}3\%\ [\mathbf{2}]_0$. Measured to 10-30% conversion (5-8 aliquots). Standard deviations ±7-15%. [d] ρ determined from slope of the plot of log k vs. σ. [e] Data from first four entries: first values from σ (r = 0.95); second from σ^- (r = 0.98). [f] Data from entries 1, 5, and 6 using σ (r = 0.98).

complete retention of the C-O bond.[13] In the latter case the oxygen is bound to a carbon that changes from sp^2 in the starting material to sp^3 in the intermediate. We suggest that this change ought to be effected very little by Y since it is insulated by the SO_2 group.

Table I (entries 1, 7, 8) contains data from reactions of **1a** with **2** and represents relative halide reactivity. The similarity of the rates independent of anion is consistent with an early transition state (irrespective of the amount of C-O bond breakage) since most relative reactivity arguments for halides in aromatic substitution are based on their size.[11] The lack of selectivity in a reaction with an early transition state is also consistent with the reactivity–selectivity principle (Hammond postulate). In addition to supporting the notion that the incipient C-X bond is long in the transition state, these data rule out the intermediacy of a $S_{RN}1$ mechanism since the differences in halide redox properties would require a much more substantial rate difference.[14]

Figure 1 represents the projection of a three-dimensional potential energy surface, a More O'Ferrall diagram. Three mechanisms are represented: S_N1, dashed line; S_N2, solid line; S_NAr, x-dash. The transition state for the last one must lie very close to the lower left corner because of the large magnitude of the ρ value (C-I bond order close to 1). The transition state for the reactions reported herein must lie less than half the way along that axis. Using the same arguments for the C-O bond order places our reaction approximately one-quarter the distance along the C-O bond coordinate. The cross-hatched area represents the intersection of these two substituent studies. It appears to resemble the S_N2 more than the "pure" S_NAr and is represented by **4**. The



4

location of the early transition state does not preclude the possibility that the reaction proceeds from it to an intermediate similar to a Meisenheimer complex.

We conclude that the use of molten salts **2** as nucleophile sources has profound effect on aromatic substitution reactions: (1) the rates of reaction of substrates with nitro or methoxy substituents differ only by a factor of about 40; (2) the halides all react about the same; (3) the transition state is early with respect to carbon–halogen bond formation, while carbon–nucleofuge bond breakage is already beginning to occur. We suggest that these are manifestations of the interaction of the solvent, the molten salt. We postpone speculation on the specific nature of these phenomena pending further investigations.[15]

(13) Precedent for the former value is taken from data on limiting S_N1 reactions involving sulfonate leaving groups on bridgehead positions in aliphatic molecules: See: Lowry, T. H.; Richardson, K. S. "Mechanism and Theory in Organic Chemistry", 2nd ed.; Harper and Row: New York, 1981; p 340 and references cited therein. The argument of analogy to reactions of carboxylate esters leads one to the same limiting value: see ref 12, pp 21-24. Leaving group abilities are also dependent on solvent and thus changes in rate may reflect differential solvation of the anionic nucleofuge. For examples and discussion in aliphatic cases, see: (a) Hartshorn, S. R. "Aliphatic Nucleophile Substitution"; Cambridge University Press: London, 1973; pp 52-58. (b) Streitweiser, A. "Solvolytic Displacement Reactions"; McGraw-Hill: New York, 1962; pp 29-33, 81. Thus, measuring leaving group propensity for the same substrate in another solvent does not necessarily provide the appropriate answer.

(14) We rule out an elimination mechanism involving benzynes because of the absence of regioisomers in the products. After completion of a kinetic run the remaining salt solution was extracted with hexane and analyzed by gas chromatography under conditions where meta and para isomers could be discriminated. An S_N1 mechanism is ruled out by the sign of ρ unless the unlikely case of the nucleophile addition to the phenonium cation were the rate-determining step.

(15) Additional preliminary studies indicate that the transition state is even earlier in $(n\text{-Bu})_4P^+I^-$ as evidenced by a smaller ρ value. An Arrhenius plot suggests that substantial rate enhancement is observed in **2c** especially for **1c** and **1d** when compared with traditional solvents. Other probes of the microscopic nature of these molten salts are being pursued. A reviewer kindly suggested that the traditional mechanism may be in force with the exception that the novel medium stabilizes the σ complex by electrostatic interaction and thereby lessens the ρ value. This is also consistent with the lower ρ value for the tetrabutylphosphonium salt but does not explain why the halides are virtually identical in reactivity. Solvation of the incipient cyclohexadienyl anion does not lessen the steric requirements for halide approach.

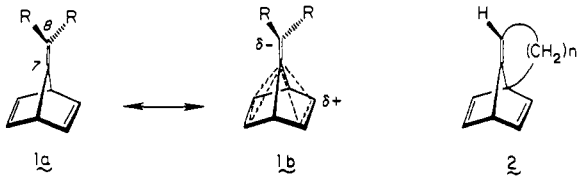
Organolithium Reagent Promoted Conversion of a Functionalized 7-Oxanorbornane to Annulated Fulvenes. An Expedient Route to 1,7-Cyclohexenonorbornadienes

Tina M. Kravetz and Leo A. Paquette*

Evans Chemical Laboratories
The Ohio State University
Columbus, Ohio 43210

Received May 6, 1985

In simple undistorted methylenenorbornadienes, homoconjugative interaction is intense and substantial ground-state electronic drift as in **1b** takes hold. The phenomenon is perhaps best revealed



by ^{13}C NMR spectroscopy. For example, if the R groups in **1** are hydrogen, C-7 resonates at 177.1 ppm,[1,2] a record downfield shift for an olefinic carbon.[3] Annulation as in **2** must induce some

(1) (a) Hofmann, R. W.; Schüttler, R.; Schäfer, W.; Schweig, A. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 512. (b) Hofmann, R. W.; Kurz, H. *Chem. Ber.* **1975**, *108*, 109. (c) Knothe, L.; Werp, J.; Babsch, H.; Prinzbach, H. *Liebigs Ann. Chem.* **1977**, 709. (d) Martin, H. D.; Mayer, B.; Hoffmann, R. W.; Riemann, A.; Rademacher, P. *Chem. Ber.* **1985**, *118*, 2514.

(2) Paquette, L. A.; Broadhurst, M. J. *J. Org. Chem.* **1973**, *38*, 1893. (b) Inagaki, S.; Fujimoto, H.; Fukui, K. *J. Am. Chem. Soc.* **1976**, *98*, 4693.

0002-7863/85/1507-6400$01.50/0 © 1985 American Chemical Society