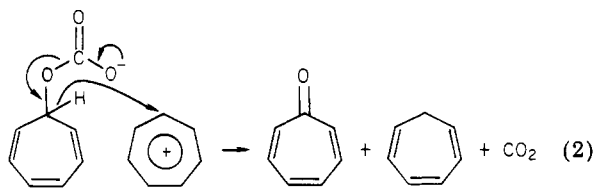


cycloheptatriene,⁸ but it is inert to the reaction conditions on our time scale. It may also be relevant that in addition to sodium carbonate, sodium bicarbonate and to a lesser extent sodium acetate⁹ and tribasic potassium phosphate also speed the reaction. Monobasic sodium phosphate has no effect.

A possible mechanism for the reaction in the presence of sodium carbonate or bicarbonate is shown in eq 2. It



accounts for the known facts about the reaction but does not explain why the process should occur. It also leaves open the question of the mechanism in the absence of added carbonate. The answers to these questions await further experimentation.

Since cycloheptatriene is a product of this reaction, the yield of tropone from tropylium salt is limited to 50%. However, tropylium fluoborate can be made from cycloheptatriene by treatment with trityl fluoborate.¹⁰ Thus, treatment of the reaction mixture containing tropone and cycloheptatriene with trityl fluoborate should regenerate tropylium salt and eventually provide more tropone.¹¹ Indeed, one should be able to start with cycloheptatriene, treat with an excess of trityl fluoborate and sodium carbonate in acetonitrile, and obtain tropone in high yield. We have been able to produce tropone by this method (30-40% yield), but even a large excess of trityl fluoborate does not remove all of the cycloheptatriene; furthermore, the large amount of triphenylmethane generated in the reaction makes isolation of the tropone difficult. Since tropylium fluoborate¹² is as easy to prepare as trityl fluoborate,¹⁰ we prefer the former intermediate.

Finally, we have noticed that troyl methyl ether, like ditroyl ether, slowly decomposes to tropone on standing.¹³ If this could be made to happen quantitatively and on a reasonable time scale, it would represent the first method for converting tropylium salts into tropone in greater than 50% yield. We have not yet found the appropriate conditions to do this, but we are continuing our search.

Experimental Section

Tropone (2). A mixture of 25 g (0.14 mol) of tropylium fluoborate, 10 g (0.095 mol) of anhydrous sodium carbonate, and 250 mL of acetonitrile was heated to reflux under nitrogen for 30 min, cooled, and stripped of solvent. The residue was swirled with 150 mL of dichloromethane, filtered, washed with water and saturated sodium chloride solution, dried, and concentrated to give 7.14 g (48%) of tropone. The product is light brown in color but pure by NMR and IR spectroscopy.⁷

Acknowledgment. We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

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(9) Surprisingly, no ditroyl ether was formed even though the trihydrate was used.

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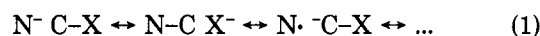
The α Effect: On the Origin of Transition-State Stabilization

Shmaryahu Hoz

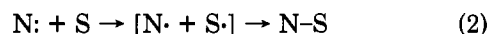
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One of the most intriguing problems in the field of nucleophilic substitution reactions is no doubt the α effect. This effect is expressed as a positive deviation of an α nucleophile (a nucleophile possessing a nonbonding pair of electrons on an atom α to the nucleophilic site) from a Brønsted-type plot of $\log k$ vs. the pK_a of the nucleophile.¹ Although the α effect has received much attention, the consensus of opinion is that its origin is still rather unclear.² This is well manifested by the multitude of explanations given to this effect.³ However, it is generally accepted that in many cases, the enhanced nucleophilic reactivity of α nucleophiles results from extra stabilization of the transition state.^{2f,3f,ij,4} In an attempt to characterize the origin of this extra stabilization we must first examine the nature of the transition state in nucleophilic reactions. Regarding bond scission, Salem has stated that a molecule with a broken bond can be partly diradical—partly zwitterionic.^{5a} Similar diradical-zwitterionic resonance structures were postulated by Walling^{5b} and subsequent workers^{5c,d} for intermediates in the decomposition reactions of certain peroxides. Since this should hold for a nucleophilic bonding process as well, it implies that one of the canonical structures describing the transition state will be diradicaloid (eq 1)



Further support for this conclusion is obtained from several recent reports of nucleophilic reactions in which a seemingly simple bond formation is found to proceed by an electron transfer to form a radical pair which subsequently collapses to yield a covalent bond (eq 2; charges omitted for clarity). The reactions of Grignard reagents



with benzophenone,⁶ the coupling of cyclopropenyl cation

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(4) Fersht, A. R.; Requena, Y. *J. Am. Chem. Soc.* 1971, 93, 3499.

(5) (a) Salem, L. *J. Am. Chem. Soc.* 1974, 96, 3486. (b) Walling, C.; Waits, H. P.; Milovanovic, J.; Pappiaonou, C. G. *Ibid.* 1970, 92, 4927. (c) Taylor, K. G.; Govindan, C. K.; Kaelin, M. S. *Ibid.* 1979, 101, 2091. (d) Pomerantz, M.; Dassanayake, N. L. *J. Am. Chem. Soc.* 1980, 102, 678.

(6) Ashby, E. C.; Bowers, J. S., Jr. *J. Am. Chem. Soc.* 1977, 99, 8504.

with cyclopropenyl anion,⁷ and the nitration of aromatics by NO₂⁺ (ref 8) are examples of this behavior. If these two steps melt into a single transition state as is believed to be the case for any "normal" nucleophilic reaction, this transition state is likely to retain a certain amount of the diradical character of its diradicaloid predecessor. Thus, the transition state should be characterized not only by its charge distribution ($\delta+$, $\delta-$) but also by its diradical character (δ).

For a given nucleophile, the pivotal question is how the nature of the substrate will affect the importance of the contribution of the diradicaloid structure. We suggest that for substrates with high electron affinity, that is, with low LUMO's (LL), the electron-transfer component will be significantly larger than for substrates having high LUMO's (HL), namely, low electron affinity.

This dichotomy between LL and HL substrates easily can be justified by noting the type of molecules which participate in electron-transfer processes.⁹ These are mainly cations, aromatics, or unsaturated compounds, all of which clearly belong to the LL family, whereas HL substrates do not usually participate in electron-transfer reactions unless reacted with extremely powerful donors (e.g., methyl chloride with sodium metal).¹⁰

Theoretical support for our suggestion can be obtained by viewing the transition state as a point of avoided crossing between the ground state and the excited potential curves of the reactants. This approach has been used, for example, by Walling¹¹ in order to explain some features of reactions between nucleophiles and peroxides and has recently been carefully developed into a detailed model by Shaik and Pross.¹² According to this model the transition state is defined by a linear combination of reactant configurations (eq 3) where D and A refer to the nucleo-

$$\psi = C_1(DA) + C_2(D^+A^-) + C_3(D^+A^*) + C_4(DA^*) + C_5(DA^{**}) + C_6(D^{2+}A^{2-}) \quad (3)$$

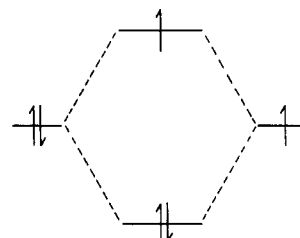
phile and the substrate, respectively. DA is the ground state of the reactants, D⁺A⁻ is an excited state in which an electron is transferred from the nucleophile to the substrate to form the diradicaloid pair, and DA* describes a mono-excited state of the electrophile with no electron transfer from the nucleophile. The other three states are di-excited and do not contribute significantly to the transition-state structure. The extent to which these configurations are mixed into the transition-state structure is governed by the energy gap between each of the indi-

vidual configurations and the ground state (DA).¹² It is immediately apparent that the amount by which the electron-transfer configuration D⁺A⁻ will contribute to the transition-state structure for a given nucleophile depends on the stability of A⁻, i.e., on the electron affinity of A and thus on the energy of its LUMO. Hence, as we have posited above, in the case of an HL substrate, the amount of electron transfer at the transition state will be significantly smaller than the extent of the electron transfer in the reaction of the same nucleophile with an LL substrate.

The importance of the role of electron transfer in the nucleophilic reactions of α nucleophiles becomes clear as a result of the quite general observation that the α effect is exhibited almost solely in the reactions of unsaturated substrates.^{2a,c,3j,13} These substrates belong to the LL family and hence in nucleophilic reactions their transition states contain a relatively large contribution of electron-transfer component. The existence of this component, in turn, is intimately linked with the question of stability of the transition state for a nucleophilic reaction with an α nucleophile as can be demonstrated by the following argument.

For the sake of simplicity let us analyze the α nucleophile in its complete radical form (e.g., HO-O· for the nucleophile HOO·). In this form, an odd electron is located α to a lone pair. The stability of radicals α to a lone pair is a well-known phenomenon and is nicely exemplified by various hydrazyl radicals (such as diphenylpicrylhydrazyl which can be isolated as a stable solid), nitroxide radicals, iminoxy radicals, and others.¹⁴

This effect is easily explained on the basis of the simple MO picture of the three electron system:



In this MO diagram there is a net energy stabilization as two electrons go down to the bonding level and only one electron goes up to the antibonding orbital. Hence, if an α nucleophile possesses partial radical character at the transition state it will stabilize it in a way which is unavailable to any normal nucleophile, thus giving rise to the α -effect phenomenon.

If the above argument is valid, then it necessarily follows that the greater the radical character α to the lone pair, the greater will be the stabilization in the transition state and thus a higher value for the α effect will result.

In order to experimentally assess this conclusion, one should first seek a sensitive probe for the degree of the electron transfer in the transition state. It was recently argued that β_{nuc} reflects this property of the transition state.^{12b} This is strongly supported by an observation made by Bordwell et al.¹⁵ that in contrast to S_N2 reactions which are usually characterized by low β_{nuc} values (0.3–0.5), electron-transfer reactions are associated with β_{nuc} values larger than unity (1.15–1.5 are typical values). On the basis

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of the reasonable assumption of continuity between these two "zones" of β_{nuc} values, one should expect a correlation between the extent of electron transfer and the value of β_{nuc} as was suggested by Shaik and Pross.^{12b} Thus, as the magnitude of the α effect depends on the extent of the electron transfer at the transition state and this on the other hand is correlated with β_{nuc} value, the α effect should be directly related to the value of β_{nuc} . Indeed, for a series of hydrazines reacting with various substrates the magnitude of the α effect was found to be directly related to the β_{nuc} value,³ⁱ confirming our aforementioned proposal. Formally, one can also expect that the increase in the degree of electron transfer upon going from an LL substrate to a substrate with a lower LUMO will also increase the magnitude of the α effect. An example of such a behavior is found in nucleophilic reactions with ArXS_2Ph where SO_2Ph is the leaving group and X varies from SO_2 to SO to S .¹⁶ The changes in X are accompanied by a parallel decrease of the α effect, giving the respective ratios: 7.3:2.4:1 for HO_2^- and 9.7:48:1 for AcNHO^- . However, it should be noted that the drastic change from an HL substrate such as methyl chloride to an LL substrate such as a carbonyl group gives rise to a relatively small change (about 2 kcal/mol) in the activation energy of an α nucleophile compared to a non α nucleophile. Therefore, a variation of the substrate within the LL family is likely to induce a much smaller effect which might be easily masked by other effects resulting from the structural changes.

In conclusion, the extra stabilization of the transition state in the reaction of α nucleophiles with LL substrates results from the partial radical character that the nucleophile acquires at the transition state. As the magnitude of this radical character increases, so should the size of the α effect.

Acknowledgment. Helpful discussions with Professor H. Basch, Dr. S. S. Shaik, and Professor J. F. Bunnett are gratefully acknowledged.

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Reaction of 3-Nitroso-2-phenylimidazo[1,2-a]pyridine with Triethyl Phosphite. A Revised Structure for the Product

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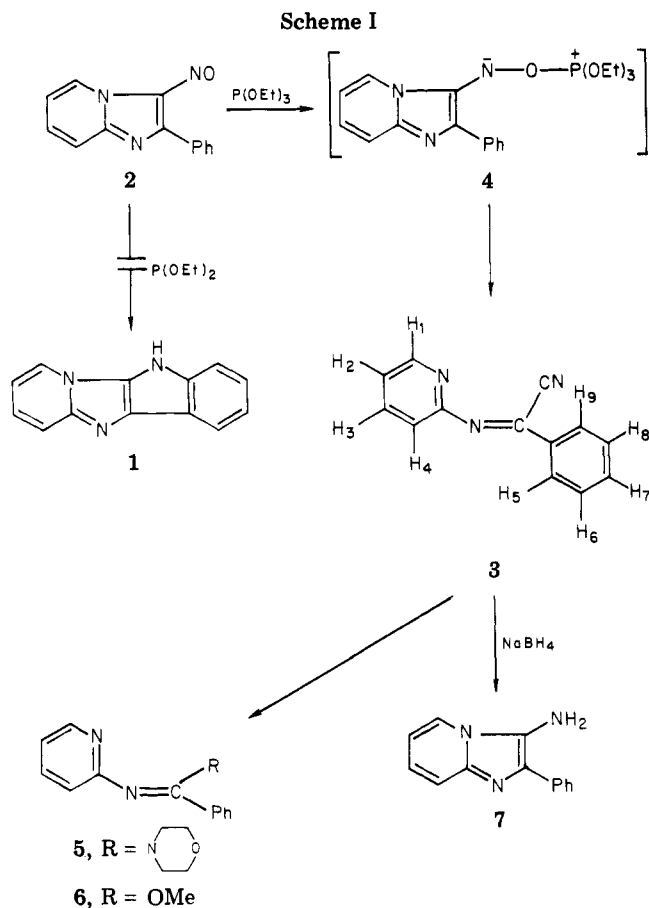
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During an investigation of the effects of various antihypertensive agents on prostacyclin and thomboxane A_2 production we required a sample of pyridino[1,2-a]-imidazo[5,4-b]indole (1), which has recently been shown to possess potent hypotensive activity in spontaneously hypertensive rats.^{1,2} The tetracycle 1 was reported to be formed by the triethyl phosphite reduction of the readily available 3-nitroso-2-phenylimidazo[1,2-a]pyridine (2,³ Scheme I).

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On repetition of the published procedure for the preparation of 1 a compound with an identical melting point and ^1H NMR spectrum was obtained. The IR spectrum of our product, however, showed none of the reported bands at 3410, 3080, or 2580 cm^{-1} but displayed strong bands at 1500 and 1540 cm^{-1} and a weak absorption at 2220 cm^{-1} . The latter band was indicative of a nitrile group. The reduction product gave a ^1H NMR spectrum identical with that reported by Adhikary, but none of the nine protons exchanged with D_2O . This failure to detect signals characteristic of the NH group in either the IR or the NMR spectra of the phosphite reduction product coupled with mechanistic considerations led us to postulate the alternative imidoyl cyanide structure 3. The cyanide would be the expected product following the loss of triethyl phosphate from the intermediate 4. A detailed examination of the proton NMR spectrum lent support to the postulated structure 3, and these assignments were confirmed by decoupling experiments (see Experimental Section).

Chemical studies on the phosphite reduction product provided evidence which also supported the assignment of structure 3. Reaction with morpholine gave the amidine 5 whereas treatment with sodium hydroxide in methanol furnished a mixture of 2-(benzoylamino)pyridine and the iminoether 6. Reduction with sodium borohydride gave rise to 3-amino-2-phenylimidazo[1,2-a]pyridine (7), an initial reduction of the imine function followed by cyclization occurring.⁴ None of these reactions could be explained by the tetracyclic structure 1.

Final confirmation of the correctness of the assignment of structure 3 to the phosphite reduction product was

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