Tetrahedron Vol. 36, pp. 1753 to 1756
Pergamon Press Ltd., 1980. Printed in Great Britain

RADICAL STABILIZING EFFECTS

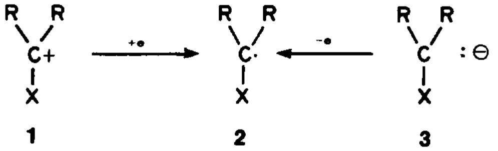
A COMPARISON OF TRANSITION STATE EFFECTS (RATES OF AZOALKANE DECOMPOSITIONS) WITH CALCULATED (*AB INITIO*) PI SPIN DENSITIES

MICHAEL F. DUBE and JACK W. TIMBERLAKE
Department of Chemistry, University of New Orleans, New Orleans, LA 70122, U.S.A.

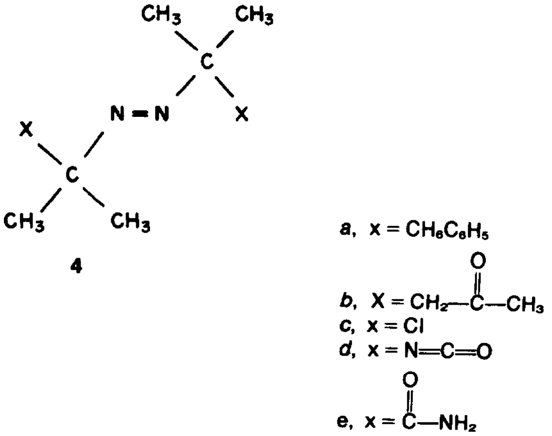
(*Received in the U.S.A.* 24 *September* 1979)

Abstract—Rate studies on five azoalkanes (**4a–e**) have been studied to assess important radical stabilizing effects. MO calculations of spin densities for three radicals with pi systems are correlated with kinetic rates of radical formation.

Traditionally, transition states leading to the formation of carbon centered radicals have been shown to be polarized (electron deficient).[1,2] However, if radicals (**2**) are considered intermediate between cations (**1**) and anions (**3**) they could be expected to display transition state characteristics of either **1** or **3** depending upon their mode of generation. One test to determine the nature of radicals is to evaluate the substituent effects on the kinetic rate of generation.[3] While all (**1**–**3**) would be stabilized by pi systems, cations would be stabilized by electron donating groups and destabilized by electron withdrawing groups; for anions the converse would be true. We have applied this test using substituted azopropanes (**4**) as the model system and report here the kinetic results on five derivatives which confirm that (a) electronic stabilization parallels carbanion—like transition states for radicals derived from azoalkanes, that (b) inductive effects are small or at least are significantly diminished with the intervention of a methylene unit, and (c) there is a reasonably good correlation between rates of generation and π spin density as determined from STO 3G calculations.



1 2 3



4

a, $x = CH_6C_6H_5$
b, $X = CH_2\text{—}\overset{\overset{\displaystyle O}{\|}}{C}\text{—}CH_3$
c, $x = Cl$
d, $x = N{=}C{=}O$
e, $x = \overset{\overset{\displaystyle O}{\|}}{C}\text{—}NH_2$

RESULTS AND DISCUSSION

Table 1 lists the rate constants for the five derivatives studied by following nitrogen evolution as a function of pressure at constant volume.[4] Table 2 contains the activation parameters and the relative rates of these five derivatives and 4, $x = CH_3$, CN, and $CH = CH_2$ for reference purposes.

The origin and magnitude of steric effects on the rate of decomposition of azoalkanes have been previously discussed by us[3,5,6] and others[7–9] and while they can in some cases be large, they can usually be qualitatively predicted. Examination of models indicates steric ground state effects are not likely to be significant for the derivatives reported here.

The difference between x = benzyl (**4a**) and x = Me (Table 2) is not outside experimental error for the extrapolation to 100°. The difference between x = benzyl (**4a**) and x = acetonyl (**4b**) a factor of 4, although small, is indeed real as indicated by a comparison of rates at all temperatures (Table 1). We would not attempt to quantify the interpretation but do note that it is in the direction expected from an inductive standpoint if the radicals are indeed stabilized by a $-I$ effect ($\sigma^*C_6H_5CH_2\text{–} = +0.25$, $\sigma^*_{CH_3COCH_2} = 0.60$).[10]

The fourth entry in Table 2 (**4c**) is a correction of our previous result[3] which probably suffered from acid catalysis resulting from facile elimination of HCl. Buffering of the reaction solutions with isoquinoline eliminates this problem. The rate enhancement of chloro over methyl, a factor of 10, is once again in the direction expected by an inductive stabilization, although we can not separate out "d-orbital" or special third row[11,12] resonance effects as has suggested to be important for sulfur substituents.[3]

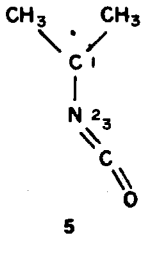
The enhancement shown by **4d** and **4e**, both of which have pi systems, is in the direction expected for "electron rich" centers and approaches that of the cyano group. Both cyano and carboethoxy are destabilizing towards cations[13] and presumably so would the isocy-

Table 1. Rate constants for azopropanes (4_{a-e})

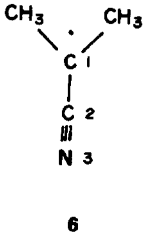
Compound	Temp, °C	k x 10^4 Sec^{-1}	Solvent
4a, x = $CH_2C_6H_5$	170.0	0.925	Diphenyl ether
	175.07	1.68	
	180.26	3.04	
	184.99	5.74	
	189.94	8.58	
	195.10	16.9	
4b, x = $CH_2-\overset{\overset{O}{\|}}{C}-CH_3$	160.01	0.78	Diphenyl ether
	165.07	1.29	
	169.99	2.25	
	175.06	4.51	
	180.26	7.95	
	184.96	12.6	
4c, x = Cl	169.78	2.72	Diphenyl ether
	175.02	3.93	Isoquinoline
	184.96	11.9	
	189.91	19.7	
	194.90	27.0	
	200.90	49.4	
4d, x = NCO	134.97	1.21	Diphenyl ether
	139.98	2.34	
	144.90	4.28	
	150.06	6.56	
	154.82	10.2	
	160.14	19.0	
4e, x = $\overset{\overset{O}{\|}}{C}-NH_2$	100.31	1.72	Ethylene glycol
	104.96	2.72	
	109.51	4.74	
	114.96	8.10	
	119.88	14.6	
	124.85	18.3	

anate and amide groups, in that they are electron withdrawing.

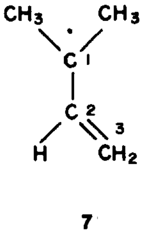
However, the magnitude of the difference between X = NCO, $CONH_2$, CN and $CH=CH_2$, all good π-systems was not what one might expect *a priori*. Conceivably the amide rate is somewhat depressed in the more polar solvent[14] (ethylene glycol versus diphenylether) as a ground state solvation effect[15] but no intuitive rationalization was obvious for the other three. Reasoning that either these effects were simply a manifestation of the degree of radical delocalization or that these transition state effects (rates) were not good reflections of radical stability, we undertook MO calculations on the radical fragments **5**, **6** and **7**.



5



6



7

In each case the radical geometries were optimized to a quasi least energy conformation using the Gaussian 70 (STO-3G basis set) approach. This was done by varying all bond lengths by 0.05A°, all bond angles by 5.0° and all dihedral angles by 10°. In all cases the variations yielded better geometries (energy minima). The methyl groups were held in identical conformations by requiring all C–H bond lengths and H–C–C bond angles to be the same. Additionally, the two methyl groups were required to vary by the same increments starting from an assumed geometry defined by the atoms H–C–C–C–H in a plane. For practical reasons (the relatively large size of these molecules thus requiring enormous amounts of computer time) no further refinements were made on the geometry. These "optimized" geometries were then subjected to single calculations using Gaussian-70 (4–31G basic set) programs. These data are displayed graphically as plots of % spin density at atom 3 ($\rho_3/\rho_1 + \rho_3$) vs relative ln k of **5**, **6** and **7**. While this degree of linearity is undoubtedly fortuitous (correlation coefficients > 0.99) and a three point correlation should be regarded with considerable reservation, it is an interesting trend none the less. Furthermore, it provides a qualitative explanation for the rate data. As the extent of positive spin density on atom

Table 2. Activation parameters and relative rates for azopropanes

	X	Rel Rate 100^o	$\Delta H^{\ddagger}$ kcal/mol	$\Delta S^{\ddagger}$ e.u.	$\Delta G^{\ddagger}$ 100^o kcal/mol
4a	$-CH_2C_6H_5$	0.8	46.5±1.2	27.1±2.3	36.4
	$-CH_3$	1.0	42.2	16.1	36.2^a
4b	$-CH_2\overset{O}{\overset{\|}{C}}CH_3$	3.4	44.3±1.1	24.1±2.5	35.3
4c	-Cl	1.1×10^1	38.9±1.3	12.0±2.7	34.4
4d	-N = C = O	3.4×10^2	36.5±1.2	12.4±2.9	31.9
4e	$-\overset{O}{\overset{\|}{C}}-NH_2$	3.4×10^4	29.0±1.3	1.4±3.5	28.5
	-CN	2.8×10^5	30.7	10.4	26.8^b
	$-CH=CH_2$	8.0×10^6	22.4	5.0	24.3^c

a. J. C. Martin and J. W. Timberlake, J. Am. Chem. Soc., 92, 978 (1970).

b. J. P. Van Hook and A. V. Tobolsky, J. Am. Chem. Soc., 80, 779 (1958).

c. P. S. Engel and D. J. Bishop, J. Am. Chem. Soc., 94, 2148 (1972).

Table 3. Pi spin densities ($\rho\pi$) calculated by STO-3G and 4-31g methods

	Compound 5		Compound 6		Compound 7	
Atom	STO-3G	4-31G	STO-3G	4-13G	STO-3G	4-31G
1.	0.613	0.612	0.836	0.844	0.775	0.760
2.	-0.136	-0.114	-0.501	-0.486	-0.587	-0.544
3.	0.086	0.101	0.606	0.599	0.773	0.747
% ρΠ at 3	12.3	14.2	42.0	41.5	49.9	49.6

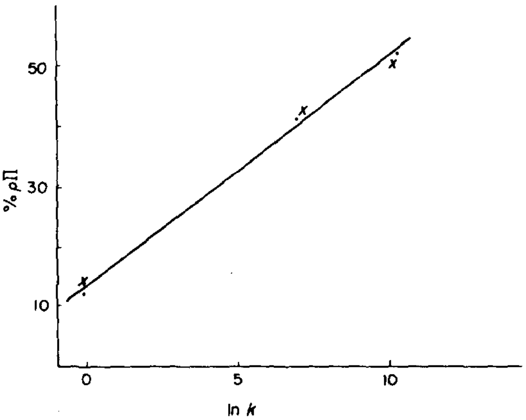


Fig. 1. Plot of % $\rho\pi$ vs ln k, STO-3G, X 4-31G.

3 increases so does the rate. It is perhaps intuitive that stability should be enhanced by electron delocalization, but rates reflect incipient radical formation and whether extensive delocalization occurs in the transition state could be questioned. It is therefore gratifying to see this trend and it argues that azoalkanes are indeed good models for measuring radical stabilities.[16,17]

From these results we conclude that transition states derived from azoalkanes are not polarized in the direction of cation centers but are minimumly stabilized by inductive electron withdrawing groups and maximumly stabilized by π systems.

EXPERIMENTAL

2-Methyl-3-phenyl-2-propanol was prepared in 61% yield from benzylmagnesium chloride[18] and acetone on a 1 mol scale: b.p. 58°/1 mm (Lit[19] 108°/11 mm).

N-1-Methyl-2-propylacetamide. To a soln of 4.5 g (0.1 mol) of acetonitrile, 100 ml of glacial AcOH and 50 ml of conc H_2SO_4 cooled to 0° was added 15.0 g (0.1 mol) of 2 - methyl - 3 - phenyl - 2 - propanol. After stirring overnight at room temp the soln was poured into 500 ml ice water and neutralized with K_2CO_3. The ether extracts were dried and concentrated to yield crude acetamide which was recrystallized from hexane to give 15.2 g (79%) of amide m.p. 91–92.5° (lit 91–92°)[20]; NMR ($CDCl_3$) δ 1.23 (s, 6H), 1.75 (s, 3H), 2.98 (s, 2H), 5.54 (br s, 1H) and 7.12 ppm (m, 5H); IR($CHCl_3$) 3440, 3338, 1682, 1500 and 1450 cm^{-1}.

2-Methyl-3-phenyl-2-propylamine. A one 1 monel autoclave charged with 19.0 g (0.1 mol) of N - 2 - methyl - 3 - phenyl - 2 - propylacetamide and 200 ml of 20% NaOH soln was heated at 220° for 24 hr. The ether extract was dried and HCl gas was passed over the soln to yield, after filtration, 14.2 g of the amine hydrochloride; m.p. 200–202° (lit 198°).[21] The free amine was recovered by neutralization of an aqueous soln of the salt and extraction with ether.

N,N′ - *Bis*(*2 - methyl - 3 - phenyl - 2 - propyl*) *diazene* (**4a**). Into a 250 ml flask under an argon atmosphere cooled to −78° was placed 75 ml of CH_2Cl_2 and 20 ml of pyridine. To this soln was added 2.61 ml (37.6 mmol) of iodine pentafluoride[22] followed by dropwise addition of 5.6 g (37.6 mmol) of 2 - methyl - 3 - phenyl - 2 - propylamine in 50 ml of CH_2Cl_2. The mixture was stirred 1 hr at −78°, allowed to warm to room temp and quenched by addition of 50 ml water. The organic layer was washed successively with 250 ml portions of 5% HCl, 5% $NaHSO_3$ and sat NaCl aq, dried over $MgSO_4$ and concentrated to give a dark brown oil. Chromatography of the oil on a neutral alumina column yielded a yellow solid which was recrystallized from $CHCl_3$–hexane to give 2.2 g (54%) of azo compound as a white solid: m.p. 67–68°; NMR($CDCl_3$) δ 1.10 (s, 12H), 2.94 (s, 4H) and 7.18 ppm (m, 10H); IR($CHCl_3$) 3072, 2966, 2928, 1492, 1452, 1379, 1361 and 1309 cm^{-1}; UV (hexane) λ_{max} = 370 nm (ϵ35).

(Found: C, 81.67; H, 8.86; N, 9.58. Calcd for $C_{20}H_{16}N_2$: C, 81.58; H, 8.90; N, 9.51%).

N,N′-*Bis*(*2-methyl-4-oxo-2-pentyl*)*diazone* (**4b**). Diacetone amine was obtained by distillation from diacetone amine hydrogen oxalate (Aldrich) and powered KOH. The keto diazene was prepared by the previously described IF_5 oxidation. Chromatography and distillation gave a 17% yield: b.p. 72–74° (0.1 mm); NMR ($CDCl_3$) δ 1.28 (s, 12H), 2.17 (s, 6H) and 2.70 ppm (s, 4H); IR ($CHCl_3$) 1719, 1465, 1427 and 1360 cm^{-1}; UV (hexane) λ_{max} 365 (ϵ31), 284 (ϵ 67) and 213 nm (ϵ 2320).

Found: C, 63.59; H, 9.91; N, 12.24. Calcd for $C_{12}H_{22}N_2O_2$: C, 63.69; H, 9.80; N, 12.38%).

N,N′-*Bis* (*2-chloro-2-propyl*)*diazene* (**4c**) was prepared according to the literature.[23]

N,N′-*Bis*(*2-methyl-2-propanamido*) *diazene* (**4d**). To 50 ml of conc H_2SO_4 was added 5 g (30 mmol) of N,N′-bis(2-cyano-2-propyl) diazene (AIBN) portionwise. The soln was stirred from 1 hr at 0° and 2 hr at room temp. The soln was poured into ice water and, after 15 min a solid separated which was filtered, washed with water, and recrystallized from $CHCl_3$–hexane to give 1.3 g (22%) of **4d** as a white solid: m.p. 96° (dec) [Lit[24] 94–95]; NMR ($CDCl_3$) δ 1.39 (s, 12H) and 1.62 ppm (s, 4H); IR ($CHCl_3$) 3511, 3400, 1691, 1598, and 1561 cm^{-1}; UV (EtOH) λ_{max} = 375 nm (ϵ 23).

(Found: C, 48.21 H, 8.27. Calcd for $C_8H_{16}N_4O_2$: C, 47.99; H, 8.05%).

N,N′-*Bis*(*2-isocyanato-2-propyl*)*diazene* (**4e**). To a cooled soln of 10 g (0.12 mol) of potassium cyanate in 200 ml of a 70% aq isopropanol soln was added 10 g (0.05 mol) of N,N′-bis (2-chloro-2-propyl) diazene in 100 ml of pentane at a rate so as to maintain the temp between 10 and 15°. The mixture was stirred 2 hr at room temp and 75 ml of water was added to dissolve the salts. A pentane extract was washed with water and 5% $NaHCO_3$, dried over $MgSO_4$ and concentrated to give a yellow solid. The solid was recrystallized repeatedly from pentane at −78° to yield 1 g of pure white **4e**: m.p. 68.5–70°[25,26]; NMR($CDCl_3$) δ 1.58 ppm (s, 12H); IR($CDCl_3$) 2232, 1458, 1383, 1366 and 1155 cm^{-1}; UV (hexane) λ_{max} = 337 nm (ϵ10).

(Found: C, 48.85; H, 6.28; N, 28.49. Calcd for $C_8H_{12}N_4O_2$: C, 48.97; H, 6.16; N, 28.55%).

Acknowledgements—The authors thank the Army Research Office for financial support and Professors Ken Houk, (LSUBR) Peter Politzer (UNO), Robert Flurry (UNO) and Ms. Lynn Garcia for assistance in obtaining and interpreting the *ab initio* data.

REFERENCES

[1] T. Koenig, *Free Radicals* (Edited by J. K. Kochi), Vol. I, Chap. 3. Wiley, New York (1973).
[2] W. H. Davis and W. A. Pryor, *J. Am. Chem. Soc.* **99**, 6365 (1977).
[3] B. K. Bandlish, A. W. Garner, M. L. Hodges, and J. W. Timberlake, *Ibid.* **97**, 5856 (1975) for Refs. on original work.
[4] J. W. Timberlake and J. C. Martin, *Rev. of Sci. Inst.* **44**, 151 (1973).
[5] A. W. Garner, J. W. Timberlake, P. S. Engel and R. A. Melaugh, *J. Am. Chem. Soc.* **97**, 7377 (1975).
[6] J. W. Timberlake and A. W. Garner, *J. Org. Chem.* **41**, 1666 (1976).
[7] C. G. Overberger, W. F. Hale, M. B. Berenbaum and A. B. Finestone, *J. Am. Chem. Soc.* **76**, 6185 (1954).
[8] W. Duismann and C. Rüchardt, *Chem. Ber.* **106**, 1083 (1973).
[9] W. Duismann and C. Rüchardt, *Tetrahedron Letters*, 4517 (1974).
[10] J. E. Leffler and E. Grunwald, *Rates and Equilibria of Organic Reactions*, p. 222. Wiley, New York (1963).
[11] Whether "d" orbital effects are important is a subject of some controversy.[12] We do not rule out the possibility that sulfur or chlorine nonbonding molecular orbitals are energetically more favorable than those of oxygen for overlap with the carbon *p* orbital; *cf* Ref. 12.
[12] F. Bernardi, N. D. Epiotis, W. Cherry, H. B. Schlegel, M-H. Whangbo and S. Wolfe, *J. Am. Chem. Soc.* **98**, 469 (1976).
[13] As determined by σ^{+}_{para} values, Ref. 10, p. 204.
[14] The amide is insoluble in diphenyl ether.
[15] W. Duismann and C. Rüchardt, *Chem. Ber.* **111**, 596 (1978).
[16] Other π substituents which will be used to test this concept include x = $CONH_2$, CHO and CH = C = CH_2.
[17] A further test underway involves calculating energy differences between radicals and parent hydrocarbons to compare with $\Delta\Delta G\ddagger$ values obtained from azoalkane decompositions.
[18] *Org. Syn.* I, 471.
[19] N. D. Zelinsky and M. W. Gawerdowskaja, *Chem. Ber.* **61**, 1049 (1928).
[20] K. N. Boltze and H. Muhlenbe, *Ger. Pat.* 1, 144, 713 (1961).
[21] *Merck Index*, 8th Edn., p. 813.
[22] T. E. Stevens, *J. Org. Chem.* **26**, 2531 (1961).
[23] E. Benzing, *Leibigs, Ann.* **631**, 1 (1960).
[24] J. Thiele and K. Hauser, *Ibid.* **290**, 1 (1896).
[25] H. C. Lange and R. E. MacLeay, U.S. Pat. 4,028,344 (1977), no physical properties were reported.
[26] J. Akers, M. F. Dube, L. M. Trefonas, J. W. Timberlake and R. Majeste, *Tetrahedron Letters* 5083 (1978); reports the X-ray structure and reactions of this compound.