by means of GLC that the compositions of the gases evolved by the reactions did not vary through the reaction courses.

Preparation of *trans*-[Pd(CH_2CD_3)$_2$($PMePh_2$)$_2$] (8) and Its Thermolysis in Toluene. *trans*-[Pd(CH_2CD_3)$_2$($PMePh_2$)$_2$] (8) was prepared by the reaction of [Pd(acac)$_2$], $PMePh_2$, and Al(CH_2CD_3)$_2$(OEt)[8g] in a similar manner to the preparation of 4. 8 was identified by means of IR spectroscopy: ν_{C-D} (KBr disk, in cm^{-1}) = 2180, 2150, 2100, 2050 cm^{-1}. The isotopic purity of 8 (97%) was determined by analyzing the ^1H NMR spectrum of $(CD_3CH_2)_2CO$ derived from 8 by the reaction with CO,[11] since 8 itself was poorly soluble in solvents to allow the accurate determination of the deuterium content in 8.

Gases evolved on thermolysis of 8 (about 0.025 mol/L) in toluene (4 mL) containing styrene (0.11 mol/L) or $PMePh_2$ (0.27 mol/L) at 25.5 °C were collected and analyzed by IR spectroscopy and mass spectrometry. The IR spectrum revealed that ethylene evolved on thermolysis consisted solely of CH_2CD_2: ν_{C-D} (cm^{-1}) 946 and 752.[8e] Evolution of $C_2D_4H_2$ was confirmed by means of mass spectrometry.

Ligand Exchange Reaction of *trans*-[$PdEt_2$(PEt_2Ph)$_2$] (3) with PMe_2Ph. To a colorless solution (3 mL) of *trans*-[$PdEt_2$(PEt_2Ph)$_2$] (0.18 g, 0.36 mmol) in Et_2O cooled at -70 °C, PMe_2Ph (0.15 mL, 1.1 mmol) was added with a syringe. After stirring of the solution for 2 h, the solution was concentrated to yield a white precipitate. The precipitate was filtered, washed with a small amount of Et_2O at -70 °C, and dried in vacuo at -10 °C. The precipitate was identified as *trans*-[$PdEt_2$(PMe_2Ph)$_2$] (1) (0.13 g, 84%) on the basis of the IR spectrum.

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α-Deuterium Isotope Effects in Benzyl Halides. 2. Reaction of Nucleophiles with Substituted Benzyl Bromides. Evidence for a Change in Transition-State Structure with Electron-Donating Substituents

V. P. Vitullo,* J. Grabowski, and S. Sridharan

Contribution from the Laboratory for Chemical Dynamics, Department of Chemistry, University of Maryland, Catonsville, Maryland 21228. *Received July 19, 1979*

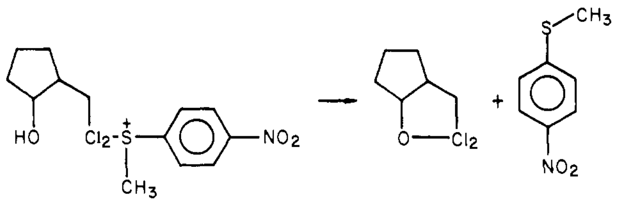
Abstract: Rates and α-D isotope effects have been determined for the following substrates and nucleophiles: *p*-methoxybenzyl bromide (Et_3N, SCN^-, N_3^-, OH^-, $S_2O_3^{2-}$), benzyl bromide (Et_3N, SCN^-, N_3^-, OH^-, $S_2O_3^{2-}$), and *p*-nitrobenzyl bromide (Et_3N, SCN^-, N_3^-, $S_2O_3^{2-}$). In nearly all cases the second-order rate constant for each nucleophile goes though a minimum for the unsubstituted compound while the α-D isotope increases monotonically in the sequence *p*-NO_2 > *p*-H > *p*-OCH_3. These results are consistent with an increasing "looseness" of the S_N2 transition state as the substituent on the aromatic ring becomes more electron donating.

Introduction

Nearly 30 years ago Kohnstam[1] suggested that as the nucleophile becomes weaker in the S_N2 reactions of *p*-methoxybenzyl chloride (I) and *p*-phenoxybenzyl chloride (II), the charge on the benzylic carbon increases. Thus, the sum of the bond orders between the α-carbon–nucleophile bond and the α-carbon–leaving group bond was less for weak nucleophiles than for strong nucleophiles. For example, I solvolyzes (S_N1) 135-fold as rapidly as II while in the S_N2 reactions of these two substrates the rate of I vs. II is dependent on the strength of the attacking nucleophile. With weak nucleophiles such as NO_3^- a 139-fold rate enhancement was observed whereas for strong nucleophiles such as N_3^- a 4.9-fold rate enhancement was found. Schematically, this may be represented as in Figure 1.

In recent years analysis of the S_N2 transition state using the reacting bond rule[2] and O'Ferrall[3]–Jencks[4] diagrams has afforded deeper insight into this reaction.[5-7] Harris[6] has summarized several predictions concerning S_N2 reactions of benzyl systems by using these O'Ferrall type reaction coordinate diagrams. For solvolysis of substituted benzyl tosylates and chlorides the experimental changes in m, k_H/k_D, k_{OTS}/k_{Cl}, and $k_{ethanol}/k_{H_2O}$ are as predicted for a transition state midway between reactants and products for a change to electron-donating substituents.

In a series of significant papers Schowen[8-10] has shown how α-D isotope effects can be used to deduce the "tightness" of the S_N2 transition state and how steric compression may lead to enzymatic accelerations in enzyme-mediated methyl transfer. Specifically, Schowen[8] has reported α-D isotope effects for reactions 1 and 2. Once again, the poorer nucleophile furnishes the looser transition state.



$$k_{H_2}/k_{D_2} = 1.17 \pm 0.02$$

Westaway and Ali[11] have studied the reaction of substituted phenyldimethylbenzylammonium ions with thiophenoxides in DMF (Figure 2). Secondary α-D isotope effects, nitrogen-leaving

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(1) G. Kohnstam, A. Queen, and T. Ribar, *Chem. Ind.*, 1287 (1962).

(2) E. R. Thornton, *J. Am. Chem. Soc.*, **89**, 2915 (1967).

(3) R. A. More O'Ferrall, *J. Chem. Soc.*, **13**, 274 (1970).

(4) W. P. Jencks, *Chem. Rev.*, **72**, 705 (1972).

(5) T. H. Lowry and K.-S. Richardson in "Mechanism and Theory in Organic Chemistry", Harper and Row, New York, 1976, pp 246–250.

(6) J. Milton Harris, S. G. Shafer, J. R. Moffatt, and A. R. Becker, *J. Am. Chem. Soc.*, **101**, 3295 (1979).

(7) P. R. Joung and W. P. Jencks, *J. Am. Chem. Soc.*, **101**, 3288 (1979).

(8) I. Mihel, J. O. Knipe, J. K. Coward, and R. L. Schowen, *J. Am. Chem. Soc.*, **101**, 4349 (1979).

(9) C. H. Gray, J. K. Coward, K. Barbara Schowen, and R. L. Schowen, *J. Am. Chem. Soc.*, **101**, 4351 (1979).

(10) M. F. Hegazi, R. T. Borchardt, and R. L. Schowen, *J. Am. Chem. Soc.*, **101**, 4359 (1979).

(11) K. C. Westaway and S. F. Ali, *Can. J. Chem.*, **57**, 1354 (1979).

0002-7863/80/1502-6463$01.00/0

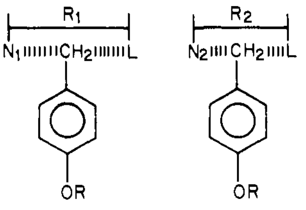


Figure 1. S_N2 transition states for benzyl chlorides reacting with nucleophiles. N_1, weak nucleophile, weak bonds to both incoming nucleophile and leaving group. N_2, strong nucleophile, strong bonds to incoming nucleophile and leaving group. Note R_1 greater than R_2 necessitates greater positive charge development at benzylic carbon for N_1.

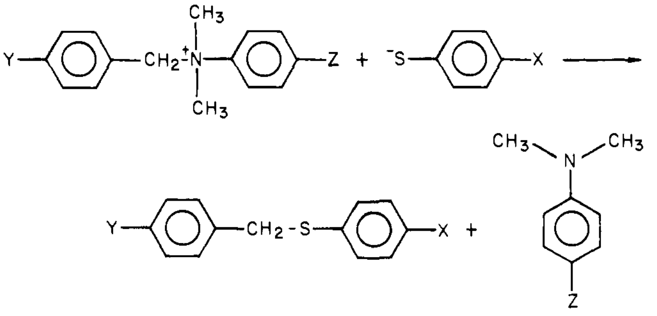
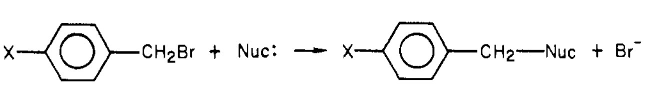


Figure 2. Reactions of substituted arylbenzyldimethylammonium ions with substituted thiophenoxides.



Ia, X = OCH_3
Ib, X = H
Ic, X = NO_2

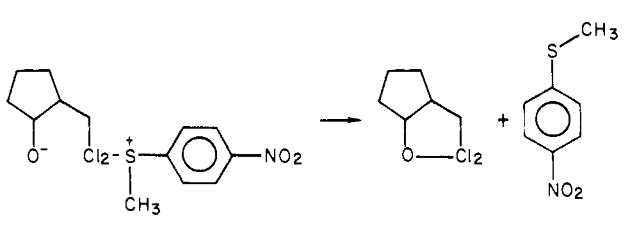
Figure 3.

Figure 4. The S_N2 Transition State.

Table I. α-Deuterium Isotope Effects[a] and Rates[b] of Reaction of Various Nucleophiles with Substituted Benzyl Bromides in 80% (v/v) Dioxane–Water at 25 °C

substd benzyl bromide	NUC	$(k_H/k_D)_D$[a]	$10^3 k_{obsd}$, $M^{-1}\ s^{-1}$	k_{rel}	ρ
p-CH_3O	Et_3N	1.014 (3)	11.4	7.40	−3.22
p-H	Et_3N	0.993 (6)	1.54	1.00	
p-NO_2	Et_3N	0.988 (9)	0.798	0.52	−0.36
p-CH_3O	KSCN	1.069 (10)	67.5	11.2	−3.89
p-H	NaSCN	1.033 (2)	6.05	1.00	
p-NO_2	NaSCN	1.026 (8)	17.8	2.94	0.60
p-CH_3O	NaN_3	1.050 (7)	77.1	8.34	−3.41
p-H	NaN_3	1.012 (7)	9.24	1.00	
p-NO_2	LiN_3	0.998 (12)	27.3	2.95	0.60
p-CH_3O	$Na_2S_2O_3$	1.045 (5)	410	4.27	−2.34
p-H	$Na_2S_2O_3$	1.031 (6)	96	1.00	
p-NO_2	$Na_2S_2O_3$	1.016 (5)	604	6.29	1.03
p-CH_3O	Et_4NOH	1.022 (22)	4.33	5.22	−2.67
p-H	Et_4NOH	0.992 (2)	0.830	1.00	
p-NO_2	Et_4NOH				

[a] Average isotope effect per D of 4–6 determinations over a range of nucleophile concentrations. Number in parentheses indicates standard deviation; e.g., 0.988 (9) is 0.988 ± 0.009. [b] Reaction rates monitored spectrophotometrically by monitoring the disappearance of reactant in a Gilford-2400 spectrophotometer. The absorbance–time data were fitted by a nonlinear least-squares regression analysis to obtain the psuedo-first-order rate constant. The second-order rate constants were obtained by correcting the observed rate constant for any solvolysis rate (Ia and Ib) and dividing the observed rate constant by the nucleophile concentration. The wavelengths used were for Ia 248 nm, for Ib 226–230 nm, and for Ic 272–276 nm.



$k_{H_2}/k_{D_2} = 0.998 \pm 0.001$

group isotope effects, and σρ-type correlations led Westaway and Ali to the following conclusions. The nucleophile–leaving group bond distance varies inversely with the magnitude of the α-D effect. In addition, they showed that..."changing to a better leaving group changes the length of the nucleophile–α-carbon bond more than the α-carbon–leaving group bond and leads to a more product-like transition state where the nucleophile–α-carbon bond formation is much less complete and the α-carbon–leaving group bond is slightly more ruptured".

In this paper we would like to present results for reactions of substituted benzyl bromides with a wide range of nucleophiles which further delineate the structure of the S_N2 transition state.

Results

In Table I are listed our results for the rates and α-D isotope effects for a series of nucleophiles with a series of benzyl bromides (Figure 3). In addition the relative rate ratio for each nucleophile and each substrate is recorded ($k_{benzyl} = 1$, for each nucleophile).

For each nucleophile $k_2^{OCH_3} > k_2^{H} < k_2^{NO_2}$ whereas the α-D isotope effects stand in the order $k_{HD}^{OCH_3} > k_{HD}^{H} > k_{HD}^{NO_2}$. Thus, while the free energy of activation is a maximum for the unsubstituted compound, the isotopic zero-point energy difference tends to be largest for the most electron-donating substituent. For all nucleophiles, the two-point ρ values obtained from the p-OCH_3 and p-H compounds (Table I) tend to be large and negative whereas the ρ values derived from the p-NO_2 and p-H compounds tend to be small, positive numbers for all nucleophiles other than Et_3N. These results suggest build up of excess positive charge for p-OCH_3 and excess negative charge for p-NO_2 at the benzylic carbon for these transition states.

Discussion

Several authors have commented on the solvolylic behavior of substituted benzyl systems.[12-15] A blend of S_N1 and S_N2 mechanisms[14,15] has been suggested, but Shiner[16] points out that an unrealistically large negative ρ is necessary to account for the observed fall off in α-D isotope effect for more electron-withdrawing substituents. He suggested that an additional mechanism is required to accommodate all the results, attack of solvent on an initially formed ion pair.

It has been noted earlier[17-23] that neutral and anionic nucleophiles react in nucleophilic displacement reactions with abnormal (nonlinear) σρ relations. But this represents the first systematic study of α-D isotope effects for various nucleophiles with various substrates in nucleophilic reactions of benzyl bromides. Several major points may be obtained by examination of these data. (1)

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(12) V. J. Shiner, Jr., *ACS Monogr.*, No. **167**, 90–159 (1970) and references contained therein.

(13) A. Fry *ACS Monogr.*, No. **167**, 377–386 (1970) and references contained therein.

(14) Y. Okamoto and H. C. Brown, *J. Org. Chem.*, **22**, 485 (1957).

(15) G. S. Hammond, C. E. Reeder, F. T. Fang, and J. K. Kochi, *J. Am. Chem. Soc.*, **80**, 568 (1958).

(16) Reference 12, p 117.

(17) T. Thorstenson, R. Eliason, and J. Songsted, *Acta Chem. Scan., Ser. A*, **A31**, 276 (1977).

(18) T. Thorstenson and J. Songsted, *Acta Chem. Scand., Ser. A*, **A30**, 724 (1976).

(19) F. P. Ballistreri, E. Maccarone, and A. Mamo, *J. Org. Chem.* **41**, 3364 (1976).

(20) A. R. Stein, *Tetrahedron Lett.*, 4145 (1974).

(21) E. C. F. Ko and K. T. Leffek, *Can. J. Chem.*, **50**, 1297 (1972).

(22) K. Kalliorinne and E. Tommila, *Acta Scand. Acta*, **23**, 2567 (1969).

(23) S. Sugden and J. B. Willis, *J. Chem. Soc.*, 1360 (1961).

Table II. Isotope Effect Dependence on Nucleophilic Reactivity

nucleophile	rel rate	substrate	k_H/k_D
SCN^-	1.0	*p*-OCH_3	1.069 (10)
$S_2O_3^{2-}$	6.1	*p*-OCH_3	1.045 (5)
SCN^-	1.0	*p*-H	1.033 (2)
$S_2O_3^{2-}$	15.8	*p*-H	1.031 (6)
SCN^-	1.0	*p*-NO_2	1.026 (8)
$S_2O_3^{2-}$	34.0	*p*-NO_2	1.016 (5)
Et_3N	1.0	*p*-OCH_3	1.014 (3)
N_3^-	6.8	*p*-OCH_3	1.050 (7)
Et_3N	1.0	*p*-H	0.993 (6)
N_3^-	6.0	*p*-H	1.012 (7)
Et_3N	1.0	*p*-NO_2	0.988 (9)
N_3^-	34.2	*p*-NO_2	0.998 (12)

All of these isotope effects are in the range expected for the S_N2 reaction. (2) For any given nucleophile the isotope effect increases with the electron-donating character of the para substituent. (3) For any given substrate the α-D isotope effect does not correlate with nucleophilicity as judged by relative rate (Table II).

Previously, theoretical[24-26] and experimental[12,27-30] isotope effect studies have been published dealing with the S_N2 reactions.

In the S_N2 reaction (Figure 4) the magnitude of the α-D isotope effect is determined by two factors principally. These are (1) the relative strengths of the nucleophile–carbon bond being formed and the carbon–leaving group bond being broken and (2) the chemical identity of the proximal atom in the leaving group and entering group.[32,33] The first of these will determine the amount of positive charge on the carbon atom being displaced. For example, in the limit where the bond to the leaving group is completely severed but bonding to the nucleophile has not yet begun (in this case N may be regarded as a "spectator" nucleophile[31]), the α-D effect will be a maximum characteristic of the leaving group. On the other hand, if the entering nucleophile and the leaving group were bound with equal strength *and* the nucleophile's proximal atom and leaving groups proximal atom were identical, the α-D effect is nearly unity. This second factor comes into play since the force field at the α-carbon will, in general, be different for these two groups bound to the α-carbon. Thus, "a tight" transition state may result in an appreciable isotope effect even if little charge develops at the α-carbon.

In Table II the results are grouped according to the identity of the attacking atom. Considering first the sulfur nucleophiles ($S_2O_3^{2-}$, SCN^-), it is apparent in all cases investigated that $S_2O_3^{2-}$ is the better nucleophile. Following Kohstam,[1] the change from $S_2O_3^{2-}$ to SCN^- results in a "loosening" of the S_N2 transition state and an attendant increase in the α-D isotope effect. The identity of the attacking atom, sulfur, in both cases, removes any substantive change in isotope effect induced by entering group variation.

Table III. Spontaneous Hydrolysis Rates and Nucleophile Concentration Range for Table II

substrate	k_0	nucleophile	concn, M
p-OCH_3	2.57×10^{-4}	Et_3N	0.0035–0.14
	2.57×10^{-4}	KSCN	0.031–0.4
	2.57×10^{-4}	NaN_3	0.025–0.1
	2.57×10^{-4}	$Na_2S_2O_3$	0.00097–0.0019
	2.57×10^{-4}	Et_4NOH	0.0042–0.0663
p-H	2.4×10^{-7}	Et_3N	0.05–0.2
	2.4×10^{-7}	NaSCN	0.006–0.025
	2.4×10^{-7}	NaN_3	0.025–0.10
	2.4×10^{-7}	$Na_2S_2O_3$	0.00097–0.0019
	2.4×10^{-7}	Et_4NOH	0.0042–0.0663
p-NO_2	~0		

The nitrogen nucleophiles (Et_3N, N_3^-) behave somewhat differently.

While Et_3N is the poorer nucleophile for all substrates, it furnishes the smaller α-D isotope effect. Unlike the $S_2O_3^{2-}$ vs. SCN^- comparison above, steric factors come into play. For bulky nucleophiles such as Et_3N the three alkyl groups impede the out-of-plane bending vibrations of the α-CH bonds. For similar nucleophile–α-carbon and α-carbon–leaving group bond orders the more sterically congested nucleophile will furnish the smaller isotope effect.[11] This appears to be the case for all three substrates, while a larger α-D isotope effect from the steric effect more than offsets this expected increase.

Experimental Section

Synthesis. The following procedure was used for the synthesis of *p*-methoxybenzyl (Ia) and benzyl bromide (Ib) labeled with deuterium at the α-position, respectively. Reduction of the methyl esters of *p*-anisic acid and benzoic acid with $LiAlD_4$ (>99 atom % D) afforded the labeled alcohols. The alcohols were converted to the bromides with $HBr/CHCl_3$ or HBr/C_6H_6: (Ia) bp 35–40 °C (0.3 mmHg), >99% D_2; (Ib) bp 74–76 °C (0.2 mmHg), >95% D_2.

The synthesis of Ic followed that of Brown.[35] The reduction of *p*-nitrobenzoic acid with $NaBD_4$ in the presence of 30 mol % $AlCl_3$ furnished labeled *p*-nitrobenzyl alcohol. Treatment of the alcohol with HBr/H_2O furnished Ic: mp 96–97 °C, 61% D_2, 34.6% HD, 4.4% H_2. The rates of reaction for deuterated substrates were corrected for incomplete deuteration as described earlier.[36] The unlabeled bromides were prepared by an analogous procedure using $LiAlH_4$ or were commercially available samples.

Kinetics. The procedure was that described in an earlier publication.[36] Reaction rates were monitored spectrophotometrically by following the change in optical density of the reactant in the thermostated cell compartment of a Gilford-2400 spectrophotometer. Absorbance-time data were fitted by a nonlinear least-squares regression analysis to obtain psuedo-first-order rate constants in the presence of at least a 10-fold excess concentration of nucleophile. The second-order rate constants were obtained by correcting the observed rate constant for any solvolysis rate (Ia and Ib) and dividing the observed rate constant by the nucleophile concentration. The wavelengths used were for Ia 248 nm, for Ib 226–230 nm, and for Ic 272–276 nm.

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(24) A. V. Willi, *Z. Phys. Chem.* (*Wiesbaden*), **66**, 317 (1969).

(25) J. Bron, *Can. J. Chem.*, **52**, 903 (1974).

(26) L. Sims, A. Fry, L. T. Netherton, J. C. Wilson, and S. W. Crook, *J. Am. Chem. Soc.*, **94**, 1364 (1972).

(27) K. M. Koshy and R. E. Robertson, *J. Am. Chem. Soc.*, **96**, 914 (1974).

(28) V. J. Shiner, Jr., M. W. Rapp, and H. R. Pinnick, *J. Am. Chem. Soc.*, **92**, 232 (1970).

(29) A. V. Willi, C.-K. Ho, and A. G. Hanba pour, *J. Org. Chem.*, **37**, 1185 (1972).

(30) V. F. Raaen, R. Juhlke, F. J. Brown, and C. J. Collins, *J. Am. Chem. Soc.*, **96**, 5928 (1974).

(31) By analogy with a term introduced by Schowen for acid–base catalysis.

(32) W. Cleland, M. H. O'Leary, and D. B. Northop, Eds., *Isot. Eff. Enzyme-Catal. React.*, *Proc. Annu. Harry Steenbock Symp.*, **6th** (1977).

(33) S. R. Hartshorn and V. J. Shiner, Jr., **94**, 9002 (1972).

(34) See, for example, ref 11.

(35) H. C. Brown and B. C. Subba Rao, *J. Am. Chem. Soc.*, **78**, 2582 (1956).

(36) V. P. Vitullo, S. Sridharan, and L. P. Johnson, *J. Am. Chem. Soc.*, **101**, 2320 (1979).