Bridgehead β-Deuterium Secondary Kinetic Isotope Effect in the Solvolysis of *endo*-Norbornan-2-yl *p*-Bromobenzenesulphonate

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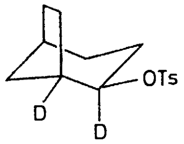
1-Deuterio- and 1,2-dideuterio-*endo*-norbornan-2-yl *p*-bromobenzenesulphonates have been prepared and the secondary deuterium kinetic isotope effects have been measured in 80% aqueous ethanol (k^H/k^D 1.000 and 1.191 respectively at 54.5°) and in buffered acetic acid (k^H/k^D 0.996 and 1.194 respectively at 64.7°). These results establish that, when a β-C–H(D) bond is orthogonal to the developing vacant orbital of an incipient carbonium ion being formed from a secondary alkyl arenesulphonate, virtually no kinetic isotope effect will be observed.

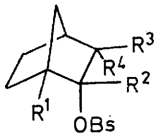
THE value of secondary deuterium kinetic isotope effect measurements in the elucidation of reaction mechanisms rests largely upon a prior knowledge of isotope effects for reactions whose mechanisms are already understood.[1,2] A β-deuterium kinetic isotope effect (β-k.i.e.) close to unity is expected for a solvolytic reaction in which the departure of a leaving group from the α-carbon is nucleophilically assisted.[1,3,4] A k.i.e. of unity is also expected for a solvolytic reaction in which the β-C–H(D) bond is orthogonal to the developing vacant *p*-orbital on the α-carbon[1] although there have been very few conformationally unambiguous examples where this has been established experimentally.

In order to measure the α-deuterium k.i.e. for the solvolysis of *endo*-bicyclo[3.2.1]octan-2-yl toluene-*p*-sulphonate without complications due to scrambling of a single deuterium label, compound (1) was used and a composite secondary k.i.e. was measured.[5] Although there was reason to assume that the effect of the bridgehead β-deuterium in (1) would be small,[6,7] no entirely satisfactory analogue was available for comparison. A suitable secondary alkyl arenesulphonate model is 1-deuterio-*endo*-norbornan-2-yl *p*-bromobenzenesulphonate (brosylate) (2a) in which the dihedral angle between the bridgehead C–H(D) bond and the bond from the leaving group to C(2) is *ca.* 80°.

Knowledge of the bridgehead β-k.i.e. for (2a) will also be helpful in the interpretation of the α-k.i.e. for the solvolysis of 2-deuterio-*exo*-norbornan-2-yl brosylate, as it is known that the deuterium of this compound becomes scrambled during the course of the solvolysis.[1,3,8-10]

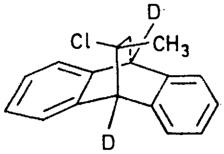


(1)



(2)

a; $R^1 = D, R^2 - R^4 = H$
b; $R^1 = R^2 = D, R^3 = R^4 = H$
c; $R^1 - R^4 = H$
d; $R^1 = R^3 = R^4 = H, R^2 = D$
e; $R^1 = R^2 = R^4 = H, R^3 = D$
f; $R^1 - R^3 = H, R^4 = D$



(3)

The preparation of the specifically labelled *endo*-norbornan-2-yl brosylates (2a and b) is illustrated in the Scheme. Norbornan-2-one was also prepared for

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[2] S. E. Scheppele, *Chem. Comm.*, 1971, 592.

[3] S. E. Scheppele, *Chem. Rev.*, 1972, **72**, 511.

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[5] H. Maskill, *J.C.S. Perkin II*, 1975, 1850.

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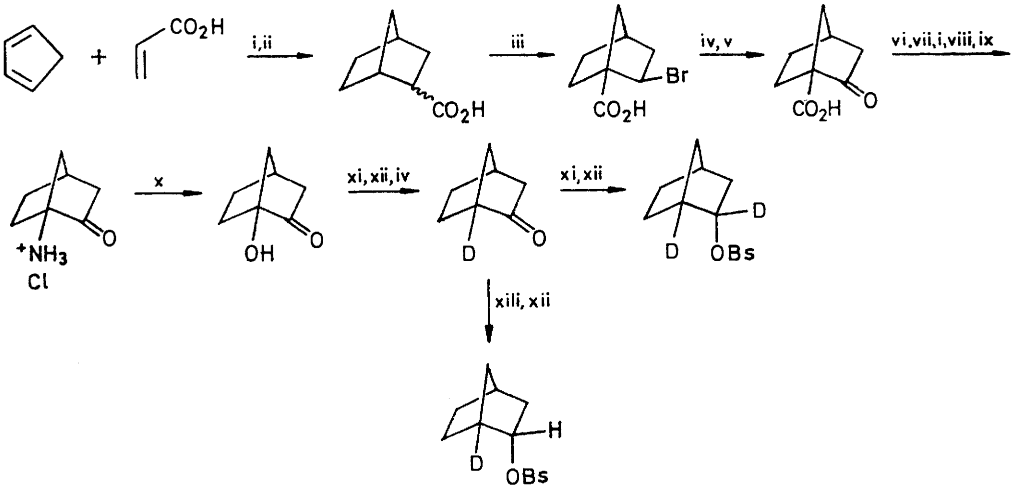
[8] C. C. Lee and E. W. C. Wong, *J. Amer. Chem. Soc.*, 1964, **86**. 2752.

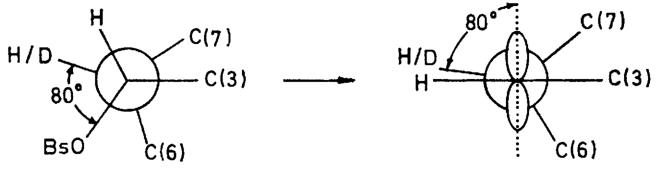
[9] B. L. Murr and J. A. Conkling, *J. Amer. Chem. Soc.*, 1970, **92**, 3462.

[10] K. Humski, R. Malojcic, S. Borcic, and D. E. Sunko, *J. Amer. Chem. Soc.*, 1970, **92**, 6534; see also D. E. Sunko and S. Borcic, ref. 1, ch. 3.

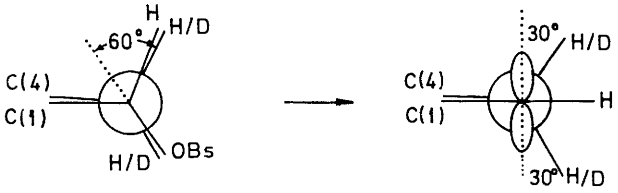
spectroscopic comparison with the key intermediate 1-deuterionorbornan-2-one. The n.m.r. spectrum of the perprotio-compound contained broad singlets at τ 7.37 and 7.51. The signal at τ 7.51 was completely absent in the n.m.r. spectrum of the deuteriated compound, and the deuterium incorporation was 100% D_1 by mass spectrometry. Similarly, of the two signals at τ 5.23 and 7.59 in the n.m.r. spectrum of *endo*-norbornan-2-yl brosylate (2c), only the former was present in the spectrum of (2a) and neither was present in that of (2b). The mass spectrometrically determined deuterium content of (2a) was $\geqslant$99% D_1 and of (2b) $\geqslant$91% D_2, $\leqslant$9% D_1.



SCHEME Reagents: i, heat; ii, H_2–catalyst; iii, Br_2–PCl_3; iv, H_2O; v, oxidation; vi, $(COCl)_2$; vii, $(C_4H_9)_4N^+N_3^-$; viii, C_2H_5OH; ix, $H_3O^+Cl^-$; x, H^+, $NaNO_2$; xi, $LiAlD_4$; xii, BsCl–C_5H_5N; xiii, $LiAlH_4$



(A)



(B)

RESULTS AND DISCUSSION

Compounds (2a—c) were solvolysed in 80% aqueous ethanol at 54.5° and in acetic acid (0·15M-CH_3CO_2K) at 64.7°. The results are shown in the Table. The values of 1.000 and 0.996 for the k.i.e. of (2a) in 80% aqueous ethanol and buffered acetic acid respectively confirm that the bridgehead deuterium of (1) introduces no serious ambiguity into the interpretation of the composite k.i.e. The low composite effect[5] cannot be due to a substantial rate-retarding isotope effect due to the α-deuterium [such as would result if the reaction of (1) were by an unassisted classical carbonium ion route] compensated in part by a rate-enhancing (inverse) kinetic effect of the bridgehead deuterium.

The results are in agreement with the value of 0.986

Rates and secondary deuterium kinetic isotope effects for solvolysis of (2) [a]

	Solvolysis medium	
	$EtOH$–H_2O(4:1) (54.5 $\mp$ 0.1°)	CH_3CO_2H–CH_3CO_2K (64.7 $\mp$ 0.1°)
10^4k^H(2c)/min^{-1}	42.61 ($\mp$0.48)	38.45 ($\mp$0.66)
k^H(2c)/k^D(2a)	1.000 ($\mp$0.011)	0.996 ($\mp$0.005)
k^H(2c)/k^D(2b)	1.191 ($\mp$0.007)	1.194 ($\mp$0.011)

[a] Compounds (2a—c) were solvolysed simultaneously in the same cell compartment and the rates were measured spectrophotometrically (276 nm). Temperature stability was better than $\mp$0.04°. Individual rate constants and standard deviations (which were usually better than 1%) were computed by a non-linear least squares programme. Rate constants which are shown are means of six values and isotope effects are means of six ratios; errors are standard errors.

for solvolysis (60% aqueous ethanol) of the tertiary chloride (3).[6] They provide firm experimental evidence that when a β-C–H(D) bond is orthogonal to the developing vacant orbital of an incipient carbonium ion from a secondary alkyl arenesulphonate, virtually no kinetic isotope effect will be observed.

The results of 1.191 and 1.194 for (2b) in 80% aqueous ethanol and buffered acetic acid are in excellent agreement with values of 1.193 [9] and 1.20 [11] reported earlier for (2d). With the knowledge of the result for (2a), this is as expected if α- and β-effects are cumulative.

Comparison of the C(1) bridgehead β-k.i.e. with the effects of the C(3) β-deuteriums [12] in (2e and f) is interesting. As can be seen from the Newman projections (A) along the C(2)–C(1) bond of (2a), there is almost no difference between the dihedral angles subtended by the C(2)–oxygen bond and by the vacant *p*-orbital on C(2) with the C(1)–H(D) bond.

On the other hand, the Newman projections (B) along the C(2)–C(3) bond of (2e and f) show that as the ionization proceeds, the dihedral angles between the developing vacant orbital on C(2) and each of the two hydrogens on C(3) change. That with the *endo*-C(3)–H(D) becomes worse for hyperconjugation as that with the *exo*-hydrogen (deuterium) improves until, at the classical carbonium ion stage, the two angles are equal. The kinetic isotope effects for (2e and f) are 1.19 and 1.12 respectively with the *exo*-C(3)–D remarkably having the greater rate-retarding effect.[12] This difference is qualitatively what would be expected if the transition state is late in the ionization reaction co-ordinate, and if the hyperconjugative interaction of the β-C–H(D) with the developing vacant orbital is more effective at the side of the α-carbon opposite to that from which the leaving group departs.[6,7,13]

EXPERIMENTAL

The 90 MHz n.m.r. spectra and the mass spectra were recorded on Perkin-Elmer R32 and JEOL D100 instruments respectively. Details of the kinetics methods have already been described.[5]

2-Oxonorbornane-1-carbonyl Chloride.—*exo*-2-Bromonorbornane-1-carboxylic acid was made by addition of freshly distilled cyclopentadiene to acrylic acid followed by hydrogenation [14] and bromination,[15,16] m.p. (light petroleum) 147—149° (lit.,[15] 150—151°), τ ($CDCl_3$) −1.9 (1 H, s), 5.80 (1 H, m), and 7.5—8.9 (9 H, m), $\bar{\nu}$(KBr) 3 300—2 200, 1 659, 1 424, 1 334, 1 307, 1 295, 1 220, 952, 939, 739, 618, and 532 cm^{-1}. Hydrolysis, oxidation,[17] and isolation by continuous ether extraction, evaporation of ether, and trituration with cold pentane gave 2-oxonorbornane-1-carboxylic acid, m.p. (light petroleum) 128—129° (lit.,[18] 128.5—129.5°), τ ($CDCl_3$) −1.6 (1 H, s), 7.27br (1 H, s), and 7.4—8.7 (8 H, m), $\bar{\nu}$(KBr) 3 300—2 600, 1 744, 1 690, 1 423, 1 323, 1 300, 1 048, and 733 cm^{-1}. Reaction with oxalyl chloride at room temperature for three days followed by fractional distillation gave 2-oxonorbornane-1-carbon chloride, b.p. 94° at 0.2 Torr, τ ($CDCl_3$) 7.24br (1 H, s) and 7.3—8.7 (8 H, m), $\bar{\nu}$ (liquid film) 2 960, 2 880, 1 790, 1 745, 1 407, 1 298, 1 262, 1 191, 1 165, 1 062, 996, 853, 783, and 696 cm^{-1}.

1-Hydroxynorbornan-2-one.[18]—The keto-acid chloride (12.9 g, 0.075 mol) in tetrahydrofuran (50 cm^3) was stirred at −60 to −40° as a solution of tetra-n-butylammonium azide [19] (*ca.* 0.09 mol) in acetone–benzene (100 cm^3) was added dropwise over 30 min. Stirring was continued as the temperature was allowed to rise to 0° during 2 h, and then for a further 1 h. Benzene (100 cm^3) was added and the solution was slowly heated under reflux as the gas evolution was measured. The heating was continued for 7 h although almost all the gas (*ca.* 2 l) was evolved in the first 2—3 h. Ethanol (50 cm^3) was added and the refluxing was continued for 15 h then toluene (120 cm^3) was added. The solution was fractionally distilled (760 Torr) until the still head temperature reached 88°. The solution was then cooled (0°) and extracted twice with cold water; the first aqueous extract was back-extracted with toluene. The combined organic phase was fractionally distilled down to *ca.* 180 cm^3, cooled, and acidified (20 cm^3 of concentrated HCl made up to 50 cm^3 with water). The mixture was then heated vigorously under reflux for *ca.* 15 h, cooled, and extracted several times with ether.

The acidic aqueous phase was cooled (0°), stirred under argon, and treated with a solution of sodium nitrite (9 g, 0.13 mol) in water (15 cm^3) over 1 h. Stirring was continued for a further 2 h then the solution was made basic with sodium hydrogen carbonate and continuously extracted with ether for 30 h. The ether extract was dried (Na_2SO_4), filtered, and fractionally distilled. The residue was evaporated briefly and chromatographed on neutral alumina using pentane–ether–ethyl acetate for elution. Automatically collected fractions were monitored by g.l.c. and combined appropriately. After fractional distillation of the solvent, the residue was sublimed at 80° and 14 Torr yielding 4.13 g (44%), m.p. (pentane–ether and further sublimation) 145—146° (lit.,[18] 146—147°), τ ($CDCl_3$) 6.60 (1 H, s), 7.47br (1 H, s), and 7.6—8.6 (8 H, m), $\bar{\nu}$(KBr) 3 400br, 2 955, 2 880, 1 743, 1 400, 1 322, 1 306, 1 172, 1 114, 1 086, 1 065, 985, and 971 cm^{-1}.

2-Deuterio-1,2-dihydroxynorbornane.—A solution of 1-hydroxynorbornan-2-one (3.0 g, 0.023 8 mol) in absolute ether (30 cm^3) was added dropwise to a stirred slurry of lithium aluminium deuteride (1.8 g, 0.043 mol) in absolute ether at 0°. After the addition was complete, the mixture was heated under reflux for 2 days. The reaction mixture was cautiously treated with aqueous ammonium chloride solution and then was continuously extracted with ether for 24 h. Fractional distillation of most of the ether and

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evaporation of the last traces left the crystalline product which was sublimed at 120° and 14 Torr yielding 2.60 g (85%).

1-*Deuterionorbornan*-2-*one*.—A solution of *p*-bromobenzenesulphonyl chloride (3.80 g, 0.015 mol) in dry pyridine (5.0 cm^3) was added to 2-deuterio-1,2-dihydroxynorbornane (1.30 g, 0.010 2 mol). The solution was cooled and kept at 0° for 2 days. The reaction mixture was warmed to room temperature, and to it were added tetrahydrofuran (50 cm^3), acetone (70 cm^3), and water (100 cm^3). The solution was heated under reflux for 27 h then was slowly fractionally distilled. After the distillation of 100 cm^3, more tetrahydrofuran (80 cm^3) was added and the distillation was continued. After a further volume (100 cm^3) of distillate had been collected, the distillation was discontinued (still-head temperature = 63°). Brine was added to the cooled residue which was then continuously extracted with pentane for 36 h. The pentane extract was fractionally distilled down to *ca.* 10 cm^3 and the residue was chromatographed on deactivated alumina. The elution was with pentane and automatically collected fractions were monitored by g.l.c. and appropriately combined. After fractional distillation, the concentrated pentane solution of ketone was reduced directly in the next step. A sample of the deuteriated ketone from a comparable preparation was isolated by preparative g.l.c. (8 ft × $\frac{1}{8}$ in 8% Apiezon L on Phaseprep A, 50 cm^3 min^{-1} N$_2$ at 40 lb in^{-2}) for spectroscopic characterization, τ (CCl$_4$) 7.37br (1 H, s) and 7.8—8.9 (8 H, m), $\bar{\nu}$(CCl$_4$) 2 960, 2 880, 2 250w, 1 745, 1 450, 1 407, 1 290, 1 256, 1 249, 1 180, 1 123, 1 086, 1 080, 931, and 862 cm^{-1}. For comparison, the i.r. and n.m.r. spectra of pure norbornan-2-one were obtained, τ (CCl$_4$) 7.37br (1 H, s), 7.51br (1 H, s), and 7.8—8.9 (8 H, m), $\bar{\nu}$(CCl$_4$) 2 960, 2 880, 1 750, 1 450, 1 407, 1 298, 1 173, 1 156, 1 128, 1 067, 1 043, 941, 863, and 851 cm^{-1}. Mass spectral analysis of deuteriated and undeuteriated analogues indicated that the former was 100% D$_1$.

1,2-*Dideuterionorbornan*-2-*ol*.—The solution of 1-deuterionorbornan-2-one (*ca.* 0.01 mol) was added to a stirred slurry of lithium aluminium deuteride (1 g, 0.024 mol) in absolute ether (15 cm^3) at −70° under argon. After 1 h the temperature was allowed to rise to room temperature during 2 h and the reaction was quenched with aqueous ammonium chloride. The product was isolated as a crystalline solid (0.49 g, 42% based upon the diol) by continuous ether extraction, fractional distillation, and sublimation at 80° and 14 Torr, and comprised *endo*- and *exo*-isomers in the ratio 97 : 3.

In an exactly analogous manner, the 1-deuterionorbornan-2-ols were prepared from 1-deuterionorbornan-2-one and lithium aluminium hydride.

1,2-*Dideuterio*-endo-*norbornan*-2-*yl* p-*Bromobenzenesulphonate*.—The 97 : 3 mixture of *endo*- and *exo*-1,2-dideuterionorbornan-2-ols (0.49 g, 4.3 mmol) and *p*-bromobenzenesulphonyl chloride (2.70 g, 10.6 mmol) were dissolved in dry pyridine (4 cm^3) and kept at 0° for 4 days. The mixture was then dissolved in acetone (75 cm^3) and water (25 cm^3) and kept at 45° for 10 min.[20] The acetone was evaporated under reduced pressure and the aqueous residue was extracted three times with ether. Each extract was washed twice with cold dilute hydrochloric acid, brine, and aqueous sodium hydrogen carbonate. The combined ether phase was dried (MgSO$_4$), treated with charcoal, filtered and evaporated finally at 0.1 Torr. The product (1.09 g, 76%) was recrystallized from light petroleum, m.p. 62—62.5°, τ (CCl$_4$) 2.32 (4 H, m), 7.78br (1 H, s), and 7.9—9.0 (8 H, m), $\bar{\nu}$(KBr) 2 960, 2 875, 2 210w, 1 574, 1 390, 1 356, 1 190, 1 084, 1 070, 1 012, 945, 922, 873, 740, 610, and 574 cm^{-1}; deuterium incorporation (mass spectroscopically determined) $\geqslant 91\%$ D$_2$, $\leqslant 9\%$ D$_1$.

By an exactly analogous method, 1-deuterio-*endo*-norbornan-2-yl *p*-bromobenzenesulphonate was prepared, m.p. 60—62°, τ (CCl$_4$) 2.33 (4 H, m), 5.24 (1 H, complex d), and 7.80br (1 H, s), and 7.9—9.2 (8 H, m), $\bar{\nu}$(CCl$_4$) 2 960, 2 870, 2 200w, 1 577, 1 473, 1 392, 1 377, 1 190, 1 179, 1 098, 1 072, 1 023, 1 015, 970, 950, 910, and 872 cm^{-1}, deuterium incorporation $\geqslant 99\%$ D$_1$.

The undeuteriated compound was made by an established procedure,[20] m.p. 60.5—62° (lit.,[20] 62—63°), τ (CCl$_4$) 2.33 (4 H, m), 5.23 (1 H, m), 7.59br (1 H, s), 7.80br (1 H, s), and 7.9—9.1 (8 H, m), $\bar{\nu}$(CCl$_4$) 2 965, 2 875, 1 578, 1 472, 1 390, 1 376, 1 190, 1 177, 1 097, 1 071, 1 014, 1 005, 977, 961, 950, 941, 915, 887, and 865 cm^{-1}.

[6/336 *Received*, 17*th February*, 1976]

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