NaH (25 mg, 1.1 mmol) in DMF (0.52 mL) was stirred at 55 °C for 22 h. To the cooled solution was added 1 mL of H_2O and 0.9 mL of 1 M HCl (pH of resulting solution ~7). The aqueous solution was washed with CH_2Cl_2 (5 × 2 mL), and the combined organic extracts were washed with brine (10 mL) and dried ($MgSO_4$). The solvent was removed in vacuo to give a yellow solid, which was chromatographed on silica gel (20:1 ethyl acetate/methanol) to afford **2** as colorless crystals (20.7 mg, 39%): mp 177–9 °C; ^1H NMR ($CDCl_3$) δ 3.69 (m, 4 H), 3.76 (m, 4 H), 3.84 (m, 4 H), 4.22 (m, 4 H), 6.94 (d, J = 7.8 Hz, 2 H), 7.07 (dt, J_d = 1 Hz, J_t = 7.7 Hz, 2 H), 7.40 (dt, J_d = 2 Hz, J_t = 7.8 Hz, 2 H), 8.15 (dd, J = 2 Hz, J = 7.8 Hz, 2 H), 8.70 (bs, 2 H); IR ($CHCl_3$) 3395, 1645 cm^{-1}; CIMS m/z (relative intensity) 415 (M^+ + 1, 100). Crystals of **2** suitable for X-ray crystallographic studies were obtained from hexanes/CH_2Cl_2 (1:1) by the isothermal distillation technique, mp 185–186.5 °C. Anal. Calcd for $C_{22}H_{26}N_2O_6$: C, 63.76; H, 6.32. Found: C, 63.52; H, 6.35.

9,10-Benzo-1,4-dioxa-7-azecin-8-one (3). A solution of **1b** (50 mg, 0.22 mmol) and NaH (60% in oil, 35 mg, 0.88 mmol) in DMF (22 mL) was stirred at 55 °C for 4 days. The solvent was removed in vacuo and the brown residue was dissolved in H_2O (10 mL) and neutralized with 1 M HCl (0.9 mL). The aqueous solution was washed with CH_2Cl_2 (3 × 15 mL), and the combined organic extracts were dried ($MgSO_4$) and concentrated to give a light brown oil. Flash chromatography (silica gel, 6:1 CH_2Cl_2/acetonitrile) afforded **3** as colorless crystals (3.0 mg, 7%) and **2**. Preparative TLC of **2** so obtained (6:1 CH_2Cl_2/acetonitrile) afforded colorless crystals (18.5 mg, 41%). **3**: mp 99–102 °C; ^1H NMR ($CDCl_3$) δ 3.62 (overlapping t's, J = 5.4, 6.2 Hz, 2 H), 3.76 (overlapping d's, J = 5 Hz, 2 H), 3.87 (overlapping d's, J = 4.1, 4.5 Hz, 2 H), 4.07 (overlapping d's, J = 4.4, 5.0 Hz, 2 H), 7.15 (dd, J = 1.2, 7.9 Hz, 1 H), 7.26 (dt, J_d = 1.2 Hz, J_t = 8.1 Hz, 1 H), 7.45 (dt, J_d = 1.9 Hz, J_t = 7.7 Hz, 1 H), 7.71 (br s, 1 H), 7.85 (dd, J = 1.9, 7.6 Hz, 1 H); IR ($CHCl_3$) 3455, 1655 cm^{-1}; CIMS m/z (relative intensity) 208 (M^+ + 1, 100). Anal. Calcd for $C_{11}H_{13}NO_3$: C, 63.76; H, 6.32. Found: C, 63.88; H, 6.48.

Isolation of 4 and Conversion to 2. A solution of **1b** (250 mg, 1.10 mmol) in DMF (5.5 mL) was added to a solution of NaH (60% in oil, 132 mg, 3.30 mmol) in DMF (5.5 mL), and the mixture was stirred for 20 h. The DMF was removed in vacuo, and the brown residue was dissolved in H_2O (20 mL). The aqueous layer was washed with ethyl acetate (3 × 20 mL). The combined organic extracts were washed with brine (30 mL) and then dried ($MgSO_4$). Removal of the solvent in vacuo and flash chromatography (silica gel, 4:3 hexane/acetone) afforded **1b** (40 mg, 16%) and **4** (123 mg, 54%) as a colorless syrup: ^1H NMR ($CDCl_3$) δ 1.95 (br s, 1 H), 3.52–3.62 (m, 6 H), 3.65–3.82 (m, 6 H), 3.90–3.96 (m, 2 H), 4.23–4.35 (m, 2 H), 6.9–7.5 (m, 7 H), 8.0 (dt, J_d = 2 Hz, J_t = 8 Hz, 1 H), 8.19 (dd, J = 2, 8 Hz, 1 H), 8.42 (br s, 1 H); IR ($CHCl_3$) 3470, 3400, 1650, 1620, 1605 cm^{-1}; desorption CIMS m/z (relative intensity) 435 (M^+ + 1, 100). Anal. Calcd for $C_{22}H_{27}N_2O_6F$: C, 60.82; H, 6.26. Found: C, 60.89; H, 6.38.

To **4** (63 mg, 0.145 mmol) in DMF (0.6 mL) was added NaH (14 mg, 0.58 mmol), and the solution was warmed to 60 °C. After stirring for 20 h the mixture was cooled, diluted with H_2O (10 mL), neutralized with 6 M HCl, and washed with CH_2Cl_2 (5 × 10 mL). The combined organic extracts were dried ($MgSO_4$) and evaporated to afford 50.6 mg (84% yield) of **2**. Flash chromatography (3:2 benzene/acetonitrile) of the product gave 29.0 mg (48%) of **2**.

9,10:16,17-Dibenzo-1,4,11-trioxa-7,14-diazacycloheptadecane-8,15-dione (5). A solution of **1b** (124 mg, 0.55 mmol), **1a** (100 mg, 0.55 mmol), and NaH (26 mg, 1.1 mmol) in DMF (6.1 mL) was stirred for 4 days. The reaction mixture was diluted with H_2O (20 mL) and neutralized with 1 M HCl, after which a colorless solid precipitated. The suspension was washed with CH_2Cl_2 (3 × 25 mL), and the combined organic extracts were dried ($MgSO_4$) and evaporated to afford a light brown solid. Flash chromatography on silica gel (3:1 benzene/acetonitrile) gave **5** (74 mg, 36%) along with recovered **1a** (12.6 mg, 10%) and **2** (13.5 mg, 12%). **5**: mp 184–7 °C; ^1H NMR ($CDCl_3$) δ 3.79 (m, 4 H), 3.95 (m, 4 H), 4.28 (m, 4 H) 6.95 (m, 2 H), 7.08 (t, J = 8 Hz, 2 H), 7.42 (complex q, 2 H), 8.14 (dd, J = 1.8, 7.7 Hz, 1 H), 8.20 (dt, J_t = 1.6 Hz, J_d = 7.8 Hz, 1 H), 8.35 (br s, 1 H), 8.85 (t, J = 5.7 Hz, 1 H); IR ($CHCl_3$) 3410, 1645 cm^{-1}; CIMS m/z (relative intensity) 371 (M^+ + 1, 45), 327 (100). Anal. Calcd for $C_{20}H_{22}N_2O_5$: C, 64.85; H, 5.99. Found: C, 64.78; H, 6.05.

9,10:19,20-Dibenzo-1,4,11,14-tetraoxa-7,17-diazacycloeicosane (6a). To a solution of **2** (135 mg, 0.33 mmol) in THF (33 mL) was added boron trifluoride etherate (0.10 mL, 0.82 mmol) and borane–dimethyl sulfide complex (0.07 mL, 10 M). The mixture was warmed to reflux and stirred for 1.5 h. The dimethyl sulfide was then removed by distillation. The remainder of the solution was refluxed for 6 h, the solvent was removed, and 10% KOH (10 mL) and MeOH (10 mL) were added. The solution was refluxed overnight, after which the organic solvents were removed in vacuo. The remaining aqueous solution was washed with CH_2Cl_2 (5 × 15 mL). The combined organic extracts were dried ($MgSO_4$), and solvent was evaporated to give a yellow solid. The solid was dissolved in CH_2Cl_2 (5 mL), the solution was washed with HCl (5 mL, 1 M) and dried ($MgSO_4$), and the solvent was evaporated to afford recovered **2** (10 mg, 7%). The aqueous layer was made basic with concentrated KOH until pH ~ 14. The resulting colorless suspension was washed with CH_2Cl_2 (3 × 5 mL). The combined organic extracts were dried ($MgSO_4$) and the solvent was evaporated to afford **6a** as colorless crystals (118 mg, 93%): mp 260–2 °C dec; ^1H NMR ($CDCl_3$) δ 2.48 (s, 2 H), 2.78 (t, J = 3.5 Hz, 4 H), 3.68 (t, J = 3.5 Hz, 4 H), 3.79 (br s, 8 H), 4.06 (br s, 4 H), 6.80 (d, J = 6.0 Hz, 2 H), 6.89 (t, J = 5.5 Hz, 2 H), 7.19 (dt, J = 1.0, 5.5 Hz, 4 H); IR ($CHCl_3$) 3325, 3000, 2935, 1600, 1595 cm^{-1}; CIMS m/z (relative intensity) 387 (M^+ + 1, 100). An acceptable analysis could not be obtained.

Preparation of 6b. A solution of **6a** (50 mg, 0.13 mmol) and NaH (8 mg, 0.3 mmol) in THF (0.65 mL) was stirred for 10 min. Benzyl bromide (0.04 mL, 0.3 mmol) was added, and the mixture was stirred overnight, diluted with H_2O (1 mL), and washed with CH_2Cl_2 (3 × 2 mL). The combined organic extracts were dried ($MgSO_4$), and the solvent was removed in vacuo. The light brown residue was chromatographed on silica gel (1:1 ethyl acetate/hexane) to afford **6b** as a light tan solid (58.8 mg, 80%); mp 106–8 °C; ^1H NMR ($CDCl_3$) δ 2.80 (t, J = 6.3 Hz, 4 H), 3.67 (s, 4 H), 3.68 (d, J = 6 Hz, 4 H), 3.76 (m, 4 H), 3.81 (s, 4 H), 4.07 (overlapping d's, J = 4.4, 6 Hz, 4 H), 6.80 (dd, J = 1.0, 7.2 Hz, 2 H), 6.91 (dt, J_d = 1.0 Hz, J_t = 7.4 Hz, 2 H), 7.1–7.4 (m, 14 H); IR ($CHCl_3$) 3000, 2920, 2865, 1595, 1585 cm^{-1}; CIMS m/z (relative intensity) 567 (M^+ + 1, 2), 386 (3), 219 (51), 196 (23), 92 (64). Crystals of **6b** suitable for X-ray crystallographic studies were obtained from hexanes/CH_2Cl_2 (1:1) by the isothermal distillation technique, mp 110–1 °C. Anal. Calcd for $C_{36}H_{42}N_2O_4$: C, 76.30; H, 7.47. Found: C, 76.42; H, 7.51.

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Registry No. **1a**, 111904-31-5; **1b**, 136538-57-3; **2**, 136538-58-4; **3**, 136538-59-5; **4**, 136538-60-8; **5**, 136538-61-9; **6a**, 136538-62-0; **6b**, 136538-63-1; 2-(2-aminoethoxy)ethanol, 929-06-6; 2-fluorobenzoyl chloride, 393-52-2.

Supplementary Material Available: Tables of crystal structure data, atomic coordinates, bond angles, bond lengths, anisotropic parameters, and hydrogen atom coordinates for **2** and **6b** (16 pages). Ordering information is given on any current masthead page.

β-Secondary Deuterium Kinetic Isotope Effect for the Insertion of Dichlorocarbene into a C–H Bond

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Large normal α- and/or β-secondary deuterium and tritium kinetic isotope effects (KIEs) have been observed in several enzyme-catalyzed hydroxylations of aliphatic carbons[1-3] and are evidence of a degree of sp^3 to sp^2 re-

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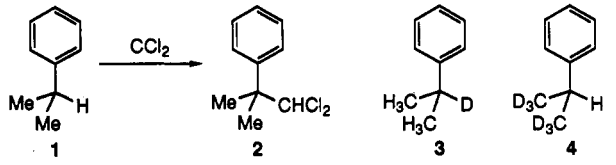
Table I. Isotopic Competition Experiment Data for β-Secondary Kinetic Isotope Effect Determinations

expt	D/H ratio of cumene starting material[a] m/z 126/120[b,c] (M^+)	D/H ratio of product 2-(dichloromethyl)-2-phenylpropane[a] m/z 208/202[b] (M^+)	m/z 125/119[b] ($M - CHCl_2$)	conversion of cumene to product (%)	k_{H6}/k_{D6} from product M^+ data	k_{H6}/k_{D6} from product $M - CHCl_2$ data
1	2.131 (25)	1.771 (65)	2.043 (61)	2.5	1.203	1.043
2	2.187 (14)	1.738 (59)	2.049 (23)	1.0	1.258	1.067
3	0.516 (11)	0.394 (23)	0.489 (10)	0.9	1.309	1.054
4	0.960	0.781	0.910	0.4	1.229	1.055
		(NMR data: 0.79)[e]			(NMR data: 1.22)	
avg					1.250 (46)[f]	1.055 (10)[f]

[a] Standard deviations are given in parentheses. [b] The value given is ratio of the sum of the intensities of the ions in each isotopic cluster. [c] The isotopic ratios determined from fragment ion data were the same as those from the M^+ data within experimental error. [d] The value given is the ratio of the intensities of the single m/z 125 and 119 ions. [e] Calculated from the integrals of the δ 5.95 resonances in the 270-MHz NMR spectrum of the isolated product. [f] The NMR measurement is not included in the average.

hybridization in the transition states of these reactions.[4] In addition, these data have been interpreted[1,2] to support the presence of carbocations or carbon radicals as intermediates in these reactions and to exclude the possibility of direct insertion of oxygen into C–H bonds of the substrate molecules (an "oxenoid" reaction mechanism[5]). The latter inferences are attractive, but given the absence in the literature of any measurement of secondary KIEs for a bona fide insertion reaction, it is perhaps premature to dismiss entirely the direct insertion mechanisms proposed for biological oxygenations.

These considerations have led us to examine the KIEs for the archetypal insertion process: the reaction of carbenes with alkanes.[6] For the purpose of KIE studies the insertion of dichlorocarbene into benzylic C–H bonds of simple alkylbenzenes is nearly ideal. Dichlorocarbene (generated by thermolysis of sodium trichloroacetate) reacts with cumene (1) to give 2-(dichloromethyl)-2-phenylpropane (2) as the predominant product.[7] With (+)-2-phenylbutane as the substrate, the insertion of dichlorocarbene (from thermolysis of $PhHgCCl_2Br$) proceeds with retention of configuration, and with 2-phenyl[2-^2H]butane, a substantial primary KIE is observed (k_H/k_D = 2.5).[8] We report herein the primary and β-secondary deuterium KIEs for the reaction of dichlorocarbene with the benzylic C–H bond of cumene and discuss the mechanistic implications of these results.



1 2 3 4

Results

Primary Kinetic Isotope Effect. 2-Phenyl[2-^2H]propane (3) was prepared by treatment of 2-bromo-2-phenylpropane[9] with lithium aluminum deuteride. This sample was in fact a 59:41 mixture of deuteriated and unlabeled molecules (D/H = 1.44) as judged by both ^1H NMR and GC–MS analyses. For the determination of the primary KIE on the insertion of dichlorocarbene into the benzylic C–H bond, a portion of sodium trichloroacetate was decomposed in the presence of a large excess of 3 at 120 °C. This reaction mixture was diluted with pentane and it (as well as a sample from a parallel reaction conducted with unlabeled cumene) was analyzed directly by GC–MS. Only the molecular ion cluster at m/z 202 retains the labeled hydrogen; the major ions in the spectra at m/z 119 and 91 have lost the dichloromethyl group. The isotopic composition of the product from the carbene reaction with 3 was measured at the molecular ion with integration of the mass spectra recorded over the entire GC peak of product, and a 36:64 mixture of deuteriated and unlabeled product molecules (D/H = 0.56) was observed.

In experiments where only intermolecular competition between isotopic molecules exists, at low fractional conversions of the isotopic substrate to product, the KIE is given by the expression $k_H/k_D = R_0/R_p$, where R_0 and R_p are the isotopic ratios (D/H) of the starting material and the product.[10] Therefore, for the reaction of dichlorocarbene with 3, R_0 = 1.44, R_p = 0.56, and k_H/k_D = 2.6 (at 120 °C). This value is, not unexpectedly, similar to the k_H/k_D = 2.5 (at 80 °C) previously observed for the reaction CCl_2 with 2-phenyl[2-^2H]butane.[8]

β-Secondary Kinetic Isotope Effect. 2-Phenyl-[1,1,1,3,3,3-$^2H_6$]propane (4) was obtained by reaction of acetone-d_6 with phenylmagnesium bromide followed by catalytic hydrogenation. This material was composed almost entirely of molecules containing six deuterium atoms; therefore, various mixtures of deuteriated and unlabeled cumenes were prepared for use in isotopic competition experiments. Dichlorocarbene was allowed to react with these mixtures under conditions identical with those employed for the primary KIE measurements. The data from four separate experiments are summarized in Table I. On each occasion, the isotopic composition of the reactants and products was analyzed by GC–MS. Since the starting material and products of this reaction contain six isotopic hydrogens, the molecular ion clusters for the deuteriated and unlabeled species are well separated (see Figure 1, spectra A and B), and a more precise estimation of the D/H ratios may be made than was possible in the primary KIE experiments. However, in the case of the product 2, the apparent D/H ratios calculated from the molecular ion data (m/z 202 and 208) are quite

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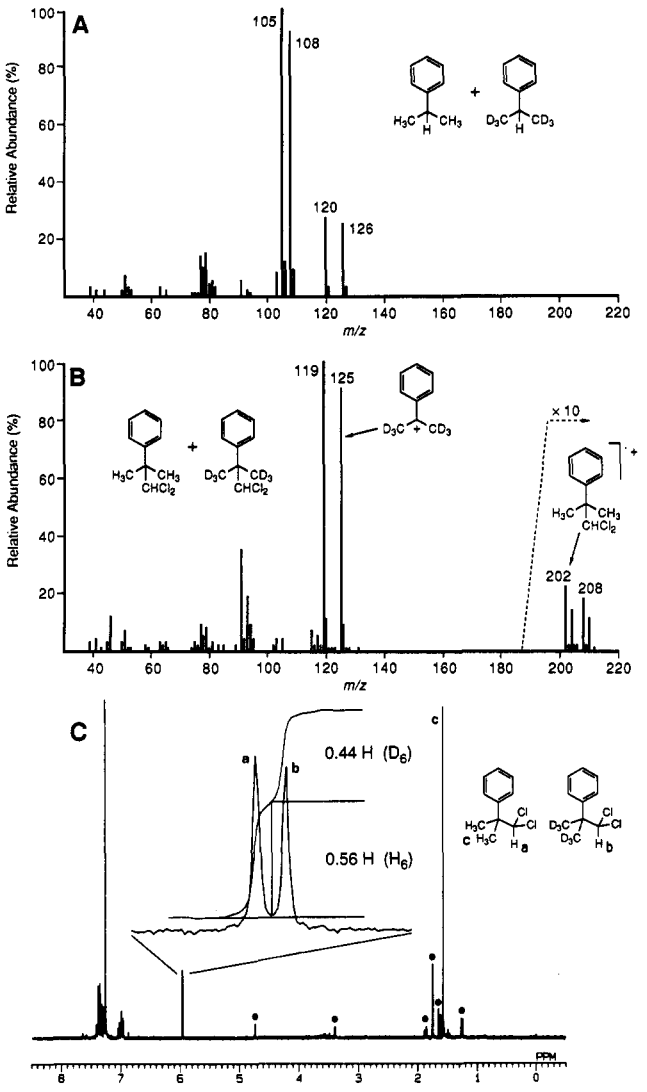


Figure 1. Spectral data from experiment 4 (Table I). (A) Mass spectrum of the initial mixture of unlabeled and deuteriated cumenes. (B) Mass spectrum of the product 2-(dichloromethyl)-2-phenylpropane. (C) ^{1}H NMR spectrum of the product 2-(dichloromethyl)-2-phenylpropane isolated by preparative GC; impurity peaks are indicated by a dot (●), and the inset shows the integration of the dichloromethyl proton resonances. See the text for the choice of reactants and reaction conditions.

different from those calculated from the base peak data (m/z 119 and 125, M − $CHCl_2$). The β-secondary KIEs calculated from these two sets of data are k_{H6}/k_{D6} = 1.250 ± 0.046 and 1.055 ± 0.010, respectively (see Table I). It seems that there must be a secondary isotope effect on the fragmentation of the product **2**.

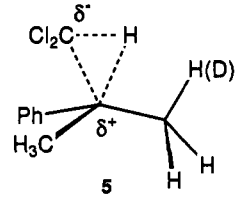
In order to obtain an independent measure of the product isotope ratio, experiment 4 (see Table I) was conducted on a large scale (five times that of prior experiments), and a portion of the reaction mixture was fractionated by preparative gas chromatography. The 270-MHz ^{1}H NMR spectrum of the isolated product **2** from this experiment is shown in Figure 1, spectrum C. Most fortunately, there is a significant difference in the chemical shifts ($\Delta\delta$ = 0.006 ppm) of the dichloromethyl protons (δ 5.95) of the protic and deuteriated products, thus allowing a direct determination of the D/H ratio. The observed NMR product D/H ratio of 0.79 (R_p; 0.44:0.56 = D_6:H_6), in combination with the starting material D/H ratio of 0.96 (R_0), yields a β-secondary KIE of k_{H6}/k_{D6} = 1.22, in good agreement with the value from the mass spectral molecular ion data. We may state with some confidence, then, that the β-secondary KIE for this carbene insertion is on the order of 1.20–1.25 for six deuteriums, or 3–4% per deuterium.

Discussion

The primary KIE for CCl_2 insertion into the benzylic hydrogen of cumene is of moderate size, larger than most primary KIEs measured for other insertions of singlet carbenes into C–H bonds[6,11] but comparable in magnitude to the KIE measured for a similar benzylic insertion reaction of CCl_2.[8] However, such primary effects provide relatively little insight into the structure of the transition state for the insertion reaction.

In contrast, secondary kinetic isotope effects are generally regarded as powerful probes of transition state structures in organic reactions, and the KIEs produced by substitution of deuterium on carbons β to a site of bond cleavage are often quite large.[4] In the most extensively studied case of S_N1 solvolyses, β-secondary KIEs are normal and typically 5–15% per deuterium atom, and such KIEs are believed to result from a weakening of the isotopic bond by hyperconjugation with the incipient carbocation in the transition state.[4] For reactions involving the formation of carbon radicals, β-secondary KIEs are smaller, ranging from 2–8% per deuterium, and they are thought to originate as well from hyperconjugation in the transition state.[12]

It is clear from our results that the β-secondary KIE for CCl_2 insertion into cumene is also normal and the magnitude is approximately 3–4% per deuterium atom. From this we conclude that hyperconjugative interactions are present in the transition state of the insertion reaction. Seyferth et al.[13] long ago proposed, on the basis of the selectivities observed for CCl_2 insertions into alkanes, a three-center transition state structure with partial charge separation (e.g., **5**). A normal β-secondary KIE, as we have observed, is consistent with this transition state structure in which hyperconjugation stabilizes the partial cation.



5

β-Secondary kinetic isotope effects have been determined for at least two enzymatic hydroxylation reactions.[1,2] Most significantly, Blanchard and Englard determined that the oxygenation of γ-butyrobetaine catalyzed by γ-butyrobetaine hydroxylase exhibits a large β-secondary tritium KIE [$^T(V/K)$ = 1.10].[1] They argued that this result [as well as the observation of an α-secondary $^T(V/K)$ = 1.31] favored a reaction mechanism involving carbocations or carbon radicals as intermediates, and excluded any reaction mechanism involving a direct insertion of oxygen. Furthermore, they predicted that an oxygen atom insertion mechanism would exhibit *inverse* secondary KIEs.[1] Dichlorocarbene is perhaps an inadequate model for an

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"oxene", but the present study demonstrates that the insertion of an electrophilic species into a C–H bond can exhibit *normal* β-secondary KIEs. For this reason, we conclude that studies of β-secondary KIEs do not permit the discrimination of concerted and stepwise mechanisms for insertion reactions in alkanes. It remains to be determined whether α-secondary KIEs are better in this regard.

Experimental Section

2-Bromo-2-phenylpropane[9] and 2-(dichloromethyl)-2-phenylpropane[7] (2) were prepared by literature procedures. Gas chromatography (GC) was performed on capillary columns (Supelco SPB-1, 30 m × 0.53 mm), as was coupled gas chromatography–mass spectrometry (GC–MS) (Hewlett-Packard HP-1 capillary column, 12.5 × 0.20 mm; Hewlett-Packard 5971A GC-MS system). Mass spectra were recorded repeatedly at close intervals across the entire peaks of emerging compounds of interest (there is substantial fractionation of protic and deuteriated species on the capillary columns), and the isotopic composition of each compound was determined from analysis of the sum of these spectra.

2-Phenyl[2-^2H]propane (3). A mixture of 2-bromo-2-phenylpropane (4.91 g, 24.7 mmol) and $LiAlD_4$ (1.00 g, 23.8 mmol, 98 atom % D) in ether (50 mL) was refluxed for 6 h and left to stir overnight. Water and dilute HCl were added, the organic layer was separated, and the aqueous phase was extracted once with ether. The combined organic phases were washed with water and then dried over anhydrous $MgSO_4$. The ethereal solution was hydrogenated over 10% Pd on C (0.3 g) at 4 atm for 3.5 h. The catalyst was filtered off, the ether was evaporated, and the residual oil was distilled to give compound 3 (1.54 g, 12.7 mmol, 51%). GC analysis indicated the purity of this material to be 98.6%: ^1H NMR ($CDCl_3$) δ 7.34 (m, 5 H, aromatic), 2.99 (septet, J_{HH} = 7 Hz, 0.41 H, benzylic), 1.35 and 1.34 [overlapping d (J_{HH} = 7 Hz) and t (J_{HD} = 1 Hz), 6 H, methyls]. The NMR spectral data indicate that 59% of the molecules contained one deuterium atom at the α-carbon. GC–MS analysis indicated the isotopic composition to be as follows: d_0, 41%; d_1, 59%; d_2, <1%. Because this material already contained a satisfactory ratio of deuteriated and unlabeled cumene, it was used directly in isotopic competition experiments.

2-Phenyl[1,1,1,3,3,3-$^2H_6$]propane (4). A mixture of phenylmagnesium bromide in ether (16 mL of a 3.0 M solution) and THF (16 mL) was cooled to 0 °C, and acetone-d_6 (3.5 mL, 52 mmol, 99.5 atom % D) was added dropwise with stirring over 15 min. The mixture was warmed to room temperature, stirred for 2 h, and then poured into water; dilute sulfuric acid was added to dissolve a white precipitate. The organic layer was separated, and the aqueous phase was extracted with ether. The combined organic extracts were dried and concentrated to give crude deuteriated 2-phenyl-2-propanol (6.0 g). This material was dissolved in 2:1 EtOAc/EtOH (225 mL), concentrated HCl (1 mL) and 10% Pd on C (0.4 g) were added, and the mixture was hydrogenated at 4 atm for 20 h. The catalyst was filtered off, hexane and water were added, and the organic layer was separated, dried, and concentrated to give 5.2 g of a yellow liquid. Distillation of this material yielded colorless compound 4 in several fractions, the best of which (1.82 g) was estimated to be >99% pure by GC: ^1H NMR ($CDCl_3$) δ 7.33 (m, 5 H, aromatic), 2.95 (s, 1 H, benzylic). The NMR spectral data indicate that the methyl groups were at least 98% deuteriated. GC–MS analysis indicated the isotopic composition to be d_6, >99%. For use in isotopic competition experiments, mixtures of 4 and unlabeled cumene was prepared. The isotopic compositions of these mixtures were determined by GC–MS and NMR analyses, which were in good agreement, but the mass spectral values were used for all calculations of kinetic isotope effects.

Isotopic competition experiments were conducted in the following manner. A known mixture of unlabeled and deuteriated cumene (200 μL, 1.44 mmol), DME (100 μL), and sodium trichloroacetate (35 mg, 0.19 mmol) was placed in a screw-capped tube. The tubes were placed in an oil bath at 120 °C for 15 h. After being cooled, the reaction mixtures were diluted with 2.0 mL of pentane and filtered through paper. The resulting solutions were analyzed directly by GC and GC–MS.

For the large-scale experiment 4, a mixture of unlabeled and deuteriated cumene (1.50 mL, 10.8 mmol), DME (0.75 mL), and sodium trichloroacetate (0.40 g, 2.2 mmol) was treated as described above. The reaction mixture was analyzed by GC and GC–MS, and then a portion of this material was fractionated by preparative GC (145 °C; column: 5% OV-17, 8 ft × 0.25 in). For ^1H NMR analysis the sample of the isolated product 2 was dissolved in deuteriochloroform and shaken with a few drops of D_2O (to remove the H_2O peak normally observed at δ ~1.6). The spectrum was recorded at 270 MHz by using a 6-s data acquisition of 65 536 points with a 15-s delay between acquisitions to ensure complete proton relaxation. Peak areas were determined by digital integration.

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Supplementary Material Available: ^1H NMR and mass spectral data from the primary kinetic isotope effect determination (2 pages). Ordering information is given on any current masthead page.

Stereospecific Photodimerization of Coumarins in Crystalline Inclusion Complexes. Molecular and Crystal Structure of 1:2 Complex of (*S*,*S*)-(−)-1,6-Bis(*o*-chlorophenyl)-1,6-diphenylhexa-2,4-diyne-1,6-diol and Coumarin

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Proximity of molecules is a crucial factor in many solid-state photochemical processes.[1,2] The biomolecular photodimerization reactions in the solid state depend on the relative geometry of reactant molecules in the crystal lattice with center-to-center distance of nearest neighbor double bonds of the order of ca. 4 Å. This fact emanates from the incisive studies of Schmidt and Cohen.[2] One of the two approaches to achieve this distance requirement is the so-called "Crystal-Engineering" of structures, which essentially involves the introduction of certain functional groups that display in-plane interstacking interactions (Cl···Cl, C–H···O, etc.) in the crystal lattice.[3,4] The chloro group is by far the most successful in promoting the β-packing mode,[2,5] though recent studies have shown its limitations.[6] Another approach involves the use of constrained media in which the reactants could hopefully be

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