Acknowledgment. We thank the National Science Foundation for partial support of this work.

References and Notes

(1) R. Hoffmann, *J. Am. Chem. Soc.*, **90**, 1475 (1968).
(2) (a) J. A. Horseley, Y. Jean, C. Moser, L. Salem, R. M. Stevens, and J. S. Wright, *J. Am. Chem. Soc.*, **94**, 279 (1972); (b) P. J. Hay, W. J. Hunt, and W. A. Goddard, III, *ibid.*, **94**, 638 (1972).
(3) X. Chapulsat and Y. Jean, *Top. Curr. Chem.*, **68**, 1 (1976).
(4) R. J. Crawford and T. R. Lynch, *Can. J. Chem.*, **46**, 1457 (1968).
(5) W. Carter and R. G. Bergman, *J. Am. Chem. Soc.*, **91**, 7411 (1969).
(6) W. v. E. Doering and K. Sachdev, *J. Am. Chem. Soc.*, **96**, 1168 (1974).
(7) H. Chmurny and D. J. Cram, *J. Am. Chem. Soc.*, **95**, 4237 (1973).
(8) J. A. Berson and J. M. Balquist, *J. Am. Chem. Soc.*, **90**, 7344 (1968).
(9) (a) J. A. Berson and L. D. Pedersen, *J. Am. Chem. Soc.*, **97**, 238 (1975); (b) J. A. Berson, L. D. Pedersen, and B. K. Carpenter, *ibid.*, **97**, 240 (1975); (c) *ibid.*, **98**, 122 (1976).
(10) M. C. Flowers and H. M. Frey, *J. Chem. Soc.*, 5550 (1961); M. C. Flowers and A. R. Gibbons, *J. Chem. Soc. B*, 612 (1971); P. J. Burkhardt, *Diss. Abstr.*, **23**, 1524 (1962).
(11) (a) J. J. Gajewski, *J. Am. Chem. Soc.*, **92**, 3688 (1970); (b) J. J. Gajewski and L. T. Burka, *ibid.*, **94**, 8865 (1972).
(12) (a) J. C. Gilbert, *Tetrahedron*, **25**, 1459 (1969); (b) J. J. Gajewski and L. T. Burka, *J. Am. Chem. Soc.*, **94**, 8857 (1972).
(13) A. D. Walsh, *Trans. Faraday Soc.*, **45**, 179 (1949).
(14) J. J. Gajewski and L. T. Burka, *J. Am. Chem. Soc.*, **94**, 8860 (1972).
(15) The stereochemical designations proximal, medial, and distal refer to the three possible distances between substituents at C-1 and C-4 of spiropentane systems; see J. J. Gajewski and L. T. Burka, *J. Org. Chem.*, **35**, 2190 (1970).
(16) W. Kirmse, "Carbene Chemistry", 2nd ed., Academic Press, New York, 1977.
(17) L. S. Skattebøl, *Chem. Ind. (London)*, 2146 (1962).
(18) J. J. Gajewski and S. K. Chou, *J. Am. Chem. Soc.*, **99**, 5696 (1977).
(19) (a) S. W. Benson, "Thermochemical Kinetics", 2nd ed., Wiley, New York, 1976; (b) S. W. Benson and H. E. O'Neal, "Kinetic Data on Gas Phase Unimolecular Reactions", NSRDS-NBS 21, U.S. Government Printing Office, Washington, D.C., 1970.
(20) For summaries see J. J. Gajewski, *J. Am. Chem. Soc.*, **93**, 4450 (1971); **98**, 5254 (1976).
(21) Professor W. L. Jorgensen has calculated, using EH theory, the A–S gap in the edge to edge diradical derived from spiropentane as 0.58 eV. In edge to edge trimethylene the gap is 0.40 eV.
(22) R. Hoffmann, C. C. Levin, and R. A. Moss, *J. Am. Chem. Soc.*, **95**, 629 (1973).
(23) Jean assumed this to be true in trajectory calculations on the cyclopropane geometric isomerization (ref 3).
(24) M. R. Willcott, III, and V. H. Cargle, *J. Am. Chem. Soc.*, **91**, 4310 (1969).
(25) For examples see (a) G. D. Andrews and J. E. Baldwin, *J. Am. Chem. Soc.*, **99**, 4853 (1977); (b) J. D. Rynbrandt and B. S. Rabinovitch, *J. Chem. Phys.*, **54**, 2275 (1971).
(26) A free-energy surface may be constructed from the kinetic data. The transition states for the TM–CS and the TP–CA interconversions are 1250 cal/mol higher than those for the TM–TP and the CA–CS interconversions. The transition state for the TM–CA interconversion is comparable in energy to that for the TM–TP and the CA–CS interconversion, and the transition state for the TP–CS interconversion is 650 cal/mol above that for the TM–TP and the CA–CS interconversions. Further, with the assumption that face to face biradicals are generated and that their rotation rate is slower than ring closure, and that the rate retardation factors f_{+p}, f_{-p}, and f_{+c} result solely from steric effects on bond rotation, it can be shown that the face to face species from TP and from CS are each roughly 650 cal/mol higher than that from TM and from CA which are comparable in stability.
(27) G. W. Cannon, A. H. Savitiii, and P. Shenian, *J. Am. Chem. Soc.*, **81**, 1660 (1959).
(28) See W. D. Emmons, *J. Am. Chem. Soc.*, **79**, 6522 (1957).
(29) See J. M. Walbrick, J. W. Wilson, Jr., and W. M. Jones, *J. Am. Chem. Soc.*, **90**, 2895 (1968).

Syn Stereospecificity in the S_N2' Reaction of an Acyclic Allylic Chloride with Secondary Amines

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Abstract: Previous theoretical and experimental investigations of the stereochemistry of the S_N2' reaction (bimolecular nucleophilic substitution with allylic rearrangement) are inconclusive and often contradictory. The reaction of isotopically labeled α-methylallyl chloride with three secondary amines is now shown to be stereospecifically syn. (*R*)-(−)-3-Chloro-(*Z*)-1-butene-*1-d* (**5**) reacts with diethylamine to give a 95:5 mixture of (*R*)-(*E*)- and (*S*)-(*Z*)-allylic amines **14** which is reduced by diimide to (*R*)-(+)- and (*S*)-(−)-*N,N*-diethyl-1-aminobutane-*1-d* (**9**). An authentic sample of (*R*)-(+)-**9** from yeast reduction of butanal-*1-d* shows an unusually large specific rotation, $[\alpha]^{25}_D$ +5.66° (ether). Comparison of the specific rotation of **9** from reduction of the S_N2' product with that of optically pure material reveals that the substitution process is stereospecific: nucleophile attacks the allylic system on the face bearing the leaving group. Similarly, reaction of the enantiomeric chloride (*S*)-(+)-**6** with both dimethylamine and piperidine proceeds with syn stereospecificity.

The S_N2' reaction (bimolecular nucleophilic substitution with allylic rearrangement) has been of synthetic and mechanistic interest for years.[1] Since the first reported example,[2] numerous instances of the process have been documented. Bordwell[1a,3] has argued that a concerted S_N2' process never occurs; rather, all such reactions proceed stepwise, often via ion-pair intermediates of the type postulated by Sneen[4] for S_N reactions in general. On the other hand, Georgoulis and Ville[5] have presented convincing evidence for direct attack by nucleophilic solvents on either the neutral substrate or a polarized species which is less ionized than an intimate ion pair.

Regardless of the precise timing of the bond-making and bond-breaking steps, one can still inquire into the stereochemistry of the reaction. Most theoretical analyses have led to a predicted preference for syn attack[6,8] (in which the nucleophile and leaving group are on the same face of the allylic system), while allowing the possibility of anti stereochemistry for certain combinations of entering and leaving groups,[8c,e]

Until recently, the definitive experimental investigation of the stereochemistry was that by Stork and White[9] who showed that *trans*-6-alkyl-2-cyclohexen-1-yl 2,6-dichlorobenzoates underwent exclusive syn attack by piperidine and malonate. Stork and Kreft[10] have now reinvestigated this system (and the related mesitoate esters of the cis and trans isomers) and have demonstrated that the stereochemistry can vary from predominantly syn to largely anti as the nucleophile is changed; a similar conclusion in support of syn attack on a closely related system was reached by Dobbie and Overton.[11] One can argue, however, that a cyclohexenyl system has certain built-in conformational biases which force syn attack, independent of any stereoelectronic requirements of the S_N2' reaction.[12]

An acyclic case, free of such complications, has been re-

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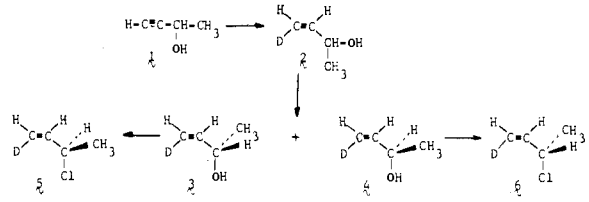
Scheme I

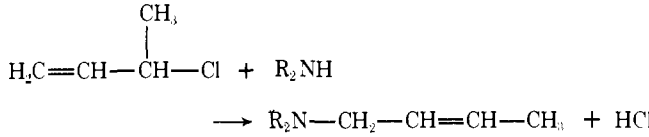


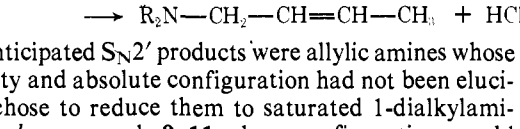
ported by Stork and Kreft,[15a] who found that internal nucleophilic attack by a thiolate anion occurred primarily anti, although a closely related intramolecular process involving carbanionic attack had proceeded syn;[15b,c] other instances of intramolecular S_N2' reactions have indicated a preference for syn stereochemistry,[16a,b] although significant anti attack can also occur.[16c] Very recently, Kirmse et al.[17] have shown that *cis*-3,4-dichlorocyclobutene undergoes consecutive syn S_N2' displacements by methoxide ion while Ikota and Ganem[18] have observed syn stereochemistry in the reaction of a bicyclic allylic mesylate with acetate ion. The only other stereochemical studies are those involving metal hydrides or organometallic reagents with allylic or propargylic systems;[19] the outcome (a nearly random blend of syn and anti) and the doubtful relevance of such reactions to a truly nucleophilic process render these experiments of little value in the present context. We now report that the intermolecular S_N2' reaction in an unbiased acyclic case proceeds with syn stereospecificity.

Results and Discussion

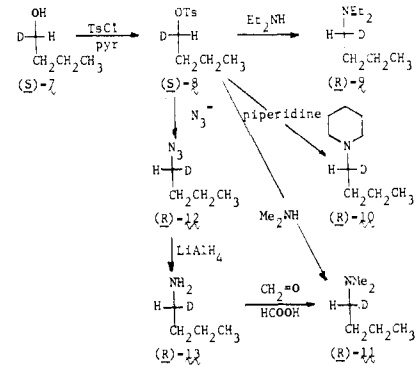
At the time we reported our preliminary results,[13] only the Stork and Kreft experiments[10,15a] from the recent explosion of activity in this area[11,17,18] had appeared. The substrates we selected, (*R*)-(−)- and (*S*)-(+)-3-chloro-(*Z*)-1-butene-*1-d* (**5** and **6**, respectively), are simply isotopic variants of α-methylallyl chloride, the compound used by Young and co-workers[2,7,20] to establish the mechanism and scope of the S_N2' reaction. *dl*-3-Butyn-2-ol (**1**) (Scheme I) was reduced to *dl*-3-buten-2-ol-(*Z*)-*4-d* (**2**) by $LiAlH_4$/THF followed by D_2O.[21] Resolution with brucine via the phthalate half-ester[22] followed by hydrolysis gave (*S*)-(+) alcohol **3**, 76.2 ± 0.3% optically pure,[22,23] and (*R*)-(−) alcohol **4**, 33.3 ± 0.4% optically pure.[22,23] Reaction of **3** and **4** with triphenylphosphine/hexachloroacetone[24] proceeded with very high regioselectivity and nearly complete inversion of configuration to chlorides **5** and **6**, respectively, 75.5 ± 0.1 and 33.1 ± 0.2% optically pure.[25]

Our principal reason for choosing substrates **5** and **6** is the nearly exclusive rearrangement that α-methylallyl chloride gives with secondary amines and other nucleophiles.[2,7,20] Because the anticipated S_N2' products were allylic amines whose optical purity and absolute configuration had not been elucidated, we chose to reduce them to saturated 1-dialkylaminobutane-*1-d* compounds **9–11** whose configurations could be related to that of (*S*)-(+)-1-butanol-*1-d* (**7**), according to Scheme II. Yeast-catalyzed reduction[26] of butanal-*1-d*[27,28]



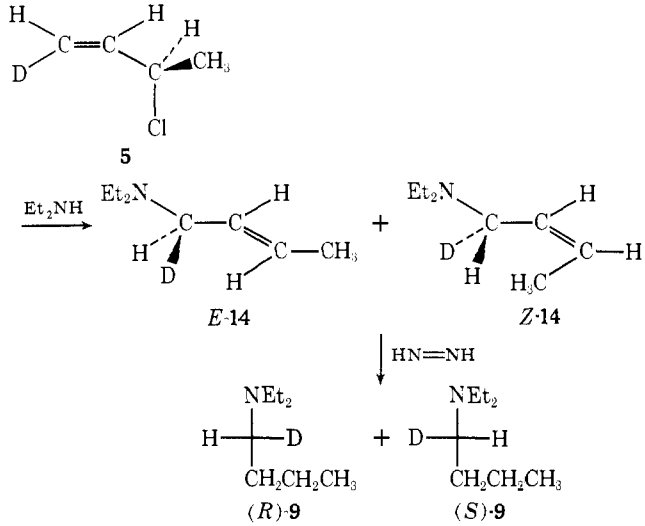


Scheme II



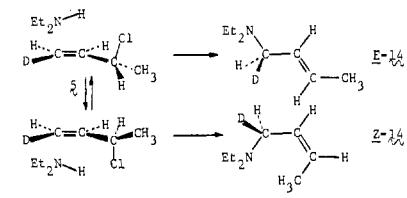
afforded (*S*)-(+)-**7**, $[\alpha]^{25}_D$ +0.39 ± 0.01° (neat),[29] which was converted into (*S*)-(−) tosylate **8**. Reaction of **8** with diethylamine gave optically pure (*R*)-(+)-**9**, $[\alpha]^{24}_D$ +5.66 ± 0.03° (ether) and $[\alpha]^{24}_{365}$ +19.14 ± 0.03° (ether).[31] Similarly, reaction of **8** with piperidine or dimethylamine produced (*R*)-(+)-**10** and (*R*)-(+)-**11**, respectively, whose specific rotations follow: **10**, $[\alpha]^{24}_D$ +4.02 ± 0.06° (ether) and $[\alpha]^{24}_{365}$ +13.46 ± 0.06° (ether); **11**, $[\alpha]^{24}_D$ +3.25 ± 0.06° (ether) and $[\alpha]^{24}_{365}$ +10.75 ± 0.06° (ether).[31] Alternatively, (*R*)-(+)-**11** can be prepared via azide displacement on tosylate **8**, reduction of (*R*)-**12** to primary amine (*R*)-**13**, and Eschweiler-Clarke methylation. Because the specific rotations of (*R*)-(+)-**11** by this route are, within experimental error, the same as those for **11** produced directly, it is reasonable to conclude that the reaction of tosylate **8** with a secondary amine, like the reaction with azide ion,[32c,d] occurs with complete inversion of configuration.

The reaction of optically active (*R*)-(−) chloride **5** with diethylamine afforded a 99:1 mixture of S_N2' and S_N2 products from which the latter could be removed by preparative gas chromatography. The major fraction, itself a 95:5 mixture (by VPC) of *E*-**14** and *Z*-**14**,[34] α^{24}_D +1.5 ± 0.1° (neat, *l* = 1), was reduced by diimide to *N*,*N*-diethyl-1-aminobutane-*1-d* (**9**),



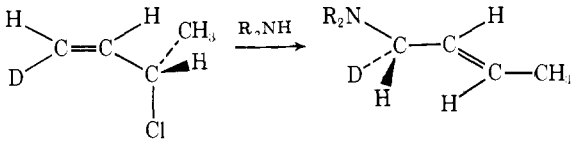
$[\alpha]^{25}_D$ +3.5 ± 0.2° (ether) and $[\alpha]^{25}_{365}$ +12.2 ± 0.2° (ether). These specific rotations for **9** must be adjusted before they can be compared with those of optically pure material. Given that

Scheme III



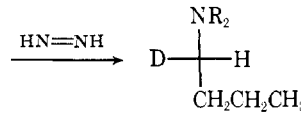
Z-**14** is present in the S_N2' mixture to the extent of 5% and that its chirality should be the opposite to that of the major isomer (assuming that they are produced by the same mechanism), the reduction product **9** is at best 90% optically pure; furthermore, starting chloride **5** was, itself, but 75.5% optically pure. Correction by these two factors and assuming reasonable error limits gives adjusted values for saturated amine **9** of +5.2 ± 0.3 and +18.0 ± 0.5° at 589 and 365 nm, respectively. With these numbers, one can calculate that the S_N2' reaction has occurred with 96 ± 2 or 97 ± 1%, respectively, syn stereochemistry (Scheme III). Given the uncertainty in the reported maximum rotation of chloride **5** and the error in determining the *E*/*Z* ratio of allylic amine **14**, it is not unreasonable to conclude that the reaction is, in fact, stereospecific.

Reaction of (*S*)-(+) chloride **6** with dimethylamine gave, again, a 99:1 mixture of S_N2' and S_N2 products. This time, however, the S_N2' product was cleanly *E*-**15**,[35] which was reduced by diimide to (*S*)-(−)-**11**, $[\alpha]^{26}_D$ −1.0 ± 0.2° (ether) and $[\alpha]^{26}_{365}$ −3.5 ± 0.2° (ether). Given that chloride **6** was



6

E-**15**, R = —CH_3
E-**16**, R = —$(CH_2)_5$—



(*S*)-**11**, R = —CH_3
(*S*)-**10**, R = —$(CH_2)_5$—

33.1% optically pure, the adjusted specific rotations are −3.0 ± 0.6 (589 nm) and −10.6 ± 0.6° (365 nm) corresponding to 95 ± 9 or 99 ± 3% syn attack. Similarly, reaction of chloride **6** with piperidine gave a 97/3 mixture of S_N2' and S_N2 materials, the former being exclusively *E*-**16**. Reduction by diimide produced (*S*)-(−)-**10**, whose adjusted specific rotations (based upon the optical purity of **6**) are −4.0 ± 0.3 (589 nm) and −13.1 ± 0.3° (365 nm) corresponding to 99 ± 4 or 99 ± 1% syn attack.

Clearly, the reaction of chiral allylic chlorides **5** or **6** with secondary amines produces rearranged products with what is essentially pure syn stereochemistry. After these experiments were completed, Oritani and Overton[36] examined the reactions of the 2,6-dichlorobenzoate esters of optically active (*R*)-3-buten-2-ol-(*Z*)-*4-d* (**4**) and (*R*)- or (*S*)-1-octen-3-ol-(*Z*)-*1-d* with optically active (*R*)- or (*S*)-α-methylbenzylamine and found that the syn/anti preference in the S_N2' product was about 1.6/1.0, dramatically different from the nearly stereospecific processes we found. These authors argue that, with Cl as leaving group, effective H bonding to the amine N–H in a six-membered cyclic transition state is responsible for the enormous preference for syn attack which we have observed. We are not yet in a position of being able to accept or reject such an explanation, although it should be noted that Young,[7,20] who first proposed this argument, also found that triethyl- and trimethylamine (for which H bonding is not a possibility) gave largely or exclusively S_N2' product. Ingold[37] also opted for the H-bonding explanation for secondary amines and decided that the S_Ni' designation was a more appropriate description. On the other hand, isotope effect studies by Fry[38a] ($^{35}Cl/^{37}Cl$ for the leaving group and $^{12}C/^{14}C$ for the α, β, and γ carbons in the reaction of α-methylallyl chloride with Et_2NH) and by Dittmer and Marcantonio[38b,c] ($^1H/^2H$ for α-methylallyl chloride with Et_2ND and $Ph(CH_3)ND$) support the notion of concerted[38a] nucleophilic attack at C_γ and rupture of the C_α–Cl bond but with no evidence[38b,c] of H bonding in the transition state. We hope that this question can be resolved by further stereochemical studies employing different entering and leaving groups.

Experimental Section

All NMR spectra were obtained with a Varian T-60 spectrometer using tetramethylsilane (Me_4Si) as internal standard; chemical shifts are recorded in δ units, parts per million downfield from Me_4Si. A Rudolph MP7A41 polarimeter was used for optical rotations. Analytical VPC was accomplished using a Hewlett-Packard Model 5750 gas chromatograph with the following columns: A, 10 ft × ⅛ in. SE-30 (10%) on Chromosorb W (silylated); B, 10 ft × ⅛ in. UCON 50-HB 280X (5%) on Chromosorb W. Preparative VPC separations were achieved with a Varian Aerograph Model 920 gas chromatograph and the following columns; C, 6 ft × ¼ in. Carbowax 20M (10%) on Chromosorb W; D, 6 ft × ¼ in. SE-30 (10%) on Chromosorb W; E, 6 ft × ¼ in. Carbowax 20M/KOH (20%) on Chromosorb W.

(*S*)-(+)- and (*R*)-(−)-3-Buten-2-ol-(*Z*)-*4-d* (3 and 4). According to the method of Grant and Djerassi,[21] *dl*-3-butyn-2-ol (8 mL, 7.1 g, 0.1 mol) in dry THF (50 mL) was treated with a 1 M lithium aluminum hydride–THF solution[39] (110 mL) overnight, then quenched with deuterium oxide (>99.7% *d*, 13 mL) in dry THF (25 mL) and dried (potassium carbonate). This procedure was repeated five times until there was a total of 0.5 mol of 3-buten-2-ol-(*Z*)-*4-d* (**2**) in THF. This alcohol–THF solution was then refluxed with phthalic anhydride (81.5 g, 0.55 mol) and pyridine (50 mL, 0.5 mol) for 1 week.[40] The THF was removed on the rotary evaporator leaving an oil which was mixed with water (100 mL). To this mixture was added an ice-cold 10 N hydrochloric acid solution (50 mL) followed by ether (250 mL). The organic layer was separated and washed with a saturated sodium chloride solution (50 mL) and dried (magnesium sulfate). The ether was removed on the rotary evaporator yielding an oil (with some phthalic anhydride crystals present) which was dissolved in benzene (100 mL) and the crystals were removed by filtration. The benzene was removed on the rotary evaporator leaving an oil (45 g) which was dissolved in acetone (200 mL); brucine dihydrate (100 g) was added and dissolved with heating. The salt which precipitated was recrystallized five times to a constant melting point 162–164 °C (lit.[40] mp 120–122 °C). Another 0.5 mol of 3-buten-2-ol-(*Z*)-*4-d* was resolved following the same procedure and the two products were combined yielding 58.4 g of salt. Hydrolysis of the salt was accomplished by shaking with 10 N hydrochloric acid (60 mL) in ice-cold water (150 mL), then extraction with three 150-mL portions of ether, and drying over magnesium sulfate. The ether was stripped off on the rotary evaporator leaving the oily phthalate ester (21.4 g) which was hydrolyzed with a 10 N sodium hydroxide solution (24 mL) and allowed to stand overnight. The aqueous phase was saturated with potassium carbonate and the organic phase was separated and dried (potassium carbonate). The product was distilled from calcium oxide (95–97 °C) yielding a clear liquid (4.1 g) which was purified by preparative VPC (column C), α^{30}_D +21.04 ± 0.01° (neat, *l* = 1) (lit.[23] α_{max} +27.6°). The mother liquor from the recrystallizations was concentrated and worked up in a similar manner yielding product (3.6 g): α^{24}_D −9.2 ± 0.1° (neat, *l* = 1); ^1H NMR (CCl_4) δ 1.20 (d, 3, *J* = 7 Hz, $-CH_3$), 2.6 (s, 1, –OH), 4.21 (dq, 1, *J* = 5, 7 Hz, –C*H*OH–), 4.95 (dd, 1, *J* = 10, 1 Hz, *H*CD=), and 5.88 (m, 1, =C*H*CH–). The vinyl hydrogens were shown to be cis by comparison with a spectrum of authentic **3**.[22]

(*R*)-(−)- and (*S*)-(+)-3-Chloro-(*Z*)-1-butene-*1-d* (5 and 6). According to the procedure developed for preparation of allylic chlorides,[24] 1.09 g (0.015 mol) of optically active (*S*)-(+)-**3** was dissolved in 20 mL of hexachloroacetone. The solution was cooled to 0 °C and triphenylphosphine (4 g, 0.015 mol) was added in small portions over a 20-min period. The mixture was warmed to room temperature and a thick slurry formed. Flash distillation (5 Torr, 30 min, ambient temperature) into a dry ice cooled receiver gave a clear, volatile material which was purified by preparative VPC (column D) yielding ca. 1.0 mL of product: α^{24}_D −46.13 ± 0.01° (neat, *l* = 1) (lit.[25] α_{max} −61.1°); ^1H NMR (CCl_4) δ 1.56 (d, 3, *J* = 7 Hz, $-CH_3$), 4.48 (dq, 1, *J* = 7, 7 Hz, –CHCl–), 5.05 (dd, 1, *J* = 10, 1 Hz, *H*CD=), and 5.97 (m, 1, =C*H*CH–). The vinyl hydrogens were shown to be cis by comparison with a spectrum of authentic **5**.[22] Similarly, a sample of (*R*)-(−)-**4** gave (*S*)-(+)-**6**, α^{24}_D +20.2 ± 0.1° (neat, *l* = 1).

(*S*)-(+)-1-Butanol-*1-d* (7). Treatment of 2-propyl-1,3-dithiane-*2-d*[27]

(34 g, 0.21 mol) with a solution of mercuric chloride (134 g, 0.495 mol) in methanol (400 mL) and water (5 mL) followed by addition of mercuric oxide (50 g, 0.23 mol) gave a voluminous precipitate. The mixture was refluxed under nitrogen for 12 h and was then cooled to room temperature. The precipitate was removed by filtration and rinsed with water (500 mL), then slurried with ether (1 L) and filtered. The aqueous phase was saturated with sodium chloride and the organic phase was separated. The precipitate was then slurried with pentane (1 L) and filtered. The aqueous phase was extracted with the pentane, and the organic phases were combined and washed with a 30% ammonium acetate solution (250 mL) and a saturated sodium chloride solution (250 mL) and dried over potassium carbonate. The ether and pentane were removed by distillation and the residue was flash distilled and collected at dry ice temperature yielding a colorless liquid (14 g, 56% yield): ^{1}H NMR (CCl_4) of 1,1-dimethoxybutane-*1-d* δ 0.9 (broadened t, 3, $-CH_2CH_3$), 1.5 (m, 4, $-CH_2CH_2CH_3$), 3.1 (s, 6, $-OCH_3$); the triplet at δ 4.3 (in the undeuterated material) due to the proton on C-1 was absent. This acetal (34 g, 0.28 mol) was shaken for 5 min with water (1 L) and hydrochloric acid (5 drops). According to the procedure of Althouse et al.,[26] the solution containing butanal-*1-d* was added to a rapidly fermenting mixture of (+)-glucose (1 kg), water (3 L), and Fleischmann's bakers' yeast (900 g) at room temperature. After 1 week, the mixture was centrifuged to remove the yeast. The liquid was distilled and everything that boiled below 100 °C was collected. The distillate was saturated with potassium carbonate and the resulting aqueous layer was separated and extracted with ether (500 mL). The combined organic phases were dried (first potassium carbonate, then 3 Å molecular sieves) and fractionated through a long Vigreux column until the residue was a 50/50 mixture of ethanol–alcohol **7.** This mixture was purified by preparative VPC (column C) yielding (*S*)-(+)-1-butanol-*1-d* (11.2 g, 54% yield), $[\alpha]^{25}_D$ +0.34 ± 0.01° (neat).[29] VPC analysis (column B) of this purified sample of **7** showed water (0.5%), ethanol (0.5%), and an optically active impurity (0.3%) present. Deuterium analysis by NMR showed 0.96 deuterium atom per molecule.[28] ^{1}H NMR (CCl_4): δ 0.9 (broadened t, 3, $-CH_3$), 1.3 (m, 4, $-CH_2CH_2CH_3$), 3.5 (m, 1, $-CH$DOH), and 4.1 (s, 1, -OH).

(*S*)-(−)-1-Butyl-*1-d* Tosylate (8). According to the procedure of Edgell and Parts,[41] to alcohol **7** (7 g, 0.095 mol) and *p*-toluenesulfonyl chloride (28 g, 0.15 mol) at 0 °C was added pyridine (130 mL) at a constant rate with rapid stirring over a period of 1 h. The reaction mixture was allowed to stand for 2 days (3 °C) and was then quenched by addition to ice–water (100 mL). The unreacted tosyl chloride was hydrolyzed by stirring the resulting suspension for 1 h. Then sulfuric acid (44 mL) in ice (150 g) was added to neutralize the pyridine. The mixture was extracted with ether (250 mL) and then pentane (250 mL). The organic phases were washed with ice-cold dilute sulfuric acid, ice–water, ice-cold dilute sodium hydroxide, and again with ice–water. The combined organic phases were dried (magnesium sulfate) and the solvent was removed by flash distillation yielding a yellow oil residue (9 g, 42% yield): α^{25}_D −0.07 ± 0.01° (neat, *l* = 1); α^{25}_{365} −0.70 ± 0.01° (neat, *l* = 1); ^{1}H NMR (CCl_4) δ 0.9 (broadened t, 3, $-CH_2CH_3$), 1.5 (m, 4, $-CH_2CH_2CH_3$), 2.4 (s, 3, ArCH_3), 4.0 (broadened t, 1, $-CH$D–), and 7.6 (AB pattern, 4, aromatic protons). Tosylate **8** was used without further purification.

(*R*)-(+)-*N,N*-Diethyl-1-aminobutane-*1-d* (9). Tosylate **8** (2.5 g, 0.011 mol) was treated with diethylamine (100 mL) at room temperature for 1 week. Ether (125 mL) followed by a 10 N sodium hydroxide solution (10 mL) in water (100 mL) was added to the diethylamine solution and the organic phase was removed. The aqueous phase was extracted with ether (100 mL) and the combined organic phases were dried (first magnesium sulfate, then potassium hydroxide pellets, and then 3 Å molecular sieves). Most of the ether and diethylamine were removed by distillation and the product was purified by preparative VPC (column C) yielding ca. 0.5 mL of product: $[\alpha]^{24}_D$ +5.43 ± 0.03° (ether) (0.348 g/mL, *l* = 0.1, α +0.189°); $[\alpha]^{24}_{365}$ +18.38 ± 0.03° (ether) (0.348 g/mL, *l* = 0.1, α +0.640°);[28] ^{1}H NMR (CCl_4) δ 0.9 (overlapping triplets, 9, methyls), 1.3 (m, 4, $-CH_2CH_2-$), 2.2 (m, 1, $-CH$D–), and 2.3 (q, 4, $N(CH_2CH_3)_2$).

(*R*)-(+)-1-Piperidinobutane-*1-d* (10). Tosylate **8** (3 g, 0.013 mol) was treated with piperidine (50 mL) at room temperature for 2 weeks. Ether (50 mL) and then a 10 N sodium hydroxide solution (10 mL) in water (10 mL) were added to the piperidine solution and the organic phase was separated. The aqueous phase was extracted with ether (50 mL) and the combined organic phases were dried (first magnesium sulfate, then potassium hydroxide pellets, and then 3 Å molecular sieves). The ether and most of the piperidine were removed by distillation through a long Vigreux column and the residue was purified by preparative VPC (column E) yielding ca. 0.7 mL of product: $[\alpha]^{24}_D$ +3.86 ± 0.06° (ether) (0.1657 g/mL, *l* = 0.1, α +0.064°); $[\alpha]^{24}_{365}$ +12.92 ± 0.06° (ether) (0.1657 g/mL, *l* = 0.1, α +0.214°);[28] ^{1}H NMR (CCl_4) δ 0.9 (broadened t, 3, $-CH_3$), 1.4 (broadened singlet with fine splitting, 10, $-CH_2CH_2CH_3$ and $NCH_2CH_2CH_2CH_2-$), and 2.2 (broadened d, 5, $-CH$D– and $-CH_2NCH_2-$).

(*R*)-(+)-1-Butyl-*1-d* Azide (12).[32c] Sodium azide (8.6 g, 0.13 mol) and tosylate **8** (11 g, 0.049 mol) in hexamethylphosphoramide (100 mL) were heated (110 °C, 24 h); ice–water (250 mL) was then added to the cooled reaction mixture. The upper layer was collected, α^{26}_D +2.22 ± 0.01° (neat, *l* = 1). The aqueous layer was extracted with two 125-mL portions of ether. The combined organic phases were washed with a saturated sodium chloride solution (100 mL) and dried (magnesium sulfate): ^{1}H NMR (CCl_4) δ 0.9 (broadened t, $-CH_3$), 1.4 (m, $-CH_2CH_2CH_3$), and 3.2 (broadened t, $-CH$D–). The alkyl azide was used as the ether solution.

(*R*)-(−)-1-Aminobutane-*1-d* (13).[32c] The above-mentioned ether solution of azide **12** was added to lithium aluminum hydride (2.2 g, 0.058 mol) in anhydrous ether (50 mL) with stirring (20 °C, 14 h). The reaction mixture was hydrolyzed (10 mL of water, 5 mL of 5 N sodium hydroxide solution, and then 10 mL of water), filtered, and dried (magnesium sulfate). The amine hydrochloride was prepared by passing in dry hydrogen chloride gas and was separated by filtering it from the ether. The free amine was obtained by treating an aqueous solution of the hydrochloride with sodium hydroxide pellets. The amine layer was separated. The aqueous layer was extracted with ether (10 mL), the combined organic phases were dried (first potassium carbonate, then 3 Å molecular sieves) and distilled, and the residue was purified by preparative VPC (column C) yielding 0.8 mL of product: $[\alpha]^{26}_D$ −0.22 ± 0.01° (neat) (neat, *l* = 0.1 α −0.016°); $[\alpha]^{26}_{365}$ −0.57 ± 0.01° (neat) (neat, *l* = 0.1, α −0.042°); ^{1}H NMR (CCl_4) δ 0.9 (broadened t, 3, $-CH_3$), 1.4 (m, 4, $-CH_2CH_2-$), and 2.6 (broadened t, 1, $-CH$D–).

(*R*)-(+)-*N,N*-Dimethyl-1-aminobutane-*1-d* (11). Method A. According to the procedure of Pine and Sanchez,[42] amine **13** (0.4 mL, 0.3 g, 0.004 mol) in an ice-cooled flask was treated with an 88% aqueous solution of formic acid (0.72 g, 0.014 mol) followed by a 36% aqueous solution of formaldehyde (1.02 g, 0.012 mol). The flask was fitted with a reflux condenser and heated (80 °C, 24 h). After the mixture was cooled, dilute hydrochloric acid (0.01 mol) was added and the mixture was extracted with ether (4 mL). The aqueous phase was made basic with a sodium hydroxide solution (0.04 mol) and extracted with ether (5 mL) and then pentane (5 mL). The combined organic phases were washed with water (5 mL) and dried (first potassium carbonate, then 3 Å molecular sieves). Most of the ether and pentane were removed by distillation. The product was purified by preparative VPC (column D) yielding 0.12 mL (26% yield) of product: $[\alpha]^{24}_D$ +3.17 ± 0.09° (ether) (0.107 g/mL, *l* = 0.1, α +0.034°); $[\alpha]^{24}_{365}$ +10.37 ± 0.09° (ether) (0.107 g/mL, *l* = 0.1, α +0.111°);[28] ^{1}H NMR (CCl_4) δ 0.9 (broadened t, 3, $-CH_2CH_3$), 1.4 (m, 4, $-CH_2CH_2-$), 2.0 (m, 1, $-CH$D–), and 2.1 (s, 6, $-N(CH_3)_2$).

Method B. In a pressure bottle, tosylate **8** (3 g. 0.013 mol) was treated with dimethylamine (50 mL) at room temperature for 1 week. After most of the dimethylamine was evaporated, water (10 mL) and a 10 N sodium hydroxide solution (10 mL) were added. The mixture was extracted with ether (50 mL) and the ether was washed with a saturated sodium chloride solution (25 mL), then dried (first magnesium sulfate, then potassium hydroxide pellets, and then 3 Å molecular sieves). Most of the solvent was removed by distillation and the product was purified by preparative VPC (column D) yielding ca. 0.5 mL of product, $[\alpha]^{24}_D$ +3.12 ± 0.06° (ether) (0.1695 g/mL, *l* = 0.1, α +0.053°); $[\alpha]^{24}_{365}$ +10.32 ± 0.06° (ether) (0.1695 g/mL, *l* = 0.1, α +0.175°).[28]

Reaction of (*R*)-(−)-5 with Diethylamine. Following the procedure of Young et al.,[7] to freshly distilled diethylamine (25 mL, 17.7 g, 0.25 mol) was added (*R*)-(−)-**5** (1 mL, 0.9 g, 0.01 mol) and the mixture was heated at reflux (20 h). After the mixture was cooled to room temperature, water (10 mL) was added, followed by a 10 N sodium hydroxide solution (18 mL). The aqueous mixture was extracted with three 25-mL portions of ether, and the combined organic phases were dried (first magnesium sulfate, then potassium hydroxide pellets, and then 3 Å molecular sieves). The ether and most of the diethylamine were removed by distillation through a long Vigreux column and the residue was purified by preparative VPC (column E) yielding ca. 0.7

mL of *N,N*-diethyl-1-aminobut-2-ene-*1-d* (**14**) which, by analytical VPC (column A), was shown to be a 95:5 mixture of *E*-**14** and *Z*-**14**: α^{24}_D +1.5 ± 0.1° (neat, *l* = 1); α^{24}_{365} +6.1 ± 0.1° (neat, *l* = 1); ^{1}H NMR (CCl_4) δ 1.0 (t, 6, *J* = 7 Hz, $-CH_2CH_3$), 1.7 (broadened d, 3, *J* = 5 Hz, $=CHCH_3$), 2.4 (q, 4, *J* = 7 Hz, $-CH_2CH_3$), 2.9 (broadened s, 1, $-HCD-$), and 5.4 (m, 2 vinyl protons). The crude reaction mixture before purification was shown by analytical VPC (column A) to be a 99:1 mixture of S_N2' and S_N2 products.

The 0.7 mL (0.6 g, 0.005 mol) of amine **14** obtained from the above reaction was placed in a flask with water (75 mL), potassium hydroxide (11.2 g, 0.2 mol), and *p*-toluenesulfonyl hydrazide (18.6 g, 0.1 mol) and heated at reflux (4 h).[43] The cooled solution was extracted with ether (40 mL) and the ether phase dried (first potassium carbonate, then 3 Å molecular sieves). Most of the ether was removed by distillation and the residue was purified by preparative VPC (column E) yielding ca. 0.1 mL of *N,N*-diethyl-1-aminobutane-*1-d* (**9**), $[\alpha]^{25}_D$ +3.5 ± 0.2° (ether) (0.054 g/mL, *l* = 0.1, α +0.019°); $[\alpha]^{25}_{365}$ +12.2 ± 0.2° (ether) (0.054 g/mL, *l* = 0.1, α +0.066°). The ^{1}H NMR spectrum matched that of compound **9** prepared from alcohol **7**. The crude reaction mixture before purification showed 24.8% of unreduced starting material (by VPC) present.

Reaction of (*S*)-(+)-6 with Dimethylamine. A pressure bottle was charged with dimethylamine (50 mL, 34 g, 0.76 mol), ether (25 mL), and (*S*)-(+)-**6** (1.5 mL, 1.4 g, 0.015 mol). The contents were allowed to stand at room temperature for 1 week, after which most of the dimethylamine was allowed to evaporate. A 10 N sodium hydroxide solution (5 mL) in water (5 mL) was added and the aqueous mixture extracted with ether (30 mL). The ether was separated and dried (first potassium carbonate, then 3 Å molecular sieves). Most of the ether was distilled off and the residue was purified by preparative VPC (column E) yielding ca. 0.5 mL of *N,N*-dimethyl-1-aminobut-2-ene-*1-d* (**15**) which, by analytical VPC (column A), was shown to be exclusively the *E* isomer: α^{24}_D −0.3 ± 0.1° (neat, *l* = 1); α^{24}_{365} −1.4 ± 0.1° (neat, *l* = 1); ^{1}H NMR (CCl_4) δ 1.6 (broadened d, 3, *J* = 5 Hz, $=CHCH_3$), 2.0 (s, 6, $-H(CH_3)_2$), 2.7 (m, 1, $-CHD-$), and 5.4 (m, 2, vinyl protons). The crude reaction mixture before purification was shown by analytical VPC (column A) to be a 99:1 mixture of S_N2' and S_N2 products.

The 0.5 mL (0.4 g, 0.004 mol) of amine **15** obtained from the above reaction was placed in a flask with water (50 mL), postassium hydroxide (11.2 g, 0.2 mol), and *p*-toluenesulfonyl hydrazide (18.6 g, 0.1 mol) and heated at reflux (4 h). The cooled solution was extracted with ether (40 mL) and the ether phase dried (first potassium carbonate, then 3 Å molecular sieves). Most of the ether was removed by distillation and the residue was purified by preparative VPC (column E) yielding ca. 0.1 mL of *N,N*-dimethyl-1-aminobutane-*1-d* (**11**), $[\alpha]^{26}_D$ −1.0 ± 0.2° (ether) (0.0549 g/mL, *l* = 0.1, α −0.006°); $[\alpha]^{26}_{365}$ −3.5 ± 0.2° (ether) (0.0549 g/mL, *l* = 0.1, α −0.021°). The ^{1}H NMR spectrum matched that of compound **11** prepared from alcohol **7**. The crude reaction mixture before purification showed 30% of unreduced starting material (by VPC) present.

Reaction of (*S*)-(+)-6 with Piperidine. To freshly distilled piperidine (10 mL, 8.6 g, 0.1 mol) was added (*S*)-(+)-**6** (1.2 mL, 1.1 g, 0.012 mol) and the mixture was heated at reflux (20 h). After cooling to room temperature, water (10 mL) was added, followed by a 10 N sodium hydroxide solution (10 mL). The aqueous mixture was extracted with two 25-mL portions of ether, and the combined organic phases were dried (first magnesium sulfate, then potassium hydroxide pellets, and then 3 Å molecular sieves). The ether and most of the piperidine were distilled off and the residue was purified by preparative VPC (column E) yielding ca. 0.8 mL of 1-piperidinobut-2-ene-*1-d* (**16**) which, by analytical VPC (column A), was shown to be exclusively the *E* isomer: α^{24}_D −0.7 ± 0.1° (neat, *l* = 1); α^{24}_{365} −2.2 ± 0.1° (neat, *l* = 1); ^{1}H NMR (CCl_4) δ 1.4 (broad s, 6, $-NCH_2CH_2CH_2CH_2-$), 1.6 (broadened d, 3, $-CH_3$), 2.3 (broad s, 4, $-CH_2NCH_2-$), 2.8 (broad s with fine splitting, 1, $-CHD-$), and 5.4 (m, 2, vinyl protons). The crude reaction mixture before purification was shown by analytical VPC (column A) to be a 97:3 mixture of S_N2' and S_N2 products.

The 0.8 mL (0.7 g, 0.005 mol) of amine **16** obtained from the above reaction was placed in a flask with water (50 mL), potassium hydroxide (11.2 g, 0.2 mol), and *p*-toluenesulfonyl hydrazide (18.6 g, 0.1 mol) and heated at reflux (4 h). The cooled solution was extracted with ether (50 mL) and the ether phase dried (first magnesium sulfate, then 3 Å molecular sieves). Most of the ether was removed by distillation and the residue was purified by preparative VPC (column E) yielding ca. 0.15 mL of 1-piperidinobutane-*1-d* (**10**), $[\alpha]^{24}_D$ −1.3 ± 0.1° (ether) (0.1038 g/mL, *l* = 0.1, α −0.013°); $[\alpha]^{24}_{365}$ −4.3 ± 0.1° (ether) (0.1038 g/mL, *l* = 0.1, α −0.045°). The ^{1}H NMR spectrum matched that of compound **10** prepared from alcohol **7**. The crude reaction mixture before purification showed 25% of unreduced starting material (by VPC) present.

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References and Notes

(1) Review articles: (a) F. G. Bordwell, *Acc. Chem. Res.*, **3**, 281 (1970); (b) R. H. DeWolfe and W. G. Young, *Chem. Rev.*, **56**, 753 (1956); (c) R. H. DeWolfe and W. G. Young in "The Chemistry of Alkenes", S. Patai, Ed., Interscience, New York, 1964, Chapter 10; (d) P. B. D. de la Mare in "Molecular Rearrangements", P. de Mayo, Ed., Interscience, New York, 1963, Chapter 2; (e) H. L. Goering, *Rec. Chem. Prog.*, **21**, 109 (1960).

(2) R. E. Kepner, S. Winstein, and W. G. Young, *J. Am. Chem. Soc.*, **71**, 115 (1949).

(3) F. G. Bordwell, P. F. Wiley, and T. G. Mecca, *J. Am. Chem. Soc.*, **97**, 132 (1975), and references cited therein.

(4) R. A. Sneen, *Acc. Chem. Res.*, **6**, 46 (1973).

(5) C. Georgoulis and G. Ville, *J. Chem. Res. (S)*, 248 (1978); *J. Chem. Res. (M)*, 3344 (1978).

(6) First suggested by S. Winstein, as quoted in ref 1b, 1c, and 7.

(7) W. G. Young, I. D. Webb, and H. L. Goering, *J. Am. Chem. Soc.*, **73**, 1076 (1951).

(8) (a) K. Fukui and H. Fujimoto, *Bull. Chem. Soc. Jpn.*, **39**, 2116 (1966); **40**, 2018 (1967); (b) W. Drenth, *Recl. Trav. Chim. Pays-Bas*, **86**, 318 (1967); (c) N. T. Anh, *Chem. Commun.*, 1089 (1968); (d) J. Mathieu, *Bull. Soc. Chim. Fr.*, 807 (1973); (e) R. L. Yates, N. D. Epiotis, and F. Bernardi, *J. Am. Chem. Soc.*, **97**, 6615 (1975); (f) C. L. Liotta, *Tetrahedron Lett.*, 523 (1975).

(9) G. Stork and W. N. White, *J. Am. Chem. Soc.*, **78**, 4609 (1956).

(10) G. Stork and A. F. Kreft, III, *J. Am. Chem. Soc.*, **99**, 3850 (1977).

(11) A. A. Dobbie and K. H. Overton, *J. Chem. Soc., Chem Commun.*, 722 (1977).

(12) This argument, hinted at in our preliminary communication,[13] has been fully and elegantly elaborated by Toromanoff[14] according to the principles of "maximum orbital overlap" (i.e., perpendicular (axial) introduction and cleavage of the reacting groups) and "minimum structural deformation." According to this analysis, a *cis*-6-alkyl-2-cyclohexen-1-yl substrate will show exclusively syn attack; for the corresponding trans system, syn stereochemistry is again predicted except in those cases for which a bulky alkyl group forces reaction to occur from a non-half-chair conformation.

(13) R. M. Magid and O. S. Fruchey, *J. Am. Chem. Soc.*, **99**, 8368 (1977).

(14) E. Toromanoff, *Tetrahedron*, **34**, 1665 (1978).

(15) (a) G. Stork and A. F. Kreft, III, *J. Am. Chem. Soc.*, **99**, 3851 (1977); (b) J. Martel, E. Toromanoff, J. Mathieu, and G. Nomine, *Tetrahedron Lett.*, 1491 (1972); (c) J. Martel, A. Blade-Font, C. Marie, M. Vivat, E. Toromanoff, and J. Buendia, *Bull. Soc. Chim. Fr.*, II-131 (1978).

(16) (a) S. C. Welch, C. P. Hagan, D. H. White, W. P. Fleming, and J. W. Trotter, *J. Am. Chem. Soc.*, **99**, 549 (1977); (b) L. Chiche, J. Coste, H. Christol, and F. Plenat, *Tetrahedron Lett.*, 3251 (1978); (c) J. J. Uebel, R. F. Mliaszewski, and R. E. Arlt, *J. Org. Chem.*, **42**, 585 (1977).

(17) W. Kirmse, F. Scheidt, and H-J. Vater, *J. Am. Chem. Soc.*, **100**, 3945 (1978).

(18) N. Ikota and B. Ganem, *J. Am. Chem. Soc.*, **100**, 351 (1978).

(19) See the following recent examples and references therein: (a) A. Claesson, L-I. Olsson, G. R. Sullivan, and H. S. Mosher, *J. Am. Chem. Soc.*, **97**, 2919 (1975); (b) H. L. Goering and V. D. Singleton, Jr., *ibid.*, **98**, 7854 (1976); (c) B. M. Trost and T. R. Verhoeven, *J. Org. Chem.*, **41**, 3215 (1976); (d) J. P. Marino and J. S. Farina, *ibid.*, **41**, 3213 (1976); (e) A. Kreft, *Tetrahedron Lett.*, 1035 (1977); (f) B. Fraser-Reid, S. Y-K. Tam, and B. Radatus, *Can. J. Chem.*, **53**, 2005 (1975); (g) Y. Tanigawa, H. Ohta, A. Sonoda, and S-I. Murahashi, *J. Am. Chem. Soc.*, **100**, 4610 (1978); (h) O. J. Muscio, Jr., Y. M. Jun, and J. B. Philip, Jr., *Tetrahedron Lett.*, 2379 (1978); (i) A. Claesson and L-I. Olsson, *J. Chem. Soc., Chem. Commun.*, 621 (1978); (j) W. H. Pirkle and C. W. Boeder, *J. Org. Chem.*, **43**, 1950, 2091 (1978).

(20) (a) W. G. Young and R. Clement, *Science*, **115**, 488 (1952); (b) W. G. Young, R. A. Clement, and C-H. Shih, *J. Am. Chem. Soc.*, **77**, 3061 (1955); (c) W. G. Young and I. J. Wilk, *ibid.*, **79**, 4793 (1957).

(21) B. Grant and C. Djerassi, *J. Org. Chem.*, **39**, 968 (1974).

(22) R. M. Magid and E. C. Nieh, *J. Org. Chem.*, **36**, 2105 (1971).

(23) K. G. Oliver and W. G. Young, *J. Am. Chem. Soc.*, **81**, 5811 (1959).

(24) (a) R. M. Magid, O. S. Fruchey, and W. L. Johnson, *Tetrahedron Lett.*, 2999 (1977); (b) R. M. Magid, O. S. Fruchey, W. L. Johnson, and T. G. Allen, *J. Org. Chem.*, **44**, 359 (1979).

(25) W. G. Young and F. F. Caserio, Jr., *J. Org. Chem.*, **26**, 245 (1961).

(26) V. E. Althouse, D. M. Feigl, W. A. Sanderson, and H. S. Mosher, *J. Am. Chem. Soc.*, **88**, 3595 (1966).

(27) D. Seebach, B. W. Erickson, and G. Singh, *J. Org. Chem.*, **31**, 4303 (1966).

(28) Because the aldehyde as well as alcohol **7** was 0.96 d_1 (by NMR integration), the rotations given for **7**–**13** in the text have been adjusted to values expected for completely deuterated materials; the raw data are given in the Experimental Section.

(29) Yeast reduction is a stereospecific process, but this value is only 83% of that cited for optically pure material.[26] Within the limits of detection by the camphanate ester method,[30] the compound is optically pure. The diminished [α] is due to the presence of a small amount of a high-rotating le-

vorotatory impurity which we have succeeded in separating (but not identifying) by preparative VPC.
(30) H. Gerlach and B. Zagalak, *J. Chem. Soc., Chem. Commun.*, 274 (1973).
(31) The unusually large specific rotations of tertiary amines **9**, **10**, and **11** are unprecedented among saturated chiral deuterium compounds,[32] but can be rationalized based upon unequal populations of conformations having opposite sign rotatory powers.[33]
(32) (a) L. Verbit, *Prog. Phys. Org. Chem.*, **7**, 51 (1970); (b) D. Arigoni and E. L. Eliel, *Top. Stereochem.*, **4**, 127 (1969); (c) B. Stephenson, G. Solladié, and H. S. Mosher, *J. Am. Chem. Soc.*, **94**, 4184 (1972); (d) P. H. Anderson, B. Stephenson, and H. S. Mosher, *ibid.*, **96**, 3171 (1974); (e) W. Meister, R. D. Guthrie, J. L. Maxwell, D. A. Jaeger, and D. J. Cram, *ibid.*, **91**, 4452 (1969).
(33) A. Moscowitz, D. A. Dixon, and L. Laux, University of Minnesota, private communication.
(34) Optically active allylic amines *E*-**14** and *Z*-**14** are assumed to be *R* and *S*, respectively, for reasons developed in the text.
(35) Exclusive formation of one geometric isomer in the reaction of α-methylallyl chloride with dimethylamine was noted by Young and Wilk.[20c]
(36) T. Oritani and K. H. Overton, *J. Chem. Soc., Chem. Commun.*, 454 (1978).
(37) C. K. Ingold, "Structure and Mechanism in Organic Chemistry", 2nd ed., Cornell University Press, Ithaca, N.Y., 1969, pp 853–861.
(38) (a) A. Fry, *Pure Appl. Chem.*, **8**, 409 (1964); (b) D. C. Dittmer and A. F. Marcantonio, *Chem. Ind. (London)*, 1237 (1960); (c) *J. Am. Chem. Soc.*, **86**, 5621 (1964).
(39) H. C. Brown, "Organic Syntheses via Boranes", Wiley-Interscience, New York, 1975, p 258.
(40) J. Kenyon and D. R. Snellgrove, *J. Chem. Soc.*, 1169 (1925).
(41) W. F. Edgell and L. Parts, *J. Am. Chem. Soc.*, **77**, 4899 (1955).
(42) S. H. Pine and B. L. Sanchez, *J. Org. Chem.*, **36**, 829 (1971).
(43) R. S. Dewey and E. E. van Tamelen, *J. Am. Chem. Soc.*, **83**, 3729 (1961).

Ketyls of Cyclic α,β-Unsaturated Ketones. 2. Formation of Radical Anions by Electron Transfer Using Trimethylsilylsodium or Dimethyl Sulfoxide–Potassium *tert*-Butoxide[1]

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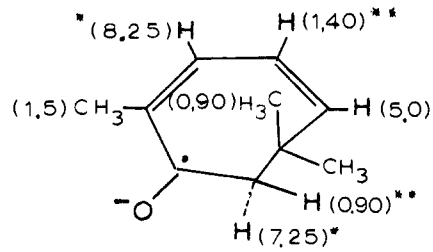
Abstract: Trimethylsilylsodium in HMPA readily reduces eucarvone, 4-substituted 2,5-cyclohexadienones, *N*-methyl-2-pyridone, maleic anhydride, phthalic anhydride, *N*-methylphthalimide, pyromellitic diimide, or *trans*-2,2,7,7-tetramethyl-4-octene-3,6-dione to the corresponding radical anions in a flow system wherein the radical anion can be detected within 0.1 s after mixing. Potassium *tert*-butoxide in Me_2SO gives only 1,4- and 1,2-semidiones from eucarvone in a flow system. Potassium *tert*-butoxide in Me_2SO converts diphenylcyclopropenone to diphenylcyclobutene-1,2-semidione, 3,7-cyclooctadiene-1,2-dione to a 5-substituted 3,6-cycloheptadiene-1,2-semidione, and cycloheptatriene to a 3-substituted tropone ketyl.

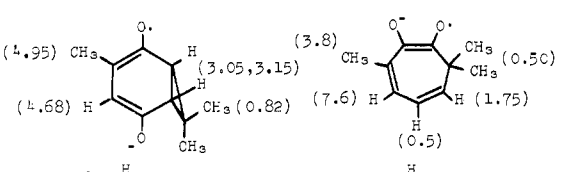
Ketyls have been detected from α,β-unsaturated ketones reduced electrolytically (DMF),[3] or by alkali metals in liquid ammonia.[4] In the present work we have treated a series of α,β-unsaturated carbonyl compounds statically or in a flow system with trimethylsilylsodium in HMPA,[5] or by potassium *tert*-butoxide in Me_2SO.[6]

α,β-Unsaturated ketones containing enolizable hydrogen atoms α to either the carbonyl or the double bond form highly unstable ketyl radical anions, which can be detected by ESR spectroscopy in solution only under special conditions (e.g., flow experiments with alkali metals in liquid ammonia).[4] Flow experiments with trimethylsilylsodium in HMPA at 25 °C with 2-cyclohexenone or 2-cyclopentenone failed to produce any appreciable ESR signal. The only α,β-unsaturated ketone with an α-hydrogen atom that we have been able to convert to the ketyl radical anion in this system has been eucarvone. Mixing eucarvone in HMPA and trimethylsilylsodium in HMPA under argon gave a well-resolved ESR signal in a flow system 90 ms after mixing (Figure S1a). Under stopped flow the spectrum of **1** disappeared immediately. The ketyl (**1**) is not a planar molecule as evidenced by the magnetic nonequivalence of the α-hydrogen atoms. The carbonyl groups and the four vinyl carbons can form a coplanar arrangement with one hydrogen atom of the α-methylene group and one methyl group of the *gem*-dimethyl in an equatorial position. This leads to the assignment of hfsc as shown.[7] It has been previously recognized that carbon atoms of conjugated vinyl groups β or δ to the ketyl or semidione spin labels carry considerable spin density.[3,4,8]



1, a^H in gauss
*, **, hfsc could be reversed

As a test of the relative reducing ability of the system potassium *tert*-butoxide in Me_2SO, eucarvone was subjected to flow and stopped-flow experiments. Ketyl **1** was never observed. Instead, oxidation products **2** (Figure S1b) and **3** (Figure S1c) were detected even with carefully deoxygenated solutions. Potassium *tert*-butoxide in Me_2SO is not only a poorer reducing agent than trimethylsilylsodium in HMPA, but it is more apt to give oxidation products from traces of oxygen remaining in the solution. At flow rates between 0.1 and 20 s between mixing and detection the previously described bicyclic 1,4-semidione **2**[9] was observed. Under stopped flow **2** decayed and the spectrum of **3** could be detected for ap-



2, a^H in gauss **3**, a^H in gauss

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