derived amides (13.4, 13.8, 14.2, 14.5), and a single primary C-H-derived amide (17.0). Similarly, *trans*-**10** gave one tertiary C-H-derived amide (11.0), four secondary C-H-derived amides (12.6, 12.8, 12.9, 13.3), and a single primary C-H-derived amide (15.2). Assuming identical detector response factors for all these compounds, the calculated selectivities (tertiary:secondary:primary) are 1:0.6:0.19 or 1:0.4:0.1 for cis and 1:0.6:0.18 or 1:0.4:0.1 for trans, in hydrocarbon or fluorinated solvents, respectively. The tertiary C-H-derived amides were found to be identical with the two amides resulting from the reaction between diethoxyphosphoryl chloride and the mixture of *cis*- and *trans*-1,2-dimethylcyclohexylamines.[15] The primary and secondary C-H-derived amides were not analyzed. The tertiary C-H-derived amides were easily separated by the GC. No amide (<1%) with a retention time of 11.0 was detected for the cis compound, and no amide with a retention time of 12.2 was observed in the reaction of the trans compound, either in hydrocarbon solution or in perfluorohexane, indicating that the reaction is completely stereospecific. Similar trans products usually have shorter retention times,[14] and therefore, retention of the configuration is the implicated course of the insertion reaction. A study to strictly elucidate absolute stereochemistry of the insertion is in progress and will be reported elsewhere.

For reactions under an argon atmosphere, all reagents and solvents were deoxygenated prior to mixing, and for reactions run under O_2, they were saturated with oxygen. The reaction samples were prepared in argon-filled (or oxygen-filled) 3-mL quartz test tubes closed with subaseal septa (Aldrich). The solvents and reagents were transferred via gas-tight syringes. For competition experiments, a measured volume of a solution of the azide in perfluorohexane was transfer to the sealed test tube. Then, appropriate volumes of hydrocarbons were injected. The total volume of the sample was ca. 3.0 mL to minimize the empty space above the solution. The samples were irradiated for 25-50 min at 22 °C on a merry-go-round with a 450-W medium-pressure Hanovia lamp through a Vycor filter. The solution of internal standard (tetradecane) was then injected, and the volatiles (solvent) were removed at 20 °C under reduced pressure. The residue was dissolved in CH_2Cl_2 and analyzed by GC. The yields of all reactions were determined after corrections for detector response. The calibration was performed with the authentic samples of reaction products by multiple injection. The concentration of the azide stock solution was determined in the same way. The results obtained for the azide (retention time 3.9 min) were in excellent agreement with those calculated from the weight of the azide used to prepare the stock solution. Double injection was used to determine the products yields for most samples. The data for runs 21, 22, 25, and 27 in Table II were obtained from six or seven injections. The reproducibility of the data was good. Average values are listed in Tables I-III.

A similar procedure was followed for reactions run in a hydrocarbon solvent. The isotope effects were obtained by multiple analysis of samples by mass spectrometry. The starting mixtures of cyclohexane-h_{12}/cyclohexane-d_{12} as well as cyclohexane-d_6 were analyzed on the same instrument. The amide hydrogens were completely exchanged prior to the analysis.

Acknowledgment. I thank Professor P. S. Skell for helpful discussions. This work was partially supported by the Camille and Henry Dreyfus Foundation (New Faculty Award).

Supplementary Material Available: Appendices A and B containing derivation of the kinetic equations used (5 pages). Ordering information is given on any current masthead page.

Photochemical Transformations. 48. The Nonconcertedness of Nucleofuge Loss and *anti*-Aryl Migration in Photochemical Wagner-Meerwein Rearrangements[1]

Stanley J. Cristol,* Mahfuza B. Ali, and Iyer V. Sankar

Contribution from the Department of Chemistry & Biochemistry, University of Colorado, Boulder, Colorado 80309-0215. *Received April 5, 1989*

Abstract: Preparation of the two diastereomers of 3-(3,5-dimethoxyphenyl)-2-butanol and of their 2-deuterio analogues has been carried out. When the methanesulfonate esters of the diastereomers were solvolyzed by heating at reflux in 50% aqueous methanol, the resulting alcohols and methyl ethers were formed with complete retention of diastereomeric identity and without measurable hydride migration to give the 2-aryl-2-butyl isomer. Similar treatment of the methanesulfonates of the deuterio analogues gave complete deuterium scrambling, that is, gave equal mixtures of 3-aryl-2-deuterio-2-butyl and 3-aryl-3-deuterio-2-butyl derivatives. These results of ground-state solvolyses are consistent with aryl participation coincident with nucleofuge loss, with bridged phenonium ions as sole intermediates. On the other hand, irradiations of the methanesulfonates with 300-nm light in the same solvent gave photosolvolysis with considerable diastereomeric mixing, although again complete deuterium scrambling was observed here as well. In addition, significant amounts of 2-aryl-2-butanol were formed. The excited-state results require a much more complicated reaction course than the ground-state results, probably involving *syn*-hydrogen migration to give the tertiary alcohol, along one path, and requiring that the observed aryl migrations, along another path, occur later than, rather than concerted with, nucleofuge loss.

Since the first example of photosolvolysis involving carbocations of β-arylethyl (homobenzyl) systems was reported by Jaeger,[2] members of our research group,[3] as well as others,[4,5] have devoted considerable effort in elucidating the mechanism of these intramolecular excitation-transfer processes, which result in the activation of remote functional groups. Although the first example reported by Jaeger[2] dealt with an acyclic homobenzylic system, almost all of the work done in the intervening years involved cyclic systems.[3-5] Much has been learned from these studies and from

(1) Part 47: Cristol, S. J.; Vanden Plas, B. J. *J. Org. Chem.* **1989**, *54*, 1209.

(2) Jaeger, D. A. *J. Am. Chem. Soc.* **1976**, *98*, 6461.

(3) (a) Cristol, S. J.; Stull, D. P.; Daussin, R. D. *J. Am. Chem. Soc.* **1978**, *100*, 6674. (b) Cristol, S. J.; Opitz, R. J.; Bindel, T. H.; Dickenson, W. A. *Ibid.* **1980**, *102*, 7977. (c) Cristol, S. J.; Dickenson, W. A.; Stanko, M. K. *Ibid.* **1983**, *105*, 1218. (d) Cristol, S. J.; Seapy, D. G.; Aeling, E. O. *Ibid.* **1983**, *105*, 7337. (e) Cristol, S. J.; Ali, M. Z. *Tetrahedron Lett.* **1983**, 5839. (f) Cristol, S. J.; Aeling, E. O.; Heng, R. *J. Am. Chem. Soc.* **1987**, *109*, 830 and references therein.

(4) (a) Morrison, H.; Miller, A.; Bigot, B. *J. Am. Chem. Soc.* **1983**, *105*, 2398. (b) Morrison, H.; De Cárdenas, L. M. *Tetrahedron Lett.* **1984**, *25*, 2527. (c) Morrison, H.; Muthuramu, K.; Pandey, G.; Severance, D.; Bigot, B. *J. Org. Chem.* **1986**, *51*, 3358. (d) Morrison, H.; Muthuramu, K.; Severance, D. *Ibid.* **1986**, *51*, 4681. (e) Morrison, H. *Rev. Chem. Intermed.* **1987**, *8*, 125.

(5) Jaeger, D. A.; Bernhardt, E. A. *Tetrahedron Lett.* **1983**, *24*, 4521.

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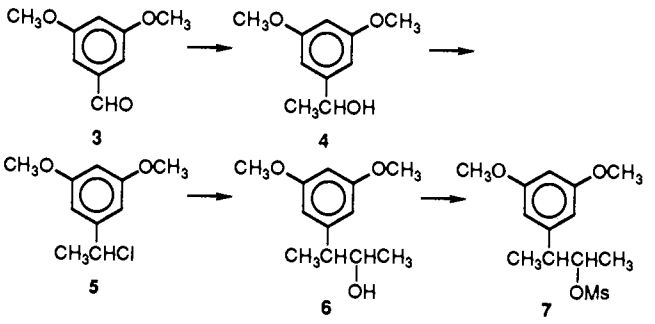
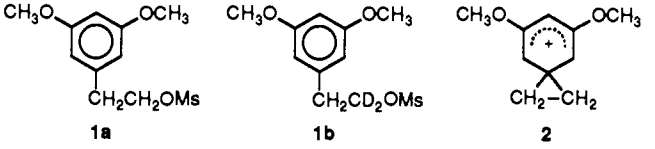
Scheme I



a systematic investigation of functionalized benzo and dibenzo bicyclic systems.[3]

Our research group has proposed that the activation of the remote functional groups (including halogens, mercurials, or methanesulfonates) occurs via intramolecular electron transfer from the photoactivated aromatic ring to the nucleofugal group. In these compounds, the aromatic ring absorbs all of the incident light, as the nucleofugal group is substantially transparent. It was also noted that the proposed electron transfer from the activated aromatic ring to the nucleofugal group is preferred when the two groups are anti to each other, over similar rings and/or groups cis to each other. It was also observed that there is often a propensity for syn migration over anti migration in the later steps of the process, which ultimately results in the photo-Wagner–Meerwein rearranged products.

It was of obvious interest to us to study the stereochemical nature of the photosolvolysis in an acyclic homobenzylic system. In his original study, Jaeger[2] investigated the photosolvolysis of 2-(3,5-dimethoxyphenyl)ethyl methanesulfonate (**1a**) in aqueous



methanol. From the results of solvolysis of **1a** and its deuterio analogue **1b**, which gave β-aryl products with deuterium scrambled between α and β positions, he proposed the phenonium ion **2** as an intermediate. However, he did not have information to determine the nature of the interaction between the excited 3,5-dimethoxyphenyl and methanesulfonate groups. Further, since the system is achiral, nothing could be said about the timing of the formation of **2**, that is, whether or not it could be considered as concerted with methanesulfonate loss, as suggested by Jaeger and Bernhardt.[5]

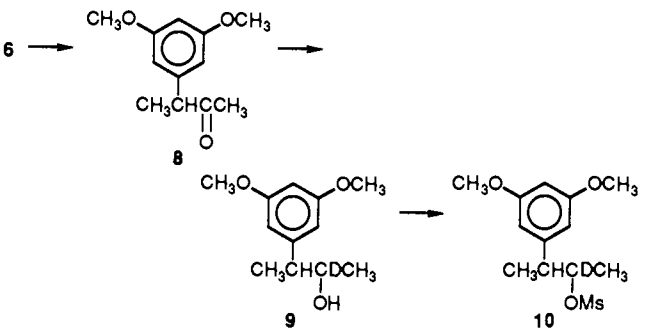
In this paper we describe our study of a diastereomeric homobenzylic system, which allows us to address the details of such reactions. We have chosen to study the 3-aryl-2-butyl systems (threo and erythro), with the aryl group being 3,5-dimethoxyphenyl.

Preparation of Compounds

The diastereomeric methanesulfonates were synthesized by the procedure depicted in Scheme I. Treatment of 3,5-dimethoxybenzaldehyde (**3**) with methylmagnesium bromide gave 1-(3,5-dimethoxyphenyl)ethanol (**4**). The alcohol **4** was converted to 1-(3,5-dimethoxyphenyl)ethyl chloride (**5**) by treatment with concentrated hydrochloric acid. **5** was converted to its Grignard reagent, which, upon treatment with excess acetaldehyde, gave a mixture of the two diastereomeric alcohols **6** in a ratio of 6:1. The diastereomers were separated by column chromatography on silica gel. The isomers were readily distinguished by their ^{1}H NMR spectra. The major isomer had a single peak at δ 1.12 for the two methyl groups, while the minor isomer had peaks at δ 1.00 and 1.20. The separated alcohols were converted to the methanesulfonates **7** following standard procedures.

The deuterated analogue **9** was prepared following Scheme II. The alcohol mixture **6** was oxidized by Jones reagent to the

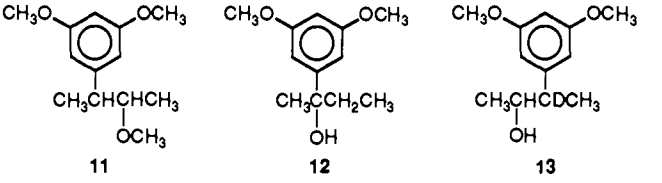
Scheme II



3-aryl-2-butanone **8**. **8** was reduced with lithium aluminum deuteride or with sodium borodeuteride to the deuterated alcohols **9**. The diastereomers were found to be in the ratio 4:1, independent of reducing agent. Again, the δ 1.12 isomer was formed in greater amount. The diastereomers were separated by silica gel chromatography. Each alcohol was converted to its methanesulfonate **10**.

The Grignard preparation of the alcohols **6** outlined in Scheme I followed closely that of Elphinoff-Felkin and Felkin[6] for the preparation of the diastereomeric 3-phenyl-2-butanols. As they found that the erythro isomer was the major product, we initially assumed that this was true as well for the **6** isomers. Our confidence in this analogy was shaken by the observation that the reductions of **8** led to the same major isomer. One would anticipate[7] that the reductions should lead rather to the threo isomer in larger amount. As, in particular, the sodium borohydride reduction, carried out in ethanol, should not be complicated by any prereaction complexing, or electron-transfer process, while this might not be true for the Grignard reaction, we have been tempted to give the major isomer the threo designation. For the purposes of the present investigation, the correctness (or incorrectness) of the tentative assignment is not critical and we have therefore not pursued the question further, although this could be done in a straightforward fashion.[8] In view of this uncertainty, we have simply given the designation **6a** to the major isomer and **6b** to the minor isomer.

Ether **11a** was prepared from the corresponding alcohol **6a** by treatment with sodium hydride followed by addition of methyl iodide. One of the photoproducts, 2-(3,5-dimethoxyphenyl)-2-butanol (**12**), was prepared by reaction of 3,5-dimethoxyacetophenone with ethylmagnesium bromide.



Ground-State Solvolyses. Initial work on ground-state solvolyses of 3-aryl-2-butyl arenesulfonates was reported by Cram,[8] who noted that the threo and erythro diastereomeric *p*-toluenesulfonates gave rise to the corresponding acetates upon acetolysis. The acetolyses were reported to proceed with at least 95% retention of diastereomeric purity and with loss of optical activity with active threo isomer and retention with active erythro isomer. Cram also noted[9] that 4–8% of hydride migration product, 2-phenyl-2-butyl acetate (racemic), was produced in optically active 3-phenyl-2-butyl *p*-bromobenzenesulfonate acetolyses. He ascribed the reactions to give the 3-aryl-2-butyl acetates to the formation of a

(6) Elphinoff-Felkin, I.; Felkin, H. *Bull. Soc. Chim. Fr.* **1957**, 450.
(7) (a) Cram, D. J.; Abd Elhafez, F. A. *J. Am. Chem. Soc.* **1952**, *74*, 5828. (b) Chêrest, M.; Felkin, H.; Frudent, N. *Tetrahedron Lett.* **1968**, 2201. (c) Chêrest, M.; Felkin, H. *Ibid.* **1968**, 2205. (d) Anh, N. T.; Eisenstein, O. *Nouv. J. Chim.* **1977**, 61.
(8) For example, see: Cram, D. J. *J. Am. Chem. Soc.* **1949**, *71*, 3863.
(9) Cram, D. J. *J. Am. Chem. Soc.* **1952**, *74*, 2137.

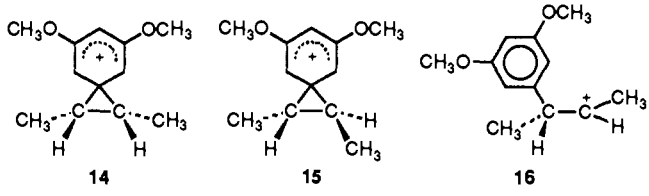
bridged phenonium ion and the hydride migration product to the intervention of a classical (unbridged) ion.

The 3,5-dimethoxyphenyl group has been shown[10] to produce a rate of acetolysis in the primary system 2-arylethyl *p*-bromobenzenesulfonate approximately 0.9 times that of the phenyl group, so one might infer that the isomeric **7** methanesulfonates would give results similar to 3-phenyl-2-butyl sulfonates. It was not clear, however, what a change in solvent to 50% aqueous methanol would do, as this is a substantially more powerful ionizing solvent[11] than acetic acid and surely more nucleophilic as well.

Solvolysis of the methanesulfonate **7a** was carried out at reflux in 50% aqueous methanol containing sodium acetate to neutralize the methanesulfonic acid produced. The product was a mixture of alcohol **6a** and ether **11a** in a ratio of 5.3 to 1. Within the limits of ^{1}H NMR analysis (±1%), no diastereomeric product **6b** or tertiary alcohol **12** was produced and no other ether was seen. Similarly the methanesulfonate **7b** gave alcohol **6b** and ether **11b** in a ratio of 7 to 1. Neither the alcohol nor the ether showed presence of the **a** series, and **12** was also not present.

When the deuterio analogue **10a** was solvolyzed and the product alcohols were analyzed by ^{2}H NMR spectroscopy, the formation of equal amounts of **9a** and of 3-(3,5-dimethoxyphenyl)-3-deuterio-2-butanol (**13a**) was noted. Similar deuterium scrambling was seen with a 50:50 mixture of **10b** and **10a**. When a 50:50 mixture was solvolyzed to about 50%, approximately equal reactivities were noted for **10a** and **10b**. The residual starting material had no evidence of deuterium scrambling from C-2 to C-3.

These results make it clear that these ground-state solvolyses proceed with stereospecific anti participation of the aryl group, which is undoubtedly concerted with cleavage of the carbon–methanesulfonate bond. Thus the threo methanesulfonate gives the meso-bridged ion **14**, while the erythro isomer gives the *dl*-



14 **15** **16**

bridged ion **15**. No evidence for intervention of the classical ion **16** in these thermal solvolyses is adduced. It is of interest that, under these conditions, the aryl group with two, presumably electron-withdrawing, *m*-methoxy groups gives results consistent only with aryl participation. In contrast to the results[12] on acetolysis of the arenesulfonates of 3-phenyl-2-butanol, failure to see deuterium scrambling in recovered starting **10** species indicates that there is no ion-pair return in solvolysis in this system in aqueous methanol. Formation of solvent-separated ion pairs from the initially produced tight ion pairs must obviously be relatively rapid. It seems most likely that this is due to the much higher ionizing power of the aqueous methanol ($Y = +1.97$) compared with acetic acid ($Y = -1.64$).[11]

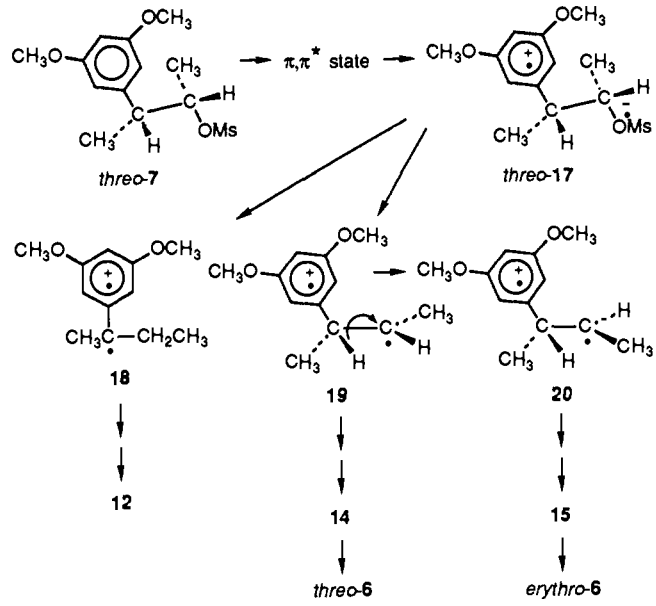
Excited-State Reactions. Irradiation with 300-nm light of these methanesulfonate esters gave results that were remarkably different from those of ground-state solvolysis.

When the isomer **7a** was irradiated, alcohol **6** and ether **11** were produced in a ratio of 3 to 1. Unlike the thermal reaction, irradiation led to diastereomeric scrambling, with both the alcohol and ether produced in approximately equal **a** and **b** configurations. In addition, also unlike the thermal reaction, the hydride migration product, alcohol **12**, was also produced, in about 9% yield.

Similar irradiation of the isomer **7b** led to alcohol **6** and ether **11** in a ratio of 4.5 to 1. Analysis of the **6** again showed diastereomeric scrambling, with about 80% **6b** and 20% **6a** formed. (The ether product was not analyzed.) Again, hydride migration was seen, with about 15% of **12** being formed.

(10) Winstein, S.; Heck, R. *J. Am. Chem. Soc.* **1956**, *78*, 4801.
(11) Fainberg, A. H.; Winstein, S. *J. Am. Chem. Soc.* **1956**, *78*, 2770.
(12) Cram, D. J. *J. Am. Chem. Soc.* **1952**, *74*, 2129.

Scheme III



Irradiation of the deuterium-labeled methanesulfonates **10a** and **10b** showed complete deuterium scrambling in the product alcohols; that is, **9a** and **13a** were formed in equal amounts, as were **9b** and **13b**. In a short-irradiation experiment, recovered methanesulfonates **10a** and **10b** were unchanged; that is, no methanesulfonate related to **13** was present.

Discussion of Results

Clearly, in the ground state, this system is a well-behaved one, with stereochemistry and aryl migration occurring as anticipated[7] for a system undergoing solvolysis with concerted aryl participation.

The photochemical results require a considerably more complicated reaction path. On the one hand, there must be an intermediate that allows for diastereomer scrambling. As both isomeric methanesulfonates do not give the same mixture of diastereomeric alcohols, that is, the diastereomeric scrambling is incomplete in at least one case, that intermediate must be short-lived. It must, of course, be converted to the set of intermediates **14** and **15** to accommodate the complete deuterium scrambling observed. If the classical ion **16** were that intermediate, it would be necessary to assume that it could rotate around the C-2–C-3 bond and/or close to **14** or **15** before any capture by solvent, an assumption that appears unlikely to us. Of course, the complete deuterium scrambling rules out any photo S_N2 reaction. Finally, an alternative reaction path leading to **12** is required.

Ideas from the previous work of our group are consistent with these results. Thus, we have proposed that π^* electron transfer to the carbon–nucleofuge bond from the π,π^* state produced by photoexcitation gives a zwitterionic biradical (**17** in Scheme III). Such electron transfer is favored[3] when the aromatic ring is anti to the carbon–nucleofuge bond, as drawn in **17**. The zwitterionic biradical may suffer one of two fates.[3] Syn migration (of H in **17**), concerted with methanesulfonate loss, may occur, to give the biradical cation **18**, which is an excited state of the tertiary cation leading to **12**. Alternatively, **17** could lose methanesulfonate without attendant migration to give the biradical cation **19**. **19** could decay to the meso-bridged cation **14** or rotate around the C-2–C-3 bond to give the stereoisomeric biradical cation **20** leading to the racemic ion **15**. **14** is, of course, the progenitor of *threo*-**6** and **15** that of *erythro*-**6**.

Our data do not permit us to explain the difference in capture ratio by water and by methanol of **14** or **15** in the same solvent, when the ions are produced in the ground state as opposed to the excited state. In each case more ether was formed in the photoprocess, although the difference was small in the **7a** case. Although the schemes consider only ions as intermediates, the

first-formed species are clearly tight ion pairs and solvent capture cannot occur until the solvent-separated ion-pair stage or free-ion stage is reached. The time required may allow for different "solvent sortings"[11] to occur in the two types of processes. The difference in temperature of the ground-state solvolyses and the photosolvolyses may also contribute to (or account for) the differences in product composition.

In this regard, Morrison and co-workers[4a] have noted that photosolvolysis of *exo*-5-chlorobenzonorbornene gave a capture ratio of the resulting benzonorbornenyl cation (methanol to water) of 1.36, while the cation generated by silver ion promoted ground-state reaction at room temperature gave a capture ratio of 0.66. They ascribe these results to production of a "hot carbocation" in the photochemical reaction. While interpretation of their results is not clouded by temperature effects, differences in ion pairing (or lack thereof in silver ion reactions) also complicate the picture in the benzonorbornenyl case, as they do in the 3-aryl-2-butyl case.

It has been noted[13] that experiments using fast laser spectroscopy demonstrate that ion pairs produced by photochemically induced heterolysis are often in an excited state (thermal or electronic). Our results, added to those published earlier,[3] demonstrate that much interesting chemistry occurs after photoexcitation, but before transformation to ground-state cations (or ion pairs). It is therefore necessary to be cautious in the use of photoproduced cations as models for ground-state cations.

Experimental Section

The boiling points quoted in this paper are the glass-oven temperature of the Büchi Kugelrohr apparatus. ^{1}H NMR spectra were recorded on a Bruker WM 250 or a Varian EM 390 instrument. Chemical shifts are reported in parts per million (ppm) relative to tetramethylsilane as internal standard. Mass spectra and exact mass were obtained on a Varian MAT-CH5 spectrometer. Elemental analyses were performed by Galbraith Laboratories, Inc. Irradiations were carried out in deoxygenated solvents with 300-nm light in a Srinivasan-Griffin photochemical reactor, hereafter referred to as a "Rayonet". All solvents and reagents were commercially available, reagent grade and were used without further purification unless otherwise stated.

Preparation of 1-(3,5-Dimethoxyphenyl)ethanol (4). A three-neck round-bottom 250-mL flask equipped with a stirrer, reflux condenser, dropping funnel, and nitrogen inlet was charged with 10.0 g (0.060 mol) of 3,5-dimethoxybenzaldehyde (Aldrich Chemical Co.) and 100 mL of anhydrous ethyl ether in an atmosphere of nitrogen. To this well-stirred solution was added 19 mL of 3.2 M methylmagnesium bromide dropwise so as to maintain a gentle reflux. After the addition, the reaction mixture was stirred at room temperature for another 2 h and then quenched with an aqueous solution of ammonium chloride. Normal workup followed by drying ($MgSO_4$) and removal of solvent gave 10.6 g (97%) of **4** as a pale yellow syrup. An aliquot of the sample was carefully distilled in the Kugelrohr apparatus (bp 110 °C/0.2 mm). **4** was found to dehydrate when heated above this temperature. ^{1}H NMR ($CDCl_3$): δ 1.44 (d, 3 H, CH_3, J = 6 Hz), 1.86 (br s, 1 H, OH), 3.77 (s, 6 H, 2 OCH_3), 4.84 (q, 1 H, CH, J = 6 Hz), 6.35 (t, 1 H, H-4′, Ar, J = 2 Hz), 6.59 (d, 2 H, H-2′, H-6′, J = 2 Hz). Mass spectrum: m/e (relative intensity) 182 (M^+, 50); 165 (100); 139 (20). Exact mass: calcd, 182.0943; found, 182.0940.

1-(3,5-Dimethoxyphenyl)ethyl Chloride (5). A mixture of 10.0 g (0.054 mol) of **4** and 20 mL of concentrated hydrochloric acid was stirred vigorously at room temperature until all of the **4** reacted, approximately 8 h. The mixture was then poured onto 200 g of ice and extracted several times with ether. The combined ethereal layer was washed with water, saturated aqueous $NaHCO_3$, and finally with water. Drying ($MgSO_4$) and removal of the solvent followed by careful Kugelrohr distillation gave 10.7 g (94%) of **5** as a colorless viscous liquid (bp 98 °C/0.2 mm). ^{1}H NMR ($CDCl_3$): δ 1.81 (d, 3 H, CH_3, J = 6.8 Hz), 3.80 (s, 6 H, OCH_3), 5.00 (q, 1 H, CH, J = 7 Hz), 6.40 (t, 1 H, H-4, Ar, J = 2.2 Hz), 6.58 (d, 2 H, H-2, H-6, Ar, J = 2.2 Hz). ^{13}C NMR ($CDCl_3$, relative to TMS): δ 145.22 (C-1), 104.67 (C-2, C-6), 160.89 (C-3, C-5), 100.06 (C-4), 58.29 (CH), 55.20 (OCH_3), 26.34 (CH_3). Mass spectra: m/e (relative intensity) 200 (40), 165 (100). Exact mass: calcd, 200.0604; found, 200.0616.

3-(3,5-Dimethoxyphenyl)-2-butanol (6a and 6b). A dry three-neck round-bottom 250-mL flask equipped with a nitrogen inlet, reflux condenser, dropping funnel, and stirrer, was charged with 4.0 g (0.16 mol) of magnesium. The magnesium was dried by heating with a Bunsen burner in an atmosphere of nitrogen. After the flask was cooled, 50 mL of anhydrous ethyl ether was added to the flask at room temperature.

A solution of 2.00 g (10 mmol) of **5** in 100 mL of anhydrous ether was added dropwise over a period of 4–5 h while the flask and contents were being sonicated. The Grignard reagent thus obtained was chilled to 0 °C, and excess acetaldehyde was slowly added under vigorous stirring. The reaction mixture was allowed to warm to room temperature and was then quenched with saturated ammonium chloride solution. The organic layer was separated, and the aqueous layer was extracted several times with ether. The combined ethereal layers were washed with water and dried ($MgSO_4$). Removal of the solvent at room temperature gave a pale yellow liquid, whose ^{1}H NMR spectrum was consistent with that of a mixture of **6a** and **6b** in the ratio 6:1, along with the dimer of the radical of **5**. The alcohols (0.90 g, 43%) were separated from each other and from the dimer by column chromatography on silica gel. Elution with 5% ether in *n*-hexane gave **6a** eluting before **6b**, with rather pure materials present in initial and final fractions and mixtures in middle fractions.

6a. ^{1}H NMR ($CDCl_3$): δ, 1.12 (d, 6 H, 2 CH_3, J = 6 Hz), 1.83 (br s, 1 H, OH), 2.53 (quintet, 1 H, H-3), 3.78 (br s, 7 H, 2 OCH_3, H-2), 6.35 (t, 1 H, H-4′), 6.38 (d, 2 H, H-2′ and H-6′, Ar). Mass spectrum: m/e (relative intensity) 210 (M^+, 43), 195 (10), 165 (100). Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.57; H, 8.57. Found: C, 67.98, H, 8.70.

6b. ^{1}H NMR ($CDCl_3$): δ 1.00 (d, 3 H, CH_3, J = 6.5 Hz), 1.20 (d, 3 H, CH_3, J = 6.5 Hz), 1.79 (br s, 1 H, OH), 2.61 (quintet, 1 H, H-3), 3.69 (s, 7 H, 2 OCH_3, H-2), 6.37 (t, 1 H, H-4′), 6.52 (d, 2 H, H-2′, H-6′). Mass spectrum: (relative intensity) m/e 210 (M^+, 40); 195 (10); 165 (100).

3-(3,5-Dimethoxyphenyl)-2-butyl Methanesulfonate (7a and 7b). A solution of 100 mg (0.46 mmol) of **6a** and 84 mg of triethylamine in 4 mL of anhydrous methylene chloride at −10 °C was treated with 70 mg (0.6 mmol) of methanesulfonyl chloride and stirred at −10 °C for 30 min.[14] The reaction mixture was diluted with more CH_2Cl_2 and washed with ice-cold water, 10% hydrochloric acid, water, saturated aqueous $NaHCO_3$, and finally brine. Drying ($MgSO_4$) and removal of the solvent gave 130 mg (98%) of **7a** as a pale yellow liquid. ^{1}H NMR ($CDCl_3$): δ 1.28 (d, 3 H, CH_3, J = 7.5 Hz), 1.40 (d, 3 H, CH_3, J = 7.5 Hz), 2.53 (s, 3 H, SO_2CH_3), 2.93 (quintet, 1 H, H-3, J = 7.5 Hz), 3.78 (s, 6 H, 2 OCH_3), 4.82 (quintet, 1 H, H-2, J = 7.5 Hz), 6.32 (t, 1 H, H-4′, J = 2.2 Hz), 6.38 (d, 2 H, H-2′, H-6′, J = 2.2 Hz). Mass spectrum: m/e (relative intensity) 288 (M^+, 51), 193 (25); 165 (27); 164 (100). Anal. Calcd for $C_{13}H_{20}O_5S$: C, 54.16; H, 6.94. Found: C, 53.98; H, 6.75.

In a similar fashion, **7b** was prepared from **6b**. ^{1}H NMR ($CDCl_3$): δ, 1.33 (d, 3 H, CH_3, J = 6.3 Hz), 1.36 (d, 3 H, CH_3, J = 6.3 Hz), 2.80 (s, 3 H, SO_2CH_3), 2.85 (quintet, 1 H, H-3, J = 6.3 Hz), 3.79 (s, 6 H, OCH_3), 4.86 (quintet, 1 H, H-2), 6.35 (t, 1 H, H-4′), 6.40 (d, 2 H, H-2′, H-6′). Mass spectrum: m/e (relative intensity) 288 (M^+, 48), 193 (28), 165 (30), 164 (100).

3-(3,5-Dimethoxyphenyl)-2-butanone (8).[16] A solution of 150 mg (0.71 mmol) of a mixture of **6a** and **6b** in 12 mL of acetone was treated with an excess of Jones reagent[15] at room temperature. After 30 min of vigorous stirring, isopropyl alcohol (2 mL) was added to the mixture. Water was added slowly, and the mixture was then extracted with ether. The organic layer was washed with water, saturated aqueous $NaHCO_3$, and water. Drying ($MgSO_4$) and removal of the solvent gave 140 mg (94%) of **8**. ^{1}H NMR ($CDCl_3$): δ, 1.26 (d, 3 H, H-4, J = 6 Hz), 1.92 (s, 3 H, H-1, CH_3), 3.59 (q, 1 H, H-3, J = 6 Hz), 3.66 (s, 6 H, OCH_3), 6.29 (br s, 3 H, Ar).

3-(3,5-Dimethoxyphenyl)-2-deuterio-2-butanol (9a and 9b). An ethereal solution of 140 mg (0.70 mmol) of **8** was slowly added to 24 mg (0.57 mmol) of lithium aluminum deuteride in 10 mL of anhydrous ethyl ether. The resulting mixture was heated at reflux for about 30 min, cooled, and quenched with water. Normal workup followed by flash chromatography on a silica gel column gave the isomeric alcohols in a 4:1 ratio (**9a**:**9b**).

9a. ^{1}H NMR ($CDCl_3$): δ, 1.10 (m, 6 H, H-1, H-4), 1.66 (b, 1 H, OH), 2.53 (q, 1 H, H-3, J = 6 Hz), 3.70 (s, 6 H, OCH_3), 6.39 (m, 3 H, Ar). ^{2}H NMR ($CDCl_3$): δ, 3.70 (b, 1 D, D-2). Mass spectrum: m/e (relative intensity) 211 (M^+, 58), 196 (18), 165 (100), 150 (49).

9b. ^{1}H NMR ($CDCl_3$): δ 1.00 (d, 3 H, H-4), 1.20 (s, 3 H, H-1), 1.66 (br, 1 H, OH), 2.56 (q, 1 H, H-3, J = 6 Hz), 3.70 (s, 6 H, OCH_3), 6.40 (m, 3 H, Ar). Mass spectrum: m/e (relative intensity) 211 (M^+, 42), 165 (100), 150 (21). ^{2}H NMR ($CDCl_3$): δ, 3.70 (br, 1 D, D-2).

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When reduction of **8** was carried out with sodium borodeuteride in ethanol in the usual fashion,[17] **9a** and **9b** were again produced in a 4:1 ratio.

3-(3,5-Dimethoxyphenyl)-2-deuterio-2-butyl Methanesulfonate Isomers (10a and 10b). The isomers of **10** were prepared from those of **9** as described above for the synthesis of **7a** and **7b**.

10a. ^{1}H NMR ($CDCl_3$): δ 1.33 (d, 3 H, H-4, J = 6 Hz), 1.40 (s, 3 H, H-1), 2.56 (s, 3 H, SO_2CH_3), 3.00 (q, 1 H, H-3), 3.80 (s, 6 H, $2OCH_3$), 6.30–6.40 (m, 3 H, Ar). ^{2}H NMR ($CHCl_3$): δ 4.80 (br s, D-2).

10b. ^{1}H NMR ($CDCl_3$): δ 1.30 (d, 3 H, H-4, J = 6 Hz), 1.39 (s, 3 H, H-1), 2.80 (s, 3 H, SO_2CH_3), 2.89 (q, 1 H, H-3, J = 6 Hz), 3.79 (s, 6 H, OCH_3), 6.33–6.41 (m, 3 H, Ar). ^{2}H NMR ($CHCl_3$): δ 4.80 (br s, D-2).

2-(3,5-Dimethoxyphenyl)-2-butanol (12). 1-(3,5-Dimethoxyphenyl)-ethanol (0.86 g, 4.72 mmol) was oxidized by Jones reagent as described for the synthesis of **8** to obtain 3,5-dimethoxyacetophenone[18] in almost quantitative yield. ^{1}H NMR ($CDCl_3$): δ 2.53 (s, 3 H, CH_3), 3.83 (s, 6 H, OCH_3), 6.66–6.70 (m, 3 H, Ar).

The addition of 0.86 g of 3,5-dimethoxyacetophenone in 10 mL of ethyl ether to 1.72 mL of 2.5 M ethylmagnesium bromide in 20 mL of ethyl ether, followed by 1-h stirring, normal workup, and chromatography on silica gel gave 950 mg (95%) of **12**[19] as a pale yellow liquid. ^{1}H NMR ($CDCl_3$): δ 0.73 (t, 3 H, H-4, J = 7 Hz), 1.40 (s, 3 H, H-1), 1.72 (q, 2 H, H-3, J = 7 Hz), 3.70 (s, 6 H, OCH_3), 6.25–6.66 (m, 3 H, Ar). Mass spectrum: m/e (relative intensity) 210 (M^+, 68), 181 (99), 164 (100). Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.57, H, 8.57. Found: C, 68.82; H, 8.69.

3-(3,5-Dimethoxyphenyl)-2-butyl Methyl Ether (11a). A mixture of 270 mg (1.30 mmol) of **6a** and 100 mg (2.1 mmol) of 50% sodium hydride in mineral oil in 20 mL of anhydrous ether was stirred for 1 h at room temperature. After the addition of 2 mL of methyl iodide, the mixture was stirred at room temperature for 24 h. Washing with three portions of water was followed by drying ($MgSO_4$) and evaporation of the solvent. Preparative thin-layer chromatography on silica gel with 1:10 ether–hexane as eluent gave **11a** as an oil. ^{1}H NMR ($CDCl_3$): δ 1.03 (d, 3 H, CH_3, J = 6 Hz), 1.20 (d, 3 H, CH_3, J = 6 Hz), 2.86 (quintet, 1 H, H-3, J = 6 Hz), 3.26 (s, 3 H, OCH_3), 3.40 (quintet, 1 H, H-2, J = 6 Hz), 3.76 (6 H, OCH_3), 6.30–6.53 (m, 3 H, Ar). Mass spectrum: m/e (relative intensity): 224 (M^+, 50), 209 (25), 193 (13), 165 (49). Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.64; H, 8.92. Found: C, 69.50; H, 8.67.

Ground-State Solvolysis of 7a and 10a. A solution of 75 mg (0.27 mmol) of **7a** and 21 mg of sodium acetate in 50 mL of 50% (v/v) aqueous methanol was heated at reflux for 24 h. Solvent was then removed by rotary evaporation in vacuo and the residue extracted with ether. The ethereal solution was washed with water and dried ($MgSO_4$). Evaporation of the solvent left 70 mg of an oil whose ^{1}H NMR spectrum indicated that it was comprised of 84% **6a** and 16% **11a**. Peaks used for analysis were the δ 1.12 resonance for C-1 and C-4 methyl protons in **6a** and the δ 3.26 resonance for the C-2 methoxy group in **11a**, and other peaks confirmed the results. Chromatographic separation of the alcohol fraction from the ether fraction was carried out, and ^{1}H NMR analysis showed the absence of **6b** (absence of peaks at δ 1.00 and 1.20) and of **12** (absence of peaks at δ 0.73, 1.40, and 1.72).

Thermal solvolysis of 20 mg of **10a** was carried out as described for **7a**. Analysis of the alcohol fraction by integration of ^{2}H NMR resonances indicated that the material was, within experimental error (±5%), half **9a** (δ 3.7) and half **13a** (δ 2.5).

Ground-State Solvolysis of 7b and 10b. A solution of 26 mg of **7b** and 7 mg of sodium acetate in 20 mL of 50% aqueous methanol was treated as described above to give a mixture of 88% of **6b** and 12% of **11b**. No evidence for the formation of **6a**, **11a**, or **12** was seen.

When 26 mg of a 60:40 mixture of **10b** and **10a** was solvolyzed as above, ^{2}H NMR analysis revealed that the product alcohol was half **9** and half **13**. We did not separate the diastereomeric alcohols, but as the experiment above showed that **10a** gave equal amounts of **9a** and **13a**, the results require that **10b** must give half **9b** and half **13b**.

Short-Term Ground-State Solvolysis of 10a and 10b. When 67 mg of a 60:40 mixture of **10b** and **10a** was treated as above, but heated at reflux for only 1 h, approximately half of each methanesulfonate reacted. The residual starting material was separated from the products by thin-layer chromatography on silica gel (elution with 1:10 ether–hexane). ^{2}H NMR of the starting material showed no deuterium scrambling (δ 4.8 peak present, δ 2.9–3.0 peak absent). The alcohol product had equal ^{2}H NMR peaks at δ 2.5 and 3.7.

Photosolvolysis of 7a and 10a. A solution of 31 mg (0.10 mmol) of **7a** and 8 mg of sodium acetate in 50 mL of 50% aqueous methanol, in a Pyrex tube, was deoxygenated by nitrogen bubbling for 45 min. Irradiation in a Rayonet with 300-nm light was carried out for 24 h. (A similar tube covered with aluminum foil showed no reaction.) The solvent was removed in vacuo and the residue extracted three times with ether. The combined ether layers were dried ($MgSO_4$), and the solvent was removed in vacuo to give 29 mg of an oil. ^{1}H NMR analysis indicated that the mixture was comprised of 68% **6**, 22% **11**, and 9% **12**. Thin-layer chromatography gave the alcohol (**6** + **12**) fraction whose ^{1}H NMR spectrum showed that **6** was half **6a** and half **6b**.

A solution containing 30 mg of **10a** was irradiated as described for the nondeuterated methanesulfonate **7a**. The mixture of alcohols contained half **9** and half **13**. A larger experiment (218 mg of **10a**), followed by chromatographic separation, gave an early fraction that was half **9a** and half **13a**. A later fraction that was 60% deuterated **6b** and 40% deuterated **6a** had a ^{2}H NMR spectrum that indicated that the deuterium was completely scrambled between C-2 and C-3.

Photosolvolysis of 7b and 10b. Irradiation of 33 mg (0.10 mmol) of **7b** and 9 mg of sodium acetate in 50 mL of 50% aqueous methanol with 300-nm light and workup were carried out as described above for **7a** to give 30 mg of an oil. ^{1}H NMR analysis indicated that the oil was comprised of 55% **6b**, 14% **6a**, 15% **11**, and 15% **12**. (No reaction occurred in the dark.)

When 20 mg of the deuterio analogue **10b** was irradiated, **9** and **13** were produced in equal amounts. The diastereomeric alcohols were not separated, but as **10a** gave complete scrambling, the results require that **10b** did as well.

Short-Term Irradiation of 10a and 10b. A 60:40 mixture of **10a** and **10b** (30 mg) was irradiated in 50% aqueous methanol for 1 h, and worked up as described above. ^{1}H NMR analysis indicated that 70% of the starting material had reacted. After chromatography, ^{2}H NMR spectroscopy showed that both **10a** and **10b** suffered no scrambling of deuterium, while the diastereomeric alcohol fraction showed equal amounts of **9** and **13**.

Acknowledgment. We are indebted to the National Science Foundation (Grant CHE 85-03422 and predecessor grant) for partial support of this work.

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