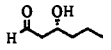
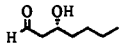
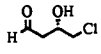
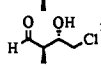
Table I. Substrate Specificity of DERA[a]

Donor	Acceptor	Presumed Product	R_f
		—	
			0.38(1)
			0.41(1)
			0.6(2)
			0.26(1)
			0.34-0.55(1)
		—	
			0.6(1)
			0.78(1)
			0.26(1)
			0.56(2)
			0.39(2)
			0.65(2)
		—	
			0.6(2)

[a] Reactions were conducted in a 1-mL solution containing 0.1 M triethanolamine, 0.1 mM EDTA, 0.1 M donor, 0.1 M acceptor, and 30 units of DERA. A control reaction was performed containing all components except the enzyme. After incubation overnight, TLC (silica gel) was used to identify the appearance of product by staining with *p*-anisaldehyde reagent. Solvent systems: 1, ether:hexane = 9:2; 2, ether:$CHCl_3$ = 1:1. The rate of each reaction is about 1% of the rate of the natural reaction. [b] Stereochemistry at the α position was not determined.

Table II. Relative Activities of Carbohydrates as Acceptor Substrates (100 mM) in DERA-Catalyzed Reactions at pH 7.5 with Acetaldehyde (25 mM)

acceptor substrates	V_{rel}
D-glyceraldehyde 3-phosphate	100
D-glyceraldehyde	0.40
L-glyceraldehyde	0.40
D-ribose	0.44
D-ribose 5-phosphate	0.36
D-arabinose	0.30
D-glucose	0.40
D-glucose 6-phosphate	0.05
2-deoxy-D-glucose	0.23
N-acetylglucosamine	0.25

^1H NMR (200 MHz, $CDCl_3$) δ 0.87 (m, 6 H), 1.63 (m, 1 H), 2.15 (s, 3 H), 2.64 (m, 2 H), 3.0 (br, 1 H), 3.78 (m, 1 H); ^{13}C NMR (50 MHz, $CDCl_3$, APT) δ 17.71, 18.29 (CH_3), 30.79 (CH_3), 32.99 (CH), 46.96 (CH_2), 72.17 (CH), 210.32 (CO). Anal. Calcd for $C_7H_{14}O$ (114.5): C, 73.68; H, 12.28. Found: C, 73.70; H, 12.22.

(*S*)-1-Fluoro-3-hydroxy-4-methylhexan-2-one. To a 66-mL solution containing 0.2 M fluoroacetone, 0.1 M isobutyraldehyde, 0.1 TEA, and 1 mM EDTA was added 2000 units of DERA in a dialysis bag. After reaction for 1 day, 0.6 mL of isobutyraldehyde was added and the solution was stirred for an additional 2 days. The product was isolated as described above to yield 750 mg (40% yield): $[\alpha]_D$ -46.3° (*c* 0.8, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$) δ 0.89 (d, 3 H, J = 3.6 Hz), 0.93 (d, 3 H, J = 3.7 Hz), 1.7 (m, 1 H), 2.5 (br s, 1 H), 2.65 (m, 2 H), 3.88 (q, 1 H), 4.82 (d, 2 H, J_{HF} = 47.6 Hz); ^{13}C NMR (50 MHz, $CDCl_3$, APT) δ 17.59, 18.27 (CH_3), 33.32 (CH), 42.22 (CH_2), 71.8 (CH), 85.14 (d, CFH_2, $^1H_{CF}$ = 183.9 Hz), 207.79 (C, $^2J_{CF}$ = 18.9 Hz). Anal. Calcd for $C_7H_{13}OF$ (122.4): C, 68.85; H, 10.66. Found: C, 68.84; H, 10.61.

2-Deoxyribose 5-phosphate was prepared similarly from a 100-mL solution containing 0.3 M acetaldehyde, 0.1 M D-glyceraldehyde 3-phosphate, and 100 units of DERA. After 6 h, $BaCl_2$ (14 mmol) was added, followed by addition of ethanol (200 mL) to obtain a precipitate, which contained 86% 2-deoxyribose 5-phosphate and 10% inorganic phosphate.[7]

In summary, we have made available the enzyme DERA for use in stereocontrolled aldol condensations and have established that the enzyme accepts a number of aldehydes as acceptors and propionaldehyde, acetone, and fluoroacetone, in addition to acetaldehyde, as donors. The enzyme appears to be a useful catalyst for synthesis of a number of β-hydroxy aldehydes and ketones. Work is in progress to optimize the conditions to increase the yield and to explore new substrates for the enzyme.

Supplementary Material Available: Details of the production, purification, stability, pH profile, and kinetic analyis of the enzyme DERA (3 pages). Ordering information is given on any current masthead page.

(7) For enzymatic determination of deoxyribose 5-phosphate, see: Bergmeyer, H. U. *Methods of Enzymatic Analysis*; Verlag Chemie: Weinheim, 1974. For inorganic phosphate analysis, see: Ames, B. N. *Methods Enzymol.* **1966**, *8*, 115. D-Glyceraldehyde 3-phosphate was prepared from (*R*)-glycidaldehyde diethyl acetal and inorganic phosphate as outlined below.

Infrared Multiple Photon Dissociation of Butyrophenone Cation. A Stepwise McLafferty Rearrangement

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Although the McLafferty rearrangement[1] (eq 1) is one of the most extensively studied unimolecular reactions in mass spectrometry,[2] its mechanism is still controversial. Theoretical studies

(1)

have supported both stepwise[3] and concerted[4] pathways. Experimental studies on the benzyl ethyl ether cation rearrangement have also supported conflicting mechanisms.[5] For a few systems,

(1) (a) McLafferty, F. W. *Anal. Chem.* **1956**, *28*, 306. (b) McLafferty, F. W. *Anal. Chem.* **1959**, *31*, 82.

(2) Kingston, D. G. I.; Bursey, J. T.; Bursey, M. M. *Chem. Rev.* **1974**, *74*, 215.

(3) (a) Boer, F. P.; Shannon, T. W.; McLafferty, F. W. *J. Am. Chem. Soc.* **1968**, *90*, 7239. (b) Hudson, C. E.; Griffin, L. L.; McAdoo, D. J. *Org. Mass Spectrom.* **1989**, *24*, 866. (c) Dorigo, A. E.; Loncharich, R. J.; Houk, K. N., submitted.

(4) (a) Dougherty, R. C. *J. Am. Chem.* **1968**, *90*, 5788. (b) Ha, T.-K.; Radloff, C.; Nguyen, M. T. *J. Phys. Chem.* **1986**, *90*, 2991.

(5) (a) Stone, D. J. M.; Bowie, J. H.; Underwood, D. J.; Donchi, K. F.; Allison, C. E.; Derrick, P. J. *J. Am. Chem. Soc.* **1983**, *105*, 1688. (b) Wesdemiotis, C.; Feng, R.; McLafferty, F. W. *J. Am. Chem. Soc.* **1985**, *107*, 715. (c) Allison, C. E.; Stringer, M. B.; Bowie, J. H.; Derrick, P. J. *J. Am. Chem. Soc.* **1988**, *110*, 6291. (d) Tureček, F.; Drinkwater, D. E.; McLafferty, F. W., submitted.

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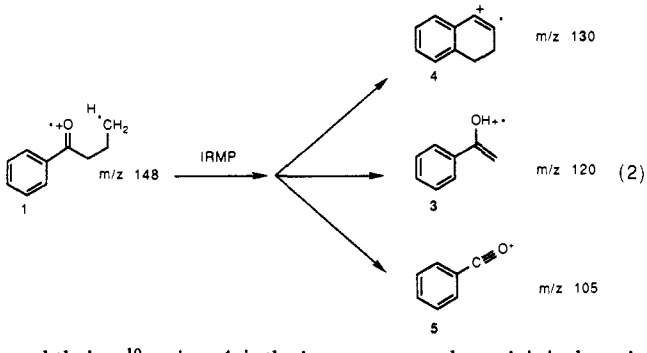
a stepwise pathway has been advanced on the basis of hydrogen scrambling.[6] In this communication we report a novel application of infrared multiple photon (IRMP) activated dissociation of the butyrophenone molecular cation which shows that the reaction is *not* a simple unimolecular rearrangement and must involve an intermediate (eq 1). A particularly interesting aspect of these experiments is the evidence for unimolecular isomerization during the laser pulse which affects product yield. These results directly implicate the existence of an intermediate, very likely the distonic ion,[7] **2**, and indicate a barrier to its formation from **1**.

IRMP dissociation of butyrophenone cation was investigated by using Fourier transform ion cyclotron resonance (FT-ICR) spectrometry[8] coupled with both pulsed CO_2 TEA and continuous-wave (cw) CO_2 lasers. To compare results from different pulse lengths, the temporal profile of the pulsed laser can be shortened from a "long" pulse of ca. 4 μs to a "short" pulse of ca. 200 ns by removing the nitrogen component of the laser gas mixture. Total fluences are reported as twice the incident fluence, since the laser light is reflected back colinearly through the FT-ICR cell.[8]

In addition to the enol[9] McLafferty product, **3**, two other products are formed by IRMP dissociation of butyrophenone cation with the pulsed laser (eq 2). Production of 1,2-dihydro-



(2)

naphthalene[10] cation, **4**, is the lowest energy channel; it is the only product formed by IRMP dissociation with a cw laser.[11] IRMP dissociation of **3** produces benzoyl cation, **5**, in high yield. For these low-energy experiments, the major pathway to **5** is via a secondary process[12] involving **3** and not direct dissociation of **1** or **2**.

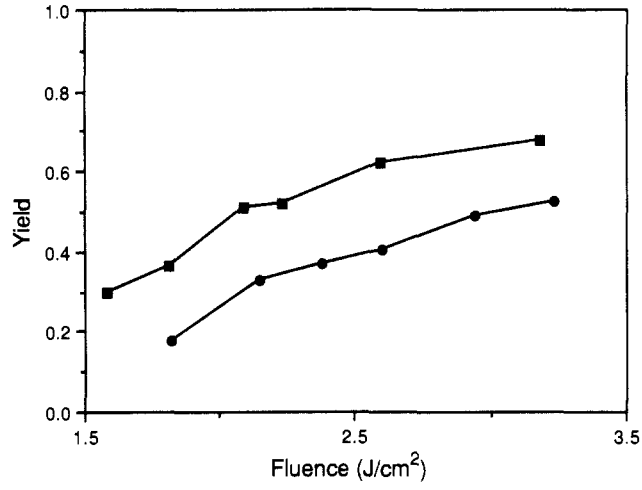


Figure 1. Dependence of total product yield on fluence for long and short laser pulses with equal spot sizes. Product ion yield reported as the fraction of total ions; (■) long pulse; (●) short pulse.

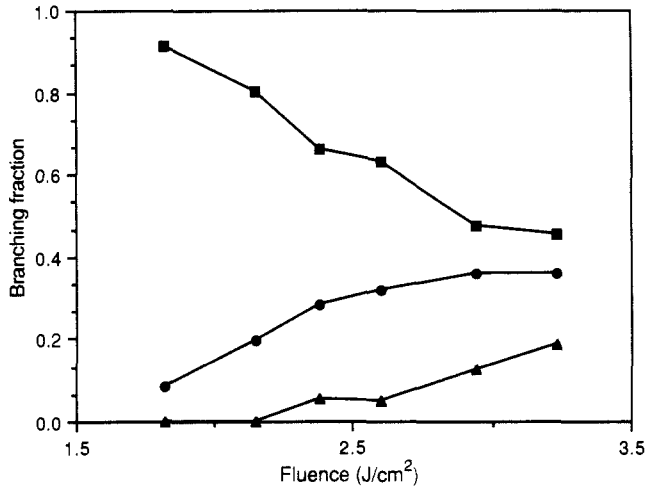


Figure 2. Dependence of branching fractions on fluence for a 200-ns laser pulse; (■) phenylcyclohexene cation, **4**; (●) acetophenone enol cation, **3**; (▲) benzoyl cation, **5**.

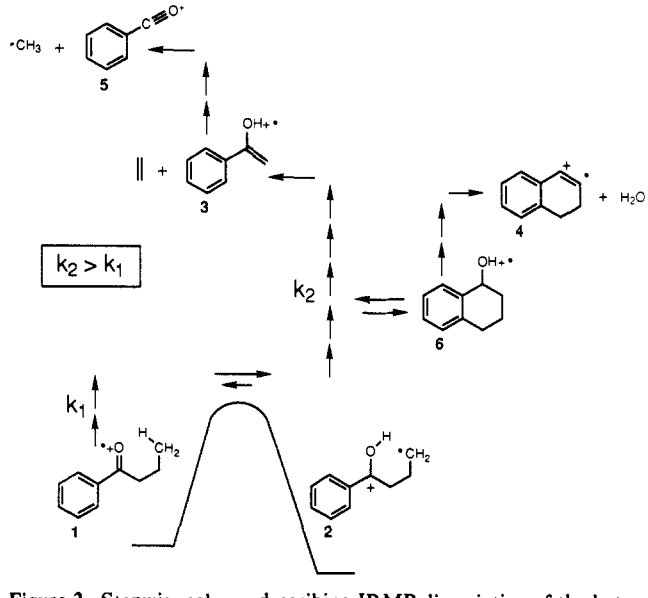


Figure 3. Stepwise scheme describing IRMP dissociation of the butyrophenone cation. The vertical axis does not correspond to an energy scale but shows qualitative appearance energy requirements.

There are two ways to increase the laser intensity: (1) by maintaining a constant pulse length while increasing fluence or

(6) (a) Smith, J. S.; McLafferty, F. W. *Org. Mass Spectrom.* **1971**, *5*, 483. (b) Briggs, P. R.; Shannon, T. W.; Vouros, P. *Org. Mass Spectrom.* **1971**, *5*, 545. (c) McAdoo, D. J.; Hudson, C. E.; McLafferty, F. W.; Parks, T. E. *Org. Mass Spectrom.* **1984**, *19*, 353.

(7) (a) Radom, L.; Bouma, W. J.; Nobes, R. H.; Yates, B. F. *Pure Appl. Chem.* **1984**, *56*, 1831. (b) Bouchoux, G. *Mass Spectrom. Rev.* **1988**, *7*, 1. (c) Hammerum, S. *Mass Spectrom. Rev.* **1988**, *7*, 123. (d) Bouchoux, G. *Mass Spectrom. Rev.* **1988**, *7*, 203.

(8) Experiments were performed with an IonSpec FTMS2000 mass spectrometer attached to a home-built vacuum system. Ions were trapped in a 1-in. cubic cell with the total gas pressure ca. 10^{-6} Torr. Electron energy for ion formation was nominally 17 V. All reactant ions were isolated by standard notched ejection techniques. Modifications for infrared photochemical experiments are described in the following: Jasinski, J. M.; Rosenfeld, R. N.; Meyer, F. K.; Brauman, J. I. *J. Am. Chem. Soc.* **1982**, *104*, 652.

(9) Beynon, J. H.; Caprioli, R. M.; Shannon, T. W. *Org. Mass Spectrom.* **1971**, *5*, 967.

(10) Deuterium labeling studies of butyrophenone and 1-tetralol have shown that loss of water proceeds via 1,4-elimination through the fused tetralol structure and not a cyclobutanol structure as has been suggested for straight-chain aldehydes. See: (a) Gross, M. L.; Chiu, E.; Pokorny, D.; DeRoos, F. L. *Org. Mass Spectrom.* **1977**, *12*, 55. (b) Audier, H. E.; Bouchoux, G.; Moustapha, C.; Denhez, J. P. *Tetrahedron Lett.* **1981**, *22*, 2875. The ultimate structure of the (M – H_2O) ion is uncertain. In ref 10a, Gross and co-workers suggested the 1,2-dihydronaphthalene structure, **4**. The distonic ion, structure **2**, was also implicated in their suggestion of a stepwise decomposition of 1-tetralol cation to benzoyl cation. Subsequently Gross and co-workers have found that the 1,2-dihydronaphthalene structure will also rearrange at higher energies. See: Dass, L.; Gross, M. L. *J. Am. Chem. Soc.* **1983**, *105*, 5724.

(11) Bomse, D. S.; Woodin, R. L.; Beauchamp, J. L. *J. Am. Chem. Soc.* **1979**, *101*, 5503.

(12) This pathway has been observed in metastable ion mass spectrometry as well as collisional activation mass spectrometry. See, in addition to ref 9: (a) Tomer, K. B.; Djerassi, C. *Org. Mass Spectrom.* **1972**, *6*, 1285. (b) Tomer, K. B.; Guenat, C. R.; Deterding, L. J. *Anal. Chem.* **1988**, *60*, 2232.

(2) by maintaining a constant fluence while shortening the pulse length. Results from case 1 experiments, for both long and short laser pulses, are consistent with what would be expected for simple IRMP dissociation. Product yield (total product ion abundance divided by parent ion plus product ion abundances) increases with fluence[8,13] as shown in Figure 1. Branching fractions (individual product yield divided by total product yield) of higher energy products increase with fluence[13] (intensity) at the expense of the lowest energy channel, see[14] Figure 2. However, results from case 2 experiments are completely unexpected. Inspection of Figure 1 shows that, for long and short laser pulses of equal fluence, the short pulse (higher intensity) results in *lower* product yield. This is surprising because the product yield for the short pulse would not be expected to decrease.[8,13,15] To our knowledge there are no previous reports[16] of such behavior.

These results can be explained, however, by a stepwise mechanism that introduces intermediate **2** in the absorption ladder (Figure 3). The lifetime for unimolecular rearrangement of activated **1** to **2** should be[17] comparable to the length of the short laser pulse (200 ns). If **1** has a smaller steady-state cross section for absorption than **2**, the yield for the short pulse will decrease because the more strongly absorbing structure **2** is not present for most of the laser pulse. Presumably the same amount of **1** decomposes from both length laser pulses. It should also be noted that significant decomposition occurs after the laser pulse is completed.[13] Since it is impossible to detect production of **2** (same mass to charge ratio as **1**), the short pulse appears to have a lower product yield. For the long pulse, the higher yield of detectable products arises because of an increased number of ions with structure **2** *during* the laser pulse. If structure **2** has a larger absorption cross section than **1**, the overall photon absorption is greater, leading to a higher product yield.

In summary, IRMP dissociation of butyrophenone cation unexpectedly displays a lower yield for a shorter laser pulse. This is inconsistent with the generally accepted model for IRMP dissociation of a single structure, which would predict a dissociation yield depending only on the number of photons and not on their rate of delivery.[8,13] These results are consistent, however, with a stepwise mechanism for the McLafferty rearrangement in which the butyrophenone molecular cation is formed initially and then, when energized, isomerizes to the distonic ion. Subsequent activation of the distonic ion yields products. These experiments represent the first spectroscopic evidence for the simultaneous existence of a distonic ion and the molecular cation.

Acknowledgment. We are grateful to the National Science Foundation for support of this work. The San Francisco Laser Center provided the cw CO_2 laser.

Registry No. Butyrophenone, 495-40-9.

(13) (a) Thiele, E.; Goodman, M. F.; Stone, J. *Chem. Phys. Lett.* **1980**, *72*, 34. (b) Quack, M.; Humbert, P.; van den Bergh, H. *J. Chem. Phys.* **1980**, *73*, 247. (c) Quack, M. *J. Chem. Phys.* **1978**, *69*, 1282. (d) Lupo, D. W.; Quack, M. *Chem. Rev.* **1987**, *87*, 181. Decreased yield has been predicted for very high intensities (case D) but would require pulses 10^3 times more intense than those used in these experiments.

(14) Comparable results are obtained for the long (4 μs) laser pulse.

(15) This phenomenon is not a result of inefficient ion trapping due to a larger kinetic energy of product fragments formed in the short-pulse experiment. A plot essentially identical with Figure 1 can be generated by using (1 - parent ion fraction). In other words, parent ion decomposition (which is independent of fragment ion kinetic energy) mirrors the product yield behavior displayed in Figure 1.

(16) A change in fragment ion product distribution from benzene ions formed by UV multiphoton ionization with shortened (20 ps) laser pulses has been observed. This was attributed to insufficient time, during the laser pulse, for complete stepwise fragmentation of the benzene ion. Hering, P.; Maaswinkel, A. G. M.; Kompa, K. L. *Chem. Phys. Lett.* **1981**, *83*, 222.

(17) The energy-dependent unimolecular rate constant for **1** → **2** can vary from 0 at threshold up to about 10^{10} s^{-1} at energies that are still below the threshold for other reactions. In general, however, a rate constant of ca. 10^7 s^{-1} would be expected for medium-sized molecules or ions within a few kilocalories per mole (1 infrared photon) of a modest critical activation energy (ca. 10 kcal/mol). See: Robinson, P. J.; Holbrook, K. A. *Unimolecular Reactions*; Wiley-Interscience: New York, 1972.

A New Photochemical Method for Selective Fluorination of Organic Molecules

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While excellent synthetic methods exist for the preparation of perfluorinated organic compounds,[1] the techniques available for selective fluorination are relatively few in number. Broadly speaking, useful reagents for selective fluorination fall into two classes:[2] elemental fluorine[3,4] and compounds prepared either directly from it (acyl hypofluorites,[4,5] fluoroxysulfate,[6] halogen fluorides,[7] and *N*-fluoro compounds[8]) or from other strong oxidants (e.g., $FClO_3$, prepared from $HSO_3F/KClO_4$), and weak oxidants derived from fluoride, such as HF, KF and other metal fluorides, BF_4^-, COF_2, and SF_4. While the range of available techniques is somewhat limited, the need for selectively fluorinated compounds, particularly for biomedical applications,[9] has made their use extremely productive.

We report a new method for selective fluorination, in which oxidizing equivalents are supplied by an illuminated semiconductor (titanium dioxide) and the fluorinating agent is F^-. This method employs safe, easily handled reagents and obviates the need for elemental fluorine and its derivatives. It is applicable to easily oxidized organic substrates, particularly those that form stable carbocations upon oxidation, as well as olefins, phosphines, and phosphites. In a typical reaction, 5 mmol of the substrate is loaded into a 10-mm-diameter borosilicate glass or translucent Teflon FEP tube with an equal weight of rutile TiO_2 powder; 5 mL of acetonitrile and a stoichiometric quantity (10 mmol) of AgF are added.[10] The mixture is deaerated with argon and then illuminated at ambient temperature with a mercury–xenon lamp, typically for 1–2 days. During the course of the reaction, Ag^+, which serves as a scavenger for conduction-band electrons, is reduced to elemental silver. The TiO_2/Ag particles are then recovered from the reaction mixture by filtration. Table I shows the results of some representative photochemical fluorination reactions using TiO_2 and AgF. In almost all cases, only a single fluorinated compound is produced. Control experiments establish that TiO_2, AgF, and light are all essential components of the reaction.

(1) (a) Adcock, J. L.; Lagow, R. J. *J. Am. Chem. Soc.* **1974**, *96*, 7588. (b) Abe, T.; Nagase, S. In *Preparation, Properties, and Industrial Applications of Organofluorine Compounds*; Banks, R. E., Ed.; John Wiley & Sons: New York, 1982; pp 19–43.

(2) Banks, R. E.; Tatlow, J. C. In *Fluorine: the First Hundred Years*; Banks, R. E., Sharp, W. A., Tatlow, J. C., Eds.; Elsevier: New York, 1986; pp 227–346.

(3) Purrington, S.; Kagen, B. S.; Patrick, T. B. *Chem. Rev.* **1986**, *86*, 997.

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(6) (a) Ip, D. P.; Arthur, C. D.; Winans, R. E.; Appleman, E. H. *J. Am. Chem. Soc.* **1981**, *103*, 1964. (b) Appleman, E. H.; Bsaile, L. J.; Hayatsu, R. *Tetrahedron* **1984**, *40*, 189. (c) Stavber, S.; Zupan, M. *J. Chem. Soc., Chem. Commun.* **1981**, 148. (d) Patrick, T. B.; Darling, D. *J. Org. Chem.* **1986**, *51*, 3242.

(7) (a) Rozen, S.; Brand, M. *J. Org. Chem.* **1986**, *51*, 222. (b) Rozen, S.; Brand, M. *J. Org. Chem.* **1985**, *50*, 3342.

(8) Barnette, W. E. *J. Am. Chem. Soc.* **1984**, *106*, 452.

(9) (a) Filler, R., Kobayashi, Y., Eds. *Biomedical Aspects of Fluorine Chemistry*; Elsevier: New York, 1982. (b) Filler, R., Ed. *Biochemistry Involving Carbon–Fluorine Bonds*; ACS Symposium Series 26; American Chemical Society: Washington, DC, 1978. (c) Schlosser, M. *Tetrahedron* **1978**, *34*, 3.

(10) A stoichiometric amount of solid KF is also added if HF is one of the reaction products. HPLC grade acetonitrile and 99.9% AgF (Aldrich) were used without purification.

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(12) Scheibel, J. J.; Cantrell, G.; Patrick, T. B. *J. Org. Chem.* **1981**, *46*, 3917.

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(14) Merritt, R. F. *J. Org. Chem.* **1966**, *31*, 3871.

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