Diketo Compounds with (Trifluoromethyl)trimethylsilane: Double Nucleophilic Trifluoromethylation Reactions†

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Reactions of various diketo compounds with (trifluoromethyl)trimethylsilane (Me_3SiCF_3) in the presence of catalytic amounts of cesium fluoride have been studied. γ-Ketoesters, $CH_3COCH_2CH_2CO_2R$ (R = Et, Bu), were reacted with 2 equiv of Me_3SiCF_3 at room temperature to give $CH_3C(OH)(CF_3)CH_2CH_2COCF_3$ in good yield after hydrolysis. α-Diketones, R_1COCOR_2 ($R_1 = R_2 =$ Ph; $R_1 =$ Ph, $R_2 =$ Me; $R_1 = R_2 =$ Me; $R_1 =$ Me, $R_2 =$ Et), when reacted with Me_3SiCF_3, formed 1:1 or 1:2 addition products depending on the reaction conditions and stoichiometry used. Reactions of diones $CH_3COXCOCH_3$ (X = $-CH_2CH_2-$, $-C_6H_4C_6H_4-$, $-CH_2-$) with Me_3SiCF_3 also led to the formation of the mono- or diaddition products depending on reaction conditions. With various kinds of substituted arylglyoxals, 2 equiv of Me_3SiCF_3 produced monoaddition products in 70−75% yield and diaddition products in 5−10% yield. One of the monoalcohols and two of the diols have been characterized by single-crystal X-ray analysis, and the presence of inter- and intramolecular hydrogen bonding has been confirmed.

Introduction

The trifluoromethyl group is a highly important substituent in the field of organic chemistry. The introduction of a trifluoromethyl group into an organic compound can bring about some remarkable changes in the physical, chemical, and biological properties that result in new compounds/materials suitable for diverse applications in the areas of materials science, agrochemistry, and industry.[1−5] Its powerful electron-withdrawing ability and relatively small size (only 2.5 times the volume of a methyl group) lead to significant changes in the chemistry of substituted compounds when compared with their nonfluorinated analogues. The influence of the trifluoromethyl group in biologically active molecules is often associated with increased lipophilicity[6] that this substituent imparts giving active pharmaceutical and agrochemical compounds with improved transport characteristics *in vivo* and facilitates lower doses rates. While a wide variety of methods have been developed for introducing trifluoromethyl groups into organic compounds,[7] the utilization of (trifluoromethyl)trimethylsilane (Me_3SiCF_3) as a nucleophilic trifluoromethylating reagent is rapidly becoming the method of choice.[8] Recently we and others have reported the reactions of keto compounds with Me_3SiCF_3 in the presence of fluoride ions.[8,9] However, little effort has been devoted to diketo systems.[10] We became interested in the double nucleophilic trifluoromethylation reactions of different kinds of dicarbonyl

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(1) For the general applications of organofluorine compounds, see: *Organofluorine Chemistry: Principles and Commercial Applications*; Banks, R. E., Smart, B. E., Tatlow, J. C., Eds.; Plenum: New York, 1994.

(2) For the use of organofluorine compounds in medicinal and biomedical chemistry, see: (a) *Biomedical Frontiers of Fluorine Chemistry*; Ojima, I., McCarthy, J. R., Welch, J. T., Eds.; ACS Symposium Series 639; American Chemical Society: Washington, DC, 1996. (b) *Organic Chemistry in Medicinal Chemistry and Biomedical Applications*; Filler, R., Ed.; Elsevier: Amsterdam, 1993. (c) Welch, J. T.; Eswaraksrishnan, S. *Fluorine in Bioorganic Chemistry*; John Wiley and Sons: New York, 1991. (d) Filler, R.; Kirk, K. *Biological Properties of Fluorinated Compounds*. In *Chemistry of Organic Fluorine Compounds II: A Critical Review*; Hudlicky, M., Pavlath, A. E., Eds.; ACS Monograph 187; Americal Chemical Society: Washington, DC, 1995. (e) Elliot, A. J. *Fluorinated Pharmaceuticals*. In *Chemistry of Organic Fluorine Compounds II*; ACS Monograph 187; Americal Chemical Society: Washington, DC, 1995. (f) Sholoshonok, V. A., Ed. *Enantiocontrolled Synthesis of Organo-Fluorine Compounds: Stereochemical Challenge and Biomedical Targets*; John Wiley and Sons: 1999.

(3) For the use of of organofluorine compounds in agrosciences, see: (a) Cartwright, D. *Recent Developments in Fluorine-Containing Agrochemicals*. In *Organofluorine Chemistry: Principles and Commercial Applications*; Banks, R. E., Smart, B. E., Tatlow, J. C., Eds.; Plenum: New York, 1994. (b) Lang, R. W. Fluorinated Agrochemicals. In *Chemistry of Organic Fluorine Compounds II*; ACS Monograph 187; American Chemical Society: Washington, DC, 1995.

(4) The ability of fluorine to change the properties of organic molecules has been discussed extensively elsewhere. For example, see: Smart, B. E. Characteristics of C−F systems. In *Organofluorine Chemistry*: *Principles and Commercial Applications*; Banks, R. E., Smart, B. E., Tatlow, J. C., Eds.; Plenum: New York, 1994.

(5) For recent discussions on the controversial topic of fluorine hydrogen bonds, see: (a) O'Hagan, D. O.; Rzepa, H. S. *J. Chem. Soc., Chem. Commun.* **1997**, 645. (b) Dunitz, J. D.; Taylor, R. *Eur. Chem. J.* **1997**, *3*, 89−92. (c) Howard, J. A. K.; Hoy, V. J.; O'Hagan, D. O.; Smith, G. T. *Tetrahedron* **1996**, *52*, 12613−12622.

(6) (a) *Organofluorine Chemicals and Their Industrial Applications*; Banks, R. E., Ed.; Ellis Harwood Ltd.: Chichester, 1979. (b) Welch, J. T. *Tetrahedron* **1987**, *43*, 3123−3197.

(7) For general discussion on the synthesis of organofluorine compounds, see: (a) Olah, G. A.; Prakash, G. K. S.; Chambers, R. D. *Synthetic Fluorine Chemistry*; Wiley and Sons: New York, 1992. (b) Furin, G. G. *Synthetic Aspects of the Fluorination of Organic Compounds*; Harward Academic Publisher: London, 1991. McClinton, M. A.; McClinton, D. A. *Tetrahedron* **1992**, *48*, 6555−6666.

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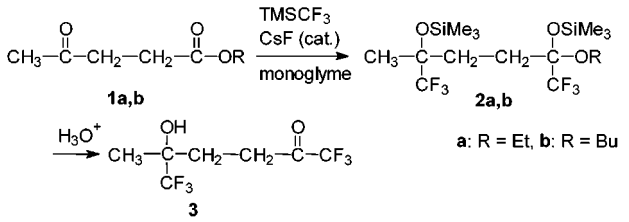
Scheme 1



compounds in order to examine the effect that substituents on the carbonyl moieties had on the formation of mono and/or diaddition products. Here we report the cesium fluoride catalyzed trifluoromethylation reactions of various α, β and γ diketo compounds with (trifluoromethyl)trimethylsilane.

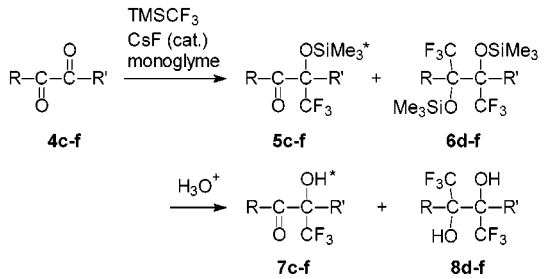
Results and Discussion

On the basis of a survey of the chemical literature, it was obvious that the routes to compounds with at least two methylene groups geminally substituted with trifluoromethyl and hydroxy moieties are difficult or are nonexistent. Little work has been done with nucleophilic trifluoromethylations of dicarbonyl compounds with Me_3SiCF_3.[10] The reactions of aldehydes and ketones with Me_3SiCF_3 are well explored in the literature.[9,10b] We and others also reported conditions where esters can be converted directly to the corresponding trifluoromethyl ketones.[11] Earlier studies examined the reactions of different kinds of α-ketoesters[10b] and α-ketoamides[10c] with Me_3SiCF_3 in the presence of tetrabutylammonium fluoride or cesium fluoride as fluoride ion initiator. But, in both cases, only the α-keto group was found to be reactive even in the presence of excess Me_3SiCF_3.

With γ-keto esters (**1a**,**b**) as substrates, the reaction with two equivalents of Me_3SiCF_3 ($TMSCF_3$) proceeded smoothly in the presence of a catalytic amount of cesium fluoride. The corresponding double addition disilyl ether intermediates (**2a**,**b**) were obtained in good yields and, when hydrolyzed with aqueous HCl, gave the expected product **3** with concomitant formation of Me_3SiOR and Me_3SiOH. (Scheme 1).

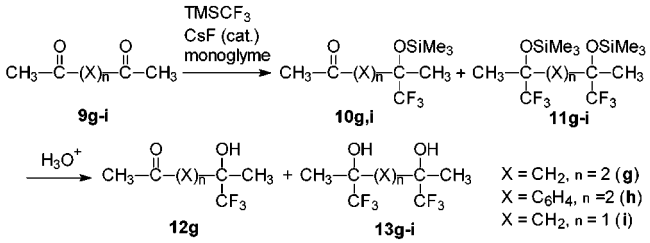
The reactions of diones with Me_3SiCF_3 are very dependent on the nature of the substituents vicinal to the keto functionalities. For example, the reaction of benzil (**4c**) with 2.25 equivalents of Me_3SiCF_3, in the presence of a catalytic amount of cesium fluoride, gave the corresponding monoaddition silyl ether intermediate (**5c**) in 96% which upon hydrolysis produced the diphenyl keto alcohol (**7c**) in 94% yield [8a] (Scheme 2). Use of more than 3 equiv of Me_3SiCF_3 with concomitant heating (60 °C) gave a complex mixture. Under similar reaction conditions, **4d** gave a mixture of monoaddition (**5d**) and diaddition (**6d**) products which upon hydrolysis yielded **7d** and **8d** as the final products (Scheme 2). When the reaction mixture was heated at 60 °C for 12 h (with 3.25 equiv of Me_3SiCF_3 in monoglyme), the diaddition product **6d** (75%) was the main product, and after hydrolysis **8d** (78%). Similarly, **4e**,**f** reacted with excess Me_3SiCF_3 at 60 °C to produce **5e**,**f** (minor) and **6e**,**f** (major) which upon hydrolysis yielded **7e**,**f** (minor) and **8e**,**f** (major).

Scheme 2



c: R = Ph, R' = Ph; **d**: R = Ph, R' = Me;
e: R = Me, R' = Me;
f: R = Me, R' = Et (* addition occurred at either carbonyl)

Scheme 3

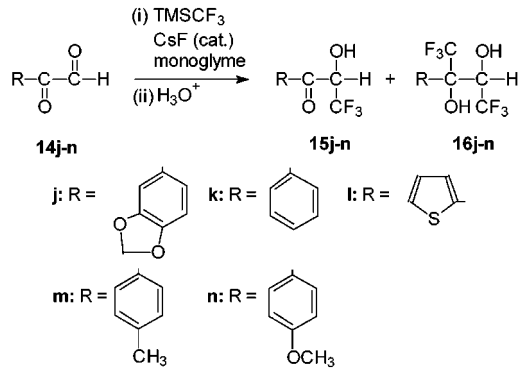


The β and γ diones where the two keto groups are separated by one or two methylene spacers or an aromatic moiety were also examined. Reaction of **9g** with 3.25 equiv of Me_3SiCF_3 in the presence of a catalytic amount of CsF in monoglyme at room temperature gave **10g** as a minor and **11g** as a major product, which upon hydrolysis gave **12g** and **13g** (Scheme 3). Heating the reaction mixture to 60 °C for several hours produced **11g** exclusively which, upon hydrolysis with aqueous HCl, yielded **13g** as a colorless solid in 78% yield (Scheme 3). The crystal and molecular structure of **13g** have been determined by single-crystal X-ray analysis as discussed below. Reaction with **9h** was essentially analogous at 60 °C with excess Me_3SiCF_3 to produce mainly the diaddition product (**11h**) in 90% yield which upon hydrolysis afforded **13h** as a colorless solid in 85% yield. Reaction of acetylacetone (**9i**) was also tried with excess Me_3SiCF_3 at 60 °C which produced a mixture of the monoaddition product (**10i**) as minor, the diaddition product (**11i**) as the major and also the formation of some unidentified products (based on GCMS) (Scheme 3). The use of excess Me_3SiCF_3 is necessary due to the fact that the enol form of acetylacetone also consumes Me_3SiCF_3 to form CF_3H. At 60 °C the initial formation of the monoaddition product (**10i**) as the major one was confirmed by GCMS. The concentration of **10i** decreases because of conversion into the diaddition product along with some decomposition products. The diaddition product (**11i**) was isolated in 30% yield after thin-layer chromatography and characterized by spectroscopic analyses. Hydrolysis of **11i** with 6 N HCl in THF at 55 °C gave a trace amount of diol (**13i**) along with formation of some unidentified product.

Arylglyoxal is a system where the two carbonyl groups are vicinal but one is ketonic and one is aldehydic. The reaction of **14j** with 2 equiv of Me_3SiCF_3 in the presence of a catalytic amount of cesium fluoride at room temperature produced a mixture of monoaddition and diaddition silyl ether intermediates which upon hydrolysis with aqueous HCl, produced the corresponding monoalcohols (**15j**, major) and dialcohol (**16j**, minor) (Scheme 4).

(11) (a) Wiedeman, J.; Heiner, T.; Mloston, G.; Prakash, G. K. S.; Olah, G. A. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 820−821. (b) Singh, R. P.; Cao, G.; Kirchmeier, R. L.; Shreeve, J. M. *J. Org. Chem.* **1999**, *64*, 2873−2876.

Scheme 4



Essentially similar reactivity was also observed with **14k**−**n**. With 2 equiv of Me_3SiCF_3, the reactions of **14k**−**n** yielded the corresponding silyl ether intermediates which gave **15k**−**n** (major) and **16k**−**n** (minor) after hydrolysis.

X-ray Crystal Structures of 13g, 15j, and 16j. Compounds **13g**, **15j**, and **16j** crystallized from a mixture of pentane and ether, and their structures were confirmed by single-crystal X-ray analyses. Compounds **13g**, **15j**, and **16j** crystallize in the following respective monoclinic space groups: *P*2(1)/*n*, *P*2(1)/*c*, and *C*2/*c*. All compounds form discrete molecular units; however, in the solid state, hydrogen bonding and weak H···F bonding are evident. Compound **13g** is centrosymmetric with two-half molecules in the asymmetric unit. It is a complex three-dimensional network of hexanediol units cross-linked via hydrogen bonding. Both hydroxyl groups of the diol are involved in intermolecular hydrogen bonding resulting in a "square" of O−H..O interactions (2.7578(19) and 2.7086(18) Å) related by symmetry. These hydrogen-bonded units extend along the *b*-axis with the staggered squares parallel to the *c*-axis. **15j** possesses an extended two-dimensional structure linked via one weak intermolecular hydrogen bond (3.4465(19) Å) and a weak F···F close contact (2.84(2) Å) with a different molecule. This gives rise to an "S" shaped moiety, which extends along the *b*-axis. The "S"-shaped extensions interweave but are not connected by close contacts or hydrogen bonding. Compound **16j** shows a greater range of hydrogen-bonding interactions, both inter- and intramolecular. In both **15j** and **16j** molecules an aromatic hydrogen from the piperonal moiety is in close proximity (2.753(7), 2.686(5) Å) to the oxygen of the first alcohol group. Each molecule also forms hydrogen bonds with two other molecules (2.978(7), 2.687(10), and 2.755(9) Å) to form a twisted "stack" which extends along the *c*-axis with the aromatic units of the piperonal moiety parallel to the *b*-axis. Every fourth repeat of this stack is hydrogen bonded through one of the methylene hydrogens of the piperonal to the adjacent oxygen on another molecule (3.024(10) Å), which causes the solid-state structure to be three-dimensional.

In summary, in an effort to synthesize both mono(trifluoromethyl)alcohols and bis(trifluoromethyl) diols, we have studied the reactions of α, *β*, and *γ* dicarbonyl compounds with Me_3SiCF_3. Not unexpectedly *γ*-ketoesters and *γ*-diketones are excellent precursors to both mono(trifluoromethyl)alcohols and, for the latter, bis(trifluoromethyl)diols in much larger yields. With α-ketodiones, varying products were found apparently as a function of the substitutent groups. For example, in the case of benzil only the monoaddition product was achieved whereas when one phenyl group was replaced with methyl (1-phenyl-1,2-propanedione), the diaddition product was the major one when an excess of Me_3SiCF_3 was utilized. This difference in products may arise from a reduction in steric hindrance for the latter. With the *β*-diketone, 2,4-pentanedione, in the presence of a large excess of Me_3SiCF_3, conversion to the diaddition product occurred. This reaction appears to occur stepwise with the preference to react once with all of the starting material before reaction begins at the second carbonyl. In the *γ*-diketone system where the link between carbonyl groups is either $-CH_2CH_2-$ or $-C_6H_4C_6H_4-$, the diaddition product is the major product for the former and the sole product for the latter. Reactions of various arylglyoxals with 2.5 equiv of Me_3SiCF_3 gave monoaddition at the aldehyde as the major product. Attempts to react the arylglyoxals with a large excess of Me_3SiCF_3 at 60 °C in order to achieve diaddition as the major product resulted only in a complex mixture.

Experimental Section

General Methods. All the reactions were performed under dry nitrogen. (Trifluoromethyl)trimethylsilane was prepared by published procedures.[12] Cesium fluoride was placed in an oven at 200 °C and repeatedly ground until it remained as a finely divided powder. Once this stage is reached, it may be used in the reactions. Storing in an oven at 200 °C retains the compound in its finely divided state indefinitely. The arylglyoxals were purchased from SynChem and all of the other diketo compounds were obtained from Aldrich and were used as received. Ethylene glycol dimethyl ether (monoglyme) of high purity (Aldrich) was used as solvent. ^1H, ^{19}F, and ^{13}C NMR spectra were recorded in $CDCl_3$ on a spectrometer operating at 200, 188, and 50 MHz, respectively. Chemical shifts are reported in ppm relative to the appropriate standard, $CFCl_3$ for ^{19}F and TMS for ^1H and ^{13}C NMR spectra. IR spectra were recorded using NaCl plates for neat liquids and KBr pellets for solids. Mass spectra were measured on an electron impact 70 ev spectrometer and high-resolution mass spectra (HRMS) were obtained using a suitable mass spectrometer. Elemental analyses were performed by Desert Analytics Laboratory, Tucson, AZ.

X-ray Crystallographic Studies. The crystals were removed from the flask and covered with a layer of hydrocarbon oil. A suitable crystal was selected, attached to a glass fiber and placed in the low-temperature nitrogen stream.[13] Data for **13g**, **15j**, and **16j** were collected near 203 K using a Siemens SMART 1000 instrument (Mo α radiation, $\alpha = 0.717\ 03$ Å) equipped with a Siemens LT-2A low-temperature device. The SHELXTL v. 5.10 program package was used for structure solution and refinement.[14] An absorption correction was applied to **13g** and **15j** using SADABS.[15] The structures were solved by direct methods and refined by full matrix least squares procedures. All non-hydrogen atoms were refined anisotropically. The data were restricted to $2\alpha = 45°$ for **15j** as there was little high angle data. Some details of the data collection and refinement are given in the Experimental Sections. Further details are provided in the Supporting Information.

Trifluoromethylation of *γ*-Keto Esters. In a typical experiment, *γ*-keto esters (5 mmol) (**1a,b**) were dissolved in

(12) (a) Nelson, D. W.; O'Reilly, N. J.; Speier, J.; Gassman, P. G. *J. Org. Chem.* **1994**, *59*, 8157−8171. (b) Ramaiah, P.; Krishnamurty, R.; Prakash, G. K. S. *Organic Syntheses*; Wiley: New York, 1998; Collect Vol. IX, pp 711−715.

(13) Hope, H. *Prog. Inorg. Chem.* **1995**, *41*, 1−3.

(14) SHELXTL Ver. 5.10 PCNT Bruker AXS, Madison, WI, **1998**.

(15) SADABS (Siemens Area Detector ABSorption correction program), an empirical absorption program by G. M. Sheldrick using the method described by Blessing: Blessing, R. H. *Acta Crystallogr.* **1995**, *A51*, 33.

monoglyme (5 mL) and cooled to 0 °C. Me_3SiCF_3 (5.25 mmol) and a catalytic amount of cesium fluoride (0.1 mmol) were added sequentially. The bath temperature was allowed to rise to room temperature and the reaction solution was stirred for 6 h. Glyme and excess Me_3SiCF_3 were removed at reduced pressure and THF (2 mL) was added to the residue. It was cooled to 0 °C and 6 N HCl (8 mL) was added dropwise. The solution was stirred at room temperature for 3 h. Volatile materials were removed at reduced pressure and the product was extracted with diethyl ether (40 mL). Purification was accomplished via column chromatography using an ether/pentane mixture to yield **3** in 60% yield.

2a: yield 90%; liquid; IR (film) 1632, 1428, 1255, 970 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.13 (s, 9H), 0.15 (s, 9H), 1.15 (t, 3H, J = 7 Hz), 1.34 (s, 3H), 1.81 (m, 2H), 3.57 (q, 2H, J = 7 Hz); ^{19}F NMR ($CDCl_3$) δ -80.26 (s, 3F), −81.69 (s, 3F); ^{13}C NMR ($CDCl_3$) δ 1.40, 1.86, 15.25, 21.36, 29.85, 31.96, 60.49, 75.56 (q, J_{C-C-F} = 28 Hz) 98.10 (q, J_{C-C-F} = 29 Hz), 121.87 (q, J_{C-F} = 143 Hz), 127.61 (q, J_{C-F} = 138 Hz); MS (EI) *m/z* (species, rel int) 429 (M^+ + H, 8), 413 ($M^+ - CH_3$, 5), 359 ($M^+ - CF_3$, 46), 271 [$M^+ - CF_3$, + $SiMe_3$ + CH_3), 42), 215 [$C(OSiMe_3)(CF_3)O_2C_2H_5^+$, 81], 143 ($CH_3COCH_2CHCO_2C_2H_5^+$, 37), 73 ($Me_3Si^+$, 100).

3: yield 60%; liquid; IR (film) 3250, 1762, 1250, 972 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.32 (s, 3H), t (2.40, t, 2H, J = 6.5 Hz), 2.65 (t, 2H, J = 6.5 Hz); ^{19}F NMR ($CDCl_3$) δ −78.5, −82.2; MS (EI) *m/z* (species, rel int) 238 (M^+, 11), 221 (M^+ − OH, 62), 169 ($M^+ - CF_3$, 55), 148 [M^+ − (HF + CF_3H), 70), 116 [M^+ − (HF + CH_3 + CF_3 + H_2O), 100), 69 (CF_3, 21).

General Trifluoromethylation of α, β and γ Diketones. Diketones (5 mmol) were dissolved in monoglyme (5 mL) and cooled to 0 °C. The required amount of Me_3SiCF_3 and a catalytic amount of cesium fluoride (0.1 mmol) were added sequentially. The bath temperature was allowed to rise to room temperature, and the reaction solution was heated to 60 °C with stirring until all the diketones were consumed. Reactions were monitored by GCMS. Glyme was removed at reduced pressure, and THF (2 mL) was added to the residue. It was cooled to 0 °C, and 6 N HCl (8 mL) was added dropwise. The solution was stirred at room temperature for 3 h. Volatile materials were removed at reduced pressure, and the product was extracted with diethyl ether. Purification was accomplished via column chromatography using an ether/pentane mixture to yield the pure products.

5c: yield 96%; viscous liquid; IR (film) 1780, 1598, 1492, 1208, 1090, 988, 750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.04 (s, 9H), 7.0−8.0 (m, 10H); ^{19}F NMR ($CDCl_3$) δ −74.18 (s, 3F); ^{13}C NMR ($CDCl_3$) δ 0.97, 83.73 (q, J_{C-C-F} = 31 Hz), 123.50 (q, J_{C-F} = 286 Hz), 126.29, 128.03, 128.51, 129.24, 130.86, 133.25, 135.18, 193.43; MS (EI) *m/z* (species, rel int) 352 (M^+, 6), 275 (M^+ − Ph, 38), 247 (M^+ − PhCO, 70), 105 ($PhCO^+$ 100), 69 (CF_3^+, 35), 73 (Me_3Si^+, 42).

6d: yield 77%; viscous liquid; IR (film) 2962, 1494, 1456, 1251, 1201, 1013, 976, 849 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.16 (s, 9H), 0.28(s, 9H), 1.73 (s, 1H), 7.37 (m, 3H), 7.64 (m, 2H); ^{19}F NMR ($CDCl_3$) δ −66.32 (s, 3F), −73.64 (s, 3F); ^{13}C NMR ($CDCl_3$) δ 1.68, 19.28, 81.06 (q, J_{C-C-F} = 26 Hz), 83.21 (q, J_{C-C-F} = 26 Hz), 125.10 (q, J_{C-F} = 288 Hz), 125.50 (q, J_{C-F} = 288 Hz), 126.81, 128.23, 133.60, 135.81; MS (EI) *m/z* (species, rel int) 417 ($M^+ - CH_3$, 2), 363 ($M^+ - CF_3$, 2), 247 [PhC(OSiMe$_3$)(CF$_3$)C$^+$, 40], 185 [MeC(OSiMe$_3$)(CF$_3$)C$^+$, 30], 105 ($PhCO^+$, 65), 69 (CF_3^+, 1), 73 ($SiMe_3^+$, 100); HRMS calcd for $C_{17}H_{26}F_6O_2Si_2$ 432.1375, found 432.1370.

7c: yield 94%; IR (film) 3268, 1560, 1450, 1270, 991 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.8 (broad, s, 1H), 7.0−8.0 (m, 10H); ^{19}F NMR ($CDCl_3$) δ −73.47 (s, 3F); MS (EI) *m/z* (species, rel int) 280 (M^+, 5), 263 (M^+ − OH, 6), 175 (M^+ − PhCO, 28), 105 ($PhCO^+$ 100), 77 (Ph^+, 24), 69 (CF_3^+, 18); HRMS calcd for $C_{15}H_{11}F_3O_2$ 280.0711, found 280.0704.

8d: yield 68%; IR (KBr) 3422, 1658, 1500, 1458, 1246, 1168, 1089, 930 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.01 (s, 3H), 3.17 (s, 1H), 3.70 (s, 1H), 7.0−7.6), m, 5H); ^{19}F NMR ($CDCl_3$) δ −70.30 (q, J = 9 Hz), −75.40 (q, J = 9 Hz); MS (EI) *m/z* (species, rel int) 268 (M^+ − HF, 5), 175 ($Ph(CF_3)(OH)C^+$, 76), 105 ($PhCO^+$, 100), 77 (Ph^+, 35), 69 (CF_3^+, 9), 43 (CH_3CO^+, 32); HRMS calcd for $C_{11}H_9F_5O_2$ (M^+ − HF) 268.0523, found 268.0521.

10i: ^1H NMR ($CDCl_3$) δ 0.13 (s, 9H), 1.49 (s, 3H), 1.53 (s, 3H), 2.20 (s, 1H); ^{19}F NMR ($CDCl_3$) δ −83.07 (s, 3F); MS (EI) *m/z* (species, rel int) 243 (M + H, 1), 32], 185 ($M^+ - CH_3COCH_2$, 7), 173 [$M^+ - CF_3$, 115 [$M^+ - (CF_3 + CH_3 + CH_3$-CO), 86], 69 ($CF_3$, 8), 43 ($CH_3CO^+$, 100).

11g: yield 81%; liquid; IR (film) 2960; ^1H NMR ($CDCl_3$) δ 0.13 (s, 18H), 1.34(s, 6H), 1.72 (t, 3H, J = 5 Hz), 1.89 (t, 2H, J = 5 Hz); ^{19}F NMR ($CDCl_3$) δ −83.05 (s, 3F), 83.57 (s, 3F); MS (EI) *m/z* (species, rel int) 398 (M^+, 1), 363 [M^+- (HF + CH_3), 1], 329 ($M^+ - CF_3$, 1), 185 ($CH_3C(OSiMe_3)$, 20], 73 ($SiMe_3$, 94), 43 (CH_3CO^+, 100).

11h: yield 90%; colorless viscous liquid; IR (film) 2960, 1668, 1498, 1462, 1380, 1296, 1255, 1169, 995 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.13 (s, 18H), 1.85 (s, 6H), 7.2−7.6 (m, 8H); ^{19}F NMR ($CDCl_3$) δ −83.68 (s, 6F); ^{13}C NMR ($CDCl_3$) δ 2.00, 22.73, 76.53 (q, J_{C-C-F} = 31 Hz); 125.30 (q, J_{C-F} = 280.5 Hz), 126.66, 127.01, 127.31, 139.32, 140.42; MS (EI) *m/z* (species, rel int) 522 (M^+, 8), 453 ($M^+ - CF_3$, 100), 73 ($SiMe_3$, 84).

11i: yield 30%; colorless liquid; ^1H NMR ($CDCl_3$) δ 0.02 (s, 18H), 1.40 (s, 6H), 2.10 (s, 2H); ^{19}F NMR ($CDCl_3$) δ −78.80 (s, 3F); MS (EI) *m/z* (species, rel int) 385 (M^+ + H, 1), 369 [$M^+ - CH_3$, 1], 315 ($M^+ - CF_3$, 1), 185 ($CH_3C(CF_3)(OSiMe_3$, 15), 69 (CF_3, 4), 43 (CH_3CO^+, 100); HRMS calcd for $C_{13}H_{26}F_6O_2Si_2$ 384.1375, found 384.1369.

13g: yield 72%; colorless solid; mp 89−90 °C; IR (KBr) 3425, 1660, 1505, 1450, 1245, 1160, 1090, 920; cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.38 (s, 3H), 1.40 (s, 3H), 1.81 (t, 2H), 1.98 (t, 2H), 2.35 (broad, s, 1H), 2.53 (broad, s, 1H); ^{19}F NMR ($CDCl_3$) δ −83.05 (s, 3F); ^{13}CNMR ($CDCl_3$) δ 20.46, 21.03, 27.66, 28.29, 73.30 (J_{C-C-F} = 28 Hz), 73.70 (J_{C-C-F} = 28 Hz), 124.30 (J_{C-F} = 282 Hz), 129.0 (J_{C-F} = 282 Hz); MS (EI) *m/z* (species, rel int) 254 (M^+, 1), 201 [M^+ − (2 × OH + F), 6], 185 ($M^+ - CF_3$, 7), 167 [M^+ − (H_2O + CF_3), 4], 113 ($CH_3C(OH)CF_3^+$, 8), 69 (CF_3, 5), 43 (CH_3CO^+, 100). Anal. Calcd for $C_8H_{12}F_6O_2$: C, 37.78; H, 4.76. Found: C, 38.02; H, 4.99. X-ray crystallographic data: crystal system, monoclinic; space group, *C*2/*c*; unit cell diamensions, a = 18.022(2) Å, b = 12.0302(14) Å, c = 10.4922-(12) Å, α = 90°, β = 106.675(2)°, λ = 90°; Z = 8; $F(000)$ = 1040; crystal size = 0.43 × 0.30 × 0.30 mm^3; $R1$ = 0.0483, wR2 = 0.1379.

13h: yield 89%; colorless solid; mp 118 °C; IR (film) 3410, 2946, 1650, 1462, 1385, 1273, 1157, 1071, 930, 818 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.80 (s, 6H), 2.47 (s, 2H), 7.2−7.6 (m, 8H); ^{19}F NMR ($CDCl_3$) δ −81.34 (s, 6F); ^{13}C NMR ($CDCl_3$) δ 23.90, 74.77, 29 (q, J_{C-C-F} = 31 Hz), 125.53 (q, J_{C-F} = 283 Hz), 126.56, 127.01, 137.65, 140.60; MS (EI) *m/z* (species, rel int) 378 (M^+, 21), 309 ($M^+ - CF_3$, 46), 240 ($M^+ - 2 \times CF_3$), 43 (CH_3CO, 100). Anal. Calcd for $C_{18}H_{16}F_6O_2$: C, 57.13; H, 4.26. Found: C, 56.92; H, 4.16.

13i: ^1H NMR ($CDCl_3$) δ 1.50 (s, 6H), 2.03 (s, 2H), 2.95 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 26.20, 62.82, 74.09 (q, J_{C-C-F} = 28.3 Hz), 125.75 (q, J_{C-F} = 285 Hz); ^{19}F NMR ($CDCl_3$) δ −83.81 (s, 6F); MS (EI) *m/z* (species, rel int) 241 (M^+ + H, 1), 225 ($M^+ - CH_3$, 1), 207 [M^+ − (CH_3 + H_2O), 1], 187 [M^+ − (CH_3 + H_2O + HF), 4], 171 ($M^+ - CF_3$, 6), 113, 69 (CF_3^+, 4), 43 (CH_3CO^+, 100).

Trifluoromethylation of Arylglyoxal. Arylglyoxal (5 mmol) and $TMSCF_3$ (10.25 mmol) were dissolved in monoglyme (50 mL), and the mixture was cooled with water/ice (about 0 °C). To the stirred solution was added powdered cesium fluoride (0.1 mmol). Heat was generated as the reaction began. After 1 h, the water bath was removed, and the reaction mixture was stirred for additional 5 h. Volatile materials were removed. THF (5 mL) was added followed by the addition of 6 N HCl (10 mL), and the solution was stirred for 3 h at room temperature. Products were extracted with diethyl ether and dried over anhydrous $MgSO_4$. Removal of solvent left the products which were purified by column chromatography.

15j: yield 80%; mp 122 °C; IR (KBr) 3419, 1664, 1595, 1500, 1452, 1244, 1152, 1091, 1031, 991, 927 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.26 (d, 1H, J = 8 Hz), 5.28 (m, 1H), 6.08 (s, 2H), 6.89 (d, 1H, J = 8.2 Hz), 7.42 (s, 1H), 7.55 (d, 1H, J = 8.2 Hz); ^{19}F NMR ($CDCl_3$) δ −74.28 (d, 3F, 6.8 Hz); ^{13}C NMR ($CDCl_3$) δ 70.27 (q, J_{C-C-F} = 31 Hz), 102.39, 108.26, 108.68, 122.33 (q, J_{C-F} = 282.5 Hz), 126.81, 127.87, 148.62, 153.81, 190.55; MS

(EI) *m*/*z* (species, rel int) 248 (M^+, 8), 179 ($M^+ - CF_3$, 1), 149 (M^+ - $CH(OH)CF_3$, 100), 121 ($M^+ - COCH(OH)CF_3$, 32). Anal. Calcd for $C_{10}H_7F_3O_4$: C, 48.38; H, 2.84. Found: C, 48.07; H, 2.80. X-ray crystallographic data: crystal system, monoclinic; space group, *P*2(1)/*n*; unit cell diamensions, $a = 11.22160(10)$ Å, $b = 5.33550(10)$ Å, $c = 16.2074(3)$ Å, $\alpha = 90°$, $\beta = 98.2470(10)°$, $\lambda = 90°$; $Z = 4$; $F(000) = 500$; crystal size $= 0.50 \times 0.25 \times 0.13$ mm^3; $R1 = 0.0495$, $wR2 = 0.1060$.

15k: yield 82%; mp 128 °C; IR (KBr) 3379, 1683, 1600, 1402, 1313, 1224, 1182, 1122, 972, 854, 829 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.28 (d, 1H, $J = 8$ Hz), 5.42 (m, 1H), 7.20−7.67 (m, 5H), 7.73 (d, 1H, $J = 6.4$ Hz), 8.04 (d, 1H, $J = 8.4$ Hz); ^{19}F NMR ($CDCl_3$) δ −74.01 (d, 3F, 6.7 Hz); MS (EI) *m*/*z* (species, rel int) 204 (M^+, 5), 107 ($M^+ - COCOCF_3$, 71), 105 [M^+ − CH(OH)-CF_3, 100], 78 [$M^+ - COC(OH)CF_3$, 40], 77 ($M^+ - COC(OH)$-CF_3, 71), 76 ($C_6H_4^+$, 13), 69 (CF_3^+, 1), Anal. Calcd for $C_9H_7F_3O_2$: C, 64.27; H, 3.96. Found: C, 64.00; H, 4.01.

15l: yield 78%; mp 125 °C; IR (KBr) 3383, 1659, 1516, 1415, 1325, 1228, 1178, 1126, 869, 812 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.15 (broad, d, 1H), 5.18 (m, 1H), 7.21 (m, 1H), 7.84 (m, 2H); ^{19}F NMR ($CDCl_3$) δ −74.73 (d, 3F); ^{13}C NMR ($CDCl_3$) δ 71.91 (q, $J_{C-C-F} = 31.5$ Hz), 122.22 (q, $J_{C-F} = 282.2$ Hz), 128.83, 135.46, 137.43, 139.53, 184.56; MS (EI) *m*/*z* (species, rel int) 210 (M^+, 2), 141 ($M^+ - CF_3$, 1), 111 ($M^+ - CF_3CHOH$, 100), 83 ($S - C_4H_3^+$, 11), 69 (CF_3, 4). Anal. Calcd for $C_7H_5F_3O_2S$: C, 40.00; H, 2.40. Found: C, 39.70; H, 2.35.

15m: yield 72%; mp 97−98 °C; IR (KBr) 3442, 1678, 104, 1300, 1247, 1226, 1175, 1126, 968, 864 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.43 (s, 3H), 4.29 (d, 1H, $J = 8.2$ Hz), 5.36 (m, 1H), 7.30 (d, 2H, $J = 8.2$ Hz), 7.86 (d, 2H, $J = 8.2$ Hz); ^{19}F NMR ($CDCl_3$) δ −74.16 (d, 3F, $J = 6.7$ Hz); ^{13}C NMR ($CDCl_3$) δ 21.84, 70.74 (q, $J_{C-C-F} = 31.0$ Hz), 122.36 (q, $J_{C-F} = 282.3$ Hz), 129.03, 129.66, 130.80, 192.34; MS (EI) *m*/*z* (species, rel int) 218 (M^+, 1), 149 ($M^+ - CF_3$, 1), 119 ($M^+ - CF_3CHOH$, 100), 91 ($CH_3C_6H_4^+$, 64), 69, CF_3, 1). Anal. Calcd for $C_{10}H_9F_3O_2$: C, 55.03; H, 4.16. Found: C, 55.02; H, 4.16.

15n: yield 70%; viscous liquid; IR (KBr) 3437, 2950, 1677, 1602, 1572, 1514, 1463, 1421, 1249, 1180, 1130, 1028, 974, 867, 833 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.79 (s, 3H), 4.35 (d, 1H, $J = 8.1$ Hz), 5.31 (m, 1H), 6.97 (d, 2H, $J = 8$ Hz), 7.94 (d, 2H, $J = 8$ Hz); ^{19}F NMR ($CDCl_3$) δ −74.32 (d, 3F, $J = 6.7$ Hz); ^{13}C NMR ($CDCl_3$) δ 21.84, 70.74 (q, $J_{C-C-F} = 31.0$ Hz), 122.36 (q, $J_{C-F} = 282.3$ Hz), 129.03, 129.66, 130.80, 192.34; MS (EI) *m*/*z* (species, rel int) 234 (M^+, 3), 165 ($M^+ - CF_3$, 1), 135 ($M^+ - CF_3CHOH$, 100), 107 ($M^+ - COCF_3CHOH$, 15), 92 [$M^+ - (COCF_3CHOH + CH_3]$, 14). Anal. Calcd for $C_{10}H_9F_3O_3$: C, 51.27; H, 3.88. Found: C, 51.24; H, 3.88.

16j: yield 10%; mp 123 °C; IR (KBr) 3300, 1618, 1450, 1348, 1126, 919 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.58 (broad, s, 2H), 5.24 (m, 1H), 6.01 (s, 2H), 6.78 (d, 1H, $J = 8$ Hz), 7.00 (d, 1H, $J = 8$ Hz), 7.18 (s, 1H); ^{19}F NMR ($CDCl_3$) δ −73.40 (m, 3F), 76.10 (m, 3F); MS (EI) *m*/*z* (species, rel int) 318 (M^+, 20), 248 ($M^+ - CF_3H$, 2), 219 ($M^+ - CH(OH)CF_3$, 82), 149 [$M^+ - (CF_3H + CH(OH)CF_3)$, 100], 99 ($CH(OH)CF_3$, 90), 69 ($CF_3$, 11). X-ray crystallographic data: crystal system, monoclinic; space group, *P*2(1)/*c*; unit cell dimensions, $a = 11.7029(7)$ Å, $b = 19.1585(12)$ Å, $c = 10.7623(7)$ Å, $\alpha = 90°$, $\beta = 96.669(2)°$, $\lambda = 90°$; $Z = 8$; $F(000) = 1280$; crystal size $= 0.35 \times 0.08 \times 0.05$ mm^3; $R1 = 0.1514$, $wR2 = 0.1759$.

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Supporting Information Available: Crystal data and structure refinement, atomic coordinates, bond lengths and bond angles, anisotropic displacement parameters, hydrogen coordinates, ORTEP drawings, and crystal packing diagrams for **13g**, **15j,** and **16j**. This material is available free of charge via the Internet at http://pubs.acs.org.

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