JOC*Note*

# One-Pot Route to New α,α-Difluoroamides and α-Ketoamides

Rajendra P. Singh and Jean'ne M. Shreeve*

*Department of Chemistry, University of Idaho, Moscow, Idaho 83844-2343*

*jshreeve@uidaho.edu*

*Received April 16, 2003*

**Abstract:** New α,α-difluoroamides (**4a**−**d**, **6a**−**d**) and α-ketoamides (**5a**−**d**, **7a**−**d**) result from one-pot reactions of α-ketoacids, $RCOCO_2H$ (R = $C_6H_5$, $CH_3$, $CH_3CH_2$, thienyl) (**1a**−**d**) with bis(2-methoxyethyl)aminosulfur trifluoride [$(CH_3OCH_2CH_2)_2NSF_3$] (**2**) (Deoxofluor) or diethylaminosulfur trifluoride [$(CH_3CH_2)_2NSF_3$)] (**3**) (DAST). Product yields depend on reaction times and the ratio of reagents used. Longer reaction times (∼36 h) with a 1:2 ratio of α-ketoacids and **2** or **3** gave major yields of the α,α-difluoroamides, and shorter reaction times (∼l h) produced α-ketoamides as the major products. Reactants in a 1:1 ratio resulted in α-ketoamides only.

Direct fluorination of cyclic amides with Deoxofluor [bis(2-methoxyethyl)aminosulfur trifluoride][1] or DAST [diethylaminosulfur trifluoride][2] occurs in good yields. However, regardless of the conditions employed, a similar methodology was not successful with acyclic α-ketoamides. These two reagents are also utilized frequently to generate acid fluorides from simple aliphatic or aromatic acids.[3−5] α-Ketoamides and α,α-difluoroamides are important constituents of many biologically significant materials.[6−8] Syntheses of α-ketoamides are often accomplished in a multistep process involving the dicarbonylation of aryl, heteroaryl, and vinyl halides in the presence of carbon monoxide and a catalytic amount of palladium compound and a secondary amine,[9−15] or the ruthenium-catalyzed oxidation of alkynylamines can be utilized.[16] N-Terminally blocked aminoaldehydes with an isonitrile and a carboxylic acid give amino-α-acyloxy carboxamides, which can be deprotected to form, e.g., peptidyl α-ketoamides.[17] The syntheses of α,α-difluoroamides have not been reported via a direct fluorination route but rather by utilizing, e.g., α,α-difluoro-*β*-ketoesters with amines.[18]

We now report that α-ketoamides as well as α,α-difluoroamides are readily obtained in one-pot reactions of α-ketoacids with the nucleophilic fluorinating reagents, Deoxofluor and DAST. While earlier we demonstrated the direct fluorination of cyclic amides,[3] neither reagent could be reacted successfully with acyclic α-ketoamides. In an effort to synthesize α-ketoacid fluorides and α,α-difluoroacid fluorides by using Deoxofluor and DAST as fluoride ion sources, we found that, in contrast with the reactions of these reagents with monocarboxylic acids, α-ketoacids did not yield isolable acid fluorides but rather α,α-difluoroamides. We have demonstrated the application of Deoxofluor and DAST with α-ketoacids to generate α,α-difluoroamides or α-ketoamides as the major product as a function of reaction time and reaction stoichiometry used.

Initially, benzoylformic acid (**1a**) was reacted with Deoxofluor (**2**) in 1:2 molar ratio at room temperature in dichloromethane. After 1 h, the reaction was quenched with aqueous sodium bicarbonate solution. The dichloromethane layer was analyzed by GCMS, which showed the complete conversion of benzoylformic acid into the corresponding mixture of α,α-difluoroamide (**4a**) and α-ketoamide (**5a**) in a ratio of 14:86. When the reaction was carried out using DAST (**3**) under similar conditions, the α,α-difluoroamide (**6a**) and the α-ketoamide (**7a**) were obtained in a ratio of 25:75. Interestingly, prolonging the reaction time increases the yield of the α,α-difluoroamide. For example, when **1a** was reacted either with **2** or **3** under similar conditions for 36 h, the yields of the α,α-difluoroamides, **4a** and **6a**, were increased to ∼90%. It has also been found that the reaction of **1a** either with **2** or **3** in a 1:1 ratio in methylene chloride for 1 h or even after 36 h gave the respective α-ketoamide **5a** or **7a** in >92% yields (Table 1). Under these conditions, only very small amounts of the α,α-difluoroamide were obtained. Reaction of pyruvic acid (**1b**) with **2** or **3** (1:2 ratio) also produced a mixture of α,α-difluoroamides (**4b** or **6b**) and α-ketoamides (**5b** or **7b**), and their yields were variable with time. Compounds **1c** and **1d** were similarly converted into the corresponding α,α-difluoroamides (**4c**, **4d**, **6c**, **6d**) and α-ketoamides (**5c**, **5d**, **7c**, **7d**) by reacting either with **2** or **3** (Scheme 1, Table 1).

All the compounds are found to be stable in air and water. Since α,α-difluoroamides are less polar than α-ketoamides, these two products were easily separated

(1) Singh, R. P.; Majumder, U.; Shreeve, J. M. *J. Org. Chem.* **2001**, *66*, 6263−6267.
(2) Middleton, W. J.; Bingham, E. M. *J. Org. Chem.* **1980**, *45*, 2883−2887.
(3) Singh, R. P.; Shreeve, J. M. *Synthesis* **2002**, 2561−2579 and references therein.
(4) Hudlický, M. *Org. React.* **1988**, *35*, 513−637.
(5) Lal, G. S.; Pez, G. P.; Pesaresi, R. J.; Prozonic, F. M.; Cheng, H. *J. Org. Chem.* **1999**, *64*, 7048−7054.
(6) Lyons, W. E.; Dteiner, J. P.; Snyder, S. H.; Dawson, T. M. *J. Neurosci.* **1995**, *15*, 2985−2988.
(7) Dubowchik, G. M.; Vrudhula, V. M.; Dasgupta, B.; Ditta, J.; Chen, T.; Sheriff, S.; Sipman, K., Witmaer, M.; Tredup, J.; Vyas, G. M.; Verdoon, T. A.; Bollini, S.; Vinitsky, A. *Org. Lett.* **2001**, *3*, 3987−3990.
(8) Hamilton, G. S.; Steiner, J. P. *J. Med. Chem.* **1998**, *41*, 5119−5123. Gold, B. G. *Mol. Neurobiol.* **1997**, *73*, 285−289.
(9) Uosumi, Y. JP 2003002869, January 8, 2003; *Chem. Abstr.* **2003**, *138*, 73088.
(10) Ozawa, F.; Soyama, H.; Yanahihara, H.; Aoyama, I.;.Takino, H.; Izawa, K.; Yamamoto, T.; Yamamoto, A. *J. Am. Chem. Soc.* **1985**, *107*, 3235−3245.
(11) Kobayashi, T.; Tanaka, M. *J. Organomet. Chem.* **1982**, *233*, C64−C66.
(12) Mutin, R.; Lucas, C.; Thivolle-Cast, J.; Dufaud, V.; Dany, F.; Basset, J. M. *J. Chem. Soc., Chem. Commun.* **1998**, 896−897.
(13) Sakamoto, M.; Shimizu, I.; Yamamoto, A. *Chem. Lett.* **1995**, 1101.
(14) Ozawa, F.; Soyama, H.; Yamamoto, T.; Yamamoto, A. *Tetrahedron Lett.* **1982**, *23*, 3383−3386.
(15) Kobayashi, T.; Tanaka, M. *J. Organomet. Chem.* **1982**, *233*, C64−C66.
(16) Muller, P.; Godoy, G. *Tetrahedron Lett.* **1982**, *23*, 3661−3664.
(17) Semple, J. E.; Levy, Odile, E. WO 2000035868, June 22, 2000; *Chem. Abstr.* **2000**, *133*, 59100.
(18) Watanabe, S.; Fujita, T.; Sakamoto, M.; Takeda, H.; Kitazume, T.; Yamazaki, T. *J. Fluorine Chem.* **1997**, *82*, 1−7.

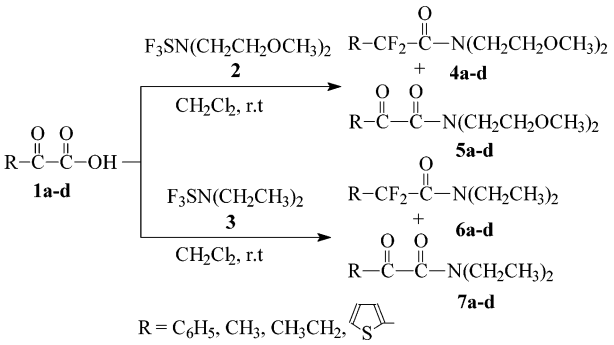
10.1021/jo034487g CCC: $25.00 
Published on Web 06/27/2003

**TABLE 1. Reaction of Deoxofluor (2) and DAST (3) with α-Ketoacid[a]**

| $RCOCO_2H$ R | Fluorinating reagent | Time (h) | Products (%)[b] |
|---|---|---|---|
| Ph(**1a**) | **2** | 1 | **4a/5a** (14/86) |
| Ph(**1a**) | **2** | 8 | **4a/5a** (60/40) |
| Ph(**1a**) | **2** | 36 | **4a/5a** (90/10) |
| Ph(**1a**) | **2** | 1 | **4a/5a** (6/94)[c] |
| Ph(**1a**) | **3** | 1 | **6a/7a** (19/81) |
| Ph(**1a**) | **3** | 36 | **6a/7a** (92/8) |
| $CH_3$(**1b**) | **2** | 36 | **4b/5b** (60/40) |
| $CH_3$(**1b**) | **3** | 36 | **6b/7b** (62/38) |
| $CH_3CH_2$(**1c**) | **2** | 36 | **4c/5c** (52/48) |
| $CH_3CH_2$(**1c**) | **3** | 36 | **6c/7c** (55/45) |
|  (**1d**) | **2** | 36 | **4d/5d** (67/33) |
|  (**1d**) | **2** | 36 | **6d/7d** (66/34) |

[a] All reactions were carried out at 25 °C with 5 mmol of α-keto acid and 10 mmol of Deoxofluor or DAST in 15 mL of methylene chloride. [b] Relative % yield was determined by GC. [c] Reaction was carried out with a 1:1 molar ratio of **1a** and **2**.

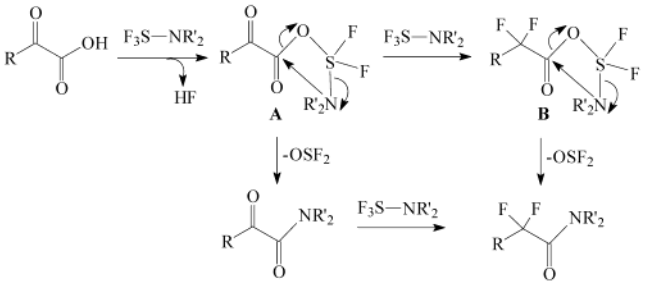
**SCHEME 1**




by silica gel chromatography using ethyl acetate and hexane mixtures (2:1). The new compounds were characterized by IR, NMR ($^1H$, $^{19}F$, $^{13}C$), and MS spectral and elemental analyses. Known compounds were characterized by comparing their spectroscopic data with that reported in the literature.

Amide formation was not observed when benzoic acid or monoaliphatic acids were reacted with **2** and **3**.[1−3] This suggests that the α-keto group in the substrate plays a major role. A possible reaction mechanism is proposed in Scheme 2. It is known that acids react similarly to alcohols with Deoxofluor or DAST. The first step is the formation of intermediate **A** with the loss of HF. Since α-keto esters such as A react selectively with Deoxofluor or DAST only at the α-carbonyl group, we believe the fluorination proceeds in the presence of an additional equivalent of **2** or **3** to give intermediate **B**. The intermediates **A** and **B** are hydrolytically unstable, and, on hydrolysis, amides are formed as the final products with the release of $SOF_2$ (Scheme 2) that was identified as a

**SCHEME 2**




volatile product via $^{19}F$ NMR spectral analysis. No evidence is found for the intermediate formation of the possible acid fluoride (RCOCOF) intermediate from the α-ketoacid on the basis of $^{19}F$ NMR studies during the course of the reaction. The intermediacy of **A** and **B** has also been supported by $^{19}F$ NMR spectra. Since reactions of monocarboxylic acids do not yield amides with **2** or **3**, we are convinced that in the case of α-ketoacids, the α-carbonyl in **A** and the $CF_2$ group in **B** cause the adjacent carbonyl to be very electron deficient and subject to facile attack by the $NR'_2$ group to give the amides as the final products.

In summary, the present report describes a straightforward one-pot synthetic route to α,α-difluoroamides and α-ketoamides in good yields. Depending on the product required, it is possible to synthesize either amide in good yield by terminating the reaction after different time intervals or by utilizing suitable stoichiometric ratios.

## Experimental Section

*Caution:* Deoxofluor and DAST react rapidly and exothermically with water, liberating HF. Reactions with these compounds should be carried out at <80 °C.

In a typical experiment, α-ketoacid (**1a**) (5 mmol) was dissolved in dichloromethane (15 mL), and Deoxofluor (**2**) or DAST (**3**) (10 mmol) in dichloromethane was added dropwise at room temperature. The reaction mixture was stirred at 25 °C for 36 h, and then the reaction was quenched by the slow addition of aqueous $NaHCO_3$ solution until effervescence was complete. The dichloromethane layer was separated, dried over anhydrous $MgSO_4$, and filtered. Removal of solvent gave a mixture of **4a**/**5a** (90:10 based on GC) or **6a/7a** (92:8 based on GC). Products were separated by silica gel chromatography using an ethyl acetate and hexane mixture (2:1).

**Compound 4a:** isolated yield = 84%; viscous liquid; IR (Nujol mull) 2928, 1668, 1448, 1365, 1257, 1114, 1082, 1019, 1082, 1019, 974, 920, 800, 775, 736, 700, 646 $cm^{-1}$; $^{19}F$ NMR ($CDCl_3$) $\delta$ −94.44 (s, 2F); $^1H$ NMR ($CDCl_3$) $\delta$ 3.19 (s, 3H), 3.24 (s, 3H), 3.31 (t, 2H, $J$ = 5.5 Hz), 3.43 (t, 2H, $J$ = 5.5 Hz), 3.51 (t, 2H, $J$ = 5.2 Hz), 3.63 (t, 2H, $J$ = 5.2 Hz), 7.30−7.55 (m, 5H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 48.89, 49.21 (t, $J$ = 3.6 Hz), 59.6, 59.7, 70.80, 72.86, 116.4 (t, $J_{C-F}$ = 248.7 Hz), 126.1 (t, $J$ = 5.6 Hz), 129.5, 131.68 (t, $J$ = 1.6 Hz), 134.5 (t, $J$ = 24.8 Hz), 164.5 (t, $J$ = 29.7 Hz); MS (EI) $m/z$ (species, rel int) 286 ($M^+$ − H, 1), 2 72 ($M^+$ − $CH_3$, 1), 255 [$M^+$ − ($OCH_3$ + H), 24), 210 ($M^+$ − $C_6H_5$, 42), 127 ($C_6H_5$-$CF_2^+$, 100), 77 ($C_6H_5^+$, 23), 59 ($CH_3OCH_2CH_2^+$, 33). Anal. Calcd for $C_{14}H_{19}F_2NO_3$: C, 58.53; H, 6.67. Found: C, 58.00; H, 6.53.

**Compound 4b:** viscous liquid; IR (Nujol mull) 2930, 1664, 1455, 1388, 1255, 1177, 1117, 1019, 927, 758 $cm^{-1}$; $^{19}F$ NMR ($CDCl_3$) $\delta$ −92.66 (q, 2F, $J$ = 20 Hz); $^1H$ NMR ($CDCl_3$) $\delta$ 1.77 (t, 3H, $J$ = 20 Hz), 3.27 (s, 3H), 3.28 (s, 3H), 3.48 (overlapped t, 4H, $J$ = 5.5 Hz), 3.59 (t, 2H, $J$ = 5.5 Hz), 3.72 (t, 2H, $J$ = 5.2 Hz); $^{13}C$ NMR ($CDCl_3$) $\delta$ 32.1 (t, $J$ = 25.5 Hz), 47.9, 48.1, 58.9, 70.1, 72.1, 119.4 (t, $J_{C-F}$ = 250.2 Hz), 163.8 (t, $J$ = 30.5 Hz); MS (EI) $m/z$ (species, rel int) 225 ($M^+$, 1), 210 ($M^+$ − $CH_3$, 1), 193 [$M^+$ − ($OCH_3$ + H), 22), 180 ($M^+$ − $CH_2OCH_3$, 77), 150

$[M^+ - (CH_2OCH_3 + 2CH_3)$, 69], 65 ($CH_3CF_2^+$, 37), 58, ($CH_3OCH_2$-$CH^+$, 100). Anal. Calcd for $C_9H_{17}F_2NO_3$: C, 47.99; H, 7.61. Found: C, 48.12; H, 7.56.

**Compound 4c:** viscous liquid; IR (Nujol mull) 2892, 1665, 1452, 1363, 1273, 1182, 1116, 1012, 974, 756 $cm^{-1}$; $^{19}F$ NMR ($CDCl_3$) $\delta$ −93.50 (t, 2F, $J$ = 18.5 Hz); $^1H$ NMR ($CDCl_3$) $\delta$ 0.97 (t, 3H, $J$ = 7.5 Hz), 2.11 (tq, 2H, $J$ = 18.5 Hz, $J$ = 7.5 Hz), 3.25 (s, 3H), 3.26 (s, 3H), 3.47 (overlapped triplet, 4H), 3.57 (t, 2H, $J$ = 5.5 Hz), 3.69 (t, 2H, $J$ = 5.5 Hz); $^{13}C$ NMR ($CDCl_3$) $\delta$ 6.2, 28.6 (t, $J$ = 24.5 Hz), 48.3, 48.5, 59.2, 70.5, 72.5, 120.2 (t, $J_{C-F}$ = 254.0 Hz), 164.2; MS (EI) *m/z* (species, rel int) 239 ($M^+$, 1), 224 ($M^+ - CH_3$, 1), 207 [$M^+ - (OCH_3 + H)$, 14), 194 ($M^+ - CH_2OCH_3$, 33), 164 [$M^+ - (CH_2OCH_3 + 2CH_3)$, 100], 79 ($CH_3$-$CF_2^+$, 37), 59 ($CH_3OCH_2CH_2^+$, 58), 58 ($CH_3OCH_2CH^+$, 46). Anal. Calcd for $C_{10}H_{19}F_2NO_3$: C, 50.20; H, 8.00. Found: C, 50.26; H, 7.92.

**Compound 4d:** viscous liquid; IR (Nujol mull) 2930, 1662, 1441, 1372, 1261, 1110, 1080, 1015, 972, 918, 801, $cm^{-1}$; $^{19}F$ NMR ($CDCl_3$) $\delta$ −94.05 (s, 2F); $^1H$ NMR ($CDCl_3$) $\delta$ 3.18 (s, 3H), 3.26 (s, 3H), 3.28 (t, 2H, $J$ = 5.5 Hz), 3.45 (t, 2H, $J$ = 5.5 Hz), 3.50 (t, 2H, $J$ = 5.2 Hz), 3.65 (t, 2H, $J$ = 5.2 Hz), 7.28 (dd, 1H, $J$ = 5.02, Hz, 2.0 Hz), 7.94 (d, 1H, $J$ = 5 Hz), 8.52 (d, 1H, $J$ = 5.0 Hz); $^{13}C$ NMR ($CDCl_3$) $\delta$ 48.7, 49.1, 59.9, 59.2, 70.5, 72.5, 116.5 (t, $J_{C-F}$ = 248.5 Hz), 127.1, 128.8, 131.0 (t, $J$ = 28.5 Hz), 164.4 (t, $J$ = 29.5 Hz); MS (EI) *m/z* (species, rel int) 293 ($M^+$, 1), 278 ($M^+ - CH_3$, 1), 261 [$M^+ - (OCH_3 + H)$, 7], 216 [$M^+ - (2OCH_3 + H)$, 12], 160 ($C_4H_2SCF_2^+$, 29), 133 ($C_4H_3SCF_2^+$, 100), 59 ($CH_3OCH_2CH_2^+$, 20), 58 ($CH_3OCH_2CH^+$, 7). Anal. Calcd for $C_{12}H_{17}F_2NO_3S$: C, 49.14; H, 5.84. Found: C, 49.14; H, 5.80.

**Compound 5a.** Yield from a run where **1a** and **3** were used in a 1:1 ratio and the reaction was stopped after 1 h: 87%; viscous liquid; IR (Nujol mull) 2962, 1678, 1639, 1446, 1446, 1366, 1260, 1179, 1114, 1015, 969, 865, 798, 772, 687 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 3.07 (s, 3H), 3.34 (s, 3H), 3.38 (t, 2H, $J$ = 5.6 Hz), 3.48 (t, 2H, $J$ = 5.6 Hz), 3.60 (t, 2H, $J$ = 5.2 Hz), 3.72 (t, 2H, $J$ = 5.4 Hz), 7.20−7.90 (m, 5H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 45.7, 48.7, 59.0, 59.3, 70.9, 71, 129.0, 130.3, 134.6, 168.1, 191; MS (EI) *m/z* (species, rel int) 265 ($M^+$, 48), 160 ($M^+ - C_6H_5CO$, 97), 105 ($C_6H_5CO^+$, 100), 77 ($C_6H_5^+$, 60), 59 ($CH_3OCH_2CH_2^+$, 68). Anal. Calcd for $C_{14}H_{19}NO_4$: C, 63.38; H, 7.22. Found: C, 63.67; H, 6.97.

**Compound 5b:** viscous liquid; IR (Nujol mull) 2960, 1665, 1448, 1370, 1255, 1170, 1123, 1021, 928, 762 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.78 (s, 3H), 3.22 (s, 3H), 3.26(s, 3H), 3.42 (overlapped t, 4H, $J$ = 5.5 Hz), 3.60 (t, 2H, $J$ = 5.5 Hz), 3.71 (t, 2H, $J$ = 5.2 Hz); MS (EI) *m/z* (species, rel int) 203 ($M^+$, 19), 160 ($M^+ - CH_3$-CO, 100), 133 [$N(CH_2CH_2OCH_3)_2$]$^+$, 4), 59 ($CH_3OCH_2CH_2^+$, 78). Anal. Calcd for $C_9H_{17}NO_4S$: C, 53.19; H, 8.43. Found: C, 53.02; H, 8.30.

**Compound 5c:** viscous liquid; IR (Nujol mull) 2935, 1639, 1449, 1363, 1207, 1195, 1119, 1047, 972, 808; $^1H$ NMR ($CDCl_3$) $\delta$ 1.00 (t, 3H, $J$ = 7.2 Hz), 2.70 (q, 2H, $J$ = 7.2 Hz), 3.19 (s, 3H), 3.24 (s, 3H), 3.33 (t, 2H, $J$ = 5.2 Hz), 3.47 (overlapped triplet, 4H), 3.53 (t, 2H, $J$ = 5.5 Hz); $^{13}C$ NMR ($CDCl_3$) 6.8, 32.9, 45.7, 48.3, 58.7, 58.9, 70.1, 70.7, 168.2, 201.6; MS (EI) *m/z* (species, rel int) 217 ($M^+$, 7), 160 ($M^+ - CH_3CH_2CO$, 100), 59 ($CH_3OCH_2$-$CH_2^+$, 91), 57 ($CH_3CH_2CO^+$, 46). Anal. Calcd for $C_{10}H_{19}NO_4$: C, 55.28; H, 8.81. Found: C, 55.30; H, 8.76.

**Compound 5d:** low-melting solid; IR (Nujol mull) 2965, 1672, 1642, 1438, 1362, 1271, 1180, 1115, 1012, 958, 864, 791 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 3.07 (s, 3H), 3.34 (s, 3H), 3.38 (t, 2H, $J$ = 5.6 Hz), 3.48 (t, 2H, $J$ = 5.6 Hz), 3.60 (t, 2H, $J$ = 5.2 Hz), 3.72 (t, 2H, $J$ = 5.4 Hz), 7.28 (dd, 1H, $J$ = 5.0, Hz, 2.0 Hz), 7.98 (d, 1H, $J$ = 5 Hz), 8. 56 (d, 1H, $J$ = 5.0 Hz); MS (EI) *m/z* (species, rel int) 271 ($M^+$, 12), 160 ($M^+ - C_4H_3SCO$, 41), 111 ($C_4H_3SCO^+$, 100), 83 ($C_4H_3S^+$, 6), 59 ($CH_3OCH_2CH_2^+$, 42). Anal. Calcd for $C_{12}H_{17}NO_4S$: C, 53.12; H, 6.32. Found: C, 53.22 H, 6.24.

**Compound 6a:** isolated yield = 85% (36 h reaction time); viscous liquid; IR (Nujol mull) 2929, 1662, 14451, 1365, 1115, 1081, 1084, 1020, 971, 920, 801, 775, 736, 645 $cm^{-1}$; $^{19}F$ NMR ($CDCl_3$) $\delta$ −95.23 (s, 2F); $^1H$ NMR ($CDCl_3$) $\delta$ 0.95 (t, 3H, $J$ = 7.0 Hz), 1.09 (t, 3H, $J$ = 7.0 Hz), 3.16 (q, 3H, $J$ = 7.0), 3.49 (q, 2H. $J$ = 7.0 Hz), 7.30−7.50. (m, 5H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 13.0, 14.6, 42.2, 42.8 (t, $J$ = 4 Hz), 116.3 (t, $J_{C-F}$ = 248.6 Hz), 126.0 (t, $J$ = 5.6 Hz), 129.5, 131.5 (t, $J$ = 1.8 Hz), 134.6 (t, $J$ = 24.8 hz), 163.6 (t, $J$ = 29.7 Hz); MS (EI) *m/z* (species, rel int) 227 ($M^+$, 1), 2 12 ($M^+ - CH_3$, 1), 198 [$M^+ - CH_2CH_3$, 1), 127 ($PhCF2^+$, 37), 100 [$CON(CH_2CH_3)_2^+$, 100], 72 [$N(CH_2CH_3)_2^+$, 59]. Anal. Calcd for $C_{12}H_{15}F_2NO$: C, 63.42; H, 6.65. Found: C, 64.00; H, 6.53.

**Compound 6b:** IR (Nujol mull) 2935, 1660, 1462, 1380, 1245, 1170, 1035, 930, 752, 642 $cm^{-1}$; $^{19}F$ NMR ($CDCl_3$) $\delta$ −92.93 (q, 2F, $J$ = 20 Hz); $^1H$ NMR ($CDCl_3$) $\delta$ 0.94 (t, 3H, $J$ = 7.0 Hz), 1.08 (t, 3H, $J$ = 7.0 Hz), 1.75 (t, 3H, $J$ = 20 Hz), 3.15 (q, 2H, $J$ = 7.0), 3.49 (q, 2H. $J$ = 7.0 Hz); MS (EI) *m/z* (species, rel int) 165 ($M^+$, 52), 150 ($M^+ - CH_3$, 32), 100 ($M^+ - CONEt_2$, 91), 72 ($NEt_2^+$, 100), 65 ($CH_3CF_2$, 51). Anal. Calcd for $C_7H_{13}F_2NO$: C, 50.90; H, 7.93. Found: C, 50.83; H, 7.85.

**Compound 6c:** viscous liquid; IR (Nujol mull) 2890, 1670, 1455, 1363, 1275, 1179, 1112, 1015, 978, 745 $cm^{-1}$; $^{19}F$ NMR ($CDCl_3$) $\delta$ −93.25 (t, 2F, $J$ = 18.6 Hz); $^1H$ NMR ($CDCl_3$) $\delta$ 0.96 (t, 3H, $J$ = 7.0 Hz), 0.97 (t, 3H, $J$ = 7.5 Hz), 1.08 (t, 3H, $J$ = 7.0 Hz), 2.11 (tq, 2H, $J$ = 18.5 Hz, $J$ = 7.5 Hz), 3.15 (q, 2H, $J$ = 7.0), 3.50 (q, 2H, $J$ = 7.0 Hz); MS (EI) *m/z* (species, rel int) 179 ($M^+$, 28), 164 ($M^+ - CH_3$, 15), 100 ($M^+ - CONEt_2$, 91), 79 ($CH_3$-$CH_2CF_2^+$, 20), 72 ($NEt_2^+$, 72). Anal. Calcd for $C_8H_{15}F_2NO$: C, 53.60; H, 8.44. Found: C, 53.42; H, 8.46.

**Compound 6d:** viscous liquid; IR (Nujol mull) 2935, 1666, 1455, 1361, 1112, 1087, 1022, 972, 918, 800, 771, 732 $cm^{-1}$; $^{19}F$ NMR ($CDCl_3$) $\delta$ −95.82 (s, 2F); $^1H$ NMR ($CDCl_3$) $\delta$ 0.95 (t, 3H, $J$ = 7.0 Hz), 1.08 (t, 3H, $J$ = 7.0 Hz), 3.16 (q, 3H, $J$ = 7.0), 3.47 (q, 2H. $J$ = 7.0 Hz), 7.27 (dd, 1H, $J$ = 5.0, Hz, 2.1 Hz), 7.97 (d, 1H, $J$ = 5 Hz), 8.58 (d, 1H, $J$ = 5.0 Hz); MS (EI) *m/z* (species, rel int) 233 ($M^+$, 2), 133 ($C_4H_3SCF_2^+$, 31), 100 [$CON(CH_2CH_3)_2^+$, 100], 72 [$N(CH_2CH_3)_2^+$, 73]. Anal. Calcd for $C_{10}H_{13}F_2NOS$: C, 51.49; H, 5.62. Found: C, 51.55; H, 5.60.

**Compound 7a.** Isolated yield when the reaction was stopped after 1 h using **1a** and **3** in a 1:2 ratio: 74%. This product was characterized by comparison with the spectroscopic data reported.[10]

**Compound 7d:** viscous liquid; IR (Nujol mull) 2938, 1671, 1458, 1358, 1108, 1076, 1012, 968, 913, 812, 771 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 0.95 (t, 3H, $J$ = 7.0 Hz), 1.08 (t, 3H, $J$ = 7.0 Hz), 3.16 (q, 3H, $J$ = 7.0), 3.47 (q, 2H. $J$ = 7.0 Hz), 7.30 (dd, 1H, $J$ = 5.0, Hz, 2.0 Hz), 7.96 (d, 1H, $J$ = 5 Hz), 8.55 (d, 1H, $J$ = 5.0 Hz); MS (EI) *m/z* (species, rel int) 211 ($M^+$, 3), 111 ($C_4H_3SCO^+$, 37), 100 [$CON(CH_2CH_3)_2^+$, 83], 72 [$N(CH_2CH_3)_2^+$, 100]. Anal. Calcd for $C_{10}H_{13}NO_2S$: C, 56.85; H, 5.62. Found: C, 56.76; H, 5.58.

**Acknowledgment.** We are grateful to Drs. G. Knerr and A. Blumenfeld for measuring MS and NMR spectra, respectively.

JO034487G