Table I. Reduction of Unsaturated Carbonyls with Sodium Borohydride Reducing Systems

compound	reagent	product ratio 1,2/1,4
2-cyclohexen-1-one	$NaBH_4$/50% EtOH	59/41[1a]
	$NaBH_4$/THF	71/29[1b]
3-methyl-2-cyclohexen-1-one	$NaBH_4$/50% EtOH	70/30[1a]
	$NaBH_4$/2-propanol	55/45[1c]
	$NaBH_4$/pyridine	0/100[1c]
	$NaBH_4$/THF	67/33[1b]
4-phenyl-3-buten-2-one	$NaBH_4$/2-propanol	77/23[1d]
	$NaBH_4$/diglyme	58/42[1d]
	$NaBH_4$/pyridine	72/28[1d]
cinnamaldehyde	$NaBH_4$/THF	95/5[1b]
citral	$NaBH_4$/THF	99/1[1b]

Table II. Reduction of Unsaturated Carbonyls with Sodium Acetoxyborohydride Reagents

compound	reagent	product ratio[a] 1,2/1,4
2-cyclohexen-1-one	$NaBH_3(OAc)$	97/3
	$NaBH_2(OAc)_2$	88/12
	$NaBH(OAc)_3$	97/3
	$NaBH_4$/HOAc	97/3
3-methyl-2-cyclohexen-1-one	$NaBH_3(OAc)$	96/4
	$NaBH_2(OAc)_2$	90/10
	$NaBH(OAc)_3$	98/2
	$NaBH_4$/HOAc	69/31

[a] Determined by vapor-phase chromatography and compared to authentic material.

gioselectivity of diacetoxyborohydride to resemble the monoacetoxy and triacetoxy species. It may be that sodium diacetoxyborohydride is not as stable as the mono- and triacetoxy species and may undergo disproportionation reactions to generate the parent borohydride anion, which would not exhibit high regioselectivity. However, at the present time this explanation is only speculative.

Thus, it appeared that either sodium monoacetoxyborohydride or sodium triacetoxyborohydride could serve as an efficient regioselective reagent for the reduction of α,β-unsaturated aldehydes and ketones. We chose to further develop sodium monoacetoxyborohydride as a regioselective reducing agent; as alluded to earlier, the triacetoxyborohydride anion is not an efficient reagent for the reduction of ketones. The results of these investigations are listed in Table III.

In summary, reduction of α,β-unsaturated aldehydes and ketones with sodium acetoxyborohydride reagents is highly regioselective, resulting in formation of the corresponding allylic alcohols. Sodium monoacetoxyborohydride is the most efficient reagent studied and should prove to be an attractive alternative to existing regioselective borohydride methods, which include $NaBH_4/CeCl_3$,[4a,b] $LiBH_3$(*n*-butyl),[4c] borohydride exchange resin,[4d] and $NaBH_4$/MeOH/THF.[4e]

Experimental Section

General Methods. Tetrahydrofuran was distilled from sodium benzophenone. Commercial sodium borohydride powder and glacial acetic acid were used directly. Vapor-phase chromatography was performed on a Hewlett-Packard HP5890A gas chromatograph equipped with a Supelco, Inc., SPB-1 capillary column, FID detector, and a Hewlett-Packard 3392A integrator. ^1H NMR spectra were recorded on a Varian EM360A spectrometer as solutions in $CDCl_3$ using tetramethylsilane as an internal standard.

Table III. Reduction of Unsaturated Carbonyls with Sodium Monoacetoxyborohydride

compound	yield,[a,b] %	product ratio[c] 1,2/1,4
2-cyclohexen-1-one	32	97/3
3-methyl-2-cyclohexen-1-one	49	96/4
trans-4-phenyl-3-buten-2-one	70	96/4
trans-cinnamaldehyde	70	99/1
citral	86	99/1

[a] Refers to chromatographed material. [b] Compounds exhibited satisfactory ^1H NMR spectra. [c] Determined by vapor-phase chromatography and compared to authentic material.

Preparation of *trans*-4-Phenyl-3-buten-2-ol (General Procedure). To a magnetically stirred suspension of sodium borohydride powder (0.43 g, 11.4 mmol) in dry THF (25 mL) at 25 °C was added over 2 min glacial acetic acid (0.65 mL, 11.4 mmol). After 0.5 h, *trans*-4-phenyl-3-buten-2-one (1.0 g, 6.8 mmol) was added, and the resulting mixture was stirred for 20 h at 25 °C. The mixture was poured into 10% aqueous NaOH (25 mL), stirred for 0.5 h, and extracted with ether (2 × 50 mL). The combined extracts were dried with Na_2SO_4, filtered, and concentrated in vacuo to afford a colorless oil (1.05 g). Flash chromatography (2:1 hexanes/ether) gave a colorless oil (0.71 g, 70%), which was homogeneous by TLC: ^1H NMR ($CDCl_3$) 7.3–7.0 (m, 5 H), 6.6–5.9 (m, 2 H), 4.5–4.1 (m, 1 H), 3.1 (broad s, 1 H), 1.3 (d, 3 H) ppm; GC (oven 125 °C, injection 270 °C, detector 270 °C, 1-μL injection) showed 96% 1,2-reduction and 4% 1,4-reduction (t_R: 2.75 and 1.95 min, respectively).

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Registry No. $NaBH_3(OAc)$, 71604-09-6; $NaBH_2(OAc)_2$, 123183-64-2; $NaBH(OAc)_3$, 56553-60-7; $NaBH_4$, 16940-66-2; (*E*)-PhCH=CHCH$_2$OH, 4407-36-7; $(CH_3)_2C{=}CH(CH_2)_2C(CH_3){=}CHCH_2OH$, 624-15-7; 2-cyclohexen-1-one, 930-68-7; 2-cyclohexen-1-ol, 822-67-3; cyclohexanone, 108-94-1; 3-methyl-2-cyclohexen-1-one, 1193-18-6; 3-methyl-2-cyclohexen-1-ol, 21378-21-2; 3-methylcyclohexanone, 591-24-2; *trans*-4-phenyl-3-buten-2-one, 1896-62-4; *trans*-4-phenyl-3-buten-2-ol, 36004-04-3; 4-phenyl-2-butanone, 2550-26-7; *trans*-cinnamaldehyde, 14371-10-9; citral, 5392-40-5.

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Ultrasound-Promoted Synthesis of α-Difluoromethylated Carboxylic Acids

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Numerous studies have shown that difluoromethyl substitution confers very interesting properties to important organic materials such as bioactive compounds.[1-3] However, except for the difluoromethyl compounds made from chlorodifluoromethane and nucleophiles,[4,5] no other

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Table I. Physical Properties of 2-(Difluoromethyl)alkanoic Acids

compound[a]	yield, %	bp, °C/(mmHg)
$C_4H_9CH(CHF_2)CO_2H$	68	86–89 (12)
$C_5H_{11}CH(CHF_2)CO_2H$	78	94–96 (15)
$C_7H_{15}CH(CHF_2)CO_2H$	81	95–96 (12)
$C_9H_{19}CH(CHF_2)CO_2H$	71	93–95 (10)
$PhCH_2CH(CHF_2)CO_2H$	77	115–118 (10)

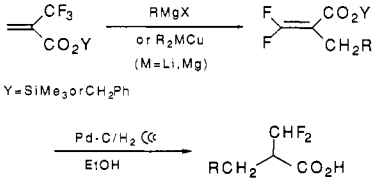
[a] The structures were confirmed by spectral data. The microanalysis was in satisfactory agreement with the calculated value (C, H; ±0.4%).

synthetic methods have been studied.

Accordingly, we have been studying simple synthetic methods for the preparation of α-difluoromethylated carboxylic acids as one of the most important and general techniques for the synthesis of a variety of functionalized compounds possessing a difluoromethyl group.

We report herein the ultrasound-promoted[6-10] hydrogenation of fluorinated acrylic acids or fluorinated benzyl acrylates. The fluorinated acrylic acids and their esters, $CF_2{=}C(R^1)CO_2R^2$, are produced from the reactions of Grignard reagents with 2-(trifluoromethyl)propenoic acid or its benzyl ester below −40 °C.[11,12] With reaction temperatures up to 0 °C, complex mixtures are obtained. Although various types of reducing reagents, such as sodium borohydride, lithium aluminum hydride, etc., were examined, the hydrogenation of fluorinated acrylic acids or their benzyl esters did not proceed under normal conditions. However, ultrasound provides a solution to this problem. Ultrasonically dispersed Pd–C in methanol had a marked effect on the hydrogenation of α-difluoromethylated carboxylic acids. Some results are listed in Table I.

The use of benzyl esters also produced the corresponding α-difluoromethyl carboxylic acids directly in this system, by hydrogenation and hydrogenolysis.



Experimental Section

General Procedure. All commercially available reagents were used without further purification. Nuclear magnetic resonance (NMR) spectra were recorded at 90 or 200 MHz for ^1H NMR and 56.5 MHz for ^{19}F NMR in $CDCl_3$. ^{19}F chemical shifts are reported in parts per million (ppm) relative to trifluoroacetic acid (δ 0.00) as an external standard.

Preparation of 2-(Difluoromethyl)heptanoic Acid via Fluorinated Benzyl Acrylate. (a) Fluorinated Benzyl Acrylate. To a solution of Bu_2LiCu, which was prepared from copper iodide (3.8 g, 20 mmol) and *n*-butyllithium (20 mmol) in freshly dried diethyl ether (30 mL) at 0 °C, was added benzyl 2-(trifluoromethyl)propenate (2.3 g, 10 mmol) by using a syringe, under an atmosphere of argon at 0 °C. After 3 h of stirring at that temperature, the mixture was quenched with saturated NH_4Cl solution (50 mL), and then the oily materials were extracted with ethyl acetate (300 mL). The extract was dried over magnesium sulfate. On removal of the solvent, distillation gave the corresponding fluorinated benzyl acrylate in 56% yield: bp 87–89 °C (24 mmHg); ^{19}F NMR ($CDCl_3$) δ −7.7, −1.9 (=CF_2); ^1H NMR ($CDCl_3$) δ 0.76–1.70 (9 H, m), 2.20 (2 H, m), 5.23 (2 H, s), 7.40 (Ar H); IR (cm^{-1}) 1740 (C=O), 1715 (C=C); high-resolution mass calcd for $C_{15}H_{18}O_2F_2$ 268.303, found 268.447. Anal. Found: C, 66.89; H, 6.84. Calcd for $C_{15}H_{18}F_2O_2$: C, 67.15; H, 6.76.

(b) Hydrogenation of Fluorinated Benzyl Acrylate. A flask containing the above fluorinated benzyl acrylate (2.68 g, 10 mmol), 10% Pd–C (0.2 g), and methanol (10 mL) under an atmosphere of hydrogen was irradiated in the water bath of an ultrasonic laboratory cleaner (32 KHz, 35 W) for 30 h. The solution was poured into a 1 N HCl solution, and the oily material was extracted with diethyl ether. After the ethereal solution was dried over magnesium sulfate, the solvent was removed. Distillation gave 2-(difluoromethyl)heptanoic acid in 78% yield: ^{19}F NMR ($CDCl_3$) δ 38.5, 45.8 (CF_AF_B, ddd, $J_{F,F}$ = 247, $J_{F,H_{gem}}$ = 51, $J_{F,H_{vic}}$ = 11.5 Hz); ^1H NMR ($CDCl_3$) δ 0.76–1.70 (9 H, m), 2.50 (1 H, m), 5.73 (1 H, ddd, $J_{H,H_{vic}}$ = 6.5 Hz), 10.8 (1 H); IR (cm^{-1}) 1710 (C=O); high-resolution mass calcd for $C_8H_{14}O_2F_2$ 180.194, found 180.430. Anal. Found: C, 53.67; H, 7.54. Calcd for $C_8H_{14}O_2F_2$: C, 53.32; H, 7.83.

Preparation of 2-(Difluoromethyl)nonanoic Acid via Fluorinated Benzyl Acrylate. (a) Fluorinated Benzyl Acrylate. To a solution of $(C_6H_{13})_2MgCu$, which was prepared from copper iodide (3.8 g, 20 mmol) and *n*-hexylmagnesium bromide (20 mmol) in freshly dried diethyl ether (30 mL) at 0 °C, was added a mixture solution of benzyl 2-(trifluoromethyl)propenate (2.3 g, 10 mmol) with a syringe under an atmosphere of argon at 0 °C. After 3 h of stirring at that temperature, the mixture was worked up similarly. Distillation gave the corresponding fluorinated benzyl acrylate in 66% yield: bp 90–93 °C (17 mmHg); ^{19}F NMR ($CDCl_3$) δ −6.8, −1.4 (=CF_2); ^1H NMR ($CDCl_3$) δ 0.86–2.07 (13 H, m), 2.27 (2 H, m), 5.25 (2 H, s), 7.35 (Ar H); IR (cm^{-1}) 1740 (C=O), 1715 (C=C); high-resolution mass calcd for $C_{17}H_{22}O_2F_2$ 296.357, found 296.630. Anal. Found: C, 68.51; H, 7.67. Calcd for $C_{17}H_{22}O_2F_2$: C, 68.90; H, 7.48.

(b) Hydrogenation of Fluorinated Benzyl Acrylate. A flask containing the above fluorinated benzyl acrylate (2.06 g, 10 mmol), 10% Pd–C (0.2 g), and methanol (10 mL) under an atmosphere of hydrogen was irradiated in the water bath of an ultrasonic laboratory cleaner (32 KHz, 35 W) for 30 h. The solution was worked up similarly. Distillation gave 2-(difluoromethyl)nonanoic acid in 81% yield: ^{19}F NMR ($CDCl_3$) δ 37.5, 44.9 (CF_AF_B, ddd, $J_{F,F}$ = 251, $J_{F,H_{gem}}$ = 53, $J_{F,H_{vic}}$ = 12.5 Hz); ^1H NMR ($CDCl_3$) δ 0.87–2.05 (15 H, m), 2.52 (1 H, m), 5.75 (1 H, ddd, $J_{H,H_{vic}}$ = 6.5 Hz), 10.9 (1 H); IR (cm^{-1}) 1710 (C=O); high-resolution mass calcd for $C_{10}H_{18}O_2F_2$ 208.242, found 208.533. Anal. Found: C, 57.41; H, 8.98. Calcd for $C_{10}H_{18}F_2O_2$: C, 57.68; H, 8.71.

Preparation of 2-(Difluoromethyl)undecanoic Acid via Fluorinated Benzyl Acrylate. (a) Fluorinated Benzyl Acrylate. To a solution of $(C_8H_{17})_2MgCu$, which was prepared from copper iodide (3.8 g, 20 mmol) and n-octylmagnesium bromide (20 mmol) in freshly dried diethyl ether (30 mL) at 0 °C, was added a mixture solution of benzyl 2-(trifluoromethyl)propenate (2.3 g, 10 mmol) with a syringe under an atmosphere of argon at 0 °C. After 3 h of stirring at that temperature, the mixture was worked up similarly. Distillation gave the corresponding fluorinated benzyl acrylate in 63% yield: bp 104–107 °C (19 mmHg); ^{19}F NMR ($CDCl_3$) δ −6.5, −1.3 (=CF_2); ^1H NMR ($CDCl_3$) δ 0.92–1.97 (17 H, m), 2.24 (2 H, m), 5.35 (2 H, s), 7.25 (Ar H); IR (cm^{-1}) 1740 (C=O), 1715 (C=C); high-resolution mass calcd for $C_{19}H_{26}O_2F_2$ 324.411, found 324.006. Anal. Found: C, 70.51; H, 7.67. Calcd for $C_{19}H_{26}O_2F_2$: C, 70.35; H, 8.08.

(b) Hydrogenation of Fluorinated Benzyl Acrylate. A flask containing the above fluorinated benzyl acrylate (2.06 g, 10 mmol), 10% Pd–C (0.2 g), and methanol (10 mL) under an atmosphere of hydrogen was irradiated in the water bath of an ultrasonic laboratory cleaner (32 KHz, 35 W) for 30 h and then worked up similarly. Distillation gave 2-(difluoromethyl)undecanoic acid in 71% yield: ^{19}F NMR ($CDCl_3$) δ 38.2, 45.7 (CF_AF_B, ddd, $J_{F,F}$ = 248, $J_{F,H_{gem}}$ = 49, $J_{F,H_{vic}}$ = 12.0 Hz); ^1H NMR ($CDCl_3$) δ 0.91–2.04

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(19 H, m), 2.51 (1 H, m), 5.93 (1 H, ddd, $J_{H,H_{vic}}$ = 6.0 Hz), 10.7 (1 H); IR (cm^{-1}) 1710 (C=O); high-resolution mass calcd for $C_{12}H_{22}O_2F_2$ 236.302, found 236.415. Anal. Found: C, 60.91; H, 9.73. Calcd for $C_{12}H_{22}O_2F_2$: C, 60.99; H, 9.39.

Preparation of 2-(Difluoromethyl)hexanoic Acid via Fluorinated Acrylic Acid. (a) Reaction of 2-(Trifluoromethyl)propenoic Acid with *n*-Propylmagnesium Bromide. Into a solution of 2-(trifluoromethyl)propenoic acid (2.80 g, 20 mmol) and trimethylsilyl chloride (1.0 g) in tetrahydrofuran (30 mL) was added a solution of *n*-propylmagnesium bromide prepared from *n*-propyl bromide (6.15 g, 50 mmol) and magnesium (1.2 g, 50 mmol) in tetrahydrofuran (70 mL) at -40 °C under an atmosphere of nitrogen. After stirring for 5 h at that temperature, the mixture was quenched with saturated NH_4Cl solution below -20 °C. Oily materials were extracted with diisopropyl ether, and then the ethereal layer was washed with water and dried over anhydrous sodium sulfate. After the solvent was removed, the residue was distilled to give the corresponding fluorinated acrylic acid in 37% yield: bp 94-96 °C (25 mmHg); ^{19}F NMR ($CDCl_3$) δ -7.4, -2.3 (=CF_2); ^1H NMR ($CDCl_3$) δ 0.90 (3 H, t, $J_{H,H}$ = 6.0 Hz), 1.40 (4 H, m), 2.20 (2 H, m), 12.10 (1 H); IR (cm^{-1}) 3500-3000 (COOH), 1700 (C=O); high-resolution mass calcd for $C_7H_{10}O_2F_2$ 164.153, found 164.375. Anal. Found: C, 51.48; H, 6.54. Calcd for $C_7H_{10}O_2F_2$: C, 51.22; H, 6.14.

(b) Hydrogenation of Fluorinated Acrylic Acid. A flask containing the above fluorinated acrylic acid (1.64 g, 10 mmol), 10% Pd-C (0.2 g), and methanol (10 mL) under an atmosphere of hydrogen was irradiated in the water bath of an ultrasonic laboratory cleaner (32 KHz, 35 W) for 30 h. The solution was poured into a 1 N HCl solution, and the oily material was extracted with diethyl ether. After the ethereal solution was dried over magnesium sulfate, the solvent was removed. Distillation gave 2-(difluoromethyl)hexanoic acid in 68% yield: ^{19}F NMR ($CDCl_3$) δ 38.3, 45.8 (CF_AF_B, ddd, $J_{F,F}$ = 249, $J_{F,H_{gem}}$ = 50, $J_{F,H_{vic}}$ = 11.8 Hz); ^1H NMR ($CDCl_3$) δ 0.97-1.76 (9 H, m), 2.85 (1 H, m), 6.02 (1 H, ddd, $J_{H,H_{vic}}$ = 6.5 Hz), 10.8 (1 H); IR (cm^{-1}) 1710 (C=O); high-resolution mass calcd for $C_7H_{12}O_2F_2$ 166.169; found 166.463. Anal. Found: C, 50.26; H, 7.43. Calcd for $C_7H_{12}O_2F_2$: C, 50.60; H, 7.28.

Preparation of 2-(Difluoromethyl)heptanoic Acid via Fluorinated Acrylic Acid. (a) Reaction of 2-(Trifluoromethyl)propenoic Acid with *n*-Butylmagnesium Bromide. Into the above reaction, 2-(trifluoromethyl)propenoic acid (2.33 g, 16.7 mmol), *n*-butylmagnesium bromide (50 mmol), and trimethylsilyl chloride (1.0 g) in tetrahydrofuran (70 mL) were used. Distillation gave the corresponding fluorinated acrylic acid in 48% yield: bp 92-94 °C (19 mmHg); ^{19}F NMR ($CDCl_3$) δ -7.9, -3.3 (=CF_2); ^1H NMR ($CDCl_3$) δ 1.03-2.45 (11 H, m), 12.07 (1 H); IR (cm^{-1}) 3500-3000 (COOH), 1700 (C=O); high-resolution mass calcd for $C_8H_{12}O_2F_2$ 178.178, found 178.006. Anal. Found: C, 52.81; H, 6.86. Calcd for $C_8H_{12}O_2F_2$: C, 53.93; H, 6.79.

(b) Hydrogenation of Fluorinated Acrylic Acid. A flask containing the above fluorinated acrylic acid (1.98 g, 10 mmol), 10% Pd-C (0.2 g), and methanol (10 mL) under an atmosphere of hydrogen was irradiated in the water bath of an ultrasonic laboratory cleaner (32 KHz, 35 W) for 30 h and then worked up similarly. Distillation gave 2-(difluoromethyl)heptanoic acid in 73% yield: high-resolution mass calcd for $C_8H_{14}O_2F_2$ 180.194, found 180.318.

Preparation of 2-(Difluoromethyl)nonanoic Acid via Fluorinated Acrylic Acid. (a) Reaction of 2-(Trifluoromethyl)propenoic Acid with *n*-Hexylmagnesium Bromide. In the above reaction, 2-(trifluoromethyl)propenoic acid (2.80 g, 20 mmol), *n*-hexylmagnesium bromide (50 mmol), and trimethylsilyl chloride (1.0 g) in tetrahydrofuran (100 mL) were used. Final purification was the distillation, giving the fluorinated acrylic acid in 45% yield: bp 128-130 °C (26 mmHg); ^{19}F NMR ($CDCl_3$) δ -6.8, -1.2 (=CF_2); ^1H NMR ($CDCl_3$) δ 1.07-2.30 (15 H, m), 12.14 (1 H); IR (cm^{-1}) 3500-3000 (COOH), 1710 (C=O); high-resolution mass calcd for $C_{10}H_{16}O_2F_2$ 206.232, found 206.391. Anal. Found: C, 57.94; H, 7.53. Calcd for $C_{10}H_{16}O_2F_2$: C, 58.24; H, 7.82.

(b) Hydrogenation of Fluorinated Acrylic Acid. A flask containing the above fluorinated acrylic acid (2.06 g, 10 mmol), 10% Pd-C (0.2 g), and methanol (10 mL) under an atmosphere of hydrogen was irradiated in the water bath of an ultrasonic laboratory cleaner (32 KHz, 35 W) for 30 h and then worked up similarly. Final purification was the distillation, giving 2-(difluoromethyl)nonanoic acid in 64% yield: high-resolution mass calcd for $C_{10}H_{18}O_2F_2$ 208.242, found 208.457.

Preparation of 3-Phenyl-2-(difluoromethyl)propanoic Acid via Fluorinated Acrylic Acid. (a) Reaction of 2-(Trifluoromethyl)propenoic Acid with Phenylmagnesium Bromide. Into the above reaction, 2-(trifluoromethyl)propenoic acid (2.33 g, 16.7 mmol), phenylmagnesium bromide (50 mmol), and trimethylsilyl chloride (1.0 g) in tetrahydrofuran (70 mL) were used. Final purification was the distillation, giving the fluorinated acrylic acid in 55% yield: bp 107-110 °C (32 mmHg); ^{19}F NMR ($CDCl_3$) δ -11.3, -8.6 (=CF_2); ^1H NMR ($CDCl_3$) δ 3.47 (2 H, m), 7.20 (Ar H), 12.17 (1 H); IR (cm^{-1}) 3500-3000 (COOH), 1710 (C=O); high-resolution mass calcd for $C_{10}H_8O_2F_2$ 198.168, found 198.402. Anal. Found: C, 60.46; H, 4.24. Calcd for $C_{10}H_8O_2F_2$: C, 60.61; H, 4.07.

(b) Hydrogenation of Fluorinated Acrylic Acid. A flask containing the above fluorinated acrylic acid (2.00 g, 10 mmol), 10% Pd-C (0.2 g), and methanol (10 mL) under an atmosphere of hydrogen was irradiated in the water bath of an ultrasonic laboratory cleaner (32 KHz, 35 W) for 30 h and then worked up similarly. Final purification was the distillation, gaving 2-(difluoromethyl)nonanoic acid in 77% yield: ^{19}F NMR ($CDCl_3$) δ 38.6, 44.9 (CF_AF_B, ddd, $J_{F,F}$ = 247, $J_{F,H_{gem}}$ = 48, $J_{F,H_{vic}}$ = 12.0 Hz); ^1H NMR ($CDCl_3$) δ 2.79 (1 H, m), 3.51 (2 H, d, $J_{H,H}$ = 3.0 Hz), 5.88 (1 H, ddd, $J_{H,H_{vic}}$ = 6.5 Hz), 11.4 (1 H); IR (cm^{-1}) 1710 (C=O); high-resolution mass calcd for $C_{10}H_{10}O_2F_2$ 200.184, found 200.337. Anal. Found: C, 60.28; H, 5.57. Calcd for $C_{10}H_{10}O_2F_2$: C, 60.00; H, 5.34.

Registry No. $PhCH_2OC(O)C(=CH_2)CF_3$, 111339-17-4; Bu_2LiCu, 24406-16-4; $CH_3(CH_2)_4C(=CF_2)CO_2CH_2Ph$, 123186-66-3; $CH_3(CH_2)_4CH(CHF_2)CO_2H$, 123186-67-4; $CH_3(CH_2)_5MgBr$, 3761-92-0; $CH_3(CH_2)_6C(=CF_2)CO_2CH_2Ph$, 123186-68-5; $CH_3(CH_2)_6CH(CHF_2)CO_2H$, 123186-69-6; $CH_3(CH_2)_7MgBr$, 17049-49-9; $CH_3(CH_2)C(=CF_2)CO_2CH_2Ph$, 123186-70-9; $CH_3(CH_2)_8CH(CHF_2)CO_2H$, 123186-71-0; $CF_3C(=CH_2)CO_2H$, 381-98-6; $CH_3(CH_2)_2MgBr$, 927-77-5; $CH_3(CH_2)_3C(=CF_2)CO_2H$, 123186-72-1; $CH_3(CH_2)_3CH(CHF_2)CO_2H$, 123186-73-2; $CH_3(CH_2)_3MgBr$, 693-03-8; $CH_3(CH_2)_4C(=CF_2)CO_2H$, 123186-74-3; $CH_3(CH_2)_6C(=CF_2)CO_2H$, 123186-75-4; PhMgBr, 100-58-3; $PhCH_2C(=CF_2)CO_2H$, 99764-29-1; $PhCH_2CH(CHF_2)CO_2H$, 70219-17-9.

Novel Synthesis of Piperidinecarboxamides via Aryl Isocyanate Acylation of α-Amino Carbanions

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In support of one of our drug discovery programs we required access to piperidinecarboxamides of general structure **1**. We decided our approach would focus on their synthesis from **2**. The key transformation in this sequence would be the metalation of activated phenylpiperidine **3**[1] followed by its reaction with a suitable electrophile to yield an adduct such as **5**. By the choice of an appropriate electrophile in this sequence, **5** could then be easily converted into **1**. Based on related examples,[1c-e,3] it was not

(1) We chose to utilize the formamidine activating group of Meyers. (a) For leading references, see: Gonzalez, M. A.; Meyers, A. I. *Tetrahedron Lett.* **1989**, *30*, 43. (b) For a review, see: Meyers, A. I. *Aldrichimica Acta* **1985**, *18*, 59. (c) Meyers, A. I.; Edwards, P. D.; Riecker, W. F.; Bailey, T. R. *J. Am. Chem. Soc.* **1984**, *106*, 3270. (d) Meyers, A. I.; Edwards, P. D.; Bailey, T. R.; Jagdmann, G. E., Jr. *J. Org. Chem.* **1985**, *50*, 1019. (e) Meyers, A. I.; Dickman, D. A.; Bailey, T. R. *J. Am. Chem. Soc.* **1985**, *107*, 7974.

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