(3 H, t, J = 7 Hz), 2.0 (3 H, d, J = 7 Hz), 2.7 (2 H, q, J = 7 Hz), 5.9 (1 H, q, J = 7 Hz), 7.5 (5 H, m); mass spectrum, m/z 146 (M^+); HRMS calcd for $C_{11}H_{14}$ 146.1092, found 146.1078. (*Z*)-3-Phenyl-3-octene (**9b**): IR (neat) 3040, 1600 cm^{-1}; ^1H NMR (CCl_4) δ 0.93 (6 H, t, J = 7 Hz), 1.27 (4 H, m), 1.80 (2 H, q, J = 7 Hz), 2.27 (2 H, q, J = 7 Hz), 5.40 (1 H, tt, J = 7, 1.5 Hz), 7.23 (5 H, m); mass spectrum, m/z 188 (M^+); HRMS calcd for $C_{14}H_{20}$ 188.1560, found 188.1543.

General Procedure for the Preparation of Alkenes 10. The β-hydroxy silanes **8** obtained above were treated with KH in THF at 0 °C for 1 h. The reaction mixture was poured into a saturated ammonium chloride solution. After extraction with CH_2Cl_2, the solvent was evaporated and the residue was purified by column chromatography (silica gel) using hexane/ethyl acetate (19:1) as eluent. (*E*)-3-Phenyl-2-pentene (**10a**): IR (neat) 3040, 1610 cm^{-1}; ^1H NMR (CCl_4) δ 0.80 (3 H, t, J = 7 Hz), 1.56 (3 H, d, J = 7 Hz), 2.25 (2 H, q, J = 7 Hz), 5.43 (1 H, q, J = 7 Hz), 7.0 (5 H, m); mass spectrum, m/z 146 (M^+); HRMS calcd for $C_{11}H_{14}$ 146.1092, found 146.1075. (*E*)-3-Phenyl-3-octene (**10b**): IR (neat) 3040, 1600 cm^{-1}; ^1H NMR (CCl_4) δ 0.9-1.7 (10 H, m), 2.23 (2 H, m), 2.57 (2 H, q, J = 7 Hz), 5.60 (1 H, t, J = 7 Hz), 7.23 (5 H, m); mass spectrum, m/z 188 (M^+); HRMS calcd for $C_{14}H_{20}$ 188.1560, found 188.1573.

General Procedure for the Preparation of Alkenes 11. To a solution of vinyl iodide **7a** (0.07 g, 0.27 mmol) in ether (5 mL) at -50 °C was added dropwise *n*-butyllithium/hexane (0.33 mmol). The mixture was slowly warmed to -10 °C and then the appropriate electrophile was added (vide supra). After warming to room temperature, the reaction mixture was poured into saturated ammonium chloride solution, extracted with ether, washed with brine, and dried ($MgSO_4$). The solvent was removed by a rotary evaporator, and the residue was purified by column chromatography (silica gel) using hexane/ethyl acetate (9:1) as eluent. (*Z*)-4-Phenyl-3-hexen-2-ol (**11a**): IR (neat) 3350, 1060 cm^{-1}; ^1H NMR (CCl_4) δ 0.97 (3 H, t, J = 7 Hz), 1.2 (3 H, d, J = 6 Hz), 1.63 (1 H, br s), 2.30 (2 H, dq, J = 7, 1 Hz), 4.12 (1 H, dq, J = 9, 7 Hz), 5.37 (1 H, dt, J = 9, 1 Hz), 7.37 (5 H, m); mass spectrum, m/z 176 (M^+); HRMS calcd for $C_{12}H_{16}O$ 176.1197, found 176.1202. (*Z*)-2-Methyl-4-phenyl-3-hexen-2-ol (**11b**): IR (CCl_4) 3400, 1150 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.93 (3 H, t, J = 7 Hz), 1.20 (6 H, s), 1.47 (1 H, br s), 2,23 (2 H, q, J = 7 Hz), 5.60 (1 H, t, J = 1 Hz), 7.23 (5 H, m); mass spectrum, m/z 190 (M^+); HRMS calcd for $C_{13}H_{18}O$ 190.1353, found 190.1370. (*Z*)-3-Phenyl-2-pentenal (**11c**): IR (CCl_4) 2850, 2770, 1675 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.10 (3 H, t, J = 7 Hz), 2.58 (2 H, q, J = 7 Hz), 6.20 (1 H, dt, J = 8, 1 Hz), 7.37 (5 H, m), 9.47 (1 H, d, J = 8 Hz); mass spectrum, m/Z 160 (M^+); HRMS calcd for $C_{11}H_{12}O$ 160.0885, found 160.0867. (*Z*)-5-Phenyl-4-hepten-2-ol (**11d**): IR (CCl_4) 3400, 1080 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.97 (3 H, t, J = 7 Hz), 1.12 (2 H, q, J = 6 Hz), 1.55 (1 H, br s), 2.07 (2 H, m), 2.37 (2 H, q, J = 7 Hz), 3.77 (1 H, sextet, J = 7 Hz), 5.50 (1 H, tt, J = 7, 1 Hz), 7.23 (5 H, m); mass spectrum, m/z 190 (M^+); HRMS calcd for $C_{13}H_{18}O$ 190.1353, found 190.1358.

Acknowledgment. Financial support of this work by the National Science Council of the Republic of China is gratefully acknowledged.

Registry No. 1 (R′ = Ph), 536-74-3; 1 (R′ = *n*-Bu), 693-02-7; **2a**, 68669-68-1; **2b**, 68669-62-5; **2c**, 118226-86-1; **2d**, 94286-32-5; **2e**, 118226-87-2; **3**, 68669-61-4; **4**, 118226-81-6; **5a**, 64245-21-2; **5b**, 57086-65-4; **5c**, 64245-20-1; **5d**, 56422-91-4; **6a**, 118226-82-7; **6b**, 118226-88-3; **7a**, 118226-83-8; **7b**, 78463-05-5; **7c**, 78463-03-3; **7d**, 52812-63-2; **8a**, 118226-84-9; **8b**, 118226-92-9; **9a**, 4165-78-0; **9b**, 118226-89-4; **10a**, 4165-86-0; **10b**, 77161-68-3; **11a**, 118226-85-0; **11b**, 118226-90-7; **11c**, 36872-10-3; **11d**, 118226-91-8; acetaldehyde, 75-07-0; propylene oxide, 75-56-9; methylmagnesium chloride, 676-58-4; ethylmagnesium bromide, 925-90-6; butylmagnesium bromide, 693-03-8.

Synthesis of Organofluorine Building Blocks. 3. An Electrochemical Preparation and Reaction of Dimethyl 2,3-Bis(2,2,2-trifluoroethyl)succinate

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Dimethyl 2,3-bis(2,2,2-trifluoroethyl)succinate (**2**) was prepared in a 50% yield by electrochemical oxidation of trifluoroacetic acid (TFA) and methyl acrylate. Electrolysis was conducted in an MeCN-H_2O (7:1)-NaOH (0.1 equiv to TFA) system by using platinum electrodes under a constant current density (83 mA/cm^2) in an undivided cell. The succinate **2** was a 1:1 mixture of *meso* (**2a**) and *dl* (**2b**) that was separable by fractional crystallization. One of the methoxycarbonyl groups of **2** was transformed to isocyanate, *tert*-butoxy carbamate, or amino groups. Heterocyclic compounds bearing two 2,2,2-trifluoroethyl groups such as γ-lactone (**15**), β-lactam (**16**), succinic anhydride (**17**), succinimide (**18**), acyloin bis(trimethylsilyl ether) (**21**), and pyrimidinedione (**19** and **20**) were prepared from **2**.

Organofluorine compounds have attracted increasing attention for medicinal and agricultural usage and for material science.[1] Among them the trifluoromethylated compounds are promising so that a variety of trifluoromethylated compounds have been prepared. Transformations of the trichloromethyl group with hydrogen fluoride[2] and the carboxyl group with sulfur tetrafluoride[3] to the trifluoromethyl group have been employed for the industrial-scale productions of aromatic trifluoromethylated compounds. On the other hand, preparations of trifluoromethylated aliphatic compounds are not straightforward because of the requirement of the milder reaction conditions. Trifluoromethylation by the use of metal complexes of trifluoromethyl iodide,[4] *N*-(trifluoromethyl)-*N*-nitrosotrifluoromethanesulfonamide,[5] and perfluoroacyl peroxide[6] has been extensively investigated.

(1) (a) Filler, R.; Kobayashi, Y. *Biomedicinal Aspects of Fluorine Chemistry*; Kodansha: Tokyo, 1982. (b) Hudlicky, M. *Chemistry of Organic Fluorine Compounds*; Ellis Horwood: New York, 1976.
(2) Tullock, C. W.; Fawcett, F. S.; Smith, W. C.; Coffman, D. D. *J. Am. Chem. Soc.* **1960**, *82*, 539.
(3) Gerstenberger, M. R. C.; Haas, A. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 647.
(4) (a) Kobayashi, Y.; Yamamoto, K.; Kumadaki, I. *Tetrahedron Lett.* **1979**, 4071. (b) Kitazume, T.; Ishikawa, N. *Chem. Lett.* **1982**, 1453. (c) Fuchigami, T.; Ojima, I. *Tetrahedron Lett.* **1984**, *25*, 303.
(5) Umemoto, T.; Ando, A. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 447.

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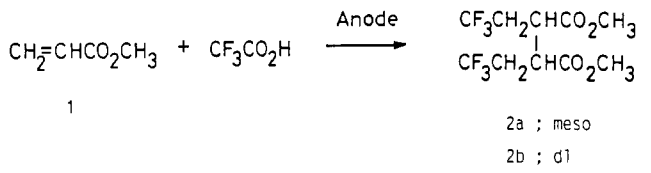
Scheme I



However, these methods are not feasible for large-scale production due to the high cost and instability of the trifluoromethylation reagents. Recently, the electroreductive generation of the active trifluoromethyl species from trifluoromethyl iodide[7] and bromide[8] and the electrooxidative generation of the trifluoromethyl radical from trifluoroacetic acid (TFA) have been reported. For example, Renaud,[9] Brookes,[10] and Muller[11] have demonstrated feasibility of the electrochemical trifluoromethylation of various olefins. Trifluoroacetic acid is the most available and economically feasible starting material for trifluoromethylation; therefore, the development of simple methods for the preparation of any trifluoromethylated building blocks and their utilization for the synthesis of the desired trifluoromethylated compounds are essential for organofluorine chemistry. We describe a modification of the electrooxidative trifluoromethylation of methyl acrylate (1) so as to prepare dimethyl 2,3-bis(2,2,2-trifluoroethyl)succinate (2) on a large scale and the chemical transformation of 2 to various trifluoromethylated amino acids and heterocycles (Scheme I).

Results and Discussion

Electrooxidation of TFA in the Presence of 1. Renaud demonstrated the electrooxidative trifluoromethylation of 1 in an AcOH–AcONa–Pt system in the presence of 4 equiv of TFA.[9] The electrolysis was conducted in a divided cell under 70–140 mA/cm^2 (1.5 F/mol), yielding 28% of 2. Meanwhile, Brookes electrolyzed 1 in the presence of 3 equiv of TFA in an MeCN–H_2O–NaOH–Pt system under 160 mA/cm^2 (2.2 F/mol), yielding 47% of 2.[10] The reported conditions require excess amounts of TFA and electricity and a divided cell so that it is not easy to purify the major product 2 in a molar scale electrolysis.[12] On this basis it is more practical from both the economical feasibility and the easy workup to employ a slight excess of methyl acrylate to TFA and to consume TFA completely in the electrolysis.

A current–voltage relation was examined at first. Figure 1 shows a plot of the terminal voltage vs quantity of electricity in the constant current (50 mA/cm^2) electrolysis of 1 and TFA in an MeCN–H_2O–NaOH–Pt system, revealing a sharp increase of the voltage after 1 equiv of electricity was applied. The result clearly demonstrates that TFA is almost completely consumed within 1–1.1 F/mol of electricity in the electrolysis system, suggesting that the current efficiency for the electrooxidative decarboxylation of TFA is satisfactory under the present electrolysis conditions. A rather lower current density electrolysis is preferable in the present electrochemical preparation of 2. A practical molar scale electrolysis of TFA in MeCN–H_2O (7:1) in the presence of 0.1 equiv of sodium hydroxide to TFA was conducted in an undivided cell under 50–85 mA/cm^2 for 1.2 F/mol. The electrolyzed solution was almost neutral at the end of electrolysis and the simple distillation of the crude extract provided 2 as crystals in a 50% yield.

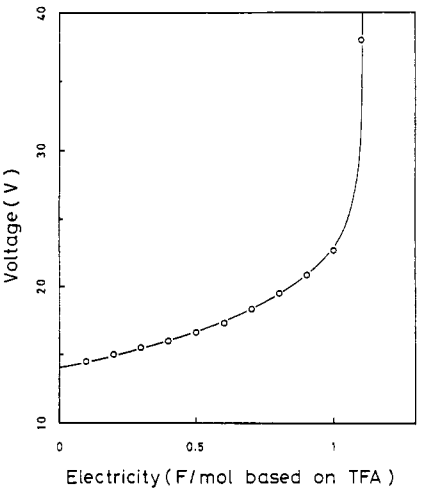
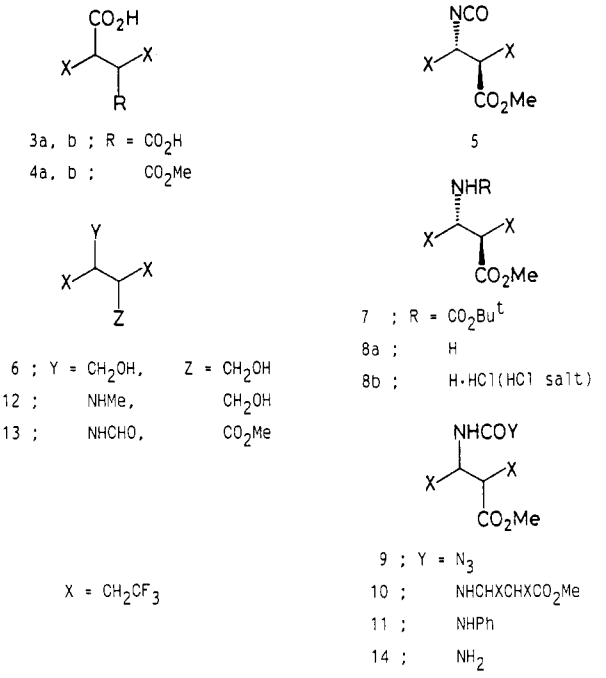


Figure 1. Terminal voltage increase dependent on the applied electricity (F/mol based on TFA) in an MeCN–H_2O–NaOH–TFA–(Pt) system.

Chart I



Chemical Modification of 2. In order to prepare amino acid and β-lactam derivatives bearing trifluoromethyl groups, chemical modifications of 2 were examined in detail. The electrochemically prepared 2 was found to be a 1:1 mixture of **2a** (*meso*) and **2b** (*dl*) by ^{19}F NMR and VPC analyses; both isomers were separable by recrystal-

(6) (a) Yoshida, M.; Amemiya, H.; Kobayashi, M.; Sawada, H.; Hagii, H.; Aoshima, K. *J. Chem. Soc., Chem. Commun.* **1985**, 234. (b) Sawada, H.; Yoshida, M.; Hagii, H.; Aoshima, K.; Kobayashi, M. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 215.

(7) Calas, P.; Moreau, P.; Commeyras, A. *J. Chem. Soc., Chem. Commun.* **1982**, 433.

(8) Sibille, S.; d'Incan, E.; Leport, L.; Perichon, J. *Tetrahedron Lett.* **1986**, *27*, 3129.

(9) (a) Renaud, R. N.; Champagne, P. J. *Can. J. Chem.* **1975**, *53*, 529. (b) Renaud, R. N.; Champagne, P. J.; Savard, M. *Ibid.* **1979**, *57*, 2617.

(10) (a) Brookes, C. J.; Coe, P. L.; Owen, D. M.; Pedler, A. E.; Tatlow, J. C. *J. Chem. Soc., Chem. Commun.* **1974**, 323. (b) Brookes, C. J.; Coe, P. L.; Pedler, A. E.; Tatlow, J. C. *J. Chem. Soc., Perkin Trans. 1* **1978**, 202.

(11) (a) Muller, N. *J. Org. Chem.* **1983**, *48*, 1370. (b) Muller, N. *Ibid.* **1984**, *49*, 2826. (c) Muller, N. *Ibid.* **1984**, *49*, 4559. (d) Muller, N. *Ibid.* **1986**, *51*, 263.

(12) In contrast to the reported method, the present electrochemical method provided 2 as crystals by a simple distillation of the extracted reaction mixture.

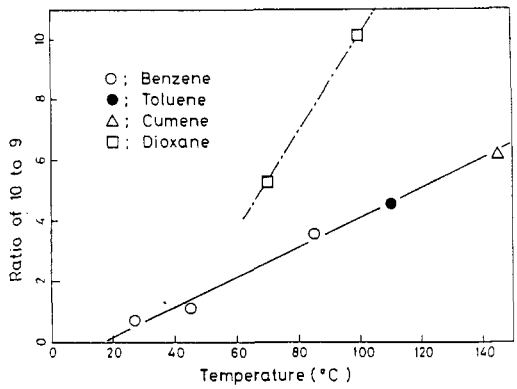
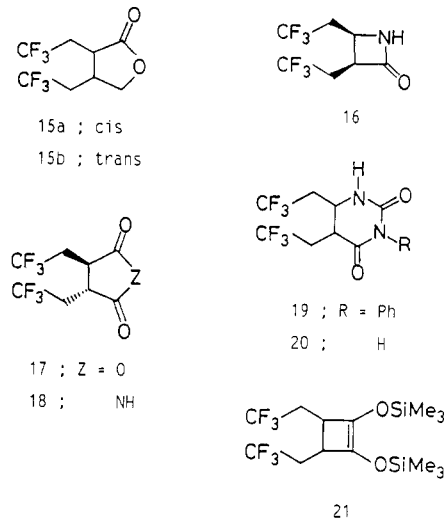


Figure 2. Temperature-dependent product distribution of **9** and **10** in denitrogenation of the acyl azide from **4a** in an aqueous medium.

lization. The stereochemistry of the *meso* isomer **2a** was clarified by the transformation to the lactone **15a**. Thus, reduction of **2a** with lithium aluminum hydride provided **6** whose capillary VPC showed a single peak. A modified sodium bromite oxidation[13] of **6** gave lactone **15a** (77%) whose 500-MHz ^{1}H NMR spectrum revealed a coupling constant of 8.2 Hz due to the cis geometry of the two methine protons. The chemical shifts of the two methylene carbons of the 2,2,2-trifluoroethyl groups in the ^{13}C NMR spectrum of **15a** appeared at 29.7 and 31.0 ppm, both of which were higher fields than those (34.0 and 35.7 ppm) of the corresponding signals from the trans lactone **15b** which was obtained from **2b**, clearly supporting the cis geometry of **15a**. In the oxidative lactonization, a longer reaction time induced partial epimerization.[14]

An alkaline hydrolysis of **2a** gave a mixture of **3a** and **3b**[15] quantitatively in refluxing methanol and **4a** and **4b** in a 90% yield at room temperature, respectively, showing complete epimerization.[16] No dehydrofluorination was observed under the basic conditions employed. However, the acid-catalyzed hydrolysis of **2a** provided a mixture of **3a** and **4a** (Chart I) whose stereochemistries were retained.[16] The monocarboxylic acid **4a** was transformed stereospecifically[17] to **5** by the action of thionyl chloride followed by sodium azide in aqueous acetone and successive thermal denitrogenation in benzene.[18] The *tert*-butyl carbamate **7** was obtained in 72% yield from **4a** via **5**. The hydrogen chloride catalyzed hydrolysis of **7** provided the desired amino ester **8b** in 96% yield. Denitrogenation of the acyl azide from **4a** in an aqueous medium gave a mixture of **9** and **10** whose ratio was intensively controlled by the thermal decomposition temperature of the acid azide intermediate. Figure 2 shows that lower temperatures are preferable for the preparation of **9**. The carbamoyl azide **9** was thermally stable and was obtained as a 30:70 diastereomeric mixture, suggesting the loss of stereochemistry during the rearrangement in an aqueous medium. The nucleophilic attacks both by water and azide ion to the isocyanate group of **5** occur smoothly in the aqueous sodium azide solution, providing **8a** and **9**, respectively. The amine **8a** again attacks **5** to give the urea

Chart II



10 in these conditions. In fact, the decomposition of the acyl azide of **4a** in the presence of aniline afforded the phenylurea **11** in 82% yield.

The transformations of the carbamoyl azide group of **9** to the methyl amino (**12**, 86%) and formylamino groups (**13**, 81%) were accomplished without loss of the trifluoromethyl group by the action of lithium aluminum hydride and sodium borohydride, respectively. The catalytic hydrogenation of **9** gave **14**. In contrast to the easy conversion of **5** to **7**, the conversion of **9** to **7** was effected by catalysis with sodium trifluoroacetate. Sodium acetate was used in vain for this purpose.[19] Anhydrous conditions suppress the formation of urea **10**. In fact, the employment of 4A molecular sieves in the reaction mixture was useful.

The transformations of **2a** to the heterocyclic compounds bearing two 2,2,2-trifluoroethyl groups were examined. The ring closure of **8a** with ethylmagnesium bromide in ether provided β-lactam **16** (53%) (Chart II). The cis geometry of the two 2,2,2-trifluoroethyl groups was clarified by the coupling constants of the two methine protons (J = 5.5 Hz for cis and J = 2.8 Hz for trans) and the steric compression effect of the two methylene carbons NMR (29.0 and 35.4 ppm for cis and 32.6 and 38.7 ppm for trans). The acid-catalyzed dehydration of the mixture of **3a** and **3b** proceeds smoothly in acetic anhydride at 100 °C for 4 h to give **17** in 84% yield. The stereochemistry was completely inverted due to the thermodynamic stability of **17**.[20] The condensation of the mixture of **3a** and **3b** with urea[21] provided **18** in 83% yield. The stereochemistry was also completely inverted due to the thermodynamic stability of **18**.[22] The ureas **11** and **14** were cyclized to **19** (57%) and **20** (76%) by heating with PPA, respectively. The acyloin condensation of **2a** was effected in the presence of metallic sodium and an excess of trimethylchlorosilane in refluxing toluene (**21**, 50%). It is noteworthy that the trifluoromethyl group remains intact in prolonged heating under the basic conditions. The cyclized products **19**, **20**, and **21** were stereochemically

(13) (a) Kageyama, T.; Kawahara, S.; Kitamura, K.; Ueno, Y.; Okawara, M. *Chem. Lett.* **1983**, 1097. (b) The lactonization in the reported conditions proceeded so slowly that the conversion of **6** is only 30% even after a few days stirring.

(14) On prolonged reaction time (20 h), 13% of lactone **15a** was epimerized to **15b**.

(15) Symbol **a** denotes a compound derived from *meso* **2a** and **b** from *dl* **2b**.

(16) Both **3a** and **4a** were esterified with diazomethane and the ratio of **2a** and **2b** was analyzed by VPC.

(17) Wallis, E. S.; Lane, J. F. *Org. React* **1946**, *3*, 267.

(18) Norman, A. L.; Robert, M. C.; Edwyn, A. C. *Synthesis* **1973**, 678.

(19) Tarbell, D. S.; Mallatt, R. C.; Wilson, J. W. *J. Am. Chem. Soc.* **1942**, *64*, 2229.

(20) Treatment of **17** in refluxing methanol for 30 min provided **4b** as a sole product, which was converted to **2b** with diazomethane (91%) whose VPC clearly revealed a single peak. This stereoinversion method via anhydride–monomethyl ester sequence enables a total conversion of a stereoisomeric mixture of **2a** and **2b** to less crystalline isomer **2b**.

(21) Guthrie, J. L.; Rabjohn, N. *Org. Synth.* **1963**, *4*, 513.

(22) Treatment of **18** in the mixture of HCl (aq) and dioxane at 100 °C provided **3b**, which was converted to **2b** by the action of diazomethane of which VPC revealed a single peak with a same retention time to the corresponding *dl* isomer **2b**.

isomeric mixtures whose stereochemistries were not determined.

Experimental Section

Melting and boiling points were uncorrected. Boiling points were indicated by an air bath temperature. Infrared spectra were taken on a Hitachi 270-30 spectrometer. The ^1H, ^{13}C, and ^{19}F NMR spectra were measured on a Varian VXR-500 spectrometer using TMS for ^1H and ^{13}C and C_6F_6 for ^{19}F NMR as internal standards. Mass spectra (MS) were obtained with a Hitachi M-80 spectrometer. The VPC analyses were conducted with a Shimazu GC-12A whose capillary column was CBP5-S25-050.

Dimethyl 2,3-Bis(2,2,2-trifluoroethyl)succinate (2). Methyl acrylate (120 mL, 1.3 mol), TFA (80 mL, 1.0 mol), and NaOH (4 g, 0.1 mol) were dissolved into a mixture of acetonitrile (560 mL) and water (80 mL) in a cylindrical electrolysis cell, equipped with two platinum foils (60 mm × 40 mm). The mixture was electrolyzed under a constant current of 2.0 A (83 mA/cm^2) at 0–10 °C for 16 h (1.2 F/mol based on TFA). Acetonitrile and the unreacted methyl acrylate were almost evaporated under reduced pressure, and 100 mL of water was added to the residue. The aqueous layer was extracted three times with AcOEt. The combined extracts were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The crude product was distilled (78–102 °C/7 mmHg) to give a mixture of **2a** and **2b** (81 g, 50%) as colorless crystals. VPC analysis revealed **2a**:**2b** = 51:49. **2a** was separated by repeated recrystallization from hexane. Likewise, **2b** was recrystallized from pentane.

2a: mp 87–88 °C; IR (Nujol) 1732, 1444, 1360, 1286 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.13–2.24 (m, 2 H), 2.70–2.81 (m, 2 H), 3.04–3.10 (m, 2 H), 3.77 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 33.37 (q, J_{C-C-F} = 29.8 Hz), 41.07, 52.74, 125.66 (q, J_{C-F} = 276.8 Hz), 171.24; ^{19}F NMR ($CDCl_3$) δ 96.20 (t, J = 10.3 Hz).

2b: mp 53–54 °C; ^1H NMR ($CDCl_3$) δ 2.36–2.46 (m, 2 H), 2.76–2.87 (m, 2 H), 3.06–3.11 (m, 2 H), 3.77 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 32.99 (t, J_{C-C-F} = 29.5 Hz), 40.51, 52.75, 125.98 (q, J_{C-F} = 276.7 Hz), 171.14; ^{19}F NMR ($CDCl_3$) δ 96.25 (t, J = 10.5 Hz).

Base-Catalyzed Hydrolysis of 2a. Method A. A solution of 85% KOH (942 mg, 14.3 mmol) in 1.5 mL of methanol was added slowly to a solution of **2** (1.06 g, 3.4 mmol) in 1.5 mL of methanol. The mixture was stirred under reflux for 4 h. Usual workup and short column chromatography (SiO_2, AcOEt) gave a mixture of **3a** and **3b** in quantitative yield (960 mg) as colorless crystals.

Method B. A solution of 85% KOH (213 mg, 3.23 mmol) in 1 mL of methanol was added slowly to a solution of **2a** (1 g, 3.22 mmol) in 2 mL of methanol. The mixture was stirred at room temperature for 10 h. Twenty milliliters of water was added to the mixture, which was then extracted three times with ether. The aqueous layer was neutralized with 10% HCl (aq) to pH 6 and extracted three times with ether. The combined extracts were washed two times with brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was chromatographed through a short silica gel column (AcOEt), yielding crystals that were recrystallized from hexane–benzene to give a mixture of **4a** and **4b** (860 mg, 90%) as colorless crystals.

Acid-Catalyzed Hydrolysis of 2a. A mixture of **2a** (1 g, 3.22 mmol), 35% HCl (aq) (3 mL), and acetic acid (6 mL) was stirred at 100 °C for 8 h. After cooling, the solution was neutralized with $NaHCO_3$ to pH 6. Usual workup and chromatography (SiO_2, hexane–AcOEt) gave **3a** (654 mg, 72%) and **4a** (188 mg, 20%) as colorless crystals and recovered **2a** (9 mg, 1%). The carboxylic acids **3a** and **4a** were transformed to **2a** with diazomethane, whose capillary VPC showed a single peak.

2,3-Bis(2,2,2-trifluoroethyl)succinic acid (3a): mp 201–202 °C; IR (Nujol) 3050, 1716, 1268, 1112 cm^{-1}; ^1H NMR (acetone-d_6) δ 2.44–2.56 (m, 2 H), 2.81–2.95 (m, 2 H), 3.01–3.15 (m, 2 H), 8.57 (s, 2 H); ^{19}F NMR (acetone-d_6) δ 98.23 (br), 98.33 (br). Anal. Calcd for $C_8H_8O_4F_6$: C, 34.06; H, 2.86. Found: C, 34.24: H, 3.01.

Monomethyl 2,3-bis(2,2,2-trifluoroethyl)succinate (4a): mp 82–84 °C; IR (Nujol) 3050, 1748, 1724, 942 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.16–2.31 (m, 2 H), 2.73–2.88 (m, 2 H), 3.09–3.18 (m, 2 H), 3.78 (s, 3 H), 9.97 (s, 1 H); ^{19}F NMR ($CDCl_3$) δ 96.27 (t, J = 9.7 Hz), 96.29 (t, J = 9.7 Hz). Anal. Calcd for $C_9H_{10}O_4F_6$: C, 36.50; H, 3.40. Found: C, 36.53; H, 3.25.

[2-(Methoxycarbonyl)-4,4,4-trifluoro-1-(2,2,2-trifluoroethyl)butyl]carbamoyl Azide (9) and *N,N'*-Bis[2-(methoxycarbonyl)-4,4,4-trifluoro-1-(2,2,2-trifluoroethyl)butyl]urea (10). Method A. Under a nitrogen atmosphere, $SOCl_2$ (0.15 mL, 2.1 mmol) was added to a solution of **4a** (157 mg, 0.53 mmol) in dry CH_2Cl_2 (1.5 mL). After refluxing for 2 h, the solvent and the unreacted $SOCl_2$ were evaporated. Under cooling, the crude product dissolved in 2 mL of dry acetone was added slowly to a solution of NaN_3 (90 mg, 1.4 mmol) in 1 mL of H_2O. After 1 h, the ice bath was removed and the mixture was stirred at room temperature for 24 h. Usual workup and chromatography (SiO_2, hexane–AcOEt) gave diastereomeric mixture of **9** (82 mg, 46%, ratio of diastereomers 31:69) and **10** (32 mg, 22%) as colorless crystals.

Method B. The above-mentioned acid azide solution was added carefully to 3 mL of diglyme kept at about 150 °C, and the mixture was stirred at that temperature for 30 min. A similar workup provided **10** (121 mg, 83%) as a mixture of diastereoisomers whose VPC analysis showed three pairs of a double peak whose relative intensities are 16, 48, and 36, respectively.

9: IR (CH_2Cl_2) 3432, 2148, 1740, 1714, 1500 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.23–2.52 (m, 3 H), 2.57–2.76 (m, 1 H), 2.98–3.04 (m, 1 H), 3.04–3.09 (m, 1 H), 3.78 (s, 3 H), 4.28–4.37 (m, 1 H), 4.42–4.48 (m, 1 H), 5.37 (d, J = 8.8 Hz, 1 H), 5.88 (d, J = 9.8 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 33.2 (q, J_{C-C-F} = 30.0 Hz), 34.0 (q, J_{C-C-F} = 30.0 Hz), 35.2 (q, J_{C-C-F} = 30.0 Hz), 37.6 (q, J_{C-C-F} = 30.0 Hz), 42.1, 43.5, 46.7, 47.1, 52.9, 52.9, 125.3 (q, J_{C-f} = 277.4 Hz), 156.3, 156.7, 171.3, 172.5; ^{19}F NMR ($CDCl_3$) δ 96.44 (t, J = 11.5 Hz), 96.69 (t, J = 12.16 Hz), 97.68 (br), 97.91 (t, J = 12.2 Hz); MS, m/z (relative intensity) 337 (M^+ + 1, 1), 293 (6), 261 (11), 181 (100), 156 (21), 138 (34), 59 (29). Anal. Calcd for $C_9H_{10}N_4O_3F_6$: C, 32.15; H, 3.00; N, 16.67. Found: C, 32.38; H, 3.10; N, 16.72.

10: IR (Nujol) 3392, 1740, 1668, 1550 cm^{-1}; ^1H NMR (acetone-d_6) δ 2.26–2.73 (m, 8 H), 2.90–3.11 (m, 2 H), 3.72 (s, 6 H), 3.73 (s, 6 H), 4.28–4.41 (m, 2 H), 4.51–4.60 (m, 2 H), 5.87–6.22 (m, 2 H); ^{19}F NMR (acetone-d_6) δ 97.85 (t, J = 10.7 Hz), 97.90 (t, J = 10.9 Hz), 99.15–99.23 (m), 99.32–99.39 (m); MS, m/z (relative intensity) 560 (M^+, 36), 529 (62), 405 (23), 266 (100), 184 (52), 112 (85). Anal. Calcd for $C_{17}H_{20}N_2O_5F_{12}$: C, 36.44; H, 3.60; N, 5.00. Found: C, 36.32; H, 3.61; N, 5.21.

***meso*-2,3-Bis(2,2,2-trifluoroethyl)-1,4-butanediol (6).** Under ice cooling, a solution of **2a** (310 mg, 1.00 mmol) in 3 mL of dry THF was added dropwise to a suspension of $LiAlH_4$ (246 mg, 6.48 mmol) in 2 mL of dry THF. The mixture was stirred under a nitrogen atmosphere at room temperature for 2 h. Usual workup and chromatography (SiO_2, hexane–AcOEt) gave **6** (251 mg, 99%): bp 95–98 °C (4 mmHg); IR (neat) 3300, 1396, 1258, 1142, 1062, 1044 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.97–2.10 (m, 2 H), 2.18–2.36 (m, 4 H), 3.10 (s, 2 H), 3.70 (dd, J_1 = 6.5 Hz, J_2 = 11.3 Hz, 2 H), 3.75 (dd, J_1 = 3.1 Hz, J_2 = 11.4 Hz, 2 H); ^{19}F NMR ($CDCl_3$) δ 97.49 (t, J = 10.9 Hz). Anal. Calcd for $C_8H_{12}O_2F_6$: C, 37.80; H, 4.76. Found: C, 37.37; H, 4.67.

***N*-[2-(Methoxycarbonyl)-4,4,4-trifluoro-1-(2,2,2-trifluoroethyl)butyl]-*N*-(*tert*-butoxycarbonyl)amine (7). Method A.** Under a nitrogen atmosphere, a mixture of **9** (102 mg, 0.30 mmol), CF_3CO_2Na (96 mg, 0.71 mmol), 4A molecular sieves (116 mg), and *t*-BuOH (1 mL) was stirred at room temperature for 1 h and then at 100 °C for 24 h. After cooling, the solution was filtered with a glass filter. Usual workup and chromatography (SiO_2, hexane–AcOEt) gave **7** (96 mg, 86%) as colorless crystals.

Method B. The acid azide from **4a** was extracted three times with pentane. The combined extracts were dried over $MgSO_4$ and concentrated in vacuo. Under a nitrogen atmosphere, the crude product in 2 mL of dry *t*-BuOH was stirred at room temperature for 20 min and then at 80 °C for 30 min. Usual workup and chromatography (SiO_2, hexane–AcOEt) gave **7** in 72% yield from **4a**: mp 106–108 °C; IR (Nujol) 3388, 1744, 1694, 1532, 1162 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.44 (s, 9 H), 2.17–2.51 (m, 3 H), 2.61–2.72 (m, 1 H), 2.98–3.06 (m, 1 H), 3.77 (s, 3 H), 4.09–4.17 (m, 1 H), 4.72 (d, J = 10.0 Hz, 1 H); ^{19}F NMR ($CDCl_3$) δ 96.58 (t, J = 10.3 Hz), 98.07 (t, J = 9.8 Hz). Anal. Calcd for $C_{13}H_{19}NO_4F_6$: C, 42.51; H, 5.21; N, 3.81. Found: C, 42.47; H, 5.31; N, 4.19.

[2-(Methoxycarbonyl)-4,4,4-trifluoro-1-(2,2,2-trifluoroethyl)butyl]ammonium Chloride (8b). A solution of **7** (101 mg, 0.27 mmol) in 1 mL of dioxane and 1 mL of 10% HCl (aq)

was stirred at 70 °C for 2 h. After cooling, 3 mL of water was added to the solution. The aqueous layer was extracted five times with ether. The solvents were evaporated to give **8b** (80 mg, 96%) as colorless crystals: mp 158–160 °C; IR (Nujol) 3300–2500, 1736, 1265, 1145 cm^{-1}; ^1H NMR (CD_3OD) δ 2.55–2.72 (m, 2 H), 2.83–2.97 (m, 2 H), 3.32–3.37 (m, 1 H), 3.84 (s, 3 H), 3.94–4.00 (m, 1 H), 4.88 (s, 3 H); ^{19}F NMR (CD_3OD) δ 98.45 (t, J = 10.5 Hz), 99.26 (t, J = 10.5 Hz). Anal. Calcd for $C_8H_{12}NO_2ClF_6$: C, 31.65; H, 3.98; N, 4.61. Found: C, 31.41; H, 4.03; N, 4.79.

***N*-[2-(Methoxycarbonyl)-4,4,4-trifluoro-1-(2,2,2-trifluoroethyl)butyl]-*N'*-phenylurea (11). Method A.** Under nitrogen atmosphere, $SOCl_2$ (0.15 mL, 2.1 mmol) was added to a mixture of **4** (156 mg, 0.53 mmol) and dry CH_2Cl_2 (1.5 mL). After refluxing for 2 h, the solvent and unreacted $SOCl_2$ were evaporated. Under cooling, the crude product, dissolved in 2 mL of dry acetone, was added slowly to a solution of NaN_3 (80 mg, 1.2 mmol) in 1 mL of H_2O. After 1 h, ice bath was removed, aniline (0.1 mL, 1.1 mmol) was added to the solution, and the mixture was stirred at room temperature for 24 h. After addition of a small amount of 10% HCl (aq), usual workup and chromatography (SiO_2, hexane–AcOEt) gave **11** (167 mg, 82%) as colorless crystals.

Method B. A mixture of **9** (39 mg, 0.12 mmol), aniline (0.03 mL, 0.33 mmol), dioxane (3 mL), acetone (2 mL), and H_2O (1 mL) was stirred at 100 °C for 5 h. A similar workup provided **11** (41 mg, 91%): IR (neat) 3350, 1738, 1643, 1559, 1159 cm^{-1}; ^1H NMR (acetone-d_6) δ 2.18–2.41 (m, 3 H), 2.48–2.60 (m, 1 H), 2.90–2.94 (m, 1 H), 3.62 (s, 3 H), 4.46–4.51 (s, 1 H), 5.79 (d, J = 10.0 Hz, 1 H), 6.83–6.88 (m, 1 H), 7.09–7.14 (m, 2 H), 7.24–7.28 (m, 3 H); ^{19}F NMR (acetone-d_6) δ 96.61 (t, J = 11.5 Hz), 98.11 (t, J = 11.5 Hz); MS, m/z (relative intensity) 386 (M^+, 100), 355 (31), 112 (71), 93 (100), 43 (29). Anal. Calcd for $C_{15}H_{16}N_2O_3F_6$: C, 46.64; H, 4.17; N, 7.25. Found: C, 46.67; H, 4.17; N, 7.30.

***N*-[2-(Hydroxymethyl)-4,4,4-trifluoro-1-(2,2,2-trifluoroethyl)butyl]-*N*-methylamine (12).** Under ice cooling, a solution of **9** (226 mg, 0.67 mmol) in 2 mL of dry THF was added dropwise to a suspension of $LiAlH_4$ (123 mg, 3.24 mmol) in 1 mL of dry THF. The mixture was stirred under a nitrogen atmosphere at room temperature for 3 h. Usual workup and chromatography (SiO_2, hexane–AcOEt) gave **12** (146 mg, 86%) as a colorless liquid: bp 85 °C (5 mmHg); IR (neat) 3320, 1744, 1650, 1442, 990, 844, 666 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.71 (br, 1 H), 1.88–2.70 (m, 6 H), 2.46 (s, 3 H), 2.51 (s, 3 H), 2.99–3.04 (m, 1 H), 3.07–3.12 (m, 1 H), 3.69–3.93 (m, 2 H); ^{19}F NMR ($CDCl_3$) δ 97.34 (t, J = 12.0 Hz), 97.64 (t, J = 11.1 Hz), 97.83 (t, J = 11.1 Hz), 98.23 (t, J = 11.1 Hz). Anal. Calcd for $C_8H_{13}NOF_6$: C, 37.95; H, 5.18; N, 5.53. Found: C, 37.52; H, 5.06; N, 5.31.

***N*-[2-(Methoxycarbonyl)-4,4,4-trifluoro-1-(2,2,2-trifluoroethyl)butyl]formamide (13).** Under ice cooling, $NaBH_4$ (56 mg, 1.48 mmol) was added to a solution of **9** (209 mg, 0.62 mmol) in 2 mL of MeOH. The mixture was stirred at room temperature for 3 h. Usual workup and chromatography (SiO_2, hexane–AcOEt) gave **13** (149 mg, 81%) as colorless crystals: IR (Nujol) 3328, 1738, 1674, 1528, 1378, 1112 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.26–2.78 (m, 4 H), 3.00–3.08 (m, 1 H), 3.78 (s, 3 H), 3.79 (s, 3 H), 4.54–4.61 (m, 1 H), 4.72–4.78 (m, 1 H), 6.02 (d, J = 10.0 Hz, 1 H), 6.44 (d, J = 10.0 Hz, 1 H), 8.21 (s, 1 H), 8.25 (s, 1 H); ^{19}F NMR ($CDCl_3$) δ 96.53 (t, J = 12.2 Hz), 96.66 (t, J = 12.2 Hz), 97.83 (t, J = 12.2 Hz), 98.01 (t, J = 11.5 Hz). Anal. Calcd for $C_9H_{11}NO_3F_6$: C, 36.62; H, 3.76; N, 4.75. Found: C, 36.46; H, 4.14; N, 4.36.

***N*-[2-(Methoxycarbonyl)-4,4,4-trifluoro-1-(2,2,2-trifluoroethyl)butyl]urea (14).** Under water cooling, dry NH_3 gas was added slowly to the solution of **5** in 10 mL of dry benzene for 1 h. Usual workup and chromatography (SiO_2, hexane–AcOEt) gave **14** (88%) as colorless crystals: IR (Nujol) 3384, 1736, 1666, 1546, 1266, 1152 cm^{-1}; ^1H NMR (acetone-d_6) δ 1.99–2.24 (m, 3 H), 2.32–2.44 (m, 1 H), 2.69–2.74 (m, 1 H), 3.44 (s, 3 H), 4.19–4.24 (m, 1 H), 4.86 (br, 2 H), 5.70 (d, J = 9.3 Hz, 1 H); ^{19}F NMR (acetone-d_6) δ 96.92 (t, J = 11.5 Hz), 98.28 (t, J = 11.5 Hz). Anal. Calcd for $C_9H_{12}N_2O_3F_6$: C, 34.85; H, 3.90; N, 9.03. Found: C, 34.58; H, 3.97; N, 9.08.

***cis*-2,3-Bis(2,2,2-trifluoroethyl)-4-butanolide (15a).** A mixture of **6** (127 mg, 0.50 mmol), $NaBrO_2$ (189 mg, 1.00 mmol), CH_2Cl_2 (2 mL), and H_2O (2 mL) was stirred at room temperature for 8 h. Usual workup and chromatography (SiO_2, hexane–AcOEt) gave **15a** (96 mg, 77%, VPC analysis **15a**:**15b** = 95:5).

15a: mp 57–58 °C; IR (Nujol) 1760, 1258, 1250, 1140, 1124, 1002 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.07 (ddq, J_1 = 14.7, J_2 = 11.3, J_3 = 11.3 Hz, 1 H), 2.20 (ddq, J_1 = 11.6, J_2 = 6.1, J_3 = 11.3 Hz, 1 H), 2.23–2.35 (m, 1 H), 2.83 (ddq, J_1 = 14.1, J_2 = 2.7, J_3 = 11.3 Hz, 1 H), 3.00–3.05 (m, 1 H), 3.08 (ddq, J_1 = 2.7, J_2 = 8.2, J_3 = 11.3 Hz, 1 H), 4.33 (dd, J_1 = 9.9, J_2 = 4.4 Hz, 1 H), 4.47 (d, J = 9.9 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 2.97 (q, J_{C-C-F} = 30.3 Hz), 31.0 (q, J_{C-C-F} = 28.6 Hz), 33.4 (q, J = 2.5 Hz), 38.4 (q, J = 2.5 Hz), 69.8, 125.9 (q, J_{C-F} = 276.2 Hz), 126.1 (q, J_{C-F} = 277.2 Hz), 174.4; ^{19}F NMR ($CDCl_3$) δ 96.15 (t, J = 10.1 Hz), 98.03 (t, J = 9.8 Hz).

15b: bp 98–100 °C (3 mmHg); IR (Nujol) 1748, 1394, 1310, 1284, 1274 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.23 (ddq, J_1 = 10.3, J_2 = 10.3, J_3 = 15.6 Hz, 1 H), 2.35 (ddq, J_1 = 10.3, J_2 = 8.3, J_3 = 15.6 Hz, 1 H), 2.56 (ddd, J_1 = 3.6, J_2 = 8.7, J_3 = 11.5 Hz, 1 H), 2.68 (ddq, J_1 = 11.3, J_2 = 3.4, J_3 = 14.7 Hz, 1 H), 2.72–2.78 (m, 1 H), 2.91 (ddq, J_1 = 11.7, J_2 = 3.6, J_3 = 14.7 Hz, 1 H), 4.00 (t, J = 9.6 Hz, 1 H), 4.59 (t, J = 8.8 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 34.0 (q, J_{C-C-F} = 30.4 Hz), 35.7 (q, J_{C-C-F} = 29.4 Hz), 35.9 (q, J = 2.5 Hz), 39.2 (q, J = 2.5 Hz), 70.7, 125.7 (q, J_{C-F} = 277.0 Hz), 125.9 (q, J_{C-F} = 276.4 Hz), 174.9; ^{19}F NMR ($CDCl_3$) δ 96.81 (t, J = 10.4 Hz), 98.08 (t, J = 10.9 Hz). Anal. Calcd for $C_8H_8O_2F_6$: C, 38.41; H, 3.22. Found: C, 38.02; H, 3.19.

3,4-Bis(2,2,2-trifluoroethyl)-2-azetidinone (16). The compound **8b** (100 mg, 0.33 mmol) was transformed to **8a** in a basic aqueous solution. Under a nitrogen atmosphere, **8a** in 1.0 mL of dry ether was added to the already prepared EtMgBr in 1.0 mL of dry ether. The mixture was stirred at room temperature for 2 h. Usual workup and recrystallization (hexane–CH_2Cl_2) gave **16** (41 mg, 53%) as colorless crystals. The VPC analysis showed 98% diastereomeric excess without stereochemical purification from **4a**: ***cis*-16**: mp 104–106 °C; IR (Nujol) 3256, 1770, 1266, 1141 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.21–2.76 (m, 4 H), 3.73 (ddd, J_1 = 11.1, J_2 = 5.5, J_3 = 3.2 Hz, 1 H), 3.80 (ddd, J_1 = 11.3, J_2 = 5.5, J_3 = 2.0 Hz, 1 H), 6.40 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 29.0 (q, J_{C-C-F} = 30.8 Hz), 35.4 (q, J_{C-C-F} = 28.1 Hz), 45.8, 47.6, 125.7 (q, J_{C-F} = 276.3 Hz), 126.1 (q, J_{C-F} = 277.1 Hz), 166.2; ^{19}F NMR ($CDCl_3$) δ 96.44 (t, J = 10.5 Hz), 97.16 (t, J = 10.1 Hz). Anal. Calcd for $C_7H_7NOF_6$: C, 35.76; H, 3.00; N, 5.96. Found: C, 35.35; H, 2.89; N, 6.16.

***trans*-16**: ^1H NMR ($CDCl_3$) δ 2.21–2.76 (m, 4 H), 3.17 (ddd, J_1 = 2.8, J_2 = 3.4, J_3 = 11.9 Hz, 1 H), 3.80 (ddd, J_1 = 2.8, J_2 = 2.8, J_3 = 9.8 Hz, 1 H), 6.40 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 32.6 (q, J_{C-C-F} = 30.2 Hz), 38.7 (q, J_{C-C-F} = 28.2 Hz), 49.1, 50.7, 125.5 (q, J_{C-F} = 276.2 Hz), 125.9 (q, J_{C-F} = 275.4 Hz), 165.8; ^{19}F NMR ($CDCl_3$) δ 96.28 (t, J = 10.3 Hz), 96.42 (t, J = 10.3 Hz).

2,3-Bis(2,2,2-trifluoroethyl)succinic Anhydride (17). A mixture of **3** (282 mg, 1.00 mmol) and acetic anhydride (2 mL) was refluxed at 100 °C for 4 h. Usual workup and chromatography (SiO_2, hexane–AcOEt) gave **17** (222 mg, 84%) as colorless crystals: mp 143–145 °C; IR (Nujol) 1866, 1796, 1288, 1264, 1154, 1124, 960 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.65–2.76 (m, 2 H), 2.84–2.95 (m, 2 H), 3.31–3.36 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 33.4 (q, J_{C-C-F} = 31.0 Hz), 40.0, 125.2 (q, J_{C-F} = 277.2 Hz), 169.2; ^{19}F NMR ($CDCl_3$) δ 98.68 (t, J = 11.5 Hz); MS, m/z (relative intensity) 220 (M^+ – 44, 13), 192 (71), 123 (76), 89 (4), 59 (100). Anal. Calcd for $C_8H_6O_3F_6$: C, 36.78; H, 2.29. Found: C, 36.50; H, 2.38.

2,3-Bis(2,2,2-trifluoroethyl)succinimide (18). A mixture of **3** (557 mg, 1.97 mmol) and urea (1.2 g, 20 mmol) was heated to 140–150 °C. As soon as the vigorous evolution of CO_2 came to an end, the temperature was kept at 110–120 °C, then 10 mL of 5% Na_2CO_3 was added carefully through the condenser, and the mixture was stirred vigorously. After cooling, usual workup gave pure **18** (430 mg, 83%) as colorless crystals: mp 92–94 °C; IR (Nujol) 3192, 3088, 1784, 1712, 1242, 1148, 1090 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.56–2.67 (m, 2 H), 2.77–2.88 (m, 2 H), 3.06–3.11 (m, 2 H), 8.25 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 33.4 (q, J_{C-C-F} = 30.3 Hz), 40.8, 125.8 (q, J_{C-F} = 277.5 Hz), 175.4; ^{19}F NMR ($CDCl_3$) δ 98.78 (t, J = 10.2 Hz). Anal. Calcd for $C_8H_7NO_2F_6$: C, 36.52; H, 2.68; N, 5.32. Found: C, 36.24; H, 2.50; N, 5.42.

5,6-Bis(2,2,2-trifluoroethyl)-5,6-dihydro-3-phenyl-2,4-(1*H*,3*H*)-pyrimidinedione (19). A mixture of **11** (74 mg, 0.19 mmol) and 3 mL of polyphosphoric acid was stirred at 100 °C for 48 h. Five milliliters of water was added dropwise to decompose the PPA. Usual workup and chromatography (SiO_2, hexane–AcOEt) gave **19** (38 mg, 57%) as colorless crystals: IR (Nujol) 3340, 3288, 1738, 1642, 1564, 1162 cm^{-1}; ^1H NMR ($CDCl_3$)

δ 2.13–2.26 (m, 1 H), 2.33–2.46 (m, 2 H), 3.04–3.16 (m, 1 H), 3.44–3.50 (m, 1 H), 4.05–4.12 (m, 1 H), 6.68 (d, J = 5.0 Hz, 1 H), 7.12–7.16 (m, 2 H), 7.40–7.50 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 2.92 (q, J_{C-C-F} = 30.1 Hz), 33.1 (q, J_{C-C-F} = 27.8 Hz), 39.21, 43.40, 123.6 (q, J_{C-F} = 53.1 Hz), 125.8 (q, J_{C-F} = 52.2 Hz), 127.3, 128.0, 128.3, 133.2, 151.4, 166.7; ^{19}F NMR (acetone-d_6) δ 99.12 (t, J = 11.5 Hz), 99.50 (t, J = 11.5 Hz). Anal. Calcd for $C_{14}H_{12}N_2O_2F_6$: C, 47.47; H, 3.41; N, 7.91. Found: C, 47.49; H, 3.28; N, 8.06.

5,6-Bis(2,2,2-trifluoroethyl)-5,6-dihydro-2,4(1*H*,3*H*)-pyrimidinedione (20). A mixture of **14** (50 mg, 0.16 mmol) and polyphosphoric acid (3 g) was stirred at 100 °C for 17 h. The above-mentioned workup and chromatography (SiO_2, hexane–AcOEt) gave **20** (34 mg, 76%) as colorless crystals: IR (Nujol) 3240, 3100, 1730, 1254, 1152 cm^{-1}; ^1H NMR (acetone-d_6) δ 2.44–2.97 (m, 4 H), 2.97–3.09 (m, 1 H), 3.38–3.46 (m, 1 H), 3.94–4.00 (m, 1 H), 4.07–4.14 (m, 1 H), 7.13 (s, 1 H), 7.41 (s, 1 H), 9.40 (s, 1 H); ^{19}F NMR (acetone-d_6) δ 99.50 (t, J = 22.6 Hz), 99.80 (t, J = 21.6 Hz), 100.32 (t, J = 22.1 Hz), 100.54 (t, J = 20.7 Hz). Anal. Calcd for $C_8H_8N_2O_2F_6$: C, 34.54; H, 2.90; N, 10.07. Found: C, 34.59; H, 3.23; N, 9.96.

3,4-Bis(2,2,2-trifluoroethyl)-1,2-bis(trimethylsiloxy)-cyclobutene (21). Under a nitrogen atmosphere, a mixture of **2** (501 mg, 1.6 mmol), sodium (200 mg, 8.7 mmol), trimethylchlorosilane (1.1 mL, 8.3 mmol), and toluene (5 mL) was stirred at 100 °C for 4 h. After cooling, the mixture was filtered with a glass filter. The filtrate was fractionally distilled (130 °C/6 mmHg) to give **21** (319 mg, 50%) as a colorless liquid: IR (neat) 2968, 1730, 1312, 1256 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.20 (s, 18 H), 2.00–2.20 (m, 4 H), 2.34–2.38 (m, 2 H), 2.88–2.92 (m, 2 H); ^{19}F NMR ($CDCl_3$) δ 96.81 (t, J = 10.2 Hz), 97.67 (t, J = 11.0 Hz); MS, m/e (relative intensity) 394 (M^+, 25), 297 (7), 147 (20), 115 (6), 73 (100). Anal. Calcd for $C_{14}H_{24}O_2F_6Si_2$: C, 42.62; H, 6.13. Found: C, 42.46; H, 6.26.

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Importance of Structure of α,β-Ethylenic Ketones during Their Reductive Coupling Promoted by the $TiCl_4$–Mg Reagent

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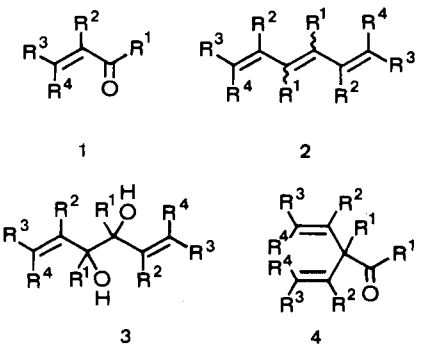
In most cases, the reductive coupling of α,β-ethylenic ketones by the $TiCl_4$–Mg reagent leads to 1,3,5-trienes and bisallylic pinacols. Some α,β-enones of *s*-cis configuration, such as (+)-pulegone, show a particular reactivity: formation of dihydro ketones in the presence of *tert*-butyl alcohol and reductive alkylation with allylic halides or benzyl bromide. Results are in accordance with a polymeric structure for the native low-valent titanium species, and in the case of some *s-cis*-enones, they can be explained by the intervention of a oxametallacyclopentene.

The reductive coupling of carbonyl compounds by a low-valent transition metal has been the subject of many studies.[1] Most of these are of practical value for the synthesis of diols or alkenes.[2] In order to extend the scope of the reaction, reductive dimerization of α,β-enones has been investigated.[3] In this paper, we emphasize the mechanistic aspects and stereochemical implications. Only those studies on Ti(0) reagents, resulting from the reduction of $TiCl_3$ by $LiAlH_4$ (McMurry's reagent), K, or Mg on saturated or aromatic ketones have been reported.[1,2,4] Surprisingly, few investigations have been reported involving the coupling of enones and the cross-coupling between enones and an excess of acetone.[1a,4b,5]

Mechanistic studies are intricate because most of the reagents used are of unknown structure. For Ti(0) reagents, the metal surface has been proposed as the active coupling species.[4b,c] Many low-valent transition metal complexes have been described,[6] but, to our knowledge,

Chart I[a]



[a] **a**, $R^1 = R^2 = R^4 = H$, $R^3 = CH_3$; **b**, $R^1 = R^3 = R^4 = CH_3$, $R^2 = H$; **c**, $R^1 = CH_3$, R^2–$R^3 = -(CH_2)_3-$, $R^4 = CH_3$.

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