tyllithium (2.5 M in hexanes) (0.88 mL, 2.2 mmol) was added, and stirring was continued for an additional 20 min. The temperature was lowered to −50 °C, and 2-chlorotropone[5c] (281 mg, 2 mmol) in 1 mL of THF was added. Stirring was continued at this temperature until all of the chlorotropone was consumed as judged by TLC analysis (1:1 petroleum ether–ether). The reaction mixture was quenched with saturated aqueous ammonium chloride solution, diluted with ether, washed with brine, and dried over anhydrous sodium sulfate. Removal of solvent in vacuo and purification of the crude product by flash chromatography (6 g of silica gel; 80% petroleum ether, 20% ether as eluent) gave 141 mg (65%) of product: IR (CCl_4) 1739, 1722, 1635, 1587, 1326 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.26 (t, J = 7 Hz, 3 H), 3.67 (s, 2 H), 3.76 (s, 2 H), 4.19 (q, J = 7 Hz, 2 H), 7.00–7.34 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 13.95, 48.97, 49.55, 61.14, 133.54, 133.88, 136.09, 137.54, 140.45, 148.74, 167.28, 186.06, 199.51; mass spectrum, m/e (%) 234 (5), 188 (16), 147 (59), 120 (100), 92 (65), 65 (31); high-resolution mass spectrum calcd for $C_{13}H_{14}O_4$ 234.0891, found 234.0895.

2-[1-(2-Oxopropyl)]-2,4,6-cycloheptatrien-1-one was prepared as described in the *general* procedure for the addition of lithium enolates to 2-chlorotropone: IR (CCl_4) 1719, 1639 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.27 (s, 3 H), 3.62 (s, 2 H), 6.93–7.25 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 30.21, 49.62, 133.48, 133.52, 135.83, 137.12, 140.40, 149.00, 186.14, 204.90; high-resolution mass spectrum calcd for $C_{10}H_{10}O_2$ 162.0878, found 162.0915.

2-(1-Carbomethoxy-4,6-heptadien-1-yl)-2,4,6-cycloheptatrien-1-one: IR (CCl_4) 1736, 1635, 1592 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.80 (q, J = 8 Hz, 2 H), 2.20 (q, J = 8 Hz, 2 H), 3.68 (s, 3 H), 3.95 (t, J = 9.5 Hz, 1 H), 5.17 (m, 2 H), 5.68 (m, 1 H), 6.10 (m, 1 H), 6.32 (m, 1 H), 7.01–7.45 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 25.80, 30.53, 48.07, 51.96, 117.34, 130.17, 131.87, 132.01, 133.46, 133.72, 135.25, 135.55, 140.93, 151.99, 173.71, 185.77; mass spectrum, m/e (%) 258 (4), 198 (9), 178 (27), 159 (18), 146 (100), 131 (16), 115 (11), 91 (15), 77 (17); high-resolution mass spectrum calcd for $C_{16}H_{18}O_3$ 258.1255, found 258.1261.

2-(1-Carbomethoxycyclobutan-1-yl)]-2,4,6-cycloheptatrien-1-one: IR (CCl_4) 1734, 1638, 1588 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.76 (m, 1 H), 2.18 (m, 3 H), 2.69 (m, 2 H), 3.58 (s, 3 H), 6.91–7.29 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 15.98, 30.61, 51.99, 53.08, 132.77, 132.97, 133.38, 135.41, 140.45, 155.84, 174.93, 185.79; mass spectrum, m/e (%) 218 (5), 186 (30), 159 (71), 141 (19), 131 (100), 115 (23), 103 (49), 91 (25), 77 (60); high-resolution mass spectrum calcd for $C_{13}H_{14}O_3$ 218.0942, found 218.0946.

2-(2,3,4,5-Tetrahydro-2-oxofuran-3-yl)-2,4,6-cycloheptatrien-1-one: IR (CCl_4) 1768, 1679, 1588 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.30–4.41 (m, 1 H), 2.47–2.60 (m, 1 H), 3.77 (t, J = 10 Hz, 1 H), 4.36 (q, J = 8.5 Hz, 1 H), 4.56 (dt, J = 8.5, 3.6 Hz, 1 H), 6.96–7.37 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 27.99, 46.96, 66.95, 133.50, 134.54, 136.17, 137.47, 141.12, 150.66, 172.24, 185.26; mass spectrum, m/e (%) 190 (5), 146 (59), 118 (100), 91 (16), 77 (15); high-resolution mass spectrum calcd for $C_{11}H_{10}O_3$ 190.1982, found 190.1979.

Acknowledgment. We thank the National Institutes of Health (Grant GM-30771) for their support of this research.

Registry No. 1, 539-80-0; 2, 3839-48-3; $MeCOCH_2CO_2Et$, 141-97-9; $H_2C{=}CHCH{=}CH(CH_2)_3CO_2Me$, 73501-25-4; MeCOMe, 67-64-1; $MeCO_2Bu$-*t*, 540-88-5; Me_2CHCO_2Et, 97-62-1; cyclohexanone, 108-94-1; methyl cyclobutanecarboxylate, 765-85-5; 2,3,4,5-tetrahydro-2-furanone, 96-48-0; 2-methyltropone, 29639-53-0; 2-(1,3-dioxolan-2-yl)ethyltropone, 115912-59-9; 2-(2-*tert*-butoxy-2-oxoeth-1-yl)cyclohepta-3,5-dien-1-one, 115912-60-2; 2-(2-oxoprop-1-yl)cyclohepta-3,5-dien-1-one, 115912-61-3; 2-(2-*tert*-butoxy-2-oxoeth-1-yl)-7-methylcyclohepta-3,5-dien-1-one, 115912-62-4; 2-(2-*tert*-butoxy-2-oxoeth-1-yl)-7-[2-(1,3-dioxolan-2-yl)ethyl]cyclohepta-3,5-dien-1-one, 115912-63-5; 2-(1,1-dimethyl-2-ethoxy-2-oxoeth-1-yl)cyclohepta-3,5-dien-1-one, 115912-64-6; 2-(2-oxocyclohex-1-yl)cyclohepta-3,5-dien-1-one, 115912-65-7; 2-(4-ethoxy-2,4-dioxobut-1-yl)-2,4,6-cycloheptatrien-1-one, 115912-66-8; 2-[1-(2-oxopropyl)]-2,4,6-cycloheptatrien-1-one, 39479-44-2; 2-(1-carbomethoxy-4,6-heptadien-1-yl)-2,4,6-cycloheptatrien-1-one, 115912-67-9; 2-(1-carbomethoxycyclobutan-1-yl)-2,4,6-cycloheptatrien-1-one, 115912-68-0; 2-(4,5-dihydro-2-oxofuran-3-yl)-2,4,6-cycloheptatrien-1-one, 115912-69-1; *tert*-butyl bromomagnesium acetate, 115912-70-4.

Electrochemical 1,2-Addition of Trifluoromethyl and Acetamide Groups to Methyl Methacrylate

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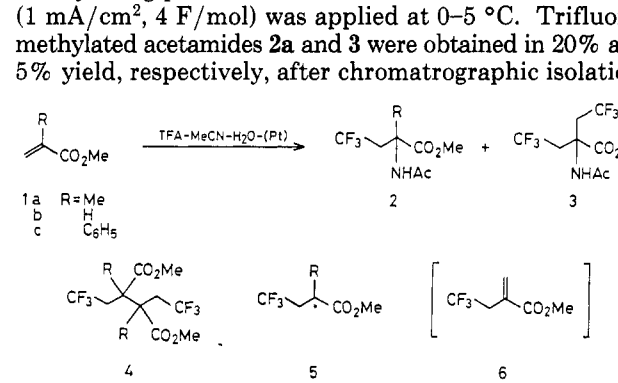
Received January 11, 1988

Organofluorine compounds have attracted increasing attention for medicinal and agricultural usage and for material science.[1] Biologically active trifluoromethylated amino acid derivatives[2] have also been prepared.[3]

Trifluoromethylation by the use of metal complexes of trifluoromethyl iodide,[4] *N*-(trifluoromethyl)-*N*-nitrosotrifluoromethanesulfonamide,[5] and perfluoroacyl peroxide[6] has been known, but no reagent can realize 1,2-addition of the trifluoromethyl group and a nucleophile to the carbon–carbon double bond. The desired 1,2-addition requires an oxidation step during the reaction course. An electrochemical trifluoromethylation of olefins would be promising for the purpose. Here we describe a novel electrochemical trifluoromethyl–acetamidation in which trifluoromethyl and acetamide groups are incorporated at the β- and α-carbons of an α,β-unsaturated carboxylate, respectively.

Electrolysis of a mixture of trifluoroacetic acid (TFA, 6 mmol) and methyl methacrylate (MMA, 2 mmol) in acetonitrile (MeCN, 20 mL)–water (3 mL) containing sodium hydroxide (0.6 mmol) was conducted in an undivided cell by using platinum foil electrodes. Constant current (1 mA/cm^2, 4 F/mol) was applied at 0–5 °C. Trifluoromethylated acetamides **2a** and **3** were obtained in 20% and 5% yield, respectively, after chromatrographic isolation.



The acetamide **2a** is easily separable by column chromatography and thus could be prepared on a large scale. This compound exhibited the following spectral characteristics consistent with the assigned structure. The ^{13}C NMR spectrum shows two quartets at 125.8 (J = 278.5 Hz) and 38.0 ppm (J = 27.5 Hz), revealing a CF_3CH_2 moiety. The ^{19}F NMR spectrum gives a triplet at 99.2 ppm (J = 10.3 Hz), suggesting a CF_3CH_2 group. The IR spectrum shows strong bands at 3258 and 1652 cm^{-1} characteristic for an

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0022-3263/88/1953-4598$01.50/0

NHAc group. A parent peak (m/e 227) was observed in the mass spectrum of **2a**.

The yield of **2a** decreased and that of **3** increased gradually by increasing current density. Dimethyl 2,3-dimethyl-2,3-bis(2,2,2-trifluoroethyl)succinate (**4a**) was also isolated in about 3% yield and identified by comparison with an authentic sample.[7] Most of the other products were unidentified because of their volatility.

It must be pointed out that Renaud has reported the formation of **4a** (9.8% yield) as the only isolated product in the electrolysis of MMA in methanol or acetic acid, but no formation of the corresponding trifluoromethyl-methoxylated or acetoxylated compound is reported.[7] In sharp contrast to MMA, the electrochemical trifluoromethylation of methyl acrylate[8] afforded dimer **4b** formed from the trifluoromethylated radical **5b**, and the corresponding acetamide **2b** was not isolated. We also observed the preferential dimer **4b** formation (40–50% yield) on the electrolysis of methyl acrylate under our experimental conditions.

The formation of different products can be rationalized as follows. The addition of the electrochemically generated trifluoromethyl radical to MMA leads to radical **5a**, which would suffer further one-electron oxidation and the successive acetamidation leading to **2a**. Alternatively, the formation of the intermediate **6**[9] by dehydrogenation from the methyl group of **5a** followed by addition of another CF_3 radical, one-electron oxidation, and acetamidation at the final stage would result in the formation of **3**. The use of a 2:1 ratio of MMA to TFA results in the decreased formation of **3** and the increase of **4a** as indicated by VPC. On the other hand, electrolysis of methyl α-phenylacrylate under similar conditions failed to produce the desired acetamide **2c** because substrate **1c** was electrooxidized much faster than TFA. In fact, the cyclic voltammogram of **1c** in MeCN–Et_4NClO_4–TFA reveals a sharp anodic current at around 1.7 V vs Ag/Ag^+, while the currents of **1a** and **1b** were observed at around 2.5 V, quite close to that of TFA in MeCN–Et_4NClO_4.

The four types of reaction modes on the electrochemical trifluoromethylation of olefins so far known are (1) addition of the CF_3 group to the carbon–carbon double bond followed by dimerization,[7-11] (2) addition of the CF_3 group followed by hydrogen abstraction,[7-10,12] (3) 1,2-addition of two CF_3 groups to olefin,[7-11] and (4) addition of the CF_3 group followed by elimination of hydrogen leading to trifluoromethylated olefin (substitution of hydrogen on sp^2 carbon with the CF_3 group).[7-10] The present electrochemical trifluoromethyl–acetamidation is the first example of 1,2–addition of a CF_3 group and a nucleophile to a carbon–carbon double bond.

Experimental Section

All reagents were commercially available and were used without further purification. Melting points were uncorrected. Infrared spectra were taken on a Hitachi 270–30 spectrometer. ^1H, ^{13}C, and ^{19}F NMR spectra were measured on a Varian VXR-500 instrument 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-M80A instrument (20 eV).

Electrolysis of TFA in the Presence of MMA. (a) Excess of TFA. MMA (200 mg, 2 mmol), TFA (0.46 mL, 6 mmol), and sodium hydroxide (24 mg, 0.6 mmol) were dissolved a mixture of acetonitrile (20 mL) and water (3 mL) in a cylindrical electrolysis cell. Two platinum foils were used as an electrode, and the mixture was electrolyzed under a constant current of 24 mA (1 mA/cm^2) at 0–5 °C for 8 h and 55 min (4 F/mol based on MMA). The solution was neutralized with saturated $NaHCO_3$, the organic layer was separated, and the aqueous layer was extracted with ethyl acetate (3 × 4 mL). The combined organic extracts were washed with saturated NaCl, dried (Na_2SO_4), and concentrated in vacuo. The residue was submitted to flash column chromatography, affording 91 mg (20%) of **2a** and 30 mg (5%) of **3**.

Methyl 2-(acetylamino)-2-methyl-4,4,4-trifluorobutyrate (2a): mp 95–97 °C; IR (KBr) 3258 (NH), 1738 (C=O), 1652 (NHC=O), 1568, 1460, 1378, 1263, 1176, 1104, 1056 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.45 (1 H, s, NH), 3.80 (3 H, s, OCH_3), 3.43 (1 H, dq, J_1 = 15.6 Hz, J_2 = 10.7 Hz, CH_2CF_3), 2.82 (1 H, dq, J_1 = 15.6 Hz, J_2 = 10.7 Hz, CH_2CF_3), 2.01 (3 H, s, Ac), 1.67 (3 H, s, CH_3); ^{13}C NMR ($CDCl_3$) δ 24.0 (s, CH_3), 24.1 (s, CH_3), 38.0 (q, J = 27.5 Hz, CH_2), 53.6 (s, OCH_3), 56.6 (q, J = 2.3 Hz, CNH), 125.8 (q, J = 278.5 Hz, CF_3), 170.3 (s, C=O), 173.6 (s, C=O); ^{19}F NMR ($CDCl_3$) δ 99.2 (t, J = 10.3 Hz); MS, m/e (relative intensity) 227 (1), 196 (1), 184 (1), 168 (32), 126 (100), 102 (8), 43 (42). Anal. Calcd for $C_8H_{12}F_3O_3N$: C, 42.29; H, 5.32; N, 6.17. Found: c, 42.50; H, 5.45; N, 6.23.

Methyl 2-(acetylamino)-2-(2,2,2-trifluoroethyl)-4,4,4-trifluorobutyrate (3): mp 58–59 °C; IR (KBr) 3436, 3388 (NH), 1754 (C=O), 1690 (NHC=O), 1512, 1376, 1354, 1256, 1212, 1166, 1100, 1048 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.68 (1 H, s, NH), 3.87 (3 H, s, OCH_3), 3.69 (2 H, dq, J_1 = 15.6 Hz, J_2 = 10.7 Hz, CH_2CF_3), 3.48 (2 H, dq, J_1 = 15.6 Hz, J_2 = 10.7 Hz, CH_2CF_3), 2.02 (3 H, s, Ac); ^{13}C NMR ($CDCl_3$) δ 23.9 (s, CH_3), 38.2 (q, J = 28.2 Hz, CH_2), 54.2 (s, OCH_3), 56.3 (q, J = 3.0 Hz, CNH), 124.9 (q, J = 278.3 Hz, CF_3), 170.7 (s, C=O), 171.1 (s, C=O); ^{19}F NMR ($CDCl_3$) δ 99.1 (t, J = 9.6 Hz); MS, m/e (relative intensity) 295 (4), 253 (1) 236 (1), 194 (78), 174 (6), 170 (10), 110 (10), 59 (4), 43 (100). Anal. Calcd for $C_9H_{11}F_6O_3N$: C, 36.62; H, 3.76; N, 4.75. Found: C, 36.90; H, 3.43; N, 4.40.

(b) Equivalent of TFA and MMA. MMA (0.22 mL, 2 mmol), TFA (228 mg, 2 mmol), and sodium hydroxide (16 mg, 0.4 mmol) were dissolved in a mixture of acetonitrile (14 mL) and water (2 mL) in a cylindrical electrolysis cell. The mixture was electrolyzed under a constant current of 60 mA (20 mA/cm^2) at 0–5 °C for 86 min (1.6 F/mol based on TFA). The residue was submitted to flash column chromatography, affording 80 mg (18%) of **2a**, a trace amount of **3**, and 20 mg (3%) of **4a**. MMA was recovered in ca. 20% yield (by VPC analysis).

Acknowledgment. We are grateful to The Mazda Foundation, The Japan Securities Scholarship Foundation, and the Ministry of Education, Science, and Culture of Japan (Scientific Research on Priority Area No. 63607521) for the finanical support and the SC-NMR Laboratory of Okayama University for the 500-MHz NMR experiment.

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Absolute Configuration of L-659,699, a Novel Inhibitor of Cholesterol Biosynthesis

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Received March 16, 1988

L-659,699, a naturally occurring β-lactone isolated from *Fusarium* sp.[1] and *Scopulariopsis* sp.,[2] is a potent, specific

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