1,1,2-Trifluoro-1,3-butadiene: A Convenient C_4 Intermediate for Functionalized Monofluoroolefins

Noritada Matsuo and Andrew S. Kende*

Department of Chemistry, University of Rochester, Rochester, New York 14627

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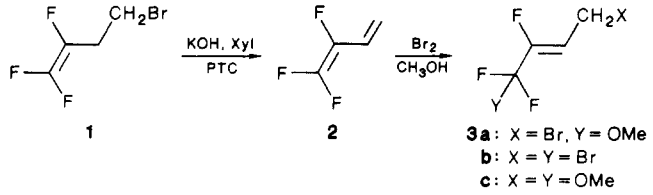
The regioselective methoxybromination of 1,1,2-trifluoro-1,3-butadiene to give (*Z*)-4-bromo-1-methoxy-1,1,2-trifluoro-2-butene (**3a**) is reported. This can easily be transformed into a wide range of (*Z*)-2-fluoro-2-alkenoates (**4a–c**, **5**). The reaction of benzenesulfenyl chloride with 1,1,2-trifluoro-1,3-butadiene leads to the formation of the 1,2-adduct, which is converted to a series of fluorinated sulfones. By use of these fluorinated compounds, the 2-fluoro analogue (**9a**) of the known insecticide piperine (**9b**) and the monofluorochrysanthemic acid derivative (**15**) are readily synthesized.

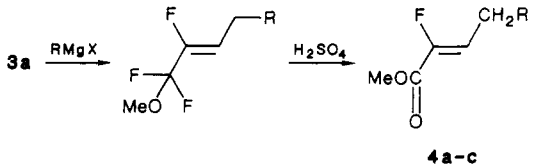
Recent interest in the synthesis of stereochemically homogeneous (*Z*)-2-fluoro-2-alkenoate esters and their derivatives[1] has underscored the scarcity of simple, general methodology for construction of these and related monofluoroalkene derivatives.[2] We describe here new chemistry of 1,1,2-trifluoro-1,3-butadiene (**2**), a readily accessible C_4 intermediate, which provides facile and versatile entry to a variety of functionalized monofluoroalkene systems.

Reaction of commercially available[3] 4-bromo-1,1,2-trifluoro-1-butene (**1**) in xylenes with potassium hydroxide solution in the presence of the phase-transfer catalyst, tetrabutylammonium bromide, at 60 °C gave a 93% yield of the known, volatile 1,1,2-trifluoro-1,3-butadiene (**2**).[4] When this diene was allowed to react in methanol with bromine in the presence of potassium carbonate, there were produced (*Z*)-4-bromo-1-methoxy-1,1,2-trifluoro-2-butene (**3a**) accompanied by the 1,4-dibromo adduct **3b** and the solvolysis product **3c**. The ratios of these products depended on reaction temperature and the amount of base (Table I). The best yield of **3a** was obtained at −70 °C by using 2 equiv of potassium carbonate.

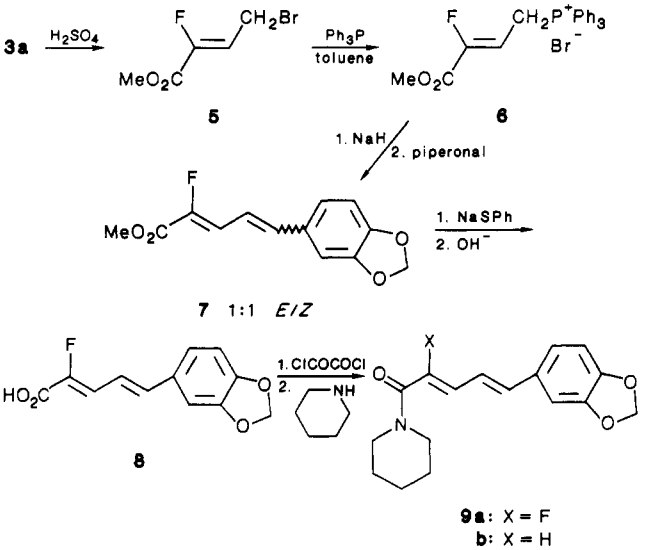


The structure of methoxy bromide **3a** was established by its mass spectrum and by its proton NMR, which revealed the diagnostic olefinic proton as a doublet (J_{FH} = 31 Hz) of triplets (J_{HH} = 9 Hz) centered at δ 5.76. The observed regiochemistry leading to **3a** is consistent with the known[5] addition of bromine to 1,1,2-trifluoro-1,3-butadiene as well as the established regiochemistry of HBr addition to trifluoroethylene.[6]

Compound **3a** contains a CF_2OMe unit[7] which may be recognized as a masked ester function. This was exploited by reaction of **3a** with a variety of Grignard reagents to yield C-4 alkylation products that were converted by hydrolysis in dilute sulfuric acid at 20 °C to the corresponding methyl esters **4a**, **4b**, and **4c** (Table II). Alternatively,



direct hydrolysis of bromide **3a** using 75% sulfuric acid in a two-phase reaction system gave 69% of the known[8] bromo ester **5**. This reacted smoothly with triphenylphosphine in toluene to give the crystalline phosphonium bromide **6**. This activated phosphonium system was



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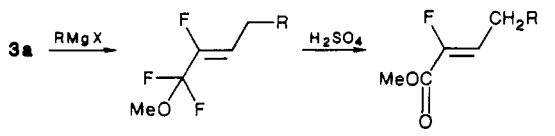
0022-3263/88/1953-2304$01.50/0

Table I

run	base (equiv)	solvent	temp, °C (time, h)	product ratios[a] 3a	3b	3c	isol yield
1	AcONa (3.3)	AcOH	0		100		56% of **3b**
2	K_2CO_3 (1.2)	MeOH	−70 (2) 20 (12)	60	40	0	
3	K_2CO_3 (2.0)	MeOH	0 (1.5)	77	23	0	
4	K_2CO_3 (2.0)	MeOH	−70 (2) 20 (12)	41		59	
5	K_2CO_3 (2.0)	MeOH	−70 (2)	92	8	0	78% of **3a**

[a] By 300-MHz ^1H NMR analysis.

Table II

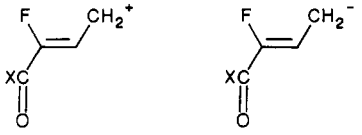


4a-c

	R =	% yield
4a	n-C_8H_{13}	52
4b	C_6H_5	42
4c	C_2H_5	48

readily transformed by sodium hydride in tetrahydrofuran to the corresponding phosphorane, which in turn reacted readily with piperonal to give the dienes **7** having a 1:1 ratio of the 4*E* to 4*Z* double bond. Isomerization of this diene mixture with sodium thiophenoxide gave cleanly the thermodynamic 2*Z*, 4*E* ester. Saponification produced the dienoic acid **8**, mp 225 °C, which was converted to the acid chloride by oxalyl chloride. Reaction with piperidine gave the crystalline piperidide **9a**, mp 97–98 °C. This new compound is the 2-fluoro analogue of the known insecticide piperine (**9b**).[9]

It is evident from the above examples that the C_4 methoxy bromide **3a** serves as the structural equivalent of either synthon **10a** or **10b**, permitting carbon–carbon bond formation at C-4 with suitable nucleophiles and electrophiles, respectively.

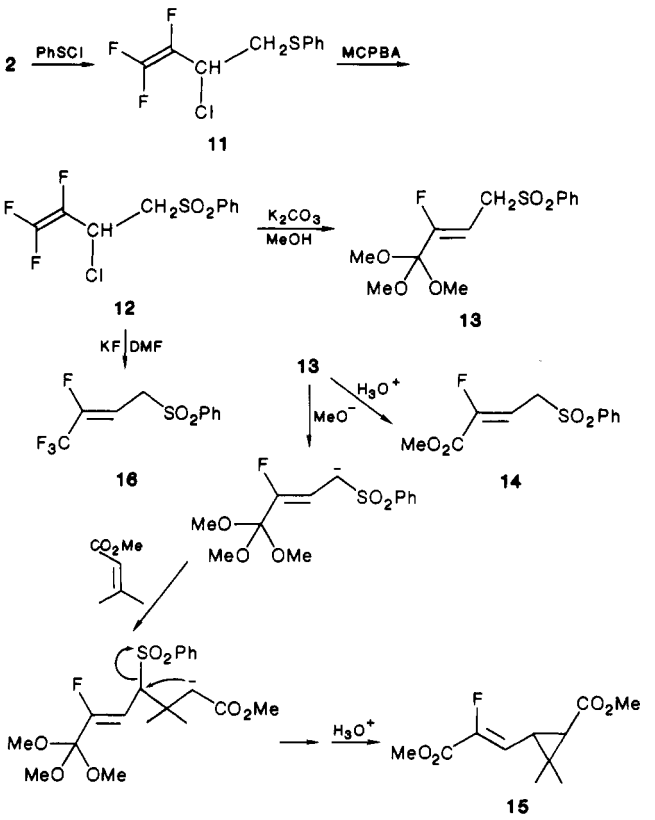


10a **10b**

Fluorinated Sulfones. A somewhat different C_4 synthon is available from the reaction of the trifluorobutadiene **2** with benzenesulfenyl chloride.[10] In this case the sole product was the 1,2 adduct **11**, isolated in nearly quantitative yield (Scheme I). Oxidation of thioether **11** with excess *m*-chloroperbenzoic acid gave the fluoro sulfone **12**, which underwent a useful transformation in methanolic potassium carbonate to produce the ortho ester **13** in 95% yield. The ortho ester structure was confirmed by 300-MHz ^1H NMR which revealed three equivalent methoxy groups, a methine proton at δ 3.98 as a doublet of triplets with J = 31 and 9 Hz corresponding to geminal H–F and geminal H–H coupling, and a two-proton doublet (J = 9 Hz) for the protons α to the phenylsulfonyl group.

Chemical evidence for ortho ester **13** was obtained by mild hydrolysis to the sulfone ester **14**, mp 105 °C, in essentially quantitative yield. On the other hand, the

Scheme I



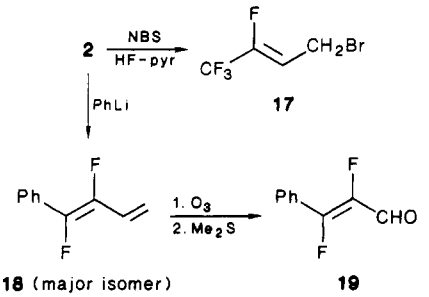
apparent stability of ortho ester **13** toward vinylogous β-elimination was illustrated by its use as an anionic C_4 monofluoroalkene synthon in the preparation of a monofluorochrysanthemic acid derivative.[11] Thus, when ortho ester **13** was stirred with methyl senecioate in dimethylformamide using 2.7 equiv of sodium methoxide, a Michael reaction of the sulfone anion followed by ring closure occurred to yield on hydrolysis the chrysanthemate analogue **15**, by the pathway shown.[12] It is noteworthy that the sulfone ester **14** did not condense at all with methyl senecioate under a variety of basic reaction conditions.

Reaction of ortho ester **13** with potassium fluoride in dimethylformamide smoothly converted it to the trifluoromethyl derivative **16**, mp 84 °C. The chemistry of this interesting tetrafluoro sulfone has not been further explored.

Bromofluorination of Diene 2. Informed by the previously described regiospecific additions we explored the use of Olah's bromofluorination conditions[13] on diene **2**. Reaction of the trifluorobutadiene **2** with *N*-bromo-

(9) Harvill, E. K.; Harzell, A.; Arthur, J. M. *Contrib. Boyce Thompson Inst.* **1943**, *13*, 87.
(10) Mueller, W. H.; Butler, P. E. *J. Am. Chem. Soc.* **1968**, *90*, 2076.
(11) Tessier, J.; Demoute, J. P. Eur. Pat. Appl. EP 114012 (Roussel-UCLAF); *Chem. Abstr.* **1985**, *102* 5763k.
(12) For an analogous synthesis of chrysanthemate esters, see: Martel, J.; Hyunh, C. *Bull. Soc. Chim. Fr.* **1967**, 985.
(13) Olah, G. A.; Nojima, M.; Kerekes, I. *Synthesis* **1973**, 780.

succinimide and HF–pyridine in dichloromethane gave a 52% yield of a product identified by proton and ^{19}F NMR as the known tetrafluoro bromide **17**.[14] Despite its ready access by this route we have not further explored the chemistry of this allylic bromide.



(*E*)-Difluorocinnamaldehyde. We have found that the trifluorobutadiene **2** serves as a valuable precursor to (*E*)-1,2-difluoroalkenes. It is known that organolithium compounds add to trifluorochloroethylene followed by loss of fluoride to give mainly (*E*)-difluoroalkenes with not more than 80% *E* selectivity.[15a] However, when phenyllithium was allowed to react with diene **2**, the resulting major product 1,2-difluoro-1-phenyl-1,3-butadiene (**18**) was obtained in 70% yield and shown by proton NMR to contain at most 10% of the *Z* isomer.[15b] When this reaction product was treated at −70 °C with a slight excess of ozone followed by dimethyl sulfide workup, we obtained in 64% yield the hitherto unknown (*E*)-2,3-difluorocinnamaldehyde (**19**), mp 32–33 °C. The latter is itself a potentially valuable arylated C_3 synthon for subsequent additions and homologations.

Conclusion. The simple trifluoro diene **2** provides a C_4 synthon in which the fluorine at C-2 may be retained in the course of a variety of electrophilic and nucleophilic operations on the diene system. By suitable stepwise functionalizations at the 1,4-termini of such intermediates, we can prepare long-chain (*Z*)-2-fluoroalkenoic acid derivatives, their 4-halo, 4-phenylthio, and 4-sulfonyl substitution products, 1,1,1,2-tetrafluoro-2-butene derivatives, and (*E*)-difluoroethylene systems. Further transformations of the various fluorinated intermediates obtained by such chemistry are under exploration.

Experimental Section

Products were identified by elemental analysis, IR spectroscopy (Perkin-Elmer 1310 infrared spectrometer), and ^1H (Nicolet QE-300 MHz), ^{19}F (Hitachi 90 N), and mass spectrometry (Nermag R10-10C). The ^{19}F figures quoted are φ chemical shifts in ppm. from internal trichlorofluoromethane and the ^1H figures are δ values in $CDCl_3$, internal tetramethylsilane standard.

1,1,2-Trifluoro-1,3-butadiene (2). To a solution of 12.0 g (214 mmol) of potassium hydroxide in 12.0 mL of water at room temperature in a 100-mL round-bottom flask with a reflux condenser was added in one portion a mixture of 4-bromo-1,1,2-trifluoro-1-butene (15.0 g, 79.4 mmol) and tetrabutylammonium bromide (0.50 g) in 20 mL of xylenes. A very fine stream of nitrogen gas was slowly bubbled into the reaction mixture through a glass tube extending into the solution, while the exit stream of nitrogen was passed through the vertical water-cooled reflux condenser, the calcium chloride tube, and then into a trap held at −78 °C. The reaction mixture was warmed to 60 °C and held there for 5 h. The desired trifluorobutadiene was collected in the cold trap as a clear liquid (7.95 g, 93% yield) and characterized by its ^1H NMR (300 MHz, $CDCl_3$): δ 5.24 (1 H, d, J = 12 Hz), 5.49 (1 H, d, J = 18 Hz), 6.20 (1 H, m). ^{19}F NMR ($CDCl_3$): φ F^3 = −15.6, F^2 = 120.0, F^1 = 103.6, $J(F^{12})$ = 66.2 Hz, $J(F^{23})$ = 107.5 Hz, $J(F^{13})$ = 28.9 Hz, $J(F^3H)$ = 24.8 Hz.

(*Z*)-4-Bromo-1-methoxy-1,1,2-trifluoro-2-butene (3a). To a solution of 5.30 g (49.1 mmol) of 1,1,2-trifluoro-1,3-butadiene in methanol (70 mL) at 0 °C in a round-bottom 250-mL flask was added 12.50 g of potassium carbonate (anhydrous powder). The flask was equipped with a magnetic stirrer, and the stirred contents were cooled to ca. −70 °C. Bromine (2.50 mL, 48.4 mmol) was slowly added to the −70 °C reaction mixture over 2 h, and the resulting mixture was stirred for a further 2 h at −50 °C. At this point the contents of the flask were poured into a large excess of ice–water, and the liquid was extracted twice with diethyl ether. The ether layers were combined, washed once with brine, and then dried over anhydrous magnesium sulfate. Evaporation of solvent gave 7.50 g (70.2%) of (*Z*)-4-bromo-1-methoxy-1,1,2-trifluoro-2-butene as a clear liquid which was distilled at 74 °C (40 mmHg). ^1H NMR (300 MHz, $CDCl_3$): δ 3.62 (3 H, s), 3.98 (2 H, d, J = 9 Hz), 5.76 (1 H, dt, J = 9, 31 Hz). Mass spectrum: m/e 218, 220 (M^+). ^{19}F NMR ($CDCl_3$): φ 79.2 (d, J = 14.2 Hz), 126.5 (dtt, J = 31.0, 14.0, 2.4 Hz).

(*Z*)-Methyl 2-Fluoro-2-decenoate (4a). To a solution of 1.0 g (4.5 mmol) of 4-bromo-1-methoxy-1,1,2-trifluoro-2-butene in 15.0 mL of tetrahydrofuran at −60 °C in a 50-mL round-bottom flask was added a solution of *n*-hexylmagnesium bromide (2 M, 5.0 mL, 10.0 mmol) in diethyl ether. The reaction mixture was stirred for 2 h at 0 °C. The contents of the flask were poured into a large excess of an aqueous ammonium chloride solution, and the liquid was extracted twice with diethyl ether. The ether layers were combined, washed once with brine, and then dried over anhydrous magnesium sulfate. Evaporation of solvent gave 1.20 g of 1-methoxy-1,1,2-trifluoro-2-decene. ^1H NMR (300 MHz, $CDCl_3$): δ 0.85 (3 H, t), 1.23 (10 H, brs), 2.12 (2 H, m), 3.60 (3 H, s), 5.39 (1 H, dt, J = 8, 34 Hz). Without further purification this crude oil was transformed to the ester as follows.

To a mixture of 3 g of 75% sulfuric acid and 15 mL of *n*-pentane at 20 °C in a round-bottom 50-mL flask was added the crude 1-methoxy-1,1,2-trifluoro-2-decene (1.2 g). The resulting mixture was stirred for 40 h at 20 °C. The reaction mixture was poured into a large excess of ice–water and the liquid was extracted twice with diethyl ether. The ether layers were combined, washed with water and brine, and then dried over anhydrous magnesium sulfate. Evaporation of solvent gave a yellow oil which was chromatographed on silica gel (5% ethyl acetate in hexanes) to give 0.59 g (64.5%) of (*Z*)-methyl 2-fluoro-2-decenoate as a clear liquid. ^1H NMR (300 MHz, $CDCl_3$): δ 0.86 (3 H, t), 1.24 (10 H), 2.22 (2 H, dq, J = 2, 8 Hz), 3.80 (3 H, s), 6.10 (1 H, dt, J = 8, 33 Hz). Mass spectrum: m/e 202 (M^+). ^{19}F NMR ($CDCl_3$): φ 131.8 (d, J = 33.0 Hz).

(*Z*)-Methyl 2-Fluoro-4-phenyl-2-butenoate (4b). To a solution of 1.0 g (4.5 mmol) of 4-bromo-1-methoxy-1,1,2-trifluoro-2-butene in 15.0 mL of tetrahydrofuran at −60 °C was added a solution of phenylmagnesium bromide (3 M, 1.6 mL, 4.8 mmol) in diethyl ether and the mixture was stirred for 1 h at −60 °C and then stirred for 12 h at 20 °C. The workup and acidic hydrolysis were done as mentioned for the synthesis of **4a** to give 0.34 g (42%) of (*Z*)-methyl 2-fluoro-4-phenyl-2-butenoate. ^1H NMR (300 MHz, $CDCl_3$): δ 3.58 (2 H, dd, J = 2, 9 Hz), 3.81 (3 H, s), 6.29 (1 H, dt, J = 9, 31 Hz), 7.18–7.34 (5 H, m). Mass spectrum: m/e 194 (M^+). ^{19}F NMR ($CDCl_3$): φ 131.3 (d, J = 31.1 Hz).

(*Z*)-Methyl 2-Fluoro-2-hexenoate (4c). 4-Bromo-1-methoxy-1,1,2-trifluoro-2-butene (1.0 g, 4.5 mmol) was allowed to react with ethylmagnesium bromide (3 M, 1.6 mL, 4.8 mmol) in diethyl ether according to the same procedure as **4b** to give 0.29 g (48%) of (*Z*)-methyl 2-fluoro-2-hexenoate. ^1H NMR (300 MHz, $CDCl_3$): δ 0.92 (3 H, t), 1.46 (2 H, q), 2.20 (2 H, dq, J = 2, 8 Hz), 3.80 (3 H, s), 6.11 (1 H, dt, J = 8, 33 Hz).

(*Z*)-Methyl 4-Bromo-2-fluoro-2-butenoate (5). To a mixture of 3.0 g of 75% sulfuric acid and 15 mL of *n*-pentane was added 1.0 g (4.6 mmol) of 4-bromo-1-methoxy-1,1,2-trifluoro-2-butene at room temperature in a 50-mL round-bottom flask. The resulting mixture was stirred for 48 h at room temperature. The reaction was added to excess ice–water and the liquid was extracted with diethyl ether. The ether layer was successively

(14) Piccardi, P.; Modena, M.; Santoro, E. *J. Chem. Soc., Perkin Trans. 1* **1972**, 1146.

(15) Reactions of organolithium compounds with simple polyfluoroethylenes are described: (a) Sauvetre, R.; Normant, J. F. *Bull. Soc. Chim. Fr.* **1972**, 3202. (b) Martin, S.; Sauvetre, R.; Normant, J. F. *J. Organomet. Chem.* **1984**, *264*, 155.

washed with water and brine and then dried over anhydrous magnesium sulfate. Evaporation of the solvent in vacuo gave the crude ester which was purified by chromatography on silica gel to give 0.62 g (68.9%) of (*Z*)-methyl 4-bromo-2-fluoro-2-butenoate. Analytical sample distilled at 90–92 °C (18 mmHg). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.84 (3 H, s), 4.40 (2 H, dd, *J* = 2.5, 9 Hz), 6.35 (1 H, dt, *J* = 9, 30 Hz). ^{19}F NMR ($CDCl_3$): φ 122.5 (d, *J* = 30.2 Hz).

[(*Z*)-3-Fluoro-3-(methoxycarbonyl)-2-propenyl]triphenylphosphonium Bromide (6). Triphenylphosphine (2.0 g, 7.6 mmol) was added to a solution of 1.50 g (7.6 mmol) of methyl 4-bromo-2-fluoro-2-butenoate in 20 mL of toluene at room temperature in a 50-mL round-bottom flask. The flask was equipped with a reflux condenser and the mixture was stirred for 10 h at 60 °C. The contents of the flask were filtered and the white precipitate was washed with excess toluene. The precipitate was purified by recrystallization from ethyl acetate and chloroform (1:1) to give 3.1 g (88.6%) of the phoshonium salt as a white powder, mp 145–147 °C dec. Anal. Calcd for $C_{23}H_{21}BrFO_2P$: C, 60.12; H, 4.61; Br, 17.41. Found: C, 59.84; H, 4.97; Br, 17.03.

(2*Z*,4*E*)-2-Fluoro-5-[3,4-(methylenedioxy)phenyl]penta-2,4-dienoic Acid (8). Sodium hydride (0.13 g, 2.7 mmol, 50% dispersion in mineral oil) was added to a mixture of 1.21 g (2.6 mmol) of [(*Z*)-3-fluoro-3-(methoxycarbonyl)-2-propenyl]triphenylphosphonium bromide in 20 mL of tetrahydrofuran at 0 °C in a 50-mL round-bottom flask under a nitrogen atmosphere. The reaction mixture was stirred for 3 h at 20 °C. Subsequently, 0.39 g (2.6 mmol) of piperonal was added to the mixture at 20 °C in one portion and the resulting mixture was stirred further for 12 h at 20 °C. Then 30 mL of hexanes was added to the reaction, and the whole mixture was filtered. The filtrate was evaporated in vacuo to give the crude pentadienoate **7** (0.8 g). This was revealed to be a 1:1 mixture of 4*E* and 4*Z* isomers according to proton NMR. ^{1}H NMR of **7** (*E*/*Z* mixture): H_2 and H_1 protons of 2*Z*,4*Z* isomer appeared at δ 6.46 as a triplet (*J* = 10 Hz) and at 7.06 as a double doublet (*J* = 12, 32 Hz), respectively. Without purification, the crude material was dissolved in 5 mL of tetrahydrofuran. To this solution were added 66 mg (0.6 mmol) of thiophenol and 28 mg (0.58 mmol) of sodium hydride (50% dispersion in mineral oil) at 20 °C. The resulting mixture was stirred for 12 h at 20 °C. The contents of the flask were poured into 10 mL of cooled 5% aqueous hydrochloric acid, and the liquid was extracted twice with diethyl ether. The ether layers were combined, washed successively with 5% sodium bicarbonate solution and brine, and then dried over anhydrous magnesium sulfate. Evaporation of solvent gave 0.7 g of crude 2*Z*,4*E* ester. This was dissolved in 5.2 mL in methanolic potassium hydroxide at 20 °C. The solution was left standing for 30 h at 20 °C. At this point the contents of the flask were poured into 10 mL of 5% aqueous hydrochloric acid and the mixture was extracted twice with ethyl acetate. The organic layers were combined, washed once with brine, and then dried over anhydrous magnesium sulfate. Evaporation of the solvent gave the crude (0.42 g) 2*Z*,4*E* acid. Recrysallization from 30% ethyl acetate in *n*-hexane gave 0.25 g (40.8% yield from **6**) of (2*Z*,4*E*)-2-fluoro-5-[3,4-(methylenedioxy)phenyl]penta-2,4-dienoic acid as white crystals, mp 225 °C dec. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.80 (2 H, s), 6.52 (dd, *J* = 12, 30 Hz). Anal. Calcd for $C_{12}H_9FO_4$: C, 61.00; H, 3.84. Found: C, 60.95; H, 3.76.

1-[(2*Z*,4*E*)-2-Fluoro-5-[3,4-(methylenedioxy)phenyl]penta-2,4-dienoyl]piperidine (9a). Oxalyl chloride (0.5 mL, 5.7 mmol) was added to a solution of 80.5 mg (0.34 mmol) of (2*Z*,4*E*)-2-fluoro-5-[3,4-(methylenedioxy)phenyl]penta-2,4-dienoic acid in 1 mL of tetrahydrofuran in a round-bottom 10-mL flask at 20 °C. The resulting solution was stirred for 1 h at 50 °C. Evaporation of solvent gave the crude acid chloride. To a solution of this acid chloride in 1 mL of benzene was added 0.3 mL (3.0 mmol) of piperidine at 20 °C. The mixture was stirred 1 h at 20 °C. The reaction mixture was poured into 2 mL of ice-cooled 5% aqueous hydrochloric acid, and the liquid was extracted once with ethyl acetate. The organic layer was washed successively with 5% aqueous sodium bicarbonate solution and brine and then dried over anhydrous magnesium sulfate. Evaporation of solvent followed by chromatography on silica gel (elution with 30% ethyl acetate in *n*-hexane) gave the white solid. This was recrystallized from 30% ethyl acetate in hexanes to give 50.0 mg (49%) of the piperidide of (2*Z*,4*E*)-2-fluoro-5-[(3,4-methylenedioxy)phenyl]-penta-2,4-dienoic acid as white crystals, mp 97.5–98.0 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.62 (6 H, m), 3.53 (4 H, m), 5.95 (2 H, s), 6.39 (1 H, dd, *J* = 10, 33 Hz), 6.62 (1 H, d, *J* = 16 Hz), 6.75 (1 H, d, *J* = 8 Hz), 6.84 (1 H, dd, *J* = 10, 16 Hz), 6.87 (1 H, d, *J* = 8 Hz), 6.98 (1 H, s). Mass spectrum: *m*/*e* 303 (M^+). Anal. Calcd for $C_{17}H_{18}FO_3N$: C, 67.29; H, 5.99; N, 4.62. Found: C, 67.22; H, 6.12; N, 4.64.

3-Chloro-4-(phenylthio)-1,1,2-trifluoro-1-butene (11). To a solution of 1,1,2-trifluoro-1,3-butadiene (8.0 g, 74 mmol) and calcium carbonate (50 mg) in 85 mL of dichloromethane at −40 °C in a 250-mL round-bottom flask was added a solution of benzenesulfenyl chloride (7.1g, 49 mmol) in 20 mL of dichloromethane over 2 h. The reaction mixture was left to stand overnight at room temperature and poured into ice–water. The organic layer was washed with aqueous 5% sodium metabisulfite solution and brine and then dried over anhydrous magnesium sulfate. Evaporation of solvent followed by distillation gave 12.1 g (97.5%) of 3-chloro-4-(phenylthio)-1,1,2-trifluoro-1-butene as a light yellow oil, bp 84–86 °C (1.0 mmHg). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.39 (2 H, d, *J* = 8 Hz), 4.58 (1 H, ttd, *J* = 1.5, 8, 33 Hz), 7.2–7.4 (5 H, phenyl protons). Mass spectrum: *m*/*e* 252,254 (M^+). ^{19}F NMR (300 MHz, $CDCl_3$): φ F^3 = −11.8, F^2 = 116.7, F^1 = 99.3, $J(F^{12})$ = 64.5 Hz, $J(F^{23})$ = 111.2 Hz, $J(F^{13})$ = 33.0 Hz, $J(F^3H)$ = 26.4 Hz.

3-Chloro-4-(phenylsulfonyl)-1,1,2-trifluoro-1-butene (12). To a solution of 7.0 g (27.7 mmol) of 3-chloro-4-(phenylthio)-1,1,2-trifluoro-1-butene in 100 mL of dichloromethane at 0 °C in a 250-mL round-bottom flask was added a solution of 15.0 g (87 mmol) of 3-chloroperoxybenzoic acid in 50 mL of dichloromethane. The mixture was further stirred for 3 h at room temperature. At this point the contents of the flask were washed with 5% aqueous sodium bisulfite solution, saturated sodium bicarbonate solution and, brine and dried over anhydrous magnesium sulfate. Evaporation of solvent gave a yellow crystalline product, which was purified by recrystallization from *n*-hexane and ethyl acetate (3:1) to obtain 7.45 g (94.7%) of 3-chloro-4-(phenylsulfonyl)-1,1,2-trifluoro-1-butene as white crystals, mp 45–47 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.63 (1 H, ddd, *J* = 1.5, 5, 14 Hz), 3.87 (1 H, dd, *J* = 10, 14 Hz), 5.10 (1 H, dm, *J* = 27 Hz), 7.6–8.0 (5 H, phenyl protons). Mass spectrum: *m*/*e* 284 (M^+). ^{19}F NMR ($CDCl_3$): φ F^1 = 97.5, F^2 = 112.8, F^3 = −13.9, $J(F^{12})$ = 60.1 Hz, $J(F^{23})$ = 113.8 Hz, $J(F^{13})$ = 33.1 Hz, $J(F^3H)$ = 24.8 Hz. Anal. Calcd for $C_{10}H_8ClF_3SO_2$: C, 42.17; H, 2.83; S, 11.27; Cl, 12.46. Found: C, 42.75; H, 2.94; S, 11.18; Cl, 12.62.

(*Z*)-3-Fluoro-4,4,4-trimethoxy-2-butenyl Phenyl Sulfone (13). Potassium carbonate (6.0 g, 43.5 mmol) was added to a solution of 3.0 g (10.5 mmol) of 2-chloro-3,4,4-trifluoro-3-butenyl phenyl sulfone in 30 mL of methanol at room temperature in a 100-mL round-bottom flask. The resulting mixture was stirred for 12 h at room temperature. The reaction was diluted with 100 mL of diethyl ether. The contents of the flask were filtered and the white solid was washed with excess diethyl ether. The ether solution was evaporated in vacuo to give 3.1 g (95%) of the crude 3-fluoro-4,4,4-trimethoxy-2-butenyl phenyl sulfone as an oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.10 (9 H, s), 3.98 (2 H, d, *J* = 9 Hz), 5.50 (1 H, dt, *J* = 9, 33 Hz), 7.50–7.90 (phenyl protons, 5 H). ^{19}F NMR ($CDCl_3$): φ 120.5 (d, *J* = 31.1 Hz). Anal. Calcd for $C_{13}H_{17}FO_5S$: C, 51.28; H, 5.63; S, 10.54. Found: C, 51.29; H, 5.61; S, 10.84.

(*Z*)-Methyl 2-Fluoro-4-(phenylsulfonyl)-2-butenoate (14). Potassium carbonate (6.0 g, 43.5 mmol) was added to a solution of 3.0 g (10.5 mmol) of 3-chloro-4-(phenylsulfonyl)-1,1,2-trifluoro-1-butene in 30 mL of methanol at room temperature in a 100-mL round-bottom flask. The resulting mixture was stirred for 12 h at room temperature. After removal of solvent in vacuo, the residue was partitioned between 50 mL of diethyl ether and 50 mL of 10% aqueous hydrochloric acid. The whole mixture was stirred for 1 h at room temperature. The ether layer was washed once with brine and then dried over anhydrous magnesium sulfate. Evaporation of solvent gave a crystalline product, which was purified by recrystallization from 30% ethyl acetate in hexanes to give 2.50 g (93.9%) of methyl 2-fluoro-4-(phenylsulfonyl)-2-butenoate as pale yellow crystals, mp 104.0–105.0 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.82 (3 H, s), 4.05 (2 H, dd, *J* = 2, 8 Hz), 6.17 (1 H, dt, *J* = 8, 30 Hz), 7.55–7.9 (phenyl protons, 5 H). Mass

spectrum: m/e 258 (M^+). ^{19}F NMR ($CDCl_3$): φ 121.4 (d, J = 31.0 Hz). Anal. Calcd for $C_{11}H_{11}FO_4S$: C, 51.16; H, 4.26. Found: C, 51.02; H, 4.37.

(*Z*)-*cis*,*trans*-Methyl 2,2-Dimethyl-3-[2-fluoro-2-(methoxycarbonyl)vinyl]cyclopropanecarboxylate (15). To a solution of 589 mg (1.94 mmol) 3-fluoro-4,4,4-trimethoxy-2-butenyl phenyl sulfone and 486 mg (4.26 mmol) of methyl senecioate in dimethylformamide (4 mL) at 20 °C in a pear-shaped 50-mL flask was added 280 mg (5.19 mmol) of sodium methoxide. The flask was equipped with a magnetic stirrer and stirred for 48 h under an N_2 atmosphere. The reaction mixture was poured into 5% aqueous hydrochloric acid and the mixture was extracted with diethyl ether. Evaporation of solvent yielded a crude liquid which was diluted with 10 mL of methanol. *p*-Toluenesulfonic acid (10 mg) was added to the solution and the resulting solution was stirred for 1 h. The reaction mixture was diluted with excess 5% sodium bicarbonate solution and diethyl ether. The ether layer was washed with brine and then dried over anhydrous magnesium sulfate. Evaporation of the solvent in vacuo gave the crude diester which was purified by chromatography on silica gel to give 178 mg (40.0%) of (*Z*)-*cis*,*trans*-methyl 2,2-dimethyl-3-[2-fluoro-2-(methoxycarbonyl)vinyl]cyclopropanecarboxylate (trans:cis = 85:15). ^1H NMR (300 MHz, $CDCl_3$): δ 1.19, 1.26 (trans *gem*-dimethyl), 1.23 (cis *gem*-dimethyl), 1.73 (trans isomer, d, J = 5.0 Hz), 2.39 (trans isomer, dd, J = 5, 10 Hz), 1.94 (cis isomer, d, J = 9 Hz), 2.10 (cis isomer, dd, J = 9, 10 Hz), 5.84 (trans isomer, dd, J = 10, 32 Hz), 6.59 (cis isomer, dd, J = 10, 31 Hz). Mass spectrum: m/e 231 ($M^+ + 1$). ^{19}F NMR ($CDCl_3$): φ 131.6 (d, J = 32.0 Hz, trans), 132.7 (d, J = 31.1 Hz, cis). Anal. Calcd for $C_{11}H_{15}FO_4$: C, 57.36; H, 6.57. Found: C, 57.25; H, 6.61.

(*Z*)-3,4,4,4-Tetrafluoro-2-butenyl Phenyl Sulfone (16). Potassium fluoride (239 mg, 3.1 mmol; Aldrich Gold Label) was added to a solution of 237 mg (0.83 mmol) of 3-chloro-4-(phenylsulfonyl)-1,1,2-trifluoro-1-butene in 2 mL of dry dimethylformamide in a 20-mL round-bottom flask. The mixture was stirred for 15 h at room temperature. At this point the contents of the flask were poured into ice-water, and the mixture was extracted with diethyl ether. The ether layer was washed once with brine and then dried over anhydrous magnesium sulfate. Evaporation of solvent yielded crude solid, which was purified by recrystallization from 30% ethyl acetate in hexanes to give 184 mg (82.5%) of 3,4,4,4-tetrafluoro-2-butenyl phenyl sulfone as white crystals, mp 83.0–84.0 °C. ^1H NMR (300 MHz, $CDCl_3$): δ 3.94 (2 H, d, J = 9 Hz), 5.73 (1 H, dt, J = 8, 31 Hz), 7.6–7.9 (5 H, phenyl protons). Mass spectrum: m/e 268 (M^+). ^{19}F NMR ($CDCl_3$): φ 72.7 (d, $J(CF_3\text{–}F)$ = 10.3), 127.3 (dqt, J(F–H trans) = 31.0 Hz, $J(F\text{–}CF_3)$ = 10.3 Hz). Anal. Calcd for $C_{10}H_8F_4SO_2$: C, 44.76; H, 3.01. Found: C, 44.58; H, 3.02.

(*Z*)-4-Bromo-1,1,1,2-tetrafluoro-2-butene (17). A solution of 3.50 g (19.7 mmol) of *N*-bromosuccinimide and 20 mL of hydrogen fluoride–pyridine complex was prepared in a 100-mL polyethylene flask at −20 °C under a nitrogen atmosphere. The flask was fitted with a gas bubbling glass tube. Into this solution was bubbled 2.30 g (21.3 mmol) of 1,1,2-trifluoro-1,3-butadiene with a stream of nitrogen gas over half an hour. The solution was stirred further for 2 h at −20 °C and let stand at room temperature overnight. The contents of the flask were poured into a large excess of ice–water, and the liquid was extracted twice with diethyl ether. The combined ether layers were washed successively with 5% aqueous potassium hydroxide solution and brine and then dried over anhydrous magnesium sulfate. Evaporation of the solvent gave crude liquid, which was distilled to obtain 2.13 g (52.4%) of (*Z*)-4-bromo-1,1,1,2-tetrafluoro-2-butene as a clear liquid, bp 73.0–75.0 °C (760 mmHg). ^1H NMR (300 MHz, $CDCl_3$): δ 4.00 (2 H, d, J = 9 Hz), 5.88 (1 H, dt, J = 9, 30 Hz). ^{19}F NMR ($CDCl_3$): φ 73.2 (d, $J(CF_3\text{–}F)$ = 10.3 Hz), 131.2 (dqt, J(F–H trans) = 28.9 Hz, $J(F\text{–}CF_3)$ = 10.3 Hz).

(*E*)-1,2-Difluoro-1-phenyl-1,3-butadiene (18). To a solution 3.2 g (29.6 mmol) of 1,1,2-trifluoro-1,3-butadiene in tetrahydrofuran (40 mL) at −70 °C in a round-bottom 100-mL flask was added 15 mL (30 mmol) of phenyllithium (2 M). The reaction mixture was stirred for 2 h at −70 °C and for 10 h at 20 °C. The contents of the flask were poured into an excess of cold 5% hydrochloric acid, and the liquid was extracted twice with diethyl ether. The ether layers were combined, washed once with brine, and then dried over anhydrous magnesium sulfate. Evaporation of solvent gave a yellow oil which was chromatographed on silica gel (hexanes) to give 3.40 g (69.4%) of (*E*)-1,2-difluoro-1-phenyl-1,3-butadiene. (It contained 10% of *Z* isomer.) ^1H NMR (300 MHz, $CDCl_3$): δ 5.32 (1 H, d, J = 12 Hz, *E* isomer), 5.62 (1 H, d, J = 16 Hz, *E* isomer), 5.26 (1 H, d, J = 12 Hz, *Z* isomer), 5.69 (1 H, d, J = 16 Hz, *Z* isomer), 6.39 (1 H, m, *Z* isomer), 6.72 (1 H, m, *E* isomer), 7.5–7.8 (phenyl protons, 5 H). Mass spectrum: m/e 167 (M + 1). ^{19}F NMR ($CDCl_3$): φ trans isomer F^1 = 154.4, F^2 = 159.0, $J(F^1F^2)$ = 113.7 Hz, $J(F^1H^3)$ = 6.2 Hz, $J(F^2H^3)$ = 26.9 Hz; cis isomer F^1 = 127.5, F^2 = 146.5 Hz, $J(F^1F^2)$ = 12.4 Hz, $J(F^2H^3)$ = 26.6 Hz.

(*E*)-2,3-Difluorocinnamaldehyde (19). To a solution of 513 mg (3.09 mmol) of 1,2-difluoro-1-phenyl-1,3-butadiene (*E*:*Z* = 90:10) in 20 mL of dichloromethane at −70 °C in a 50-mL round-bottom flask was bubbled ozone gas. As soon as the starting diene disappeared on TLC, bubbling of ozone gas was stopped. Nitrogen gas was bubbled to remove excess ozone. At this point dimethyl sulfide (2 mL) was added to the solution, the mixture was left to stand overnight at room temperature and poured into water, and the mixture was extracted with diethyl ether. The ether layer was washed once with brine and then dried over anhydrous magnesium sulfate. Evaporation of solvent yielded crude oil which was purified by recrystallization from hexanes to give 333 mg (64.0%) of (*E*)-2,3-difluorocinnamaldehyde as yellow crystals, mp 32.0–33.0 °C. ^1H NMR (300 MHz, $CDCl_3$): δ 7.4–7.6 (3 H, m, phenyl protons), 7.84 (2 H, dd, J = 2, 8 Hz, phenyl protons), 9.98 (1 H, dd, J = 2, 18 Hz). Mass spectrum: m/e 168 (M^+), 169 (M + 1), 170 (M + 2). ^{19}F NMR ($CDCl_3$): φ F^1 = 148.3, F^2 = 166.9, $J(F^1F^2)$ = 119.9 Hz, $J(F^2H)$ = 16.5 Hz. Anal. Calcd for $C_9H_6F_2O$: C, 64.27; H, 3.61. Found: C, 65.17; H, 3.61.

Optically Pure (4a*S*)-(+)- or (4a*R*)-(−)-1,4a-Dimethyl-4,4a,7,8-tetrahydronaphthalene-2,5(3*H*,6*H*)-dione and Its Use in the Synthesis of an Inhibitor of Steroid Biosynthesis

Hisahiro Hagiwara* and Hisashi Uda

Chemical Research Institute of Nonaqueous Solutions, Tohoku University, Katahira, 2-1-1, 980 Sendai, Japan

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Synthesis of the optically pure enone 1 is described. Reestimation of the optical purity and reexamination of the absolute stereochemistry of 1 have been studied. Usefulness of the enone 1 is demonstrated by a five-step synthesis of (−)-3, an inhibitor of steroid biosynthesis.

Numerous syntheses and synthetic studies of sesquiterpenes and diterpenes from the racemic Wieland–Miescher ketone analogue 1 have been described.[1] In contrast to the availability of either enantiomer of the

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