(slight excess) of ethyl cyanoacetate, and 6 ml of acetic acid in 50 ml of absolute alcohol was stirred at room temperature. Then 10 ml of diethylamine was added in small portions. The temperature rose rapidly to 45°, then began to drop as the last of the diethylamine was added. After 15 min, a white, fluffy precipitate formed. Stirring was continued for an additional 1 hr, then the mixture was cooled in an ice bath for 30 min. The white crystals were filtered, washed with water, and then recrystallized from 95% ethanol to give 16.4 g (93%) of shiny, white flakes: mp 144–149°; ir (KBr) 3260, 3000, 1730, 1725, 1670, and 1575 cm^{-1}; nmr (DMSO-d_6) δ 1.20 (3 H, t, J = 6 Hz), 3.73 (2 H, s), 4.00 (2 H, q, J = 6 Hz), 5.86 (1 H, s), and 11.50 ppm (1 H, broad s, exchanged with D_2O); uv max (CH_3OH) 233 nm (ϵ 11,000) and 284 (22,000); mass spectrum (70 eV) m/e (rel intensity) 187 (60), 173 (7), 159 (18), 142 (82), 115 (100), and 86 (40).

Anal. Calcd for $C_7H_9NO_3S$: C, 44.90; H, 4.84; N, 7.49; S, 17.12. Found: C, 44.85; H, 4.76; N, 7.47; S, 17.06.

2-Cyanomethylene-4-thiazolidinone (**3**).—Five milliliters of piperidine was added to a stirred mixture consisting of 120.17 g (1.0 mol) of ethyl mercaptoacetate, 66.07 g (1.0 mol) of malononitrile, and 5 drops of acetic acid in 200 ml of absolute ethanol. The temperature quickly rose to 60° and was subsequently maintained between 50 and 60° by intermittent use of an ice bath. After a short time, a white precipitate formed a solid mass in the reaction vessel. An additional 100 ml of ethanol was then added and the mixture was stirred for 30 min more. The mixture was then filtered and the white solid was recrystallized from a mixture (v/v) of ethanol–acetonitrile (2:1) to give 80 g (57%) of a white powder that slowly decomposed over 200°: ir (KBr), 3115, 3090, 3000, 2880, 2218, 1770, 1730, and 1600 cm^{-1}; nmr (DMSO-d_6) δ 4.00 (2 H, s), 4.90 (1 H, s), and 11.75 ppm (1 H, broad s, exchanged with D_2O); mass spectrum (70 eV) m/e (rel intensity) 139 (39), 111 (12), 73 (20), 67 (100), 66 (53), 47 (35), 46 (78), 45 (61), and 42 (33).

Anal. Calcd for $C_5H_4N_2OS$: C, 42.87; H, 2.88; N, 20.00; S, 22.84. Found: C, 42.44; H, 2.94; N, 20.01; S, 22.37.

2-Carboxamidomethylene-4-thiazolidinone (**4**).—A mixture of 10.0 g (0.094 mol) of methyl mercaptoacetate, 13.0 g (slight excess) of 2-cyanoacetamide, 2.0 g of ammonium acetate, and 50 ml of ethanol was stirred at room temperature. Then 15 ml of diethylamine was added and stirring was continued for 1 hr, during which time the temperature gradually rose to 48°. At the end of 1 hr, the temperature began to drop and a tan powder came out of solution. After an additional 0.5 hr the solution was filtered and the very insoluble powder was washed liberally with ethanol, then ether. The residue after washing weighed 4.8 g (32%) as a light brown powder that decomposed at 260° and sublimed over 200°, and was homogeneous (tlc): ir (KBr) 3400, 3160, 2783, 1730, 1675, 1630, and 1590 cm^{-1}; nmr (DMSO-d_6) δ 3.60 (2 H, s), 5.59 (1 H, s), 6.60 (1 H, broad s), 7.10 (1 H, broad s), and 10.50 ppm (1 H, broad s); mass spectrum (70 eV) m/e (rel intensity) 158 (100), 142 (16), 115 (19), 84 (28), 73 (42), 68 (42), 46 (53), 44 (53), and 42 (56).

Anal. Calcd for $C_5H_6N_2O_2S$: C, 37.98; H, 3.82; N, 17.71; S, 20.24. Found: C, 37.98; H, 3.79; N, 17.49; S, 20.19.

Desulfurization of 2-Carbethoxymethylene-4-thiazolidinone (**2**).—Three grams of **2** was dissolved in 250 ml of absolute ethanol containing approximately 18 g of W2 Raney nickel and the mixture was stirred and refluxed for 44 hr. The solution was then cooled, filtered through an asbestos plug, and then filtered by gravity through fluted paper to give a clear, colorless filtrate. Removal of the ethanol by evaporation left a colorless oil that was distilled at 137–138° (6 mm) [lit. 136° (6 mm)]: ir (liquid film) 3260, 2950, 1740, and 1650 cm^{-1}; nmr (CCl_4) δ 1.23 (3 H, t, J = 6 Hz), and 2.05 (3 H, s), 2.48 (2 H, t, J = 6 Hz), 3.28 (2 H, q, J = 6 Hz), 4.00 (2 H, q, J = 6 Hz), 7.50 ppm (1, H, broad t). The ir, nmr, and elemental analyses indicated that the product was the ethyl ester of *N*-acetyl-β-alanine.

Anal. Calcd for $C_7H_{13}NO_3$: C, 52.82; H, 8.23; N, 8.80. Found: C, 52.57; H, 8.51; N, 9.06.

2-Amino-3-carbethoxy-4-hydroxythiophene (**1b**)[8].—Nine grams (0.048 mol) of ethyl chloroacetylcyanoacetate[7] was dissolved in 90 ml of a 15% aqueous potassium hydrosulfide solution. The mixture was warmed gently on a steam bath. After a few minutes, shiny plates began to appear. After 15 min the precipitate was collected, washed with water, and recrystallized from ethanol to give 4.2 g (45%) of shiny, white flakes: mp 219–202; ir (KBr) 3350, 3080, 1673, 1625, and 1490 cm^{-1}; nmr (DMSO-d_6) δ 1.20 (3 H, t, J = 6 Hz), 3.35 (2, H, s), 4.15 (2, H, q, J = Hz), 8.87 (1 H, broad s, sharpened upon ^{14}N spin decoupling), and 9.40 ppm (1, H, broad s, sharpened upon ^{14}N spin decoupling); mass spectrum (70 eV) m/e (rel intensity) 187 (100), 143 (100), 142 (100), 141 (69), 115 (100), 85 (69), 68 (100), and 60 (65).

Anal. Calcd for $C_7H_9NO_3S$: C, 44.90; H, 4.84; N, 17.49. Found: C, 45.00; H, 4.80; N, 17.38.

Registry No.—**1b**, 38555-67-8; **2**, 24146-36-9; **3**, 3364-82-7; **4**, 27653-83-4; ethyl mercaptoacetate, 623-51-8; ethyl cyanoacetate, 105-56-6; malononitrile, 109-77-3; 2-cyanoacetamide, 107-91-5; methyl mercaptoacetate, 2365-48-2; ethyl ester of *N*-acetyl-β-alanine, 33233-68-0; ethyl chloroacetylcyanoacetate, 26390-99-8.

The Synthesis of the Fluorinated Ethers "Perfluoroglyme" and "Perfluorodiglyme" by Direct Fluorination

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The synthesis of perfluorinated ethers and polyethers using existing technology is often difficult and in many cases impossible to accomplish. A facile general synthesis with possible commercial importance has been developed in our laboratory by employing modified[1] LaMar[2] direct fluorination techniques. Perfluorinated polyethers are of interest as potential high stability fluids and as solvents. Of the reported products, only "perfluoroglyme" (perfluoro-1,2-dimethoxyethane) has been prepared in 4% yield based on the electrolytic fluorination and cleavage of 1,4-dioxane.[3]

Experimental Section

Perfluoro-1,2-dimethoxyethane.—1,2-Dimethoxyethane (4.015 g, 0.045 mol) was evaporated employing a flow of 50–100 cc of helium into gradient reactor containing four distinct zones which were maintained at −78°, a temperature below the freezing point of the ether (−58°). An initial flow of 0.5 cc/min of fluorine and 20 cc/min of helium was started and after 12 hr the fluorine was increased to 1.0 cc/min. After an additional 12 hr, zone 1 was allowed to run out of Dry Ice. Twelve hours after zone 1 was clear of Dry Ice the fluorine was increased to 1.5 cc/min while helium flow still was maintained at 20 cc/min. The fluorine flow was maintained at 1.5 cc/min. On alternate days the helium was reduced to 10 cc/min, followed by one additional zone being allowed to clear of Dry Ice. Subsequent reductions to 5-, then to 0-cc/min helium flow were followed each time by warming of one additional zone.[4] Finally, as the reactor warmed under a flow of pure fluorine, the fluorinated ether was passed through a metal trap filled with sodium fluoride pellets and into a glass trap maintained at −78°. The raw fluorocarbon ethers collected represented a mass which corresponded to between 50 and 100% of the expected yield based on moles of the parent ether. This mixture contained several hydrofluoro ethers and

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(1) R. J. Lagow and N. J. Maraschin, *J. Amer. Chem. Soc.*, **94**, 8601 (1972).

(2) R. J. Lagow and J. L. Margrave, "The Reaction of Polynuclear Hydrocarbons with Elemental Fluorine," in press; R. J. Lagow and J. L. Margrave, *Chem. Eng. News*, 40 (Jan 12, 1970).

(3) J. H. Simons, U. S. Patent 2,500,388 (1950).

(4) Warmings of successive zones allowed renewal of the reactant surface inside the reactor.

other hydrolytically unstable and corrosive products along with a smaller amount of perfluorinated fragments. The yield of the hydrofluoro ethers in most cases exceeded the yield of perfluoro ethers owing to incomplete reaction. These products were removed by aqueous alkali hydrolysis and the hydrolytically stable ethers fractionated. The bulk of the desired products was collected in the −95 and −130° traps (combined weight 2.48 g, 20.6%). Final purification was accomplished using gas–liquid chromatography using a fluorosilicone (QF-1-0065, 13% on Chromosorb p, 80–100 mesh) column.

Perfluoro-1,2-dimethoxyethane is a gas at room temperature (bp 16.7°). The molecular weight determined by the ideal gas method was 269 (*cf.* 270 for $C_4F_{10}O_2$). The ^{19}F nmr consisted of a triplet at +59.54 and a quartet at +94.19 ppm relative to $CFCl_3$[5] with coupling constant 9.2 Hz and relative intensities of 3:2. The ir spectrum exhibited bands at 1410 (w), 1295 (s), 1250 (s), 1200 (w), 1170 (sh), 1155 (s), 1105 (w), 923 (w), 887 (m), 865 (w), 819 (w), 690 (w) wavenumbers. The mass spectrum contained no parent peak but showed strong peaks at *m/e* 135 corresponding to the symmetrical cleavage of the molecule, (CF_3-O-CF_2). Other strong peaks were at *m/e* 119 (C_2F_5), 100 (C_2F_4), 69 (CF_3), 50 (CF_2), 47 (CFO). *Anal.* Calcd for $C_4F_{10}O_2$: F, 70.36. Found: C, 17.41; F, 70.08. The yield was 21%.

1-Hydrononafluoro-2,5-dioxahexane.—If the products of the previously described reaction were not hydrolyzed, a second major product may be isolated which in some cases exceeds the amount of perfluoro-1,2-dimethoxyethane. This ether was a liquid with a disagreeable odor and may be quite toxic. Its molecular weight was determined to be 251 (*cf.* 252 for $C_4HF_9O_2$). Its ^{19}F nmr spectrum exhibited a triplet at +59.22 and a quartet at +93.63 with a coupling constant of 9.4 hz and relative intensities of 2:2, a doublet centered at +88.36 (J = 70.0 Hz) split into triplets (J = 4.4 Hz), and a triplet at +92.47 ppm (J = 4.6 Hz) relative to $CFCl_3$ with relative integrals of 2:2. The proton nmr consisted of a triplet at −6.26 ppm relative to TMS (external standard) with coupling constant equal to 68.6 Hz, in good agreement with the doublet splitting in the ^{19}F nmr. If the proton was irradiated, the ^{19}F doublet decayed into a singlet. This information is consistent with a structure containing a proton in the 1 position (Chart I). The mass spectrum supports this conclusion. The two peaks corresponding to "symmetrical" cleavage at *m/e* 135 (C_2F_5O) and 117 (C_2HF_4O) were both strong with relative intensities of 1:1.5 as were the very strong peaks at *m/e* 69 (CF_3) and 51 (CHF_2) of relative intensties of 1:1.5. Other, less intense peaks support this conclusion. The ir spectrum contained a weak proton absorption at 3028 cm^{-1} in addition to carbon–fluorine and carbon–oxygen bands at 1400 (w, b), 1370 (w), 1295 (s), 1250 (s), 1192 (m), 1179 (sh), 1159 (s), 1125 (s), 1040 (m), 910 (m), 853 (w), 818 (w), 700 (w) cm^{-1}. The yield was 0–25%.

CHART I

^1H AND ^{19}F NUCLEAR MAGNETIC RESONANCE SPECTRA[a]

Perfluoro-1,2-dimethoxyethane

$CF_3—O—CF_2—CF_2—O—CF_3$
+59.54 +94.19
(9.2)

1-Hydrononafluoro-2,5-dioxahexane

$CF_3——O——CF_2——CF_2——O——CF_2——H$
+59.22 +93.63 +92.47 +88.36 −6.26[b]
(9.2) (<1) (4.5) (69.3)

Perfluorobis(2-methoxyethyl) Ether

$CF_3—O—CF_2——CF_2—O—CF_2—CF_2—O—CF_3$
+59.30 +93.84 +91.64
(9.4) (<1)

[a] ϕ in parts per million (J in hertz). $\phi_{CFCl_3(ext)} = 0$. [b] ^1H [TMS (external standard)].

Perfluorobis(2-methoxyethyl) Ether.—Bis(2-methoxyethyl) ether (1.79 g, 0.0134 mol) was evaporated at 50° into the four-zone cryogenic factor (zone 1, −40°; zones 2, 3, and 4 at −78°) using a 80–100-cc/min flow of helium gas. After 6 to 8 hr the helium flow was reduced to 20 cc/min and a 0.5-cc/min flow of fluorine was started. A similar procedure to that used for 1,2-dimethoxyethane was used to complete the reaction. The raw products were fractionated through −63, −78, −95, and −196° traps. Perfluorobis(2-methoxyethyl) ether was collected from the −78 and −95° traps (yield 0.83 g, 16.1%). Perfluorobis(2-methoxyethyl) ether is a volatile liquid, bp 60–63°). Its molecular weight was determined to be 385 (*cf.* 386 for $C_6F_{14}O_3$). The ^{19}F nmr exhibited a triplet at +59.30 and a quartet at +93.84 (J = 9.4 Hz) and a singlet at +91.64 ppm relative to $CFCl_3$. The relative integrals of the absorptions are 3:2:2. The spectrum exhibited bands at 1385 (w), 1295 (s), 1250 (s), 1220 (sh, w), 1200 (w), 1165 (s), 1145 (s), 920 (sh), 910 (m), 770 (m), 697 (w), 681 (sh) wavenumbers. The mass spectrum exhibited strong peaks at *m/e* 185 (C_3F_7O), 135 (C_2F_5O), 119 (C_2F_5), 100 (C_2F_4), 69 (CF_3), 50 (CF_2). *Anal.* Calcd for $C_6F_{14}O_3$: C, 18.67; F, 68.90. Found: C, 18.64; F, 69.94. The yield was 16%.

Discussion

The yields of perfluorinated ethers reported are not to be considered optimum. Obviously the partially fluorinated material could be recycled. A new variable temperature reactor[6] which enables reactions to be studied at temperatures other than −78° may also greatly improve the yields.

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Registry No.—Perfluoro-1,2-dimethoxyethane, 378-11-0; 1,2-dimethoxyethane, 110-71-4; fluorine, 7782-41-4; 1-hydrononafluoro-2,5-dioxahexane, 40891-98-3; perfluorobis(2-methoxyethyl) ether, 40891-99-4; bis(2-methoxyethyl) ether, 111-96-6.

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[5] Nmr samples were condensed into capillary tubes, sealed, and immersed in a solution of $CFCl_3$ (30%), tetramethylsilane (5%), and carbon tetrachloride (65%) contained in a standard nmr tube.

[6] To be published.

Carbon-13 Magnetic Resonance Study of Terpenoids. I. An Application of Heteronuclear Selective Decoupling Experiments to the Spectral Assignments of Nonproton-Bearing Carbon-13 Resonances of a Germacranolide, Melampodin

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We recently reported[2] the isolation and structure elucidation of melampodin, a new sesquiterpene lactone from *Melampodium leucanthum* Torr. & Gray. Single-crystal X-ray diffraction[3] and neutron diffraction[4] of this highly oxygenated medium-ring compound revealed that melampodin represents a new and novel germacranolide-type sesquiterpene lactone, which, in contrast to the well-known *trans,trans*-cyclodeca-1,5-

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(1) (a) Louisiana State University. (b) Varian AG.

(2) N. H. Fischer, R. Wiley, and J. D. Wander, *J. Chem. Soc. Chem. Commun.*, 137 (1972).

(3) S. Neidle and D. Rogers, *J. Chem. Soc. Chem. Commun.*, 140 (1972).

(4) I. Bernal and S. F. Watkins, *Science*, **178**, 1282 (1972).