good yield. Following evaporation to $^1/_3$ volume, the reaction solution was quickly washed with cold, saturated $NaHCO_3$ (50 mL), dried (Na_2SO_4), and evaporated to 5 mL. Addition of 30–60 °C petroleum ether (150 mL) precipitated a white solid: 2.85 g (67%); mp 130–131 °C; $[\alpha]^{20}_D$ +5.5° (c = 1.0, DMF); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.09 (s, 9 H, $C(CH_3)_3$), 1.28 (d, J = 6.4 Hz, 3 H, γ-CH_3), 2.34 (s, 3 H, CH_3), 3.67 (s, 3 H, OCH_3), 3.85 (d, J = 2.6, 1 H, α-H), 4.13 (dq, J = 6.4, 2.5 Hz, 1 H, β-H), 7.13 (d, J = 8.0 Hz, 2 H, H_{arom}), 7.77 (d, J = 8.1 Hz, 2 H, H_{arom}). Anal. Calcd for $C_{16}H_{27}NO_6S$: C, 53.16; H, 7.54; N, 3.87; S, 8.87. Found: C, 53.11; H, 7.49; N, 3.81; S, 9.11.

***N*-(9-Fluorenylmethoxycarbonyl)-*O*-*tert*-butyl-L-serine (1c). Procedure 1.** **1b** (10.0 g, 28.8 mmol) was stirred in 10% Na_2CO_3 (200 mL) at rt for 24 h and chilled (0 °C) and Fmoc-ONSu (10.2 g, 30.2 mmol) in p-dioxane (100 mL) added dropwise. After 24 h of stirring and gradual warming to rt, the mixture was washed with Et_2O (3 × 100 mL) and the aqueous phase chilled (0 °C), acidified with concd HCl to pH 2, and then extracted with Et_2O (3 × 100 mL). The combined Et_2O extracts were dried (Na_2SO_4) and evaporated to an oil, which gave white crystals from CH_3NO_2: 10.5 g (95%); mp 128.5–130 °C (lit.[4] mp 126–129 °C); $[\alpha]^{20}_D$ +26.7° (c = 1.0, EtOAc) (lit.[4] $[\alpha]^{23-25}_D$ +25.4° (c = 1.0, EtOAc)); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.40 (s, 9 H, $C(CH_3)_3$), 3.76 (dd, J = 8.5, 5.5 Hz, 1 H, β-H), 4.12 (dd, J = 8.8, 3.1 Hz, 1 H, β'-H), 4.43 (t, J = 7.0 Hz, 1 H, CH_{Fmoc}), 4.5–4.6 (m, 3 H, α-H, CH_{2Fmoc}), 5.82 (d, J = 7.6 Hz, 1 H, NH), 7.4–8.0 (m, 8 H, H_{arom}). Anal. Calcd for $C_{22}H_{25}NO_5$: C, 68.90; H, 6.58; N, 3.65. Found: C, 68.99; H, 6.50; N, 3.71.

Procedure 2. A solution of **1b** (2.00 g, 5.75 mmol) and NaOH (0.46 g, 11.5 mmol) in water (50 mL) was stirred at 0 °C for 2 h and then neutralized with concd HCl. Na_2CO_3 was added to 10% (w/v). Derivatization with Fmoc-ONSu (2.04 g, 6.04 mmol), workup, and crystallization were carried out as in procedure 1, yielding white crystals: 2.10 g (95%); mp 129–130.5 °C; $[\alpha]^{20}_D$ +25.9° (c = 1.0, EtOAc); NMR as above.

***N*-(9-Fluorenylmethoxycarbonyl)-*O*-*tert*-butyl-L-threonine (2c).** **2b** (0.58 g, 1.61 mmol) was hydrolyzed with NaOH (0.13 g, 3.22 mmol) and derivatized with Fmoc-ONSu (0.57 g, 1.69 mmol) as described in procedure 2, providing white crystals: 0.58 g (91%); mp 131–132 °C (lit.[4] mp 129–132 °C); $[\alpha]^{20}_D$ +15.3° (c = 1.0, EtOAc) (lit.[4] $[\alpha]^{23-25}_D$ + 15.5° (c = 1.0, EtOAc)); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.11 (d, J = 6.1 Hz, 3 H, γ-CH_3), 1.32 (s, 9 H, $C(CH_3)_3$), 4.21 (t, J = 7.0 Hz, 1H, CH_{Fmoc}), 4.31 (m, 2 H, α-H, β-H), 4.40 (d, J = 7.0 Hz, 2 H, CH_{2Fmoc}), 5.72 (br s, 1 H, NH), 7.2–7.8 (m, 8 H, H_{arom}). Anal. Calcd for $C_{23}H_{27}NO_5$: C, 69.49; H, 6.86; N, 3.52. Found: C, 69.47; H, 6.74; N, 3.31.

***N*-(9-Fluorenylmethoxycarbonyl)-L-tyrosine Methyl Ester (3b).** Fmoc-ONSu (37.4 g, 95.0 mmol) in p-dioxane (160 mL) was added dropwise to **3a**[7] (20.0 g, 86.3 mmol) in a mixture of 10% Na_2CO_3 (170 mL) and p-dioxane (80 mL) at 0 °C. After 20 h of stirring with gradual warming to rt, the solution was poured into ice/water (1.3 L) and extracted with Et_3O (3 × 400 mL). The extract was washed with brine (500 mL), dried (Na_2SO_4), and evaporated to an oil, which crystallized from EtOAc/hexane: 35.0 g (97%); mp 122–125 °C; $[\alpha]^{20}_D$ −17.0° (c = 1.0, DMF); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.9–3.2 (m, 2 H, β-CH_2), 3.72 (s, 3 H, OCH_3), 4.20 (t, J = 6.9 Hz, 1 H, CH_{Fmoc}), 4.3–4.7 (m, 3 H, CH_{2Fmoc}, α-H), 5.28 (d, J = 8.2 Hz, 1 H, NH), 5.69 (br s, 1 H, OH), 6.73 (d, J = 8.3 Hz, 2 H, $H_{tyr,arom}$), 6.94 (d, J = 8.3 Hz, 2 H, $H_{tyr,arom}$), 7.3–7.8 (m, 8 H, $H_{Fmoc,arom}$). Anal. Calcd for $C_{25}H_{23}NO_5$: C, 71.92; H, 5.56; N, 3.36. Found: C, 71.85; H, 5.71; N, 3.02.

***N*-(9-Fluorenylmethoxycarbonyl)-*O*-*tert*-butyl-L-tyrosine Methyl Ester (3c).** **3b** (5.00 g, 12.0 mmol), concd H_2SO_4 (0.33 mL, 6.0 mmol), and DCM (100 mL) were stirred under isobutylene gas (5 psi) for 6 h at rt. The solution was washed with cold 10% $NaHCO_3$ (2 × 100 mL) and brine (100 mL), dried (Na_2SO_4), and evaporated. The residue was dissolved in 1:1 MeOH/CCl_4 (400 mL), washed with water (300 mL), and then extracted with 1:1 MeOH/water (2 × 200 mL). The extract was dried (Na_2SO_4) and evaporated to a white solid, which was recrystallized from DCM/hexane: 4.70 g (83%); mp 90–92 °C; $[\alpha]^{20}_D$ −22.1° (c = 1.0, DMF); ^{1}H NMR ($CDCl_3$, 200 MHZ) δ 1.32 (s, 9 H, $C(CH_3)_3$), 3.07 (d, J = 5.8 Hz, 2 H, β,β'-CH_2), 3.70 (s, 3 H, OCH_3), 4.21 (t, J = 6.8 Hz, 1 H, CH_{Fmoc}), 4.3–4.6 (m, 3 H, CH_{2Fmoc}, α-H), 5.24 (d, J = 8.1 Hz, 1 H, NH), 6.90 (d, J = 8.4 Hz, 2 H, $H_{tyr,arom}$), 6.98 (d, J = 8.4 Hz, 2 H, $H_{tyr,arom}$), 7.3–7.8 (m, 8 H, $H_{Fmoc,arom}$). Anal. Calcd for $C_{29}H_{31}NO_5$: C, 73.54; H, 6.61; N, 2.96. Found: C, 73.49; H, 6.64; N, 3.15.

***N*-(9-Fluorenylmethoxycarbonyl)-*O*-*tert*-butyl-L-tyrosine (3d).** A mixture of **3c** (2.00 g, 4.22 mmol) in CH_3CN (250 mL) and 3% Na_2CO_3 (375 mL) was stirred for 15 h, then washed with hexane (3 × 500 mL), acidified with 2 N HCl to pH 3–4, and extracted with $CHCl_3$ (2 × 600 mL). The combined $CHCl_3$ fractions were washed with brine (500 mL), dried (Na_2SO_4), and evaporated to an oil, which gave white crystals from EtOAc/hexane: 1.43 g (74%); mp 150–151 °C (lit.[4] mp 150–151 °C); $[\alpha]^{20}_D$ −28.0° (c = 1.0, DMF) (lit.[4] $[\alpha]^{23-25}_D$ −27.6° (c = 1.0, DMF)); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.32 (s, 9 H, $C(CH_3)_3$), 2.9–3.2 (m, 2 H, β,β'-CH_2), 4.20 (t, J = 6.8 Hz, 1 H, CH_{Fmoc}), 4.3–4.5 (m, 2 H, CH_{2Fmoc}), 4.6–4.7 (m, 1 H, α-H), 5.22 (d, J = 8.0 Hz, 1 H, NH), 6.90 (d, J = 8.2 Hz, 2 H, $H_{tyr,arom}$), 7.03 (d, J = 8.2 Hz, 2 H, $H_{tyr,arom}$), 7.3–7.8 (m, 8 H, $H_{Fmoc,arom}$). Anal. Calcd for $C_{28}H_{29}NO_5$: C, 73.17; H, 6.37; N, 3.05. Found: C, 73.29; H, 6.48; N, 2.85.

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Registry No. **1a**, 5680-80-8; **1b**, 132776-33-1; **1c**, 71989-33-8; **2a**, 39994-75-7; **2b**, 132776-34-2; **2c**, 71989-35-0; **3a**, 3417-91-2; **3b**, 82911-79-3; **3c**, 132409-94-0; **3d**, 71989-38-3; $Me_2C{=}CH_2$, 115-11-7; Fmoc-ONSu, 82911-69-1.

Synthesis of a New Family of Chiral Fluorinated Synthons: (*R*)- and (*S*)-4-Fluoro-1-alkynes

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The synthesis and use of fluorinated biomolecules is currently an area of intense research.[1] Useful optically pure synthons bearing a chiral fluoromethylene group remain relatively rare although substantial progress has been reported recently.[2] In connection with ongoing mechanistic studies in the area of fatty acid biomodification,[3] we required a general synthesis of chiral fluorinated fatty acids. We were also spurred on by reports of new ferroelectric liquid crystalline materials bearing a pendant chiral fluoroalkyl chain.[4] We now report a facile multigram synthesis of a chiral monofluorinated terminal alkyne. In addition, we have been able to prepare the corresponding chiral 3-fluoro carboxylic acids by permanganate oxidation of the title compounds.

Results and Discussion

Our synthetic route is based on the availability of chiral homopropargyl alcohols whose configuration has been unambiguously determined.[5a,b] (See Scheme I.) Thus racemic 1-decyn-4-ol, prepared by reaction of lithium

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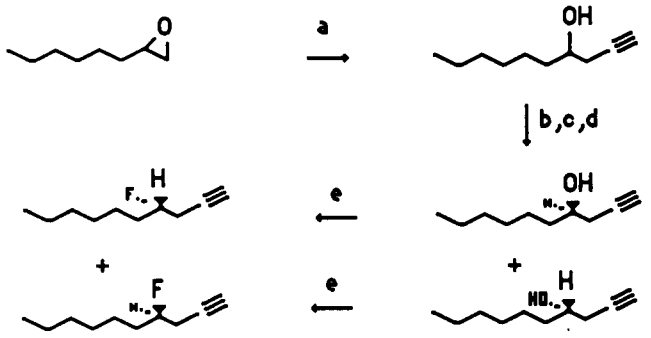
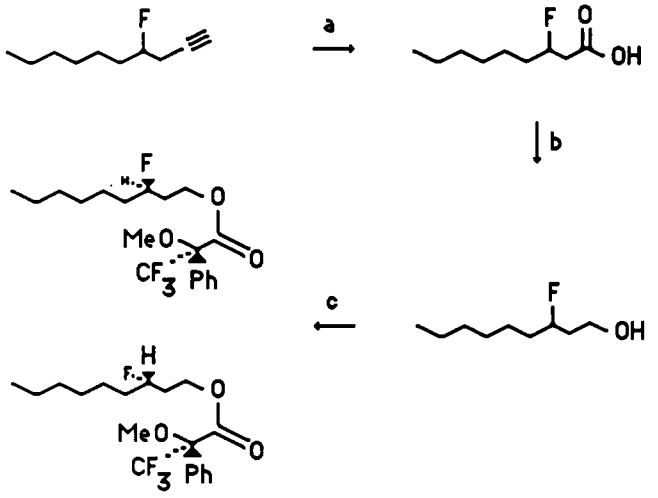
Scheme I[a]



[a] (a) HC≡C⁻Li⁺, EDA complex; (b) *O*-methylmandeloyl chloride, pyridine; (c) chromatographic separation on silica gel column; (d) KOH/50% ethanol; (e) DAST.

Scheme II[a]



[a] (a) $KMnO_4$, H^+; (b) $LiAlH_4$; (c) (+)-MTPA Cl.

acetylide with 1,2-epoxyoctane, was conveniently resolved by chromatographic separation of the corresponding (*S*)-*O*-methylmandelate esters to give the two enantiomeric decynols, each in 15% overall yield. The absolute configuration of these alcohols was straightforward to assign since the ^1H NMR data of the mandelate esters closely matched that reported in the literature for the hexynol series.[5b] Thus (*S*)-1-decyn-4-ol was prepared from the less polar mandelate ester; (*R*)-1-decyn-4-ol was obtained from the more polar diastereomer.

We selected (diethylamido)sulfur trifluoride (DAST) as our fluorinating agent because it is known to introduce fluorine with clean inversion at unactivated secondary carbinol centers.[6] The (*R*)-decynol was transformed into the (*S*)-4-fluoro-1-decyne, and the (*S*)-decynol gave rise to the (*R*)-4-fluoro-1-decyne, each in 32% isolated yield. We have made no attempt to optimize this reaction: a considerable amount of enyne is formed, which fortunately can be easily removed by flash chromatography.[7]

The optical purity of the homopropargyl fluorides was determined in the following manner. Encouraged by a recent report[2b,8] that the enantiomeric purity of 2-fluoro-

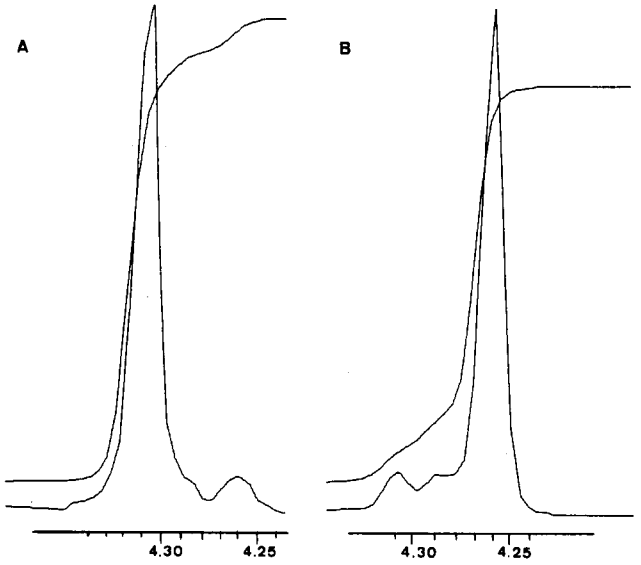


Figure 1. Estimation of % ee of chiral 4-fluoro-1-alkynes by ^{19}F NMR analysis of the (*R*)-MTPA esters of the corresponding chiral 3-fluorononanols: (A) signals due to CF_3 group of predominantly (*R*)-3-fluorononan-1-ol, (*R*)-α-methoxy-α-(trifluoromethyl)-phenylacetate; (B) signals due to CF_3 group of predominantly (*S*)-3-fluorononan-1-ol, (*R*)-α-methoxy-α-(trifluoromethyl)-phenylacetate.

hexanoic acids could be evaluated by Mosher esterification of the corresponding fluoro alcohols, we attempted oxidative cleavage of the triple bond. (See Scheme II.) We were able to prepare 3-fluorononanoic acid in 45% yield by treatment of 4-fluoro-1-decyne with acidic $KMnO_4$ solution.[9] Reduction of the acid to the corresponding alcohol with $LiAlH_4$ was uneventful as was esterification of the alcohol with (+)-MTPA chloride.[10] We were grateful to see that two signals ($\Delta\delta$ = 0.055 ppm, 4.254 and 4.310 ppm) were obtained for the CF_3 groups in the ^{19}F NMR spectrum of the (*R*)-MTPA esters of racemic 3-fluorononan-1-ol. A mirror image pattern of signals was obtained upon repeating the sequence with the two enantiomers as shown in Figure 1. On this basis, we were able to estimate the ee of our fluoroalkynes to be 90%. In addition, the signals due to the methoxyl groups appeared as overlapping quartets ($\Delta\delta$ = 0.005 ppm, 3.533 and 3.528 ppm) in the 500-MHz ^1H NMR spectrum of the (*R*)-MTPA esters of racemic fluoro alcohol. Again, this pattern simplified to essentially one quartet in the ^1H NMR spectrum of the ester derived from each enantiomer. (See Experimental Section.)

We were able to corroborate this evidence by running the GC of the (*R*)-MTPA esters of the two enantiomers on a DB 17 column as previously recommended:[2b] The *RS* Mosher ester eluted 0.29 min later than the *RR* ester; the ratios of the two diastereomers were estimated to be 94(*RS*):6(*RR*) and 95(*RR*):5(*RS*) for the MTPA derivatives of the (*S*)-3-fluorononan-1-ol and (*R*)-3-fluorononan-1-ol, respectively, in good agreement with the NMR results.

It should be mentioned that we have attempted to distinguish the enantiomeric 4-fluoroalkynes by more direct methods. Unfortunately all chiral shift reagents known to interact with halogen[11] and multiple bonds[12]

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failed to distinguish the two enantiomers. In order to encourage better shift reagent/substrate interaction, we attempted to convert our fluorodecynes to the corresponding ketone. However, all attempts to hydrate the triple bond using standard methods[13] that worked well with 1-decyne were unsuccessful when applied to our fluorinated derivatives. Also meso and *dl* dimers obtained by quantitative oxidative coupling[14] of a sample of racemic fluorodecynes could not be distinguished by high-field ^{13}C NMR and ^{1}H NMR nor by capillary GC or reversed-phase HPLC.

In summary, we have demonstrated that it is possible to prepare homopropargyl fluorides in high optical purity. These synthons are available in a variety of chain lengths since the large-scale chromatographic separation of the mandelate esters of hexynols,[5b] octynols, and decynols proved to be extremely facile. We have also been able to prepare the chiral 4-fluoro-1-octynes without any complications. (See Experimental Section.) In addition, we have provided an entry into the previously unknown 3-fluoro carboxylic acid family, the biological properties of which may prove to be interesting.

Experimental Section

NMR spectra were obtained in $CDCl_3$ unless otherwise noted. Flash chromatography was performed by using Merck silica gel 60 (230–400 mesh). Both analytical and preparative TLC was carried out by using Merck precoated silica gel G/UV254 glass plates. Visualization of UV-inactive compounds was accomplished by spraying with water: hydrophobic spots appeared as white spots on a gray background. Mosher and mandelate esters could be observed on TLC plates by using a UV lamp at 254 nm.

The capillary GC chromatograms of the Mosher esters were obtained by using FID detection and a 30 m × 0.25 mm i.d. 0.25 μm film, J & W DB 17 column which was temperature programmed from 100 to 210 °C at 2.0 °C/min.

A Waters prep LC/System 500 chromatograph equipped with two 500-mL cartridges was used to separate the (*S*)-(+)-*O*-methylmandelic esters of 1-decyne-4-ol; 5% EtOAc/hexane was used as the eluting solvent for this system.

All reagents and starting materials were purchased from Aldrich Chemical Company and used without purification. Chiral materials were used without improving their optical purity. All reactions were performed under N_2. DMSO was distilled from CaH in vacuo prior to use and stored over molecular sieves under N_2. Unless otherwise noted, organic extracts were washed with saturated $NaHCO_3$ and saturated NaCl, dried over $MgSO_4$, and evaporated on a rotary evaporator.

(*S*)-(+)-*O*-Methylmandelic acid was prepared from (*S*)-(+)-mandelic acid (Aldrich) according to the method of Reeve and Christoffel.[15]

(±)-1-Decyn-4-ol. A dark brown slurry of lithium acetylide–EDA complex (83.5 g, 0.91 mol) in dry DMSO (400 mL) was stirred with 1,2-epoxyoctane (60.0 mL, 0.39 mol) overnight at room temperature. After the reaction mixture was quenched with ice (ca. 800 g), 0.3 N H_2SO_4 (ca. 150 mL) was used to neutralize the resultant basic solution to pH 7, after which the product was extracted with ether. The ethereal solution (1.2 L) was worked up to yield the crude product as a golden free-flowing liquid (50.6 g): bp 106–110 °C (90 mm) (lit.[16] bp 107–112 °C (112 mm)); ^{1}H NMR (60 MHz) δ 2.03 (1 H, t, C≡C*H*), 2.33 (2 H, m, CHOHCH_2CCH), 3.73 (1 H, m, $CH_2CHOHCH_2$).

Resolution of (±)-1-Decyn-4-ol. Crude racemic 1-decyn-4-ol was resolved as the (*S*)-*O*-methylmandelate esters by following the method described by Roy and Deslongchamps.[5b] In this way, multigram quantities of each enantiomer were obtained in a yield of 15% based on 1,2-epoxyoctane. The properties of the diastereomeric esters were as follows.

(*R*)-1-Decyn-4-ol, (*S*)-*O*-methylmandelate ester: R_f 0.28 (silica gel, 10% EtOAc/hexane); ^{1}H NMR (300 MHz) δ 4.94 (1 H, p, C*H*CH_2C≡CH), 4.75 (1 H, s, C*H*OCH_3), 3.40 (3 H, s, OCH_3), 2.45 (2 H, m, CHCH_2CCH), 1.95 (1 H, t, C≡C*H*); $[\alpha]^{21}_D$ = +70.0° (*c* 2.1, $CHCl_3$).

(*S*)-1-Decyn-4-ol, (*S*)-*O*-methylmandelate ester: R_f 0.33 (silica gel, 10% EtOAc/hexane); ^{1}H NMR (300 MHz) δ 4.97 (1 H, p, C*H*CH_2C≡CH), 4.76 (1 H, s, C*H*OCH_3), 3.42 (3 H, s, OCH_3), 2.31 (2 H, m, CHCH_2C≡CH), 1.80 (1 H, t, C≡C*H*); $[\alpha]^{21}_D$ = +18.1° (*c* 2.2, $CHCl_3$).

The rotations of the two enantiomeric alcohols obtained by hydrolysis of the above esters were as follows: (*R*)-1-decyn-4-ol, $[\alpha]^{21}_D$ = +14.5° (neat); (*S*)-1-decyn-4-ol, $[\alpha]^{21}_D$ = −14.4° (neat). No appreciable optical rotation could be measured at normal concentrations (1–2% w/v) in $CHCl_3$. This behavior is in contrast with that reported[5b] for the corresponding optically active 1-hexyn-3-ols.

(*R*)-4-Fluoro-1-decyne. (*S*)-1-Decyn-4-ol (2.15 g, 13.9 mmol) was added to a previously cooled (−45 °C) solution of DAST (4.2 g, 26 mmol) in dry CH_2Cl_2 (20 mL) with vigorous stirring over a 10-min period. The dark orange brown solution was allowed to come to room temperature overnight, after which time it was transferred into a separatory funnel containing water and CH_2Cl_2. The organic layer was worked up to yield the crude product as a dark orange free-flowing liquid (1.78 g). This material was passed through a small pad of Florisil and then flash chromatographed with 2.5% CH_2Cl_2/hexane being used as eluant to remove a considerable amount of enyne byproduct. The title compound was obtained as a colorless liquid (0.68 g, 32% isolated yield): bp 82 °C (43 mm); ^{1}H NMR (300 MHz) δ 0.89 (3 H, t, CH_3CH_2), 1.30 (8 H, br s, $CH_3(CH_2)_4$), 1.7 (2 H, d of m, J_{HF} = 20 Hz, CH_2CHFCH$_2$C≡CH), 2.03 (1 H, t, C≡C*H*), 2.53 (2 H, d of m, J_{HF} = 19 Hz, CH_2CHFCH_2C≡CH), 4.59 (1 H, d of p, J_{HF} = 48 Hz, C*H*F); ^{13}C NMR δ 14.00, 22.56, 24.8, 25.08 (J_{CF} = 24 Hz), 29.03, 31.69, 34.07 (J_{CF} = 20 Hz), 70.5, 79.23 (J_{CF} = 10 Hz), 91.5 (J_{CF} = 174 Hz); $[\alpha]^{21}_D$ = +12.3° (*c* 1.14, $CHCl_3$). Anal. Calcd for $C_{10}H_{17}F$: C, 76.92; H, 10.90. Found: C, 76.83; H, 10.63.

(*S*)-4-Fluoro-1-decyne was prepared in the same manner from (*R*)-1-decyn-4-ol: $[\alpha]^{21}_D$ = −10.2° (*c* 1.3, $CHCl_3$).

(*R*)-4-Fluoro-1-octyne ($[\alpha]^{21}_D$ = +10.0° (*c* 2.5, $CHCl_3$)) and **(*S*)-4-fluoro-1-octyne** ($[\alpha]^{21}_D$ = −11.7° (*c* 2.1, $CHCl_3$)) were synthesized in a similar manner from the corresponding optically active octynols.

(±)-3-Fluorononanoic Acid. A solution of (±)-4-fluoro-1-decyne (250 mg, 1.5 mmol) in 1 mL of acetic acid was added in one portion to a previously cooled (0 °C) solution of $KMnO_4$ (1.0 g, 6 mmol) in 14 mL of water with vigorous stirring. The dark purple slurry was allowed to come to room temperature while being stirred overnight, after which time excess oxidant was decomposed with 4 mL of dilute sulfurous acid. Sufficient hexane was then added to extract the product. The organic layer was dried over Na_2SO_4 and evaporated in vacuo to yield a colorless crystalline material as the crude product (120 mg): mp 43–45 °C; ^{1}H NMR (300 MHz) δ 2.64 (2 H, m, CHFCH_2CO_2H), 4.92 (1 H, d of m, J_{HF} = 44 Hz, C*H*F), 5.8 (1 H, br s, COO*H*). Anal. Calcd for $C_9H_{17}O_2F$: C, 61.13; H, 9.72. Found: C, 60.81; H, 9.75.

(±)-3-Fluorononan-1-ol. A solution of (±)-3-fluorononanoic acid (24 mg, 0.14 mmol) and $LiAlH_4$ (200 mg, 5.3 mmol) in 25 mL of ether was stirred at room temperature for 10 min, after which time excess reductant was slowly decomposed with water. The ether layer was worked up to yield a colorless liquid as the crude product (22 mg): ^{1}H NMR (200 MHz) δ 1.88 (2 H, m, CHFCH_2CH_2OH), 3.78 and 3.61 (each 1 H, distorted t, CHFCH$_2$CH_2OH), 4.68 (1 H, d of m, J_{HF} = 49 Hz, C*H*F). Anal. Calcd for $C_9H_{19}FO$: C, 66.62; H, 11.80. Found: C, 66.86; H, 11.83.

(±)-3-Fluorononan-1-ol, MTPA Esters. The title compounds were prepared essentially as previously reported.[2b] Care was taken to ensure complete esterification. The two diastereomeric MTPA esters were purified by flash chromatography or preparative TLC (20% EtOAc/hexane) prior to NMR analysis.

(*R*)-3-Fluorononan-1-ol, (*R*)-α-(trifluoromethyl)phenylacetate: ^{1}H NMR δ 1.97 (2 H, m, CHFCH_2CH_2OCO), 3.533 (3 H, q, J_{HF} = 1.2 Hz, CH_3O), 4.45 (1 H, m, C*H*F, 2 H, m, CHFCH$_2$CH_2OH), 7.48 (2 H, m, phenyl), 7.4

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(3 H, m, phenyl); ^{19}F NMR (TFA ext ref) δ 4.313 (3 F, br s, CF_3), -108.21 (1 F, m, C*H*F); capillary GC (DB 17) retention time, 47.99 min.

(*S*)-3-Fluorononan-1-ol, (*R*)-α-methoxy-α-(trifluoromethyl)phenylacetate: ^{1}H NMR δ 1.97 (2 H, m, $CHFCH_2CH_2OCO$), 3.528 (3 H, q, J_{HF} = 1.2 Hz, CH_3O), 4.45 (1 H, m, C*H*F, 2 H, m, $CHFCH_2CH_2OH$), 7.48 (2 H, m, phenyl), 7.4 (3 H, m, phenyl); ^{19}F NMR (TFA ext ref) δ 4.258 (3 F, br s, CF_3), -107.8 (1 F, m, C*H*F); capillary GC (DB 17) retention time, 48.28 min.

The mass spectrum (CI, ether) for racemic Mosher esters had *m/e* 453 ($(M + 75)^+$). The mass spectrum (EI, 70 eV) had *m/e* 378 (M^+).

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Supplementary Material Available: ^{1}H NMR and CI and EI mass spectra for the MPTA esters of the two enantiomeric 3-fluorononan-1-ols (4 pages). Ordering information is given on any current masthead page.

MeCN Is a Better Solvent Than Me_2SO for Electrochemically Induced $S_{RN}1$ Substitution Reactions with Chalcogenophenoxide Anions

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Although the synthesis of aromatic substituted derivatives **1** by $S_{RN}1$ substitution (eqs 1–4)[1] is usually carried out in liquid ammonia where the hydrogen abstraction reaction (5) does not occur, dimethyl sulfoxide (DMSO) is considered as the solvent of choice among other aprotic solvents due to its low reactivity toward aryl radicals.[2]

$$ArX + e \rightleftarrows [ArX]^{\bullet -} \quad (1)$$

$$[ArX]^{\bullet -} \xrightarrow{k_1} Ar^{\bullet} + X^- \quad (2)$$

$$Ar^{\bullet} + Nu^- \xrightarrow{k_2} (ArNu)^{\bullet -} \quad (3)$$

$$(ArNu)^{\bullet -} + ArX \rightleftarrows \underset{\mathbf{1}}{ArNu} + [ArX]^{\bullet -} \quad (4)$$

$$Ar^{\bullet} + SH \xrightarrow{k_H} ArH + S^{\bullet} \quad (5)$$

$$ArX + PhE^- \xrightarrow[S_{RN}1]{} \underset{\mathbf{2}}{ArEPh} + X^- \quad (6)$$

$$Ar^{\bullet} + e \rightarrow Ar^- \quad (7)$$

Despite the fact that MeCN in slightly more reactive toward aryl radicals than DMSO,[3,4] results from Savéant, Amatore, and Thiébault[3b,5] and our group[6] have emphasized the advantages of using MeCN, which is a versatile solvent, to prepare chalcogeno derivatives **2** (E = S, Se, Te) by electrochemically induced $S_{RN}1$ substitution[7] (global reaction 6). Indeed, when the electrophilic ability of the intermediate Ar• radical is reinforced by the presence of electron-withdrawing groups such as nitrile and carbonyl functions, the key step (3) is diffusion controlled in MeCN as well as in DMSO and so the hydrogen abstraction reaction (5) becomes negligible and substitution occurs almost quantitatively as long as the cathodic reaction (7) is avoided.

Even for unactivated aryl radicals Ar• (Ar• = 4-biphenyl, 2-fluorenyl, 9-anthryl), seleno and telluro derivatives were isolated in yields ranging from 53 to 74% in MeCN.[6d] Furthermore, during the electrochemical synthesis of the 9-(phenylchalcogeno)anthracene (a, thio; b, seleno; c, telluro) derivatives **3a–c** where the nucleophilic attack (3) was not diffusion controlled, we have observed that the synthesis proceeds in better yields in MeCN than in DMSO.[6d,g] In other words, the results indicate that the ratios k_2/k_H are higher in MeCN than in DMSO since the key step (3) and the reaction (5) are the only competing reactions. For instance, this ration is 5.3 ± 0.3 times higher in MeCN than in DMSO when the electrochemical synthesis of **3a,b** is carried out, as shown by cyclic voltammetry (Table I).[6g]

Surprisingly, an opposite effect was found by Savéant et al.[5b] when the electrochemical synthesis of 1-(phenylthio)naphthalene (**4**) was carried out. Indeed, **4** was isolated in almost quantitative yield in DMSO and in 32% yield in MeCN, together with 40% naphthalene (HPLC determination), when 1-BrNaph was reduced in the presence of PhS^- in excess (10^{-1} M; 10 equiv). During these electrolyses, the key step (3) was in competition with two side reactions (5 and 7) since the intermediate $BrNaph^{\bullet -}$ radical anion was unstable ($k_1 = 2 \times 10^8$ s^{-1} in DMSO), and so Naph• was generated close to the electrode where it was reduced and then protonated to naphthalene. With the assumption that the unknown cleavage rate, k_1, of the 1-$BrNaph^{\bullet -}$ radical anion in MeCN was the same as in DMSO, it was concluded that $k_2/k_H = 15$ M^{-1} in MeCN and 40 M^{-1} in DMSO. The same latter value was also found by Helgée and Parker in DMSO.[4]

In order to be able to determine the ratio k_2/k_H in MeCN with no assumption concerning k_1 in this solvent, we have carried out the indirect reduction of 1-bromonaphthalene in MeCN and DMSO in the presence of a redox mediator (med) in order to avoid the cathodic side reaction (7). Indeed, under such conditions, $[ArX]^{\bullet -}$ and therefore Ar• are generated in the bulk of the cathodic solution through the following reactions: med + e ⇄ $med^{\bullet -}$ and $med^{\bullet -}$ + ArX ⇄ med + $[ArX]^{\bullet -}$.[1c,7-9] Hence, the

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