BiCl$_3$-Mediated Direct Functionalization of Unsaturated C–C Bonds with an Electrophilic SCF$_2$PO(OEt)$_2$ Reagent

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Supporting Information

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1. General information

All reactions were carried out using oven-dried glassware and magnetic stirring under argon unless otherwise stated. Reaction temperatures are reported as the temperature of the bath surrounding the vessel. Analytical thin layer chromatography was performed on silica gel aluminum plates with F-254 indicator and visualized by UV light (254 nm) and/or chemical staining with a KMnO₄ solution. Flash column chromatography was performed using 0.040 – 0.063 mm silica gel or a Biotage Isolera One flash purification system. ¹H NMR spectra were recorded on a Bruker DXP 300 MHz spectrometer at 300.1 MHz, ¹³C NMR spectra at 75.5 MHz, ¹⁹F NMR spectra at 282.4 MHz and ³¹P NMR at 121.5 MHz. Chemical shifts (δ) are quoted in ppm relative to TMS (¹H) and CFCl₃ (¹⁹F). Coupling constants (J) are quoted in Hz. The following abbreviations were used to show the multiplicities: s: singlet, d: doublet, t: triplet, q: quadruplet, dd: doublet of doublet, dt: doublet of triplet, td: triplet of doublet, m: multiplet. The residual solvent signals were used as references (CDCl₃: δH = 7.26 ppm, δC = 77.16 ppm or relative to external CFCl₃, δF = 0 ppm). High-resolution mass spectrometry (HRMS) was carried out on an electrospray ionization mass spectrometer with a micro-TOF analyzer. IR spectra were recorded on a PerkinElmer Spectrum 100, the wave numbers (ν) of recorded IR-signals (ATR) are quoted in cm⁻¹. Melting points were reported for new compounds, recorded on a Heizbank system kofler WME and were uncorrected.

2. Materials

Tetrahydrofuran and dichloroethane were respectively distilled from sodium/benzophenone and calcium hydride under argon. Water was provided from a Veolia Aquadem 500 system. Anhydrous bismuth(III) chloride (+98%) and 1-pentyne (99%) were purchased from Acros Organics and used as supplied. 1-phenyl-1-pentyne 1a (98%), 1-phenyl-1-propyne 1p (98%), 1-phenyl-1-butyne 1q (98%), 4-octyne (99%) 1r and diphenylacetylene 1s (98%) were purchased from Alfa Aesar and used as received. Styrene 5a (99%), 4-vinylbiphenyl 5b (97%), 4-bromostyrene 5c (98%), 4-chlorostyrene 5d (99%) and 2-phenylpropene 5h (99%) were purchased from Alfa Aesar and used as supplied. The reagent I was prepared according to the previously reported procedure.¹¹ Alkynes 1b, 1d, 1f-h and 1l-n were prepared according to the literature procedure.¹² The alkyne 1c was prepared according to the literature procedure.¹³ The alkyne 1i was prepared according to the literature procedure.¹⁴ Alkynes 1j-k were prepared according to the literature procedure.¹⁵ Alkyne 1o was prepared according to the literature procedure.¹⁶ TMS-alkynes 3a-c and 3o were prepared according to the literature procedure.¹⁷ TMS-alkynes 3d, 3i and 3j were prepared according to the literature procedure.¹⁸ TMS-alkynes 3e, 3h and 3m-n were prepared according to the literature procedure.¹⁹ TMS-alkynes 3f was prepared according to the literature procedure.¹⁰ TMS-alkynes 3g was prepared according to the literature procedure.¹¹ TMS-alkynes 3k was prepared according to the literature procedure.¹² TMS-alkynes 3l was prepared according to the literature procedure.¹³ TMS-alkynes 3p was prepared according to the literature procedure.¹⁴ Styrene 5e was prepared
according to the literature procedure. Styrene 5f was prepared according to the literature procedure. Styrene 5g was prepared according to the literature procedure.

3. General procedure for the synthesis of derivatives 2

An oven-dried tube was charged with the reagent I (106 mg, 0.3 mmol). If solid, the alkyne 1 (0.25 mmol) was added at this stage. The tube was fitted with a rubber septum, evacuated under vacuum and backfilled with argon for three times before the addition of distilled DCE (2.5 mL). If liquid, the alkyne 1 (0.25 mmol) was added at this stage. Then, water (9 µl, 0.5 mmol) was added before adding Bismuth(III) chloride (158 mg, 0.5 mmol) under an argon atmosphere and the tube was sealed with a Teflon cap. The reaction mixture was heated at 45 °C for 40 hours in a pre-heated oil bath. The resulting suspension was cooled down to room temperature, diluted with dichloromethane (5 mL), filtered over a plug of Celite® (washed with 25 mL of dichloromethane) and concentrated under reduced pressure. The crude residue was finally purified by either a Biotage Isolera One Flash Purification System or a flash column chromatography over silica gel to afford the corresponding product 2.

4. General procedure for the synthesis of derivatives 4

An oven-dried tube was charged with the reagent I (106 mg, 0.3 mmol). If solid, the alkyne 3 (0.25 mmol) was added at this stage. The tube was fitted with rubber septum, evacuated under vacuum and backfilled with argon for three times before the addition of distilled DCE (2.5 mL). If liquid, the alkyne 3 (0.25 mmol) was added at this stage. Then, water (8 µl, 0.45 mmol) was added before adding Bismuth(III) chloride (142 mg, 0.45 mmol) under an argon atmosphere and the tube was sealed with a Teflon cap. The reaction mixture was heated at 60 °C for 6 hours in a pre-heated oil bath. The resulting suspension was cooled down to room temperature, diluted with dichloromethane (5 mL), filtered over a plug of Celite® (washed with 30 mL of dichloromethane) and concentrated under reduced pressure. The crude residue was finally purified by either a Biotage Isolera One Flash Purification System or a flash column chromatography over silica gel to afford the corresponding products 4.
5. General procedure for the synthesis of derivatives 6

An oven-dried tube was charged with the reagent I (106 mg, 0.3 mmol). If solid, the styrene 5 (0.25 mmol) was added at this stage. The tube was fitted with rubber septum, evacuated under vacuum and backfilled with argon for three times before the addition of distilled DCE (2.5 mL). If liquid, the styrene 5 (0.25 mmol) was added at this stage. Then, water (8 µl, 0.5 mmol) was added before adding Bismuth(III) chloride (158 mg, 0.5 mmol) under argon atmosphere and the tube was sealed with a Teflon cap. The reaction mixture was heated at 60 °C for 6 hours in a pre-heated oil bath. The resulting suspension was cooled down to room temperature, diluted with dichloromethane (5 mL), filtered over a plug of Celite® (washed with 25 mL of dichloromethane) and concentrated under reduced pressure. The crude residue was finally purified by either a Biotage Isolera One Flash Purification System or a flash column chromatography over silica gel to afford the corresponding compound 6.

6. Purification and characterization of derivatives 2

Note that only the signals of the major isomer were depicted due to the high diastereoisomeric ratio. All reported diastereoisomeric ratios were determined by $^{19}$F NMR on the crude reaction mixture.

(E)-1-Chloro-1-phenyl-2-[(diethylphosphonodifluoromethyl)sulfanyl]pentene  2a.
Purified by silica gel column chromatography (25 g SiO$_2$ cartridge, height 80 mm, width 30 mm, eluent: pentane/EtOAc, from 90:10 to 70:30); Yield: 89% (89 mg, 0.22 mmol); Diastereoisomeric ratio: 96:4; Note that 2a was obtained in 78% (310 mg, 0.78 mmol) and a 97:3 diastereoisomeric ratio on 1 mmol scale; R$_f$ (petroleum ether/Et$_2$O = 50:50): 0.38; Light yellow oil; $^1$H NMR (300.1 MHz, CDCl$_3$): $\delta$ 7.39-7.28 (m, 5H), 4.22-3.92 (m, 4H), 2.78 (dd, $J$ = 7.5 and 7.5 Hz, 2H), 1.82-1.69 (m, 2H), 1.23 (t, $J$ = 7.2 Hz, 6H), 1.01 (t, $J$ = 7.5 Hz, 3H); $^{13}$C NMR (75.5 MHz, CDCl$_3$): $\delta$ 140.9 (dt, $J$ = 2.3 and 1.5 Hz), 138.9, 129.3, 128.7, 128.0, 126.2 (dt, $J$ = 5.3 and 1.5 Hz), 125.2 (td, $J$ = 302.0 and 213.7 Hz), 65.4 (d, $J$ = 6.8 Hz), 38.7, 20.5, 16.3 (d, $J$ = 5.3 Hz), 13.6; $^{19}$F NMR (282.4 MHz, CDCl$_3$): $\delta$ -82.8 (d, $J$ = 98.8 Hz); $^{31}$P{$^1$H} NMR (121.5 MHz, CDCl$_3$): $\delta$ 2.9 (t, $J$ = 97.2 Hz); IR (neat, cm$^{-1}$) v: 2965, 2934, 2874, 1591, 1444, 1371, 1275, 1114, 1024, 907, 872, 750, 727, 695, 537; HRMS (ESI$^+$): calcld for C$_{16}$H$_{26}$ClF$_2$NO$_3$PS $m/z$ 416.1028 [M+NH$_4$]$^+$, found 416.1027 (-0.2 ppm).
The structure of 2a was confirmed by 2D experiments.

The NOESY NMR of 2a:

The HOESY NMR of 2a:
\((E)\)-1-Chloro-1-(4-methylphenyl)-2-[(diethylphosphonodifluoromethyl)sulfanyl]pentene 2b. Purified by silica gel column chromatography (25 g SiO\(_2\) cartridge, height 80 mm, width 30 mm, eluent: pentane/EtOAc, from 90:10 to 70:30); Yield: 70\% (72 mg, 0.17 mmol); Diastereoisomeric ratio: 99:1; \(R_f\) (petroleum ether/Et\(_2\)O = 50:50): 0.34; yellow oil; \(^1\)H NMR (300.1 MHz, CDCl\(_3\)): \(\delta \) 7.23-7.18 (m, 2H), 7.15-7.09 (m, 2H), 4.23-3.90 (m, 4H), 2.76 (dd, \(J = 7.5\) and 7.5 Hz, 2H), 2.33 (s, 3H), 1.81-1.67 (m, 2H), 1.23 (t, \(J = 6.9\) Hz, 6H), 1.00 (t, \(J = 7.2\) Hz, 3H); \(^{13}\)C NMR (75.5 MHz, CDCl\(_3\)): \(\delta \) 141.1 (dt, \(J = 2.3\) and 1.5), 138.7, 136.1, 129.3, 128.6, 125.8 (dt, \(J = 4.5\) and 1.5 Hz), 125.2 (td, \(J = 302\) and 213.7 Hz), 65.4 (d, \(J = 6.0\) Hz), 38.7, 21.3, 20.6, 16.3 (d, \(J = 5.3\) Hz), 13.6; \(^{19}\)F NMR (282.4 MHz, CDCl\(_3\)): \(\delta \) -82.8 (d, \(J = 98.8\) Hz); \(^{31}\)P\({}^1\)H\) NMR (121.5 MHz, CDCl\(_3\)): \(\delta \) 2.9 (t, \(J = 98.4\) Hz); IR (neat, cm\(^{-1}\)) \(\nu \): 2965, 2933, 2873, 1602, 1508, 1457, 1394, 1274, 1113, 1022, 908, 818, 730, 643, 537; HRMS (ESI\(^+\)): calecd for C\(_{17}\)H\(_{28}\)ClF\(_2\)NO\(_3\)PS \(m/z\) 430.1184 [M+NH\(_4\)]\(^+\), found 430.1188 (0.9 ppm).

\((E)\)-1-Chloro-1-[(4-phenylphenyl)-2-(diethylphosphonodifluoromethyl)sulfanyl]pentene 2c. Purified by silica gel column chromatography (25 g SiO\(_2\) cartridge, height 80 mm, width 30 mm, eluent: pentane/EtOAc, from 90:10 to 70:30); Yield: 51\% (61 mg, 0.13 mmol); Diastereoisomeric ratio: 99:1; \(R_f\) (petroleum ether/Et\(_2\)O = 50:50): 0.37; yellow oil; \(^1\)H NMR (300.1 MHz, CDCl\(_3\)): \(\delta \) 7.62-7.54 (m, 4H), 7.48-7.33 (m, 5H), 4.22-3.92 (m, 4H), 2.81 (dd, \(J = 7.2\) and 7.2 Hz, 2H), 1.86-1.70 (m, 2H), 1.22 (t, \(J = 7.2\) Hz, 6H), 1.03 (t, \(J = 7.2\) Hz, 3H); \(^{13}\)C NMR (75.5 MHz, CDCl\(_3\)): \(\delta \) 141.6, 140.7 (dt, \(J = 2.3\) and 1.5), 140.3, 137.8, 129.9, 129.0, 127.8, 127.1, 126.7, 126.4 (d, \(J = 5.3\) and 1.5 Hz), 125.2 (td, \(J = 302.0\) and 213.7 Hz), 65.5 (d, \(J = 6.0\) Hz), 38.8, 20.6, 16.3 (d, \(J = 6.0\) Hz), 13.7; \(^{19}\)F NMR (282.4 MHz, CDCl\(_3\)): \(\delta \) -82.8 (d, \(J = 98.8\) Hz); \(^{31}\)P\({}^1\)H\) NMR (121.5 MHz, CDCl\(_3\)): \(\delta \) 3.9 (m); IR (neat, cm\(^{-1}\)) \(\nu \): 2964, 2933, 2873, 1508, 1457, 1394, 1274, 1113, 1022, 908, 818, 730, 643, 537; HRMS (ESI\(^+\)): calecd for C\(_{22}\)H\(_{30}\)ClF\(_2\)NO\(_3\)PS \(m/z\) 492.1341 [M+NH\(_4\)]\(^+\), found 492.1346 (1.0 ppm).

\((E)\)-1-Chloro-1-(4-acetoxylphenyl)-2-[(diethylphosphonodifluoromethyl)sulfanyl]pentene 2d. Purified by silica gel column chromatography (10 g SiO\(_2\) cartridge, height 60 mm, width 20 mm, eluent: pentane/CH\(_2\)Cl\(_2\), from 40:60 to 0:100); Yield: 40\% (46 mg, 0.10 mmol);
Diastereoisomeric ratio: 99:1; R<sub>f</sub> (petroleum ether/Et<sub>2</sub>O = 50:50): 0.45; light yellow oil; ¹H NMR (300.1 MHz, CDCl<sub>3</sub>): δ 7.33 (d, J = 8.7 Hz, 2H), 7.05 (d, J = 8.7 Hz, 2H), 4.23-3.95 (m, 4H), 2.77 (dd, J = 7.5 and 7.5 Hz, 2H), 2.28 (s, 3H), 1.78-1.68 (m, 2H), 1.25 (t, J = 7.2 Hz, 6H), 1.00 (t, J = 7.2 Hz, 3H); ¹³C NMR (75.5 MHz, CDCl<sub>3</sub>): δ 169.1, 150.9, 139.9 (dt, J = 2.3 and 1.5 Hz), 136.4, 130.7, 126.8 (dt, J = 5.3 and 1.5 Hz), 125.2 (td, J = 302.0 and 213.7 Hz), 121.3, 65.6 (d, J = 6.0 Hz), 38.8, 21.2, 20.6, 16.4 (d, J = 5.3 Hz), 13.7; ¹⁹F NMR (282.4 MHz, CDCl<sub>3</sub>): δ -82.8 (d, J = 96.0 Hz); ³¹P{¹H} NMR (121.5 MHz, CDCl<sub>3</sub>): δ 2.8 (t, J = 97.2 Hz); IR (neat, cm⁻¹): ν: 2966, 2874, 1766, 1596, 1503, 1370, 1274, 1194, 1166, 1015, 908, 732, 534; HRMS (ESI⁺): calcd for C<sub>18</sub>H<sub>28</sub>ClF<sub>2</sub>NO<sub>3</sub>PS m/z 474.1082 [M+NH₄]⁺, found 474.1067 (-3.2 ppm).

(E)-1-Chloro-1-(4-acetamidophenyl)-2-[(diethylphosphonodifluoromethyl)sulfanyl]pentene 2e. Purified by silica gel column chromatography (height 200 mm, width 20 mm, eluent: CH₂Cl₂/EtOAc, 65:35); Yield: 58% (66 mg, 0.14 mmol); Diastereoisomeric ratio: 99:1; R<sub>f</sub> (CH₂Cl₂/Et₂O = 50:50): 0.23; white solid; Mp: 111-114°C; ¹H NMR (300.1 MHz, CDCl<sub>3</sub>): δ 7.94 (br. s, 1H ), 7.49 (d, J = 8.4 Hz, 2H), 7.26 (d, J = 8.7 Hz, 2H), 4.22-3.99 (m, 4H), 2.76 (dd, J = 7.2 and 7.2 Hz, 2H), 2.13 (s, 3H), 1.78-1.67 (m, 2H), 1.26 (t, J = 6.9 Hz, 6H), 1.00 (t, J = 7.5 Hz, 3H); ¹³C NMR (75.5 MHz, CDCl<sub>3</sub>): δ 168.8, 140.7 (d, dt, J = 2.3 and 1.5 Hz), 138.8, 134.3, 130.1, 126.0 (dt, J = 4.5 and 1.5 Hz), 125.2 (td, J = 302.0 and 213.7 Hz), 119.0, 65.7 (d, J = 6.8 Hz), 38.8, 24.6, 20.6, 16.3 (d, J = 5.3 Hz), 13.7; ¹⁹F NMR (282.4 MHz, CDCl<sub>3</sub>): δ -82.8 (d, J = 98.8 Hz); ³¹P{¹H} NMR (121.5 MHz, CDCl<sub>3</sub>): δ 2.6 (t, J = 98.4 Hz); IR (neat, cm⁻¹) ν: 3323, 3284, 2961, 1693, 1597, 1533, 1313, 1259, 1024, 906, 858, 761, 549; HRMS (ESI⁺): calcd for C<sub>18</sub>H<sub>29</sub>ClF<sub>2</sub>N<sub>2</sub>O<sub>4</sub>PS m/z 473.1242 [M+NH₄]⁺, found 473.1234 (-1.7 ppm).

(E)-1-Chloro-1-(4-fluorophenyl)-2-[(diethylphosphonodifluoromethyl)sulfanyl]pentene 2f. Purified by silica gel column chromatography (25 g SiO<sub>2</sub> cartridge, height 80 mm, width 30 mm, eluent: pentane/EtOAc, from 90:10 to 70:30); Yield: 75% (78 mg, 0.19 mmol); Diastereoisomeric ratio: 97:3; R<sub>f</sub> (petroleum ether/Et₂O = 50:50): 0.31; light yellow oil; ¹H NMR (300.1 MHz, CDCl<sub>3</sub>): δ 7.38-7.28 (m, 2H), 7.09-6.96 (m, 2H), 4.25-3.95 (m, 4H), 2.77 (dd, J = 7.5 and 7.5 Hz, 2H), 1.81-1.66 (m, 2H), 1.27 (t, J = 7.2 Hz, 6H), 1.00 (t, J = 7.2 Hz, 3H); ¹³C NMR (75.5 MHz, CDCl<sub>3</sub>): δ 162.7 (d, J = 249.2 Hz), 139.9 (dt, J = 2.3 and 1.5 Hz), 135.0 (d, J = 3.8 Hz), 131.4 (d, J = 8.3 Hz), 126.8 (dt, J = 5.3 and 1.5 Hz), 125.2 (td, J = 301.2 and 214.4 Hz), 115.1 (d, J = 21.9 Hz), 65.5 (d, J = 6.8 Hz), 38.8, 20.5, 16.3 (d, J = 6.0 Hz), 13.6; ¹⁹F NMR (282.4 MHz, CDCl<sub>3</sub>): δ -82.9 (d, J = 98.8 Hz), -112.6 to -112.7 (m); ³¹P{¹H}
NMR (121.5 MHz, CDCl$_3$): $\delta$ 3.9-1.9 (m); IR (neat, cm$^{-1}$) $\nu$: 2966, 2935, 2874, 1596, 1505, 1498, 1275, 1024, 908, 837, 733, 533 cm$^{-1}$; HRMS (ESI$^+$): calcd for C$_{16}$H$_{25}$ClF$_3$NO$_3$PS m/z 434.0933 [M+NH$_4$$^+$]+, found 434.0927 (-1.4 ppm).

(E)-1-Chloro-1-(4-chlorophenyl)-2-[(diethyl phosphonodifluoromethyl)sulfanyl]pentene

2g. Purified by silica gel column chromatography (25 g SiO$_2$ cartridge, height 80 mm, width 30 mm, eluent: pentane/EtOAc, from 90:10 to 70:30); Yield: 69% (75 mg, 0.17 mmol); Diastereoisomeric ratio: 95:5; $R_f$ (petroleum ether/Et$_2$O = 50:50): 0.31; light yellow oil; $^1$H NMR (300.1 MHz, CDCl$_3$): $\delta$ 7.34-7.24 (m, 4H), 4.24-3.97 (m, 4H), 2.77 (dd, $J$ = 7.5 and 7.5 Hz, 2H), 1.81-1.64 (m, 2H), 1.27 (t, $J$ = 6.9 Hz, 6H), 1.00 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (75.5 MHz, CDCl$_3$): $\delta$ 139.7 (dt, $J$ = 2.3 and 1.5 Hz), 137.3, 134.7, 130.8, 128.3, 127.1 (dt, $J$ = 4.5 and 1.5 Hz), 125.1 (td, $J$ = 302.0 and 214.4 Hz), 65.5 (d, $J$ = 6.0 Hz), 38.7, 20.5, 16.3 (d, $J$ = 6.0 Hz), 13.6; $^{19}$F NMR (282.4 MHz, CDCl$_3$): $\delta$ -82.8 (d, $J$ = 98.8 Hz); $^{31}$P{$^1$H} NMR (121.5 MHz, CDCl$_3$): $\delta$ 3.9-1.7 (m); IR (neat, cm$^{-1}$) $\nu$: 2965, 2934, 2873, 1582, 1483, 1393, 1274, 1114, 1026, 1014, 908, 761, 731, 538; HRMS (ESI$^+$): calcd for C$_{16}$H$_{25}$ClF$_2$NO$_3$PS m/z 450.0638 [M+NH$_4$$^+$]$^*$, found 450.0628 (-2.2 ppm).

(E)-1-Chloro-1-(4-bromophenyl)-2-[(diethyl phosphonodifluoromethyl)sulfanyl]pentene

2h. Purified by silica gel column chromatography (25 g SiO$_2$ cartridge, height 80 mm, width 30 mm, eluent: pentane/EtOAc, from 90:10 to 70:30); Yield: 72% (86 mg, 0.18 mmol); Diastereoisomeric ratio: 96:4; $R_f$ (petroleum ether/Et$_2$O = 50:50): 0.31; light yellow oil; $^1$H NMR (300.1 MHz, CDCl$_3$): $\delta$ 7.47 (d, $J$ = 8.4 Hz, 2H), 7.20 (d, $J$ = 8.4 Hz, 2H), 4.25-3.97 (m, 4H), 2.76 (dd, $J$ = 7.5 and 7.5 Hz, 2H), 1.80-1.65 (m, 2H), 1.27 (t, $J$ = 6.9 Hz, 6H), 1.00 (t, $J$ = 7.5 Hz, 3H); $^{13}$C NMR (75.5 MHz, CDCl$_3$): $\delta$ 139.7 (dt, $J$ = 2.3 and 1.5 Hz), 137.3, 131.2, 131.1, 127.1 (dt, $J$ = 5.3 and 1.5 Hz), 125.1 (td, $J$ = 302.0 and 214.4 Hz), 123.0, 65.5 (d, $J$ = 6.0 Hz), 38.8, 20.5, 16.3 (d, $J$ = 6.0 Hz), 13.6; $^{19}$F NMR (282.4 MHz, CDCl$_3$): $\delta$ -82.8 (d, $J$ = 98.8 Hz); $^{31}$P{$^1$H} NMR (121.5 MHz, CDCl$_3$): $\delta$ 3.8-1.8 (m); IR (neat, cm$^{-1}$) $\nu$: 2965, 2934, 2873, 1582, 1483, 1393, 1274, 1114, 1026, 1014, 907, 732, 537; HRMS (ESI$^+$): calcd for C$_{16}$H$_{25}$BrClF$_2$NO$_3$PS m/z 494.0133 [M+NH$_4$$^+$]$^*$, found 494.0113 (-4.0 ppm).
(E)-1-Chloro-1-(4-(trifluoromethyl)phenyl)-2-diethylphosphonodifluoromethyl)sulfanyl pentene 2i. Purified by silica gel column chromatography (25 g SiO$_2$ cartridge, height 80 mm, width 30 mm, eluent: pentane/EtOAc, from 90:10 to 70:30); Yield: 54% (63 mg, 0.13 mmol); Diastereoisomeric ratio: 92:8; R$_f$ (petroleum ether/Et$_2$O = 50:50): 0.36; light yellow oil; $^1$H NMR (300.1 MHz, CDCl$_3$): δ 7.61 (d, $J$ = 8.1 Hz, 2H), 7.45 (d, $J$ = 8.1 Hz, 2H), 4.23-3.94 (m, 4H), 3.29 (dd, $J$ = 7.5 and 7.5 Hz, 2H), 1.83-1.67 (m, 2H), 1.24 (t, $J$ = 7.2 Hz, 6H), 1.02 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (75.5 MHz, CDCl$_3$): δ 142.4 (q, $J$ = 1.5 Hz), 139.2 (dt, $J$ = 2.3 and 1.5 Hz), 130.7 (q, $J$ = 32.5 Hz), 129.9, 127.8 (dt, $J$ = 5.3 and 1.5 Hz), 125.2 (td, $J$ = 302.0 and 214.4 Hz), 125.1 (q, $J$ = 3.8 Hz), 123.9 (q, $J$ = 271.8 Hz), 65.5 (d, $J$ = 6.8 Hz), 38.7, 20.5, 16.2 (d, $J$ = 5.3 Hz), 13.6; $^{19}$F NMR (282.4 MHz, CDCl$_3$): δ -63.3, -82.9 (d, $J$ = 98.8 Hz); $^{31}$P{$^1$H} NMR (121.5 MHz, CDCl$_3$): δ 3.8-1.6 (m); IR (neat, cm$^{-1}$) ν: 2967, 2936, 2875, 1604, 1459, 1408, 1323, 1276, 1167, 1127, 1016, 908, 733, 537; HRMS (ESI$^+$): calcd for C$_{17}$H$_{25}$ClF$_5$NO$_3$PS m/z 484.0901 [M+NH$_4$]$^+$, found 484.0894 (-1.4 ppm).

(E)-1-Chloro-1-(4-acetylphenyl)-2-[(diethylphosphonodifluoromethyl)sulfanyl]pentene 2j. Purified by silica gel column chromatography (25 g SiO$_2$ cartridge, height 80 mm, width 30 mm, eluent: pentane/EtOAc, from 90:10 to 70:30); Yield: 50% (55 mg, 0.12 mmol); Diastereoisomeric ratio: 97:3; R$_f$ (petroleum ether/Et$_2$O = 50:50): 0.19; light yellow oil; $^1$H NMR (300.1 MHz, CDCl$_3$): δ 7.91 (d, $J$ = 8.4 Hz, 2H), 7.42 (d, $J$ = 8.1 Hz, 2H), 4.26-3.92 (m, 4H), 2.77 (dd, $J$ = 7.5 and 7.5 Hz, 2H), 2.58 (s, 3H), 1.80-1.66 (m, 2H), 1.23 (t, $J$ = 6.9 Hz, 6H), 1.00 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (75.5 MHz, CDCl$_3$): δ 197.4, 143.3, 136.9, 129.7, 128.1, 127.5 (dt, $J$ = 4.5 and 1.5 Hz), 125.1 (td, $J$ = 302.0 and 214.4 Hz), 125.1 (q, $J$ = 3.8 Hz), 123.9 (q, $J$ = 271.8 Hz), 65.5 (d, $J$ = 6.8 Hz), 38.7, 20.5, 16.3 (d, $J$ = 5.3 Hz), 13.6; $^{19}$F NMR (282.4 MHz, CDCl$_3$): δ -82.9 (d, $J$ = 98.8 Hz); $^{31}$P{$^1$H} NMR (121.5 MHz, CDCl$_3$): δ 2.8 (t, $J$ = 98.4 Hz); IR (neat, cm$^{-1}$) ν: 2967, 2874, 1686, 1597, 1402, 1264, 1029, 908, 728, 538; HRMS (ESI$^+$): calcd for C$_{18}$H$_{28}$ClF$_2$NO$_4$PS m/z 458.1133 [M+NH$_4$]$^+$, found 458.1127 (-1.3 ppm).

(E)-1-Chloro-1-[4-cyanophenyl]-2-[(diethylphosphonodifluoromethyl)sulfanyl]pentene 2k. Purified by silica gel column chromatography (10 g SiO$_2$ cartridge, height 60 mm, width...
20 mm, eluent: pentane/CH$_2$Cl$_2$, from 40:60 to 0:100); Yield: 46% (49 mg, 0.12 mmol); Diastereoisomeric ratio: 93:7; R$_f$ (petroleum ether/EtOAc = 50:50): 0.30; light yellow oil; $^1$H NMR (300.1 MHz, CDCl$_3$): $\delta$ 7.67-7.61 (m, 2H), 7.50-7.42 (m, 2H), 4.26-4.01 (m, 4H), 2.77 (dd, $J = 7.5$ and 7.5 Hz, 2H), 1.80-1.66 (m, 2H), 1.27 (t, $J = 7.2$ Hz, 6H), 1.00 (t, $J = 7.2$ Hz, 3H); $^{13}$C NMR (75.5 MHz, CDCl$_3$): $\delta$ 143.2, 138.5 (dt, $J = 2.3$ and 2.3 Hz), 131.9, 130.3, 128.5 (dt, $J = 4.5$ and 1.5 Hz), 125.1 (td, $J = 302.0$ and 215.9 Hz), 118.4, 112.5, 65.5 (d, $J = 6.8$ Hz), 38.7, 20.5, 16.4 (d, $J = 5.3$ Hz), 13.7; $^{19}$F NMR (282.4 MHz, CDCl$_3$): $\delta$ -83.0 (d, $J = 98.8$ Hz); $^{31}$P{$^1$H} NMR (121.5 MHz, CDCl$_3$): $\delta$ 2.7 (t, $J = 97.2$ Hz); IR (neat, cm$^{-1}$) $\nu$: 2964, 2874, 1725, 1437, 1274, 1111, 1030, 1020, 907, 728, 539; HRMS (ESI$^+$): calcd for C$_{17}$H$_{25}$ClF$_2$N$_2$O$_3$PS m/z 441.0980 [M+NH$_4$]$^+$, found 441.0983 (0.7 ppm).

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\text{(E)-1-Chloro-1-[4-(methoxycarbonyl)phenyl]-2-[}(diethylphosphonodifluoromethyl) sulfanyl]pentene 2i. Purified by silica gel column chromatography (25 g SiO$_2$ cartridge, height 80 mm, width 30 mm, eluent: pentane/EtOAc, from 90:10 to 70:30); Yield: 54% (62 mg, 0.14 mmol); Diastereoisomeric ratio: 97:3; R$_f$ (petroleum ether/EtOAc = 50:50): 0.28; light yellow oil; $^1$H NMR (300.1 MHz, CDCl$_3$): $\delta$ 7.99 (d, $J = 8.4$ Hz, 2H), 7.39 (d, $J = 8.4$ Hz, 2H), 4.22-3.94 (m, 4H), 3.90 (s, 3H), 2.77 (dd, $J = 7.5$ and 7.5 Hz, 2H), 1.80-1.66 (m, 2H), 1.22 (t, $J = 6.9$ Hz, 6H), 0.99 (t, $J = 7.2$ Hz, 3H); $^{13}$C NMR (75.5 MHz, CDCl$_3$): $\delta$ 166.5, 143.2, 139.5 (dt, $J = 2.3$ and 1.5 Hz), 130.5, 129.5, 129.3, 127.5 (dt, $J = 4.5$ and 1.5 Hz), 125.1 (td, $J = 302.0$ and 214.4 Hz), 65.5 (d, $J = 6.8$ Hz), 52.4, 38.7, 20.5, 16.3 (d, $J = 5.3$ Hz), 13.6; $^{19}$F NMR (282.4 MHz, CDCl$_3$): $\delta$ -82.8 (d, $J = 96.0$ Hz); $^{31}$P{$^1$H} NMR (121.5 MHz, CDCl$_3$): $\delta$ 2.7 (t, $J = 97.2$ Hz); IR (neat, cm$^{-1}$) $\nu$: 2964, 2874, 1725, 1437, 1274, 1111, 1030, 1020, 907, 728, 539; HRMS (ESI$^+$): calcd for C$_{18}$H$_{28}$ClF$_2$NO$_3$PS m/z 474.1082 [M+NH$_4$]$^+$, found 474.1080 (-0.4 ppm).

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\text{(E)-1-Chloro-1-(naphthalene-1-yl)-2-[}(diethylphosphonodifluoromethyl)sulfanyl]pentene 2m. Purified by silica gel column chromatography (10 g SiO$_2$ cartridge, height 60 mm, width 20 mm, eluent: pentane/CH$_2$Cl$_2$, from 40:60 to 0:100); Yield: 44% (49 mg, 0.11 mmol); Diastereoisomeric ratio: 99:1; R$_f$ (petroleum ether/EtOAc = 50:50): 0.51; light yellow oil; $^1$H NMR (300.1 MHz, CDCl$_3$): $\delta$ 7.90-7.78 (m, 3H), 7.59-7.33 (m, 4H), 4.02-3.61 (m, 4H), 2.93 (dd, $J = 7.2$ and 7.2 Hz, 2H), 1.94-1.80 (m, 2H), 1.16-1.05 (m, 6H), 1.00 (t, $J = 7.2$ Hz, 3H); $^{13}$C NMR (75.5 MHz, CDCl$_3$): $\delta$ 166.5, 143.2, 139.5 (dt, $J = 4.5$ and 1.5 Hz), 125.1 (td, $J = 302.0$ and 212.2 Hz), 125.1, 65.4 (d, $J = 6.0$ Hz), 37.9, 20.8, 16.2 (d, $J = 6.0$ Hz), 13.8; $^{19}$F NMR (282.4 MHz,
CDCl$_3$): $\delta$ -82.5 (d, $J = 96.0$ Hz); $^{31}$P($^1$H) NMR (121.5 MHz, CDCl$_3$): $\delta$ 2.6 (t, $J = 97.2$ Hz); IR (neat, cm$^{-1}$) v: 2963, 2931, 2873, 1591, 1457, 1393, 1273, 1116, 1027, 907, 784, 729, 539; HRMS (ESI$^+$): calcd for C$_{20}$H$_{28}$ClF$_2$NO$_3$PS $m/z$ 466.1184 [M+NH$_4^+$], found 466.1196 (2.6 ppm).

![2n](image)

(E)-1-Chloro-1-[3-methylphenyl]-2-[(diethylphosphonodifluoromethyl)sulfanyl]pentene 2n. Purified by silica gel column chromatography (25 g SiO$_2$ cartridge, height 80 mm, width 30 mm, eluent: pentane/EtOAc, from 90:10 to 70:30); Yield: 80% (83 mg, 0.20 mmol); Diastereoisomeric ratio: 98:2; R$_f$ (petroleum ether/Et$_2$O = 75:25): 0.14; light yellow oil; $^1$H NMR (300.1 MHz, CDCl$_3$): $\delta$ 7.25-7.06 (m, 4H), 4.22-3.93 (m, 4H), 2.77 (dd, $J = 7.2$ and $J = 7.2$ Hz, 2H), 2.34 (s, 3H), 1.81-1.68 (m, 2H), 1.24 (t, $J = 6.9$ Hz, 6H), 1.01 (t, $J = 7.5$ Hz, 3H);

![2o](image)

(E)-1-chloro-1-(thiophen-2-yl)-2-[(diethylphosphonodifluoromethyl)sulfanyl]pentene 2o. Purified by silica gel column chromatography (25 g SiO$_2$ cartridge, height 80 mm, width 30 mm, eluent: pentane/EtOAc, from 90:10 to 70:30); Yield: 41% (41 mg, 0.10 mmol); Diastereoisomeric ratio: 99:1; R$_f$ (petroleum ether/Et$_2$O = 50:50): 0.34; brown oil; $^1$H NMR (300.1 MHz, CDCl$_3$): $\delta$ 7.43-7.27 (m, 2H), 6.99-6.93 (m, 1H), 4.34-4.15 (m, 4H), 2.79 (dd, $J = 7.5$ and 7.5 Hz, 2H), 1.78-1.65 (m, 2H), 1.37-1.30 (m, 6H), 0.99 (t, $J = 7.5$ Hz, 3H); $^{13}$C NMR (75.5 MHz, CDCl$_3$): $\delta$ 139.4, 134.3 (dt, $J = 2.3$ and 1.5 Hz), 131.2, 128.4, 126.3, 125.9 (dt, $J = 4.5$ and 1.5 Hz), 125.5 (td, $J = 302.0$ and 215.2 Hz), 65.6 (d, $J = 6.0$ Hz), 40.2, 20.7, 16.4 (d, $J = 5.1$ Hz), 13.8; $^{19}$F NMR (282.4 MHz, CDCl$_3$): $\delta$ -82.9 (d, $J = 98.8$ Hz); $^{31}$P($^1$H) NMR (121.5 MHz, CDCl$_3$): $\delta$ 2.9 (t, $J = 98.4$ Hz); IR (neat, cm$^{-1}$) v: 2965, 2933, 2873, 1567, 1457, 1394, 1275, 1113, 1022, 906, 704, 539; HRMS (ESI$^+$): calcd for C$_{18}$H$_{28}$ClF$_2$NO$_3$PS $m/z$ 422.0592 [M+NH$_4^+$], found 422.0580 (-2.8 ppm).

The structure 2o was confirmed by 2D experiments:

510
The NOESY NMR of 2o:

The HOESY NMR of 2o:

Purified by silica gel column chromatography (25 g SiO$_2$ cartridge, height 80 mm, width 30 mm, eluent: pentane/EtOAc, from 90:10 to 70:30); Yield: 82% (76 mg, 0.20 mmol); Diastereoisomeric ratio: 96:4; R$_f$ (petroleum ether/EtOAc = 5:1): 0.18; Light yellow oil; $^1$H NMR (300.1 MHz, CDCl$_3$): $\delta$ 7.40-7.27 (m, 5H), 4.22-3.95 (m, 4H), 2.47 (s, 3H), 1.24 (t, $J$ = 7.2 Hz, 6H); $^{13}$C NMR (75.5 MHz, CDCl$_3$): $\delta$ 140.3 (dt, $J$ = 2.3 and 1.5 Hz), 138.6, 129.4, 128.8, 128.1, 125.3 (td, $J$ = 302.0 and 213.7 Hz), 121.4 (dt, $J$ = 4.5 and 2.3 Hz), 65.5 (d, $J$ = 6.8 Hz), 24.8-24.7 (m), 16.3 (d, $J$ = 6.0 Hz); $^{19}$F NMR (282.4 MHz, CDCl$_3$): $\delta$ -82.8 (d, $J$ = 98.8 Hz); $^{31}$P{$^1$H} NMR (121.5 MHz, CDCl$_3$): $\delta$ 2.8 (t, $J$ = 97.2 Hz); IR (neat, cm$^{-1}$) ν: 2986, 2248, 1594, 1488, 1394, 1274, 1111, 1013, 908, 893, 728, 695, 538; HRMS (ESI$^+$): calcd for C$_{14}$H$_{22}$ClF$_2$NO$_3$PS $m/z$ 388.0715 [M+NH$_4$]$^+$, found 388.0711 (-1.0 ppm).

The structure of 2p was confirmed by 2D experiments.

The NOESY NMR of 2p:
A strong interaction between the aromatic protons H_c with the ethyl part (H_b from CH₃ and H_a from CH₂) was observed by NOESY.
The HOESY 2D of 2p:

(E)-1-Chloro-1-phenyl-2-[(diethylphosphonodifluoromethyl)sulfanyl]butene 2q. Purified by silica gel column chromatography (25 g SiO₂ cartridge, height 80 mm, width 30 mm, eluent: pentane/EtOAc, from 90:10 to 70:30); Yield: 84% (81 mg, 0.21 mmol); Diastereoisomeric ratio: 97:3; Rf (petroleum ether/EtOAc = 83:17): 0.17; Light yellow oil; ¹H NMR (300.1 MHz, CDCl₃): δ 7.39-7.28 (m, 5H), 4.21-3.93 (m, 4H), 2.82 (q, J = 7.5 Hz, 2H), 1.30-1.19 (m, 9H); ¹³C NMR (75.5 MHz, CDCl₃): δ 140.3 (dt, J = 2.3 and 1.5 Hz), 138.9, 129.4, 128.7, 128.0, 127.7 (dt, J = 4.5 and 1.5 Hz), 125.2 (td, J = 301.2 and 213.7 Hz), 65.5 (d, J = 6.0 Hz), 30.6, 16.4 (d, J = 5.3 Hz), 11.8; ¹⁹F NMR (282.4 MHz, CDCl₃): δ -82.8 (d, J = 98.8 Hz); ³¹P{¹H}
NMR (121.5 MHz, CDCl$_3$): $\delta$ 2.9 (t, $J = 9.8$ Hz); IR (neat, cm$^{-1}$) $\nu$: 2982, 2937, 1591, 1444, 1371, 1275, 1113, 1023, 907, 881, 762, 722, 537; HRMS (ESI$^+$): calcd for C$_{15}$H$_{24}$ClF$_2$NO$_3$PS $m/z$ 402.0871 [M+NH$_4$]$^+$, found 402.0876 (1.2 ppm).

(E)-4-Chloro-5-[(diethylphosphonodifluoromethyl)sulfanyl]octene 2r. Purified by silica gel column chromatography (25 g SiO$_2$ cartridge, height 80 mm, width 30 mm, eluent: pentane/EtOAc, from 90:10 to 70:30); Yield: 76% (69 mg, 0.19 mmol, at 45 °C), 87% (78 mg, 0.21 mmol, at 60 °C); R$_f$ (petroleum ether/Et$_2$O = 67:33): 0.22; yellow oil; $^1$H NMR (300.1 MHz, CDCl$_3$): $\delta$ 4.48-4.15 (m, 4H), 2.75 (dd, $J = 7.2$ and 7.2 Hz, 2H), 2.57 (dd, $J = 7.2$ and 7.2 Hz, 2H), 1.66-1.50 (m, 4H), 1.38 (t, $J = 7.2$ Hz, 6H), 0.93-0.82 (m, 6H); $^{13}$C NMR (75.5 MHz, CDCl$_3$): $\delta$ 146.5 (dt, $J = 2.3$ and 1.5 Hz), 125.5 (td, $J = 300.5$ and 216.7 Hz), 122.9 (dt, $J = 4.5$ and 1.5 Hz), 65.4 (d, $J = 6.8$ Hz), 39.6, 39.0, 21.2, 20.5, 16.4 (d, $J = 6.0$ Hz), 13.6, 13.2; $^{19}$F NMR (282.4 MHz, CDCl$_3$): $\delta$ -83.5 (d, $J = 98.8$ Hz); $^{31}$P{$^1$H} NMR (121.5 MHz, CDCl$_3$): $\delta$ 3.6 (t, $J = 100.8$ Hz); IR (neat, cm$^{-1}$) $\nu$: 2964, 2934, 2874, 1605, 1459, 1394, 1277, 1015, 982, 909, 753, 550; HRMS (ESI$^+$): calcd for C$_{13}$H$_{28}$ClF$_2$NO$_3$PS $m/z$ 382.1184 [M+NH$_4$]$^+$, found 382.1175 (-2.4 ppm).

(E)-1-Chloro-2-[[(diethylphosphonodifluoromethyl)sulfanyl]-1,2-diphenylethene 2s. Purified by silica gel column chromatography (25 g SiO$_2$ cartridge, height 80 mm, width 30 mm, eluent: pentane/EtOAc, from 90:10 to 70:30); Yield: 42% (45 mg, 0.10 mmol); R$_f$ (petroleum ether/Et$_2$O = 67:33): 0.14; yellow solid; Mp: 85-88 °C; $^1$H NMR (300.1 MHz, CDCl$_3$): $\delta$ 7.63-7.50 (m, 4H), 7.46-7.33 (m, 6H), 4.20-3.92 (m, 4H), 1.22 (t, $J = 7.2$ Hz, 6H); $^{13}$C NMR (75.5 MHz, CDCl$_3$): $\delta$ 140.4 (dt, $J = 2.3$ and 1.5 Hz), 139.3, 138.8, 129.7, 129.3, 129.1, 128.5, 128.2, 128.15, 125.2 (dt, $J = 4.5$ and 2.3 Hz), 124.8 (td, $J = 303.5$ and 213.7 Hz), 65.4 (d, $J = 6.8$ Hz), 16.3 (d, $J = 3.8$ Hz); $^{19}$F NMR (282.4 MHz, CDCl$_3$): $\delta$ -83.4 (d, $J = 96.0$ Hz); $^{31}$P{$^1$H} NMR (121.5 MHz, CDCl$_3$): $\delta$ 3.9-1.7 (m); IR (neat, cm$^{-1}$) $\nu$: 2983, 2918, 1720, 1584, 1445, 1271, 1117, 1028, 1011, 909, 740, 696, 554; HRMS (ESI$^+$): calcd for C$_{19}$H$_{24}$ClF$_2$NO$_3$PS $m/z$ 450.0871 [M+NH$_4$]$^+$, found 450.0872 (0.2 ppm).
7. Purification and characterization of derivatives 4

{2-[(Diethylphosphonodifluoromethyl)sulfanyl]ethynyl}benzene 4a. Purified by silica gel column chromatography (height 150 mm, width 25 mm, eluent: pentane/Et2O = 60:40); Yield: 81% (65 mg, 0.20 mmol); Rf (petroleum ether/Et2O = 60:40): 0.14; Light yellow oil; 1H NMR (300.1 MHz, CDCl3): δ 7.57-7.44 (m, 2H), 7.40-7.28 (m, 3H), 4.48-4.22 (m, 4H), 1.40 (t, J = 7.2 Hz, 6H); 13C NMR (75.5 MHz, CDCl3): δ 132.2, 129.4, 128.5, 123.9 (td, J = 306.5 and 218.2 Hz), 122.2, 100.5 (dt, J = 2.3 and 1.5 Hz), 68.2 (dt, J = 5.3 and 5.3 Hz), 65.9 (d, J = 6.8 Hz), 16.5 (d, J = 6.0 Hz); 19F NMR (282.4 MHz, CDCl3): δ -86.4 (d, J = 96.0 Hz); 31P{1H} NMR (121.5 MHz, CDCl3): δ 2.7 (t, J = 97.2 Hz); IR (neat, cm⁻¹) ν: 2986, 2842, 2249, 2171, 1604, 1508, 1464, 1276, 1012, 905, 833, 730, 644, 537; HRMS (ESI⁺): calcd for C13H19F2NO3PS m/z 338.0791 [M+NH4]⁺, found 338.0795 (1.2 ppm).

1-Methoxy-4-{2-[(diethylphosphonodifluoromethyl)sulfanyl]ethynyl}benzene 4b. Purified by silica gel column chromatography (height 150 mm, width 25 mm, eluent: pentane/Et2O = 60:40); Yield: 86% (75 mg, 0.21 mmol); Rf (PE/Et2O = 67:33): 0.18; Light yellow oil; 1H NMR (300.1 MHz, CDCl3): δ 7.44 (d, J = 9.0 Hz, 2H), 6.85 (d, J = 8.7, 2H), 4.42-4.28 (m, 4H), 3.81 (s, 3H), 1.40 (t, J = 7.2 Hz, 6H); 13C NMR (75.5 MHz, CDCl3): δ 160.6, 134.2, 123.8 (td, J = 305.8 and 217.4 Hz), 114.1, 114.1, 100.5 (dt, J = 2.3 and 1.5 Hz), 66.4 (dt, J = 5.3 and 5.3 Hz), 65.8 (d, J = 6.8 Hz), 55.3, 16.4 (d, J = 5.3 Hz); 19F NMR (282.4 MHz, CDCl3): δ -86.7 (d, J = 98.8 Hz); 31P{1H} NMR (121.5 MHz, CDCl3): δ 3.9-1.9 (m); IR (neat, cm⁻¹) ν: 2986, 2842, 2249, 2171, 1604, 1508, 1464, 1276, 1251, 1125, 1012, 905, 833, 730, 644, 537; HRMS (ESI⁺): calcd for C14H21F2NO4PS m/z 368.0897 [M+NH4]⁺, found 368.0895 (-0.5 ppm).

1-Methyl-4-{2-[(diethylphosphonodifluoromethyl)sulfanyl]ethynyl}benzene 4c. Purified by silica gel column chromatography (25 g SiO₂ cartridge, height 80 mm, width 30 mm, eluent: pentane/CH2Cl2, from 20:80 to 0:100); Yield: 68% (57 mg, 0.17 mmol); Rf (petroleum ether/Et2O = 67:33): 0.18; Light yellow oil; 1H NMR (300.1 MHz, CDCl3): δ 7.38 (d, J = 8.1
Hz, 2H), 7.13 (d, \(J = 7.8\) Hz, 2H), 4.44-4.27 (m, 4H), 2.35 (s, 3H), 1.40 (t, \(J = 7.2\) Hz, 6H); \(^{13}\)C NMR (75.5 MHz, CDCl\(_3\)): \(\delta\) 139.9, 132.2, 129.3, 123.9 (td, \(J = 306.5 \) and 217.4 Hz), 119.1, 100.7 (dt, \(J = 2.3\) and 1.5 Hz), 67.2 (dt, \(J = 6.0\) and 4.5 Hz), 65.9 (d, \(J = 6.0\) Hz), 21.7, 16.5 (d, \(J = 5.3\) Hz); \(^{19}\)F NMR (282.4 MHz, CDCl\(_3\)): \(\delta\) -86.6 (d, \(J = 98.8\) Hz); \(^{31}\)P{\(^{1}\)H} NMR (121.5 MHz, CDCl\(_3\)): \(\delta\) 2.8 (t, \(J = 98.4\) Hz); IR (neat, cm\(^{-1}\)) \(\nu\): 2986, 2922, 2173, 1607, 1508, 1277, 1127, 1010, 897, 815, 533; HRMS (ESI\(^{+}\)): calcd for C\(_{14}\)H\(_{21}\)F\(_2\)NO\(_3\)PS m/z 352.0948 [M+NH\(_4\)]\(^{+}\), found 352.0956 (2.3 ppm).

4d

1-Phenyl-4-\{2-[(diethylphosphonodifluoromethyl)sulfanyl]ethynyl\}benzene 4d. Purified by silica gel column chromatography (25 g SiO\(_2\) cartridge, height 80 mm, width 30 mm, eluent: pentane/CH\(_2\)Cl\(_2\), from 20:80 to 0:100); Yield: 66% (65 mg, 0.16 mmol); \(R_t\) (CH\(_2\)Cl\(_2\)): 0.56; Light yellow oil; \(^{1}\)H NMR (300.1 MHz, CDCl\(_3\)): \(\delta\) 7.63-7.54 (m, 6H), 7.48-7.41 (m, 2H), 7.40-7.33 (m, 1H), 4.45-4.29 (m, 4H), 1.42 (t, \(J = 7.2\) Hz, 6H); \(^{13}\)C NMR (75.5 MHz, CDCl\(_3\)): \(\delta\) 142.2, 140.2, 133.5, 123.8 (td, \(J = 306.5\) and 217.4 Hz), 121.9, 119.8, 99.6 (dt, \(J = 2.3\) and 1.5 Hz), 68.4 (dt, \(J = 5.3\) and 5.3 Hz), 65.9 (d, \(J = 6.0\) Hz), 21.2, 16.5 (d, \(J = 6.0\) Hz); \(^{19}\)F NMR (282.4 MHz, CDCl\(_3\)): \(\delta\) -86.4 (d, \(J = 96.0\) Hz); \(^{31}\)P{\(^{1}\)H} NMR (121.5 MHz, CDCl\(_3\)): \(\delta\) 2.6 (t, \(J = 97.2\) Hz); IR (neat, cm\(^{-1}\)) \(\nu\): 2985, 2917, 2249, 2172, 1486, 1446, 1275, 1127, 1013, 905, 840, 763, 728; HRMS (ESI\(^{+}\)): calcd for C\(_{14}\)H\(_{21}\)F\(_2\)NO\(_3\)PS m/z 414.1107 [M+NH\(_4\)]\(^{+}\), found 414.1107 (0.7 ppm).

4e

4-\{2-[(Diethylphosphonodifluoromethyl)sulfanyl]ethynyl\}phenyl acetate 4e. Purified by silica gel column chromatography (25 g SiO\(_2\) cartridge, height 80 mm, width 30 mm, eluent: pentane/EtOAc, from 90:10 to 65:35); Yield: 50% (47 mg, 0.12 mmol); \(R_t\) (petroleum ether/Et\(_2\)O = 67:33): 0.18; light yellow oil; \(^{1}\)H NMR (300.1 MHz, CDCl\(_3\)): \(\delta\) 7.49 (d, \(J = 8.7\) Hz, 2H), 7.06 (d, \(J = 8.7\) Hz, 2H), 4.40-4.27 (m, 4H), 2.28 (s, 3H), 1.39 (t, \(J = 7.2\) Hz, 6H); \(^{13}\)C NMR (75.5 MHz, CDCl\(_3\)): \(\delta\) 169.1, 151.4, 133.5, 123.8 (td, \(J = 306.5\) and 217.4 Hz), 121.9, 119.8, 99.6 (dt, \(J = 2.3\) and 1.5 Hz), 68.4 (dt, \(J = 5.3\) and 5.3 Hz), 65.9 (d, \(J = 6.0\) Hz), 21.2, 16.5 (d, \(J = 6.0\) Hz); \(^{19}\)F NMR (282.4 MHz, CDCl\(_3\)): \(\delta\) -86.4 (d, \(J = 96.0\) Hz); \(^{31}\)P{\(^{1}\)H} NMR (121.5 MHz, CDCl\(_3\)): \(\delta\) 2.6 (t, \(J = 97.2\) Hz); IR (neat, cm\(^{-1}\)) \(\nu\): 2987, 2918, 2174, 1767, 1601, 1503, 1371, 1276, 1190, 1164, 1009, 907, 844, 536; HRMS (ESI\(^{+}\)): calcd for C\(_{15}\)H\(_{21}\)F\(_2\)NO\(_3\)PS m/z 396.0846 [M+NH\(_4\)]\(^{+}\), found 396.0846 (0 ppm).
1-Acetamido-4-\{2-[(diethylphosphonodifluoromethyl)sulfanyl]ethynyl\}benzene  4f.  
Purified by silica gel column chromatography (25 g SiO$_2$ cartridge, height 80 mm, width 30 mm, eluent: pentane/EtOAc, from 70:30 to 30:70); Yield: 67% (63 mg, 0.17 mmol); R$_f$ (petroleum ether/EtOAc = 50:50): 0.14; light yellow oil; $^1$H NMR (300.1 MHz, CDCl$_3$): $\delta$ 8.47 (br. s, 1H), 7.53 (d, $J$ = 8.7 Hz, 2H), 7.38 (d, $J$ = 8.7 Hz, 2H), 4.40-4.25 (m, 4H), 2.14 (s, 3H), 1.38 (t, $J$ = 6.9 Hz, 6H); $^{13}$C NMR (75.5 MHz, CDCl$_3$): $\delta$ 169.2, 139.7, 133.2, 123.7 (td, $J$ = 306.5 and 215.9 Hz), 119.4, 117.1, 100.5 (dt, $J$ = 2.3 and 1.5 Hz), 67.2 (dt, $J$ = 6.8 and 4.5 Hz), 66.0 (d, $J$ = 6.0 Hz), 24.5, 16.4 (d, $J$ = 6.0 Hz); $^{19}$F NMR (282.4 MHz, CDCl$_3$): $\delta$ -86.6 (d, $J$ = 98.8 Hz); $^{31}$P{$^1$H} NMR (121.5 MHz, CDCl$_3$): $\delta$ 2.4 (t, $J$ = 98.4 Hz); IR (neat, cm$^{-1}$) $\nu$: 3313, 3179, 2988, 2170, 1698, 1593, 1527, 1510, 1257, 1012, 841, 731; HRMS (ESI$^+$): calcd for C$_{15}$H$_{22}$F$_2$N$_2$O$_4$PS m/z 395.1006 [M+NH$_4$]$^+$, found 395.0991 (-3.8 ppm).

2-[(Diethylphosphonodifluoromethyl)sulfanyl]ethynyl] naphthalene  4g.  
Purified by silica gel column chromatography (25 g SiO$_2$ cartridge, height 80 mm, width 30 mm, eluent: pentane/EtOAc, from 90:10 to 70:30); Yield: 68% (63 mg, 0.17 mmol); R$_f$ (petroleum ether/Et$_2$O = 67:33): 0.14; colorless oil; $^1$H NMR (300.1 MHz, CDCl$_3$): $\delta$ 8.31 (d, $J$ = 8.1 Hz, 1H), 7.90-7.83 (m, 2H), 7.73 (d, $J$ = 6.9 Hz, 1H), 7.63-7.49 (m, 2H), 7.47-7.39 (m, 1H), 4.45-4.31 (m, 4H), 1.41 (t, $J$ = 7.2 Hz, 6H); $^{13}$C NMR (75.5 MHz, CDCl$_3$): $\delta$ 133.5, 133.2, 131.4, 129.9, 128.4, 127.3, 126.8, 126.1, 125.2, 124.0 (td, $J$ = 306.5 and 217.4 Hz), 119.9, 98.8 (dt, $J$ = 2.3 and 1.5 Hz), 72.7 (dt, $J$ = 6.0 and 4.5 Hz), 65.9 (d, $J$ = 6.0 Hz), 16.5 (d, $J$ = 6.0 Hz); $^{19}$F NMR (282.4 MHz, CDCl$_3$): $\delta$ -86.2 (d, $J$ = 98.8 Hz); $^{31}$P{$^1$H} NMR (121.5 MHz, CDCl$_3$): $\delta$ 2.8 (t, $J$ = 97.2 Hz); IR (neat, cm$^{-1}$) $\nu$: 3060, 2986, 2249, 2158, 1586, 1508, 1394, 1275, 1127, 1011, 899, 799, 772, 730; HRMS (ESI$^+$): calcd for C$_{17}$H$_{22}$F$_2$NOS PS m/z 388.0948 [M+NH$_4$]$^+$, found 388.0953 (1.3 ppm).

1-Fluoro-4-\{2-[(diethylphosphonodifluoromethyl)sulfanyl]ethynyl\}benzene  4h.  
Purified by silica gel column chromatography (25 g SiO$_2$ cartridge, height 80 mm, width 30 mm, eluent: pentane/EtOAc, from 90:10 to 70:30); Yield: 58% (49 mg, 0.14 mmol); R$_f$ (petroleum ether/Et$_2$O = 67:33): 0.10; light yellow oil; $^1$H NMR (300.1 MHz, CDCl$_3$): $\delta$ 7.56-7.42 (m, 2H), 7.09-6.97 (m, 2H), 4.43-4.28 (m, 4H), 1.40 (t, $J$ = 6.9 Hz, 6H); $^{13}$C NMR (75.5 MHz, CDCl$_3$):
\[ \delta 163.2 \ (d, \ J = 252.2), 134.4 \ (d, \ J = 8.3 \ Hz), 123.9 \ (tq, \ J = 306.5 \ and \ 218.2 \ Hz), 118.4 \ (d, \ J = 3.8 \ Hz), 115.9 \ (d, \ J = 21.9 \ Hz), 99.4 \ (dt, \ J = 2.3 \ and \ 1.5 \ Hz), 68.2-67.9 \ (m), 65.9 \ (d, \ J = 6.0 \ Hz), 16.5 \ (d, \ J = 5.3 \ Hz); \] 
\[ \text{\[^{19}F\] NMR (282.4 MHz, CDCl}_3): \delta -86.4 \ (d, \ J = 98.8 \ Hz), -109.2 \ to -109.3 \ (m); \text{\[^{31}P\{\[^{1}H\} \ NMR (121.5 MHz, CDCl}_3): \delta 2.6 \ (t, \ J = 96.0 \ Hz); \] }\]

**1-Chloro-4-[2-[(Diethylphosphonodifluoromethyl)sulfanyl]ethynyl]benzene 4i.** Purified by silica gel column chromatography (25 g SiO\(_2\) cartridge, height 80 mm, width 30 mm, eluent: pentane/EtOAc, from 90:10 to 65:35); Yield: 43% (38 mg, 0.11 mmol); \(R_f\) (petroleum ether/Et\(_2\)O = 67:33): 0.17; light yellow oil; \(^1\)H NMR (300.1 MHz, CDCl\(_3\)): \(\delta 7.41 \ (d, \ J = 8.4 \ Hz, 2H), 7.30 \ (d, \ J = 8.7 \ Hz, 2H), 4.41-4.28 \ (m, 4H), 1.40 \ (t, \ J = 7.2 \ Hz, 6H); \(^13\)C NMR (75.5 MHz, CDCl\(_3\)): \(\delta 135.6, 133.3, 128.9, 123.8 \ (td, \ J = 306.5 \ and \ 218.2 \ Hz), 120.7, 99.3 \ (dt, \ J = 2.3 \ and \ 1.5 \ Hz), 69.5 \ (d, \ J = 6.0 \ Hz), 16.5 \ (d, \ J = 5.3 \ Hz); \] 
\[ \text{\[^{19}F\] NMR (282.4 MHz, CDCl}_3): \delta -86.3 \ (d, \ J = 98.8 \ Hz); \] 
\[ \text{\[^{31}P\{\[^{1}H\} \ NMR (121.5 MHz, CDCl}_3): \delta 2.6 \ (t, \ J = 96.0 \ Hz); \] }\]

**1-Acetyl-4-[2-[(Diethylphosphonodifluoromethyl)sulfanyl]ethynyl]benzene 4j.** Purified by silica gel column chromatography (25 g SiO\(_2\) cartridge, height 80 mm, width 30 mm, eluent: pentane/EtOAc, from 85:15 to 65:35); Yield: 52% (47 mg, 0.13 mmol); \(R_f\) (PE/Et\(_2\)O = 50:50): 0.13; colorless oil; \(^1\)H NMR (300.1 MHz, CDCl\(_3\)): \(\delta 7.90 \ (d, \ J = 8.7 \ Hz, 2H), 7.54 \ (d, \ J = 8.4 \ Hz, 2H), 4.43-4.28 \ (m, 4H), 2.59 \ (s, 3H), 1.41 \ (t, \ J = 7.2 \ Hz, 6H); \(^13\)C NMR (75.5 MHz, CDCl\(_3\)): \(\delta 197.3, 136.9, 131.8, 128.4, 127.0, 123.8 \ (td, \ J = 307.3 \ and \ 218.2 \ Hz), 99.7 \ (dt, \ J = 2.3 \ and \ 1.5 \ Hz), 72.3 \ (dt, \ J = 5.3 \ and 4.5 Hz), 66.0 \ (d, \ J = 6.8 \ Hz), 26.7, 16.5 \ (d, \ J = 5.3 \ Hz); \] 
\[ \text{\[^{19}F\] NMR (282.4 MHz, CDCl}_3): \delta -86.1 \ (d, \ J = 96.0 \ Hz); \] 
\[ \text{\[^{31}P\{\[^{1}H\} \ NMR (121.5 MHz, CDCl}_3): \delta 2.4 \ (t, \ J = 96.0 \ Hz); \] }\]

HRMS (ESI\(^+\)): calcd for C\(_{15}\)H\(_{18}\)F\(_2\)NO\(_4\)PS \(m/z\) 372.0402 [M+NH\(_4\)]\(^+\), found 372.0393 (-2.4 ppm).
Methyl 4-{2-[(Diethylphosphonodifluoromethyl)sulfanyl]ethynyl}benzoate 4k. Purified by silica gel column chromatography (25 g SiO$_2$ cartridge, height 80 mm, width 30 mm, eluent: pentane/EtOAc, from 85:15 to 65:35); Yield: 52% (49 mg, 0.13 mmol); $R_f$ (petroleum ether/EtOAc = 50:50): 0.18; colorless oil; $^1$H NMR (300.1 MHz, CDCl$_3$); $\delta$ 7.98 (d, $J = 8.4$ Hz, 2H), 7.51 (d, $J = 8.4$ Hz, 2H), 4.42-4.28 (m, 4H), 3.90 (s, 3H), 1.40 (t, $J = 7.2$ Hz, 6H); $^{13}$C NMR (75.5 MHz, CDCl$_3$): $\delta$ 166.4, 131.6, 130.3, 129.6, 126.8, 123.8 (td, $J = 307.3$ and 218.2 Hz), 99.7 (dt, $J = 2.3$ and 1.5 Hz), 71.8 (dt, $J = 6.0$ and 4.5 Hz), 66.0 (d, $J = 6.8$ Hz), 52.4, 16.5 (d, $J = 6.0$ Hz); $^{19}$F NMR (282.4 MHz, CDCl$_3$); $\delta$ -86.1 (d, $J = 96.0$ Hz); $^{31}$P{$_^1$H} NMR (121.5 MHz, CDCl$_3$); $\delta$ 3.5-1.5 (m); IR (neat, cm$^{-1}$) $\nu$: 2987, 2251, 2174, 1723, 1606, 1437, 1405, 1272, 1107, 1013, 900, 768, 730; HRMS (ESI$^+$): calcd for C$_{15}$H$_{21}$F$_2$NO$_5$PS m/z 396.0846 [M+NH$_4^+$], found 396.0841 (-1.3 ppm).

1-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-4-2-[(diethylphosphonodifluoromethyl)sulfanyl]ethynyl]benzene 4l. Purified by silica gel column chromatography (25 g SiO$_2$ cartridge, height 80 mm, width 30 mm, eluent: pentane/EtOAc, from 85:15 to 50:50); Yield: 20% (22 mg, 0.07 mmol); $R_f$ (petroleum ether/EtOAc = 50:50): 0.48; yellow oil; $^1$H NMR (300.1 MHz, CDCl$_3$); $\delta$ 7.76 (d, $J = 8.1$ Hz, 2H), 7.46 (d, $J = 7.8$ Hz, 2H), 4.43-4.27 (m, 4H), 1.40 (t, $J = 7.2$ Hz, 6H), 1.34 (s, 12H); $^{13}$C NMR (75.5 MHz, CDCl$_3$); $\delta$ 134.7, 131.0, 125.3, 123.8 (td, $J = 306.5$ and 217.4 Hz), 100.6 (dt, $J = 2.3$ and 1.5 Hz), 84.2, 69.7 (dt, $J = 6.0$ and 1.5 Hz), 65.9 (d, $J = 6.8$ Hz), 25.0, 16.5 (d, $J = 5.3$ Hz). One carbon is overlapped; $^{19}$F NMR (282.4 MHz, CDCl$_3$); $\delta$ -86.1 (d, $J = 96.0$ Hz); $^{31}$P{$_^1$H} NMR (121.5 MHz, CDCl$_3$); $\delta$ 2.7 (t, $J = 97.2$ Hz); IR (neat, cm$^{-1}$) $\nu$: 2981, 2933, 2249, 1607, 1357, 1274, 1142, 1015, 906, 732, 652; HRMS (ESI$^+$): calcd for C$_{19}$H$_{30}$F$_2$NO$_5$BPS m/z 464.1643 [M+NH$_4^+$], found 464.1653 (2.2 ppm).

1-Methyl-3-2-[(Diethylphosphonodifluoromethyl)sulfanyl]ethynyl]benzene 4m. Purified by silica gel column chromatography (25 g SiO$_2$ cartridge, height 80 mm, width 30 mm, eluent: pentane/EtOAc, from 90:10 to 70:30); Yield: 65% (54 mg, 0.16 mmol); $R_f$ (petroleum ether/EtOAc = 2:1): 0.11; light yellow oil; $^1$H NMR (300.1 MHz, CDCl$_3$); $\delta$ 7.50 (d, $J = 7.5$ Hz, 1H), 7.37-7.16 (m, 3H), 4.55-4.31 (m, 4H), 2.51 (s, 3H), 1.47 (t, $J = 7.2$ Hz, 6H); $^{13}$C NMR
(75.5 MHz, CDCl₃): δ 141.2, 132.3, 129.7, 129.4, 125.7, 123.9 (td, J = 305.8 and 217.4 Hz), 122.1, 99.6 (dt, J = 2.3 and 1.5 Hz), 71.4 (dt, J = 5.3 and 5.3 Hz), 65.9 (d, J = 6.0 Hz), 20.7, 16.5 (d, J = 6.0 Hz); ¹⁹F NMR (282.4 MHz, CDCl₃): δ -86.4 (d, J = 96.0 Hz); ³¹P{¹H} NMR (121.5 MHz, CDCl₃): δ 2.8 (t, J = 7.2 Hz, 6H); IR (neat, cm⁻¹) ν: 2986, 2172, 1482, 1456, 1277, 1127, 1010, 895, 707, 538; HRMS (ESI⁺): calcd for C₁₄H₂₁F₂NO₃PS m/z 352.0948 [M+NH₄]⁺, found 352.0948 (0 ppm).

1-Methyl-2-[(Diethylphosphonodifluoromethyl)sulfanyl]ethynyl]benzene 4n. Purified by silica gel column chromatography (25 g SiO₂ cartridge, height 80 mm, width 30 mm, eluent: pentane/EtOAc, from 90:10 to 70:30); Yield: 66% (55 mg, 0.16 mmol); Rᵣ (petroleum ether/Et₂O = 67:33): 0.11; light yellow oil; ¹H NMR (300.1 MHz, CDCl₃): δ 7.43 (d, J = 7.5 Hz, 1H), 7.29-7.09 (m, 3H), 4.43-4.25 (m, 4H), 2.44 (s, 3H), 1.40 (t, J = 7.2 Hz, 6H); ¹³C NMR (75.5 MHz, CDCl₃): δ 141.2, 132.3, 129.7, 129.4, 125.7, 123.9 (td, J = 306.5 and 217.4 Hz), 122.1, 99.6 (dt, J = 2.3 and 1.5 Hz), 71.4 (dt, J = 5.3 and 5.3 Hz), 65.9 (d, J = 6.0 Hz), 20.6, 16.5 (d, J = 6.0 Hz); ¹⁹F NMR (282.4 MHz, CDCl₃): δ -86.4 (d, J = 98.8 Hz); ³¹P{¹H} NMR (121.5 MHz, CDCl₃): δ 2.8 (t, J = 7.2 Hz); IR (neat, cm⁻¹) ν: 2986, 2172, 1482, 1456, 1277, 1127, 1010, 897, 756, 640, 538; HRMS (ESI⁺): calcd for C₁₄H₂₁F₂NO₃PS m/z 352.0948 [M+NH₄]⁺, found 352.0937 (-3.1 ppm).

[2-[(Diethylphosphonodifluoromethyl)sulfanyl]ethynyl]thiophene 4o. Purified by silica gel column chromatography (25 g SiO₂ cartridge, height 80 mm, width 30 mm, eluent: pentane/EtOAc, from 90:10 to 65:35); Yield: 55% (45 mg, 0.14 mmol); Rᵣ (petroleum ether/Et₂O = 67:33): 0.14; light yellow oil; ¹H NMR (300.1 MHz, CDCl₃): δ 7.41-7.31 (m, 2H), 7.03-6.97 (m, 1H), 4.40-4.27 (m, 4H), 1.40 (t, J = 7.2 Hz, 6H); ¹³C NMR (75.5 MHz, CDCl₃): δ 135.0, 129.8, 127.3, 123.7 (td, J = 307.3 and 217.4 Hz), 122.2, 93.5 (dt, J = 2.3 and 1.5 Hz), 73.0 (dt, J = 6.0 and 4.5 Hz), 65.9 (d, J = 6.0 Hz), 16.5 (d, J = 5.3 Hz); ¹⁹F NMR (282.4 MHz, CDCl₃): δ -86.6 (d, J = 96.0 Hz); ³¹P{¹H} NMR (121.5 MHz, CDCl₃): δ 3.7-1.6 (m); IR (neat, cm⁻¹) ν: 2986, 2915, 2158, 1417, 1371, 1275, 1127, 1010, 895, 707, 538; HRMS (ESI⁺): calcd for C₁₁H₁₇F₂NO₃PS m/z 344.0356 [M+NH₄]⁺, found 344.0348 (-2.3 ppm).
2-[(Diethylphosphonodifluoromethyl)sulfanyl]ethynyl]cyclohexene 4p. Purified by silica gel column chromatography (height 180 mm, width 20 mm, eluent: pentane/Et₂O = 50:50); Yield: 78% (63 mg, 0.19 mmol); R₇ (petroleum ether/Et₂O = 50:50): 0.18; Light yellow oil; ¹H NMR (300.1 MHz, CDCl₃): δ 6.28-6.17 (m, 1H), 4.40-4.23 (m, 4H), 2.16-2.06 (m, 4H), 1.66-1.53 (m, 4H), 1.39 (t, J = 7.2 Hz, 6H); ¹³C NMR (75.5 MHz, CDCl₃): δ 138.3, 123.8 (td, J = 305.0 and 217.4 Hz), 120.4, 102.5 (dt, J = 2.3 and 1.5 Hz), 65.8 (d, J = 6.8 Hz), 64.7 (dt, J = 6.0 and 5.3 Hz), 28.8, 25.9, 22.2, 21.4, 16.4 (d, J = 6.0 Hz); ¹⁹F NMR (282.4 MHz, CDCl₃): δ -86.8 (d, J = 98.8 Hz); ³¹P{¹H} NMR (121.5 MHz, CDCl₃): δ 2.8 (t, J = 98.4 Hz); IR (neat, cm⁻¹): ν: 2985, 2934, 2161, 1478, 1437, 1277, 1041, 1010, 918, 897, 735; HRMS (ESI⁺): calcd for C₁₃H₂₃F₂NO₃PS m/z 342.1104 [M+NH₄]⁺, found 342.1107 (0.9 ppm).

8. Purification and characterization of derivatives 6

1-Chloro-1-phenyl-2-[(diethylphosphonodifluoromethyl)sulfanyl]ethane 6a. Purified by silica gel column chromatography (height 130 mm, width 20 mm, eluent: CH₂Cl₂); Yield: 62% (56 mg, 0.16 mmol); Note that 6a was obtained in 64% (230 mg, 0.64 mmol) on 1 mmol scale. R₇ (CH₂Cl₂): 0.43; Light yellow oil; ¹H NMR (300.1 MHz, CDCl₃): δ 7.43-7.30 (m, 5H), 5.10 (t, J = 7.5 Hz, 1H), 4.37-4.22 (m, 4H), 3.64 (dd, J = 14.1 and 7.5 Hz, 1H), 3.52 (dd, J = 14.1 and 7.5 Hz, 1H), 1.38 (t, J = 7.2 Hz, 6H); ¹³C NMR (75.5 MHz, CDCl₃): δ 139.3, 129.1, 128.9, 127.4, 125.5 (td, J = 299.0 and 221.2 Hz), 65.69 (d, J = 6.0 Hz), 65.67 (d, J = 6.8 Hz), 61.8, 37.3-37.2 (m), 16.5 (d, J = 6.0 Hz); ¹⁹F NMR (282.4 MHz, CDCl₃): δ -85.4 (dd, J = 98.8 Hz) and -86.5 (dd, J = 98.8 Hz); ¹³C NMR (75.5 MHz, CDCl₃): δ 139.3, 129.1, 128.9, 127.4, 125.5 (td, J = 299.0 and 221.2 Hz), 65.69 (d, J = 6.0 Hz), 65.67 (d, J = 6.8 Hz), 61.8, 37.3-37.2 (m), 16.5 (d, J = 6.0 Hz); ¹⁹F NMR (282.4 MHz, CDCl₃): δ -85.4 (dd, J = 257.0 and 101.7 Hz), -86.5 (dd, J = 257.0 and 101.7 Hz); ³¹P{¹H} NMR (121.5 MHz, CDCl₃): δ 3.1 (t, J = 102.1 Hz); IR (neat, cm⁻¹): ν: 2986, 1493, 1456, 1272, 1114, 1017, 922, 731, 697, 535; HRMS (ESI⁺): calcd for C₁₃H₂₂ClF₂NO₃PS m/z 376.0715 [M+NH₄]⁺, found 376.0713 (-0.5 ppm).
86.5 (dd, J = 257.0 and 101.7 Hz); 31P {1H} NMR (121.5 MHz, CDCl3): δ 3.1 (t, J = 102.1 Hz); IR (neat, cm⁻¹) ν: 2985, 1602, 1487, 1393, 1271, 1115, 1018, 908, 729, 697, 549; HRMS (ESI⁺): calecd for C₁₉H₂₆ClF₂NO₃PS m/z 452.1028 [M+NH₄]⁺, found 452.1014 (-3.1 ppm).

1-Chloro-1-(4-bromophenyl)-2-[(diethylphosphonodifluoromethyl)sulfanyl]ethane 6c.

Purified by silica gel column chromatography (height 150 mm, width 20 mm, eluent: CH₂Cl₂);
Yield: 44% (48 mg, 0.11 mmol); Rf (CH₂Cl₂): 0.43; Light yellow oil; ¹H NMR (300.1 MHz, CDCl3): δ 7.53 (d, J = 8.7 Hz, 2H), 7.31 (d, J = 8.7 Hz, 2H), 5.10 (t, J = 7.5 Hz, 1H), 4.39-4.26 (m, 4H), 3.65 (dd, J = 14.1 and 7.2 Hz, 1H), 3.49 (dd, J = 14.1 and 8.1 Hz, 1H), 1.41 (t, J = 7.2 Hz, 6H); ¹³C NMR (75.5 MHz, CDCl3): δ 138.3, 132.1, 129.1, 125.3 (td, J = 299.7 and 221.2 Hz), 123.1, 65.7 (d, J = 6.8 Hz), 65.68 (d, J = 6.0 Hz), 60.9, 37.2-37.1 (m), 16.5 (d, J = 5.3 Hz); ¹⁹F NMR (282.4 MHz, CDCl3): δ -85.5 (dd, J = 257.0 and 101.7 Hz), -86.7 (dd, J = 257.0 and 101.7 Hz); ³¹P {¹H} NMR (121.5 MHz, CDCl3): δ 2.9 (t, J = 103.3 Hz); IR (neat, cm⁻¹) ν: 2986, 1592, 1489, 1271, 1116, 1022, 1011, 907, 728, 535; HRMS (ESI⁺): calecd for C₁₃H₁₁BrClF₂NO₃PS m/z 453.9820 [M+NH₄]⁺, found 453.9822 (0.4 ppm).

1-Chloro-1-(4-chlorophenyl)-2-[(diethylphosphonodifluoromethyl)sulfanyl]ethane 6d.

Purified by silica gel column chromatography (height 120 mm, width 20 mm, eluent: CH₂Cl₂);
Yield: 64% (63 mg, 0.16 mmol); Rf (CH₂Cl₂): 0.41; Light yellow oil; ¹H NMR (300.1 MHz, CDCl3): δ 7.41-7.29 (m, 4H), 5.07 (t, J = 7.5 Hz, 1H), 4.36-4.22 (m, 4H), 3.61 (dd, J = 14.1 and 7.2 Hz, 1H), 3.45 (dd, J = 14.1 and 7.8 Hz, 1H), 1.36 (t, J = 7.2 Hz, 6H); ¹³C NMR (75.5 MHz, CDCl3): δ 137.8, 134.9, 129.1, 128.8, 125.3 (td, J = 299.0 and 222.0 Hz), 65.7 (d, J = 6.0 Hz), 65.6 (d, J = 6.8 Hz), 60.8, 37.2-37.1 (m), 16.4 (d, J = 6.0 Hz); ¹⁹F NMR (282.4 MHz, CDCl3): δ -85.5 (dd, J = 257.0 and 101.7 Hz), -86.7 (dd, J = 257.0 and 101.7 Hz); ³¹P {¹H} NMR (121.5 MHz, CDCl3): δ 2.9 (t, J = 102.1 Hz); IR (neat, cm⁻¹) ν: 2986, 2916, 1597, 1493, 1272, 1115, 1013, 924, 750, 531; HRMS (ESI⁺): calecd for C₁₃H₁₂Cl₂F₂NO₃PS m/z 410.0325 [M+NH₄]⁺, found 410.0323 (-0.5 ppm).

1-Chloro-1-[4-(methoxycarbonyl)phenyl]-2-[(diethylphosphonodifluoromethyl)sulfanyl]ethane 6e. Purified by silica gel column chromatography (height 120 mm, width 20 mm, eluent:
CH₂Cl₂); Yield: 40% (42 mg, 0.10 mmol); R₆ (CH₂Cl₂): 0.26; Light yellow oil; ¹H NMR (300.1 MHz, CDCl₃): δ 8.03 (d, J = 8.4 Hz, 2H), 7.48 (d, J = 8.4 Hz, 2H), 5.14 (t, J = 7.5 Hz, 1H), 4.35-4.22 (m, 4H), 3.91 (s, 3H), 3.63 (dd, J = 14.1 and 7.2 Hz, 1H), 3.48 (dd, J = 14.1 and 7.5 Hz, 1H), 1.37 (t, J = 7.2 Hz, 6H); ¹³C NMR (75.5 MHz, CDCl₃): δ 166.5, 144.0, 130.8, 130.2, 127.5, 125.3 (td, J = 299.7 and 221.2 Hz), 65.74 (d, J = 6.8 Hz), 65.7 (d, J = 6.8 Hz), 60.9, 52.4, 37.2-37.0 (m), 16.5 (d, J = 5.3 Hz); ¹⁹F NMR (282.4 MHz, CDCl₃): δ -85.5 (dd, J = 259.8 and 101.7 Hz), -86.6 (dd, J = 259.8 and 104.5 Hz); ³¹P {¹H} NMR (121.5 MHz, CDCl₃): δ 2.9 (t, J = 102.1 Hz); IR (neat, cm⁻¹): v: 2987, 1721, 1613, 1437, 1278, 1111, 1019, 907, 727, 534; HRMS (ESI⁺): calcd for C₁₅H₂₆ClF₂NO₅PS m/z 434.0769 [M+NH₄]⁺, found 434.0776 (1.6 ppm).

1-Chloro-1-[4-cyanophenyl]-2-[(diethylphosphonodifluoromethyl)sulfanyl]ethane 6f. Purified by silica gel column chromatography (height 120 mm, width 20 mm, eluent: CH₂Cl₂); Yield: 31% (30 mg, 0.08 mmol); R₆ (CH₂Cl₂): 0.26; Light yellow oil; ¹H NMR (300.1 MHz, CDCl₃): δ 7.67 (d, J = 8.7 Hz, 2H), 7.53 (d, J = 8.4 Hz, 2H), 5.13 (t, J = 7.5 Hz, 1H), 4.35-4.23 (m, 4H), 3.62 (dd, J = 14.4 and 7.2 Hz, 1H), 3.45 (dd, J = 14.4 and 8.1 Hz, 1H), 1.41-1.34 (m, 6H); ¹³C NMR (75.5 MHz, CDCl₃): δ 144.2, 132.7, 128.4, 125.2 (td, J = 299.7 and 222.0 Hz), 118.3, 112.9, 65.8 (d, J = 6.8 Hz), 65.76 (d, J = 6.8 Hz), 60.5, 37.2-37.1 (m), 16.5 (d, J = 6.0 Hz); ¹⁹F NMR (282.4 MHz, CDCl₃): δ -85.6 (dd, J = 257.0 and 101.7 Hz), -86.8 (dd, J = 259.8 and 101.8 Hz); ³¹P {¹H} NMR (121.5 MHz, CDCl₃): δ 2.7 (t, J = 102.1 Hz); IR (neat, cm⁻¹): v: 2987, 2231, 1610, 1478, 1444, 1270, 1116, 1019, 908, 729, 556; HRMS (ESI⁺): calcd for C₁₄H₂₁ClF₂N₂O₃PS m/z 401.0667 [M+NH₄]⁺, found 401.0673 (1.5 ppm).

1-Chloro-1-(naphthalene-2-yl)-2-[(diethylphosphonodifluoromethyl)sulfanyl]ethane 6g. Purified by silica gel column chromatography (height 120 mm, width 20 mm, eluent: CH₂Cl₂); Yield: 48% (49 mg, 0.12 mmol); R₆ (CH₂Cl₂): 0.50; Light yellow oil; ¹H NMR (300.1 MHz, CDCl₃): δ 7.95-7.78 (m, 4H), 7.59-7.41 (m, 3H), 5.29 (t, J = 7.5 Hz, 1H), 4.39-4.19 (m, 4H), 3.75 (dd, J = 14.1 and 7.2 Hz, 1H), 3.62 (dd, J = 14.1 and 7.8 Hz, 1H), 1.36 (t, J = 7.2 Hz, 6H); ¹³C NMR (75.5 MHz, CDCl₃): δ 136.4, 133.5, 133.0, 129.1, 128.3, 127.9, 127.0, 126.9, 126.7, 125.5 (td, J = 299.7 and 221.2 Hz), 124.3, 65.7 (d, J = 6.8 Hz), 65.67 (d, J = 6.8 Hz), 60.2, 37.1-37.0 (m), 16.4 (d, J = 5.3 Hz); ¹⁹F NMR (282.4 MHz, CDCl₃): δ -85.3 (dd, J = 257.0 and 101.7 Hz), -86.4 (dd, J = 257.0 and 101.7 Hz); ³¹P {¹H} NMR (121.5 MHz, CDCl₃): δ 3.1 (t, J = 102.1 Hz); IR (neat, cm⁻¹): v: 2985, 1271, 1113, 1016, 922, 731, 535; HRMS (ESI⁺): calcd for C₁₇H₂₄ClF₂NO₃PS m/z 426.0871 [M+NH₄]⁺, found 426.0864 (-1.6 ppm).
1-[(Diethylphosphonodifluoromethyl)sulfanyl]-2-phenyl propene 6ha and 3-[(Diethylphosphonodifluoromethyl)sulfanyl]-2-phenyl propene 6hb (1:1 ratio). Purified by silica gel column chromatography (height 150 mm, width 20 mm, eluent: CH$_2$Cl$_2$); Yield: 40% (34 mg, 0.10 mmol); R$_f$ (CH$_2$Cl$_2$): 0.35; Light yellow oil; $^1$H NMR (300.1 MHz, CDCl$_3$): $\delta$ 7.52-7.27 (m, 10H), 6.58 (s, 1H), 5.52 (s, 1H), 5.42 (s, 1H), 4.40-4.22 (m, 8H), 4.09 (s, 2H), 2.21 (s, 3H), 1.44-1.34 (m, 12H); $^{13}$C NMR (75.5 MHz, CDCl$_3$): $\delta$ 142.8, 142.5, 141.3, 138.8, 128.6, 128.2, 128.0, 126.3, 125.9, 117.0, 111.0-110.7 (m), 65.6 (d, $J = 6.8$ Hz), 65.5 (d, $J = 5.3$ Hz) (CF$_2$ carbons not observed); $^{19}$F NMR (282.4 MHz, CDCl$_3$): $\delta$ -86.6 (d, $J = 101.7$ Hz), -86.62 (d, $J = 101.7$ Hz); $^{31}$P{$^1$H} NMR (121.5 MHz, CDCl$_3$): $\delta$ 3.5 (t, $J = 101.7$ Hz), 3.4 (t, $J = 103.4$ Hz); IR (neat, cm$^{-1}$) ν: 2985, 2930, 1600, 1495, 1393, 1272, 1115, 1014, 981, 750, 697, 536; HRMS (ESI$^+$): calcd for C$_{14}$H$_{23}$F$_2$NO$_3$PS m/z 354.1104 [M+NH$_4$]$^+$, found 354.1097 (-2.0 ppm).

9. Post-functionalization reactions

9.1 Cleavage of the SCF$_2$PO(OEt)$_2$ group

![Chemical structure]

To a solution of alkene 2a (60 mg, 0.15 mmol) in anhydrous THF (3 mL) was added H$_2$O (3.2 µl, 0.18 mmol) and sodium hydroxide (9 mg, 0.23 mmol). The reaction mixture was stirred for 4 hours at room temperature under argon atmosphere before adding water (10 mL). The resulting mixture was extracted by diethyl ether (3 × 10 mL) and the combined organic layers were washed by brine (2 × 20 mL), dried over magnesium sulfate, filtered and concentrated under reduced pressure. The crude residue was finally purified by flash column chromatography (Biotage System, 10 g SiO$_2$ cartridge, height 60 mm, width 20 mm, eluent: pentane/Et$_2$O, from 95:5 to 80:20) to give the desired product 7 as a colorless oil in 76% yield (30 mg, 0.11 mmol).

(E)-1-Chloro-1-phenyl-2-[(difluoromethyl)thio]pentene 7. Diastereoisomeric ratio: 98:2; R$_t$ (petroleum ether/Et$_2$O = 80:20): 0.61; Light yellow oil; $^1$H NMR (300.1 MHz, CDCl$_3$): $\delta$ 7.50-7.28 (m, 5H), 6.61 (t, $J = 56.7$ Hz, 1H), 2.83-2.63 (m, 2H), 1.82-1.68 (m, 2H), 1.04 (t, $J = 7.2$ Hz, 3H); $^{13}$C NMR (75.5 MHz, CDCl$_3$): $\delta$ 138.8 (t, $J = 2.3$ Hz), 138.75, 129.3, 129.0, 128.3, 126.8 (t, $J = 2.3$ Hz), 120.1 (t, $J = 277.1$ Hz), 38.4, 20.7, 13.7; $^{19}$F NMR (282.4 MHz, CDCl$_3$): $\delta$ -92.5 (d, $J = 56.5$ Hz); IR (neat, cm$^{-1}$) ν: 2962, 2930, 2872, 1593, 1488, 1444, 1318, 2962.
1296, 1052, 871, 749, 694; HRMS (EI\(^+\)): calcd for C\(_{12}\)H\(_{13}\)ClF\(_2\)S \(m/z\) 262.0395 [M\(^+\)], found 262.0398 (1.2 ppm).

### 9.2 Oxidation

![Chemical structure](image)

To a solution of alkene 2a (60 mg, 0.15 mmol) in anhydrous CH\(_2\)Cl\(_2\) (1.5 mL) was added \(m\)-CPBA (assay 77\%, 40 mg, 0.18 mmol) at 0 °C and the reaction mixture was allowed to warm to room temperature and stirred for 16 hours under argon atmosphere before diluted by dichloromethane (20 mL). The resulting mixture was successively washed by saturated sodium sulfite aqueous solution (2 × 20 mL), saturated sodium bicarbonate (2 × 20 mL) and brine (2 × 20 mL). The combined organic layers were dried over magnesium sulfate, filtered and concentrated under reduced pressure to give a yellow crude residue, which was finally purified by flash column chromatography (Biotage System, 10 g SiO\(_2\) cartridge, height 60 mm, width 20 mm, eluent: pentane/Et\(_2\)O, from 80:20 to 50:50) to give the desired product 8 as a colorless oil in 51\% yield (32 mg, 0.08 mmol).

\(\text{(E)-1-Chloro-1-phenyl-2-[(diethylphosphonodifluoromethyl)sulfinyl]pentene 8.}\)

Diastereoisomeric ratio: 97:3; \(R_f\) (petroleum ether/Et\(_2\)O = 50:50): 0.18; \(^1\)H NMR (300.1 MHz, CDCl\(_3\)): \(\delta\) 7.46-7.29 (m, 5H), 4.42-4.06 (m, 4H), 2.85-2.60 (m, 2H), 1.83-1.67 (m, 2H), 1.34 (t, \(J = 7.2\) Hz, 3H), 1.27 (t, \(J = 7.2\) Hz, 3H), 1.04 (t, \(J = 7.2\) Hz, 3H); \(^{13}\)C NMR (75.5 MHz, CDCl\(_3\)): \(\delta\) 145.1-145.0 (m), 139.5-139.4 (m), 135.9, 130.2, 134.9 (d, \(J = 1.6\) Hz), 128.5, 65.9 (d, \(J = 7.6\) Hz), 65.8 (d, \(J = 7.6\) Hz), 28.7, 28.68, 21.5, 21.4, 16.4 (d, \(J = 5.3\) Hz), 16.3 (d, \(J = 5.3\) Hz), 14.4 (CF\(_2\) carbon not observed); \(^{19}\)F NMR (282.4 MHz, CDCl\(_3\)): \(\delta\) -102.5 (dd, \(J = 268.3\) and 87.5 Hz), -118.3 (dd, \(J = 271.1\) and 93.2 Hz); \(^{31}\)P\(\{^1\)H\}\) NMR (121.5 MHz, CDCl\(_3\)): \(\delta\) 1.91 (t, \(J = 91.1\) Hz), 1.89 (t, \(J = 91.1\) Hz); IR (neat, cm\(^{-1}\)) v: 2968, 2934, 2874, 1617, 1594, 1445, 1394, 1278, 1093, 1011, 750, 697, 538; HRMS (ESI\(^+\)): calcd for C\(_{16}\)H\(_{23}\)ClF\(_2\)O\(_4\)PS \(m/z\) 415.0711 [M+H\(^+\)], found 415.0709 (-0.5 ppm).

### 9.3 Oxidation and cleavage

![Chemical structure](image)

To a solution of alkene 2a (60 mg, 0.15 mmol) in anhydrous CH\(_2\)Cl\(_2\) (1.5 mL) was added \(m\)-CPBA (202 mg, 0.9 mmol, assay 77\%) at 0 °C and the reaction mixture was then heated to 60 °C for 48 hours under argon atmosphere before diluted by dichloromethane (30 mL). The
resulting mixture was successively washed by saturated sodium sulfite aqueous solution (2 × 20 mL), saturated sodium bicarbonate (2 × 20 mL) and brine (2 × 20 mL). The organic layer was dried over magnesium sulfate, filtered and concentrated under reduced pressure to give a yellow crude residue, which was finally purified by flash column chromatography (Biotage System, 10 g SiO₂ cartridge, height 60 mm, width 20 mm, eluent: pentane/Et₂O, from 100:0 to 90:10) to give the desired product 9 as a colorless oil in 54% yield (24 mg, 0.08 mmol).

(E)-1-Chloro-1-phenyl-2-[[difluoromethyl]sulfonyl]pentene 9. Diastereoisomeric ratio: ¹ 98:2; Rₐ (petroleum ether/Et₂O = 91:9): 0.25; ¹H NMR (300.1 MHz, CDCl₃): δ 7.63-7.32 (m, 5H), 5.63 (t, J = 53.7 Hz, 1H), 2.93-2.69 (m, 2H), 1.89-1.72 (m, 2H), 1.07 (t, J = 7.2 Hz, 3H); ¹³C NMR (75.5 MHz, CDCl₃): δ 151.9 (t, J = 1.5 Hz), 136.3, 136.2, 130.4, 128.9 (t, J = 0.8 Hz), 128.3, 114.7 (t, J = 287.7 Hz), 34.1, 21.6, 14.1; ¹⁹F NMR (282.4 MHz, CDCl₃): δ -121.8 (d, J = 53.7 Hz); IR (neat, cm⁻¹) ν: 2968, 2876, 1612, 1590, 1445, 1352, 1285, 1166, 1119, 1098, 1016, 749, 695, 544; HRMS (EI⁺): calcd for C₁₂H₁₃ClF₂O₂S m/z 294.0293 [M]+, found 294.0293 (0.1 ppm).

10. Measurement of lipophilicities (Log P)

I- Preparation of the saturated octanol and water solutions for the determination of the lipophilicity

50 mL Octanol and 50 mL (Milli-Q water) were added into a separating funnel, which was hand-shacked for 5 min and then left to stand for 3 hours to allow a well-defined separation of the two layers. Both were collected in an oven-dried flask.

Note that to make sure that the layers were well separated, the fractions close to the separating line were not collected.

II- Determination of the calibration curve for the titration of Benzene and PhSCF₂PO(OEt)₂ in octanol and water layers.

Calibration in case of benzene

A solution of benzene in methanol (concentration 8.787 mg/mL) was prepared. Then, diluted solutions were prepared by dilution in methanol (see below).

The calibration curve of benzene was determined with the following solutions: 439.35; 219.675; 87.878; 43.935 and 17.574 µg/mL.

Each solution was injected three times, integrations were determined at 205 nm and an average integration value based on the three injections was used to plot the calibration curve, forced at

¹ E/Z ratio was determined by ¹⁹F NMR on the product 9 after hydrolysis on column chromatography.
<table>
<thead>
<tr>
<th>C µg/mL</th>
<th>Area (relative)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1 439.35</td>
<td>165.9293</td>
</tr>
<tr>
<td>C2 219.675</td>
<td>83.6564</td>
</tr>
<tr>
<td>C3 87.878</td>
<td>34.1727</td>
</tr>
<tr>
<td>C4 43.935</td>
<td>9.3338</td>
</tr>
<tr>
<td>C5 17.574</td>
<td>3.827</td>
</tr>
</tbody>
</table>

Calibration curve formula is \( f(x) = 0.377x \); correlation coefficient is \( R^2 = 0.998 \)

**III- Calibration in case of PhSCF₂PO(OEt)₂**

A solution of PhSCF₂PO(OEt)₂ in methanol (concentration 8.787 mg/mL) was prepared. Then, diluted solutions were prepared by dilution in methanol (see below).
The calibration curve of PhSCF$_2$PO(OEt)$_2$ was determined with the following solutions: 219.675; 146.45; 109.84; 54.92; 27.46; 21.97 ng/mL.

Each solution was injected three times, integrations were determined by mass spectrometry using a MRM transition between m/z 297.0819 and 64.9304 and an average integration value based on the three injections was used to plot the calibration curve.

<table>
<thead>
<tr>
<th>C ng/mL</th>
<th>Area (relative)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1 219.675</td>
<td>1158679.7</td>
</tr>
<tr>
<td>C2 146.45</td>
<td>784295.33</td>
</tr>
<tr>
<td>C3 109.84</td>
<td>627021</td>
</tr>
<tr>
<td>C4 54.92</td>
<td>318793</td>
</tr>
<tr>
<td>C5 27.46</td>
<td>162903.67</td>
</tr>
<tr>
<td>C6 21.92</td>
<td>121804</td>
</tr>
</tbody>
</table>

Calibration curve formula is \( f(x) = 5217.766x + 24258.179 \); correlation coefficient is \( R^2 = 0.998 \).
IV- Determination of the log P of Benzene, the log P of PhSCF₂PO(OEt)₂ and the Hansch-Leo π constant

To a 5 mL vial was added a sat. octanol solution (2 mL) and a sat. water solution (2 mL). Then benzene or PhSCF₂PO(OEt)₂ was added. The resulting biphasic mixture was shacked for 15 min by vortex, stand for 2 hours to give fully separated layers. Then, two samples were prepared using the same method.

A sample was taken from each layer with a pipette. The upper layer (octanol layer) was first carefully transfer to a HPLC vial. Then, a small amount of the octanol and the water layers were discarded and the water layer was transfer to a HPLC vial with a pipette.

Each octanol and water layer samples was then prepared for analysis.

a- Calculation of the lipophilicity of Benzene (log P)

Analysis were performed by HPLC at 205 nm.

<table>
<thead>
<tr>
<th>Injection</th>
<th>Area in water (no dilution)</th>
<th>Area in octanol (dilution by 50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.74</td>
<td>39.742</td>
</tr>
<tr>
<td>2</td>
<td>2.712</td>
<td>39.758</td>
</tr>
<tr>
<td>average</td>
<td>2.726</td>
<td>39.75</td>
</tr>
</tbody>
</table>

Using the calibration curve formula \( f(x) = 0.377 \times \) determined before, a concentration in water \( C_{\text{water}} = 7.2278 \mu\text{g/mL} \) and a concentration in octanol \( C_{\text{octanol}} = 5269.74 \mu\text{g/mL} \) were determined.

\[
\text{Log } P_{\text{benzene}} (C_{\text{octanol}}/C_{\text{water}}) = 2.86
\]

b- Calculation of the lipophilicity of \( C_6H_5SCF_2PO(OEt)_2 \) (Log P)

Analysis were performed by mass spectrometry in MRM mode m/z 297.0819 and 64.9304

<table>
<thead>
<tr>
<th>Injection</th>
<th>Area in water (dilution by 3)</th>
<th>Area in octanol (dilution by 5000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>172027.5</td>
<td>411534.5</td>
</tr>
</tbody>
</table>
Using the calibration curve formula \( f(x) = 5217.766 \times x + 24258.179 \) determined before, a concentration in water \( C_{\text{water}} = 0.0762 \, \mu g/mL \) and a concentration in octanol \( C_{\text{octanol}} = 32.0369 \, \mu g/mL \) were determined.

\[
\log P C_{6}H_{5}SCF_{2}PO(OEt)_{2} (C_{\text{octanol}}/C_{\text{water}}) = 3.62
\]

c- Determination of the Hansch-Leo \( \pi \) constant\cite{18}

Based on the following equation (\( \pi = \log PC_{6}H_{5}X - \log PC_{6}H_{5} \) for substituted benzenes), a Hansch-Leo \( \pi \) constant of 0.76 was determined in case of \( C_{6}H_{5}SCF_{2}PO(OEt)_{2} \).

V Instruments and methods

a- Analytical conditions for the determination of the concentration in benzene

Analytical HPLC was performed on a Thermo Scientific Ultimate 3000 RSLC instrument equipped with a PDA detector, UV chromatogram were recorded at 205 nm. The column used is a Phenomenex Prodigy ODS 30×4.6 mm; 5 \( \mu \)m. Acetonitrile and water (60/40, v/v) were used as eluents at flow rate of 1.2 mL/min. Temperature was set at 40 °C.

b- Analytical conditions for the determination of the concentration in PhSCF_{2}PO(OEt)_{2}

LC-MS data were performed on a Waters I-Class chromatographic system equipped with a column Waters BEH 100×2.1 mm; 1.9 \( \mu \)m. Acetonitrile and water (60/40, v/v) were used as eluents at flow rate of 0.45 mL/min, temperature was set at 25 °C. The system is coupled to a triple quadrupole mass spectrometer Xevo TQS Micro employing multiple reaction monitoring (MRM) where the precursor is set at 297.0819 and the fragment 64.9304 is detected.
11. References


12. X-Ray crystallographic analysis of 2s

Compound 2s (Data CCDC 1898035)
DATA COLLECTION

The crystal structure of 2s [C_{10}H_{20}ClF_{2}O_{3}] has been determined from single crystal X-Ray diffraction. The chosen crystal was stuck on a glass fibre and mounted on the full three-circle goniometer of a Bruker SMART APEX diffractometer with a CCD area detector. Three sets of exposures (a total of 1800 frames) were recorded, corresponding to three \( \omega \) scans (steps of 0.3°), for three different values of \( \phi \). The details of data collection are given in annexe 1.

The cell parameters and the orientation matrix of the crystal were preliminary determined by using SMART Software\(^1\). Data integration and global cell refinement were performed with SAINT Software\(^2\). Intensities were corrected for Lorentz, polarisation, decay and absorption effects (SAINT and SADABS Softwares) and reduced to \( F_\text{O}^2 \). The program package WinGX\(^3\) was used for space group determination, structure solution and refinement.

DATA REFINEMENT

The standard space group \( P-1 \) (n°2) was determined from systematic extinctions and relative \( F_\text{O}^2 \) of equivalent reflections. The structure was solved by direct methods\(^4\). Anisotropic displacement parameters were refined for all non-hydrogen atoms. Every Hydrogen atoms were located from subsequent difference Fourier syntheses and placed with geometrical constraints (SHELXL\(^5\)). The final cycle of full-matrix least-square refinement on \( F^2 \) was based on 4152 observed reflections and 246 variable parameters and converged with unweighted and weighted agreement factors of:

\[
R_1 = 0.0656, \quad wR_2 = 0.1754 \text{ for } 2525 \text{ reflections with } l>2\sigma(l) \quad \text{and} \quad R_1 = 0.1072, \quad wR_2 = 0.2070 \text{ for all data.}
\]

The refinement data are given in annexe 1 table 2.

CRYSTALLOGRAPHIC DATA AND STRUCTURAL DESCRIPTION

Crystallographic data

The crystal data are collected in Table 1. The full crystallographic parameters (atomic coordinates, bond length, angles and anisotropic displacements) are reported in annexe 2.
### Table 1: Crystal data

<table>
<thead>
<tr>
<th>Chemical Formula</th>
<th>[C_{19}H_{20}ClF_2O_3PS]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular Weight / g.mol⁻¹</td>
<td>432.83</td>
</tr>
<tr>
<td>Crystal System</td>
<td>Triclinic</td>
</tr>
<tr>
<td>Space Group</td>
<td>P-1 (n°2)</td>
</tr>
<tr>
<td>Z, Z’ (asymmetric units per unit cell)</td>
<td>2, 1</td>
</tr>
<tr>
<td>a / Å</td>
<td>10.099(2)</td>
</tr>
<tr>
<td>b / Å</td>
<td>10.253(2)</td>
</tr>
<tr>
<td>c / Å</td>
<td>11.362(2)</td>
</tr>
<tr>
<td>α / °</td>
<td>77.012(4)</td>
</tr>
<tr>
<td>β / °</td>
<td>67.262(4)</td>
</tr>
<tr>
<td>γ / °</td>
<td>83.234(4)</td>
</tr>
<tr>
<td>V / Å³</td>
<td>1056.6(4)</td>
</tr>
<tr>
<td>d_{calc} / g.cm⁻³</td>
<td>1.360</td>
</tr>
<tr>
<td>F(000) / e⁻</td>
<td>448</td>
</tr>
<tr>
<td>Absorption coefficient μ (MoKα₁) / mm⁻¹</td>
<td>0.388</td>
</tr>
</tbody>
</table>

### Structural description

The asymmetric unit is composed of one molecule of \[C_{19}H_{20}ClF_2O_3PS\] (Figures 1&2). These molecules establish along \(a\) axis, some π interactions in T-shape, and give rise to molecular chains in this direction (Figures 3&4).
Figure 1: asymmetric unit in thermal ellipsoidal representation

Figure 2: Asymmetric unit with atom labels

Figure 3: Projection along $a$, spreading axis of the molecular chains formed by the T-shaped $\pi$ interactions
Figure 4: Projection of a molecular chain formed by the T-shaped $\pi$ interactions

Figure 5: Projection along $a$

Figure 6: Projection along $b$
Figure 7: Projection along $c$

Sofwares:


(2)- SAINT+ V6.02 (1999), Saint software reference manual, Bruker Advanced X Ray Solutions, Inc., Madison, Wisconsin, USA.


(5)-include in WinGX suite: SHELXL-97 – a program for crystal structure refinement, G. M. Sheldrick, University of Goettingen, Germany, 1997, release 97-2.

(6)-PowderCell for Windows (version 2.4) by Kraus W. & Nolze G., Federal institute for materials Research and testing, Rudower Chausse 5, 12489 Berlin Germany.
13. NMR spectra of derivatives 2

Cl
Pr
SCF₂PO(OEt)₂

2a
SCF₂PO(OEt)₂

2m
SCF₃PO(OEt)₂

2o
14. NMR spectra of derivatives 4
15. NMR spectra of derivatives 6

![NMR spectra](image)

6a
$\text{Me} \quad \text{Ph} \quad \text{SCF}_2\text{PO(OEt)}_2 \quad + \quad \text{SCF}_2\text{PO(OEt)}_2$

$6\text{ha}/6\text{hb}$

$(1:1)$
16. NMR spectra of compounds 7, 8 and 9