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A facile synthesis of 1-*H*-2,2-difluorovinylphosphorus compounds from 2,2,2-trifluoroethyl trifluoromethanesulfonate and substitutions of their vinylic fluorines

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Dedicated to Professor Emeritus Yoshiro Kobayashi with deep respect on the occasion of his 75th birthday

Abstract

2,2-Difluorovinylphosphine as well as its oxide and borane-complex are synthesized in high yields *via* the *P*-trifluoroethylation of lithium diphenylphosphide with 2,2,2-trifluoroethyl trifluoromethanesulfonate, followed by dehydrofluorination with potassium *tert*-butoxide. The reactions of 2,2-difluorovinylphosphine oxide and borane-complex with hydride, *S*- and *N*-nucleophiles proceed *via* an addition–elimination process to afford mono- or nonfluorovinylphosphorus compounds and carbamoylmethylphosphine oxides.

Keywords: Fluorovinylphosphorus compound; Trifluoroethylation; Triflate; Dehydrofluorination; Substitution; Vinylic fluorine

1. Introduction

Vinylphosphorus compounds such as phosphonium salts, phosphonates, and phosphine oxides have received significant attention as versatile intermediates in the syntheses of heterocyclic, carbocyclic, and chain-extended systems [1–4]. In this sense, fluorine-containing vinylphosphorus species are potential building blocks for the synthesis of selectively fluorinated compounds. Fluorine substitution provides the unique advantage of markedly affecting electron density distribution and related properties. Only a limited number of methods have been available for the preparation of fluorinated vinylphosphorus compounds despite the utility of these species [2,5–8].

In our recent publication we have illustrated a new route to 2,2-difluorovinyl- and 2-fluorovinylphosphorus compounds bearing a substituent at the 1-position of the vinyl group [9]. To the best of our knowledge, there have been no reports of synthetic methods for 2,2-difluorovinylphosphorus compounds bearing no 1-substituent. We describe here a route to these simple difluorovinylphosphorus compounds starting from 2,2,2-trifluoroethyl trifluoromethanesulfonate and substitution reactions of the resulting vinylic fluorines.

2. Syntheses of 1-nonsubstituted 2,2-difluorovinylphosphorus compounds

Our synthetic plan for 2,2-difluorovinylphosphine (**3**) was (i) the introduction of a 2,2,2-trifluoroethyl group on phosphorus, followed by (ii) dehydrofluorination, which would furnish the phosphorus atom with the difluorovinyl substituent, as shown in Scheme 1. Although trifluoroethylating reagents (CF_3CH_2X) are generally poor electrophiles because of the electronegativity of the CF_3 group [10–14], the reaction depicted in Scheme 1 proceeded in high yield. Use of the potent triflate ($X{=}OSO_2CF_3$) leaving group (*O*-trifluoroethylation [15,16], *N*-trifluoroethylation [17,18], *C*-trifluoroethylation [19]) in conjunction with the strongly nucleophilic diphenylphosphide ion effectively promoted the rarely observed *P*-trifluoroethylation we desired. Dehydrofluorination of the resulting trifluoroethylphosphine with base afforded the 2,2-difluorovinylphosphine.

Lithium diphenylphosphide, generated in situ from diphenylphosphine and butyllithium, readily reacted with trifluoroethyl triflate (**1**) in tetrahydrofurane (THF) even at −78°C to afford the desired diphenyl(trifluoroethyl)phosphine (**2**)

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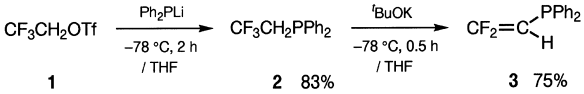
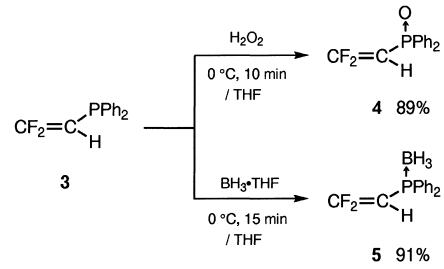


Scheme 1.

in 83% yield. Minimal trifluoroethylation occurred with trifluoroethyl iodide (X=I), confirming the potent trifluoroethylating ability of **1** [15–19]. Next, conditions employing several bases were examined to effect dehydrofluorination of **2**. Lithium diisopropylamide (LDA) and butyllithium caused the replacement of the CF_3CH_2 group at the phosphorus center. In order to prevent such nucleophilic attack, less nucleophilic bases were examined. Among lithium 2,2,6,6-tetramethylpiperidide, *tert*-butyllithium, and potassium *tert*-butoxide, only the last successfully achieved the deprotonation in THF to give (2,2-difluorovinyl)diphenylphosphine (**3**) in 75% yield.

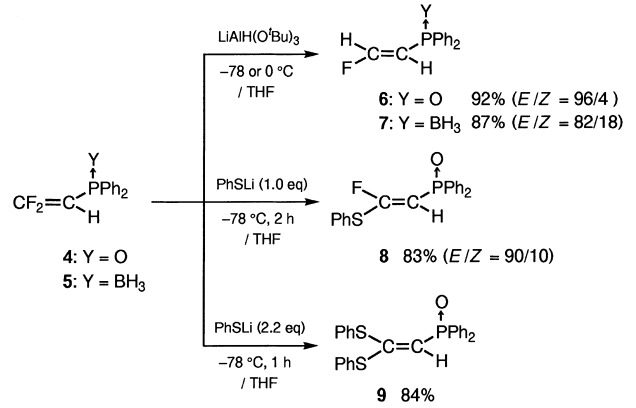
Thus obtained, **3** was transformed to several phosphorus derivatives. Treatment of **3** with hydrogen peroxide or borane provided phosphine oxide (**4**) and phosphine-borane (**5**) in 89% and 91% yields, respectively (Scheme 2).



Scheme 2.

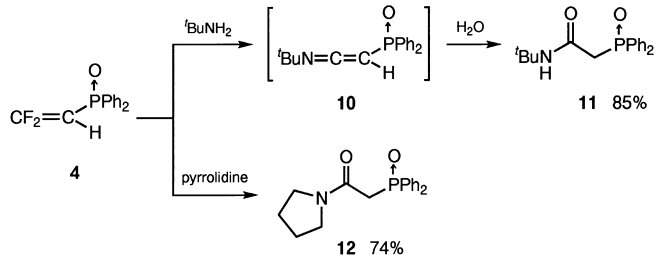
3. Vinylic fluorine substitution of 1-*H*-2,2-difluorovinylphosphorus compounds

4 and **5** have a highly electrophilic carbon–carbon double bond doubly activated by either a $P(O)Ph_2$ or $P(BH_3)Ph_2$ group and two fluorine atoms [20–23]. Reaction of these activated olefins with nucleophiles effects the substitution of the fluorines *via* an addition–elimination process, leading to mono- and/or nonfluorovinylphosphorus compounds [9]. On treatment with lithium aluminum hydride, **4** was selectively converted into the expected monofluorinated compound (**6**) in 73% yield (*Z*/*E*=95/5).[2,3] Examination of several hydride reagents revealed that $LiAlH(O^tBu)_3$ brought about better results for the reduction of both **4** and **5** to give **6** (92%, *E*/*Z*=96/4) and **7** (87%, *E*/*Z*=82/18), respectively (Scheme 3).[1,2] When benzenethiolate was employed as a nucleophile, a similar substitution of the fluorines took place to yield the mono- or di-substituted product **8** (83%, *E*/*Z*=90/10) or **9** (84%), depending on the amount of the added thiolate. This result indicates that the substitution of the two vinylic fluorines can be controlled in a stepwise fashion.



Scheme 3.

We also investigated the reaction of **4** with primary amines to produce phosphinoylketenimines (**10**) [24] through double dehydrofluorination. While **4** readily reacted with *tert*-butylamine, aqueous workup gave an 85% yield of *N*-*tert*-butyl(diphenylphosphinoyl)acetamide (**11**), probably by addition of water to the ketenimine (Scheme 4).[4] In the case of secondary amines, the same reaction followed by treatment with aqueous sodium hydroxide afforded *N*,*N*-disubstituted (carbamoylmethyl)phosphine oxides (**12**) in high yields (Scheme 4). This sequence of reactions effectively affords phosphinoylacetylation of primary and secondary amines to provide the corresponding α-phosphinoylamides.



Scheme 4.

4. Conclusions

The reactions described herein provide novel 1-*H*-2,2-difluorovinylphosphorus compounds such as free phosphine

[2]The *E*/*Z* ratio was determined by GLC analysis of the reaction mixture. The configuration was assigned by ^1H and ^{19}F NMR measurement on the basis of the vinylic ^1H–^1H, ^1H–^{31}P, ^1H–^{19}F, and ^{19}F–^{31}P coupling constants to bear the relationship of $J_{trans}>J_{cis}$.

[3]The reaction should be quenched under acidic conditions to prevent *E*/*Z* isomerization.

[4]Ketenimine **10** was detected by ^1H NMR measurement after nonaqueous workup.

(**3**), phosphine oxide (**4**), and phosphine-borane (**5**). Furthermore, 2-fluorovinylphosphorus compounds (**6–8**), 2-substituted vinylphosphine oxide (**9**), and (carbamoylmethyl)phosphine oxides (**11**, **12**) are also readily obtained from the reaction of **4** or **5** with appropriate nucleophiles. The vinylic substitutions demonstrate that fluorine acts as a powerful functional group for further synthetic elaborations as well as an electronically unique substituent.

5. Experimental details

General: IR spectra were recorded on a Shimadzu IR-408 spectrometer. NMR spectra were obtained on JEOL JNM-FX-60, JNM-FX-100, JNM-EX-270, or JNM-A-500 spectrometers. Chemical shift values were given in ppm relative to internal Me_4Si (for ^1H and ^{13}C NMR : δ-value), H_3PO_4 (for ^{31}P NMR), or C_6F_6 (for ^{19}F NMR). Mass spectra were taken with a JEOL JMS-DX-300 spectrometer. Elemental analyses were performed with a YANAKO MT-3 CHN Corder apparatus. THF was distilled from sodium benzophenone ketyl prior to use.

5.1. Diphenyl(2,2,2-trifluoroethyl)phosphine (2)

To a solution of diphenylphosphine (80 mg, 0.43 mmol) in THF (2 ml) was added butyllithium (0.31 ml, 1.53 M in hexane, 0.47 mmol) at −78°C over 10 min under an argon atmosphere. After the reaction mixture was stirred for 30 min at −78°C, 2,2,2-trifluoroethyl trifluoromethanesulfonate (**1**, 100 mg, 0.39 mmol) in THF (1 ml) was added to the mixture. The reaction was quenched with degassed water after stirring for 2 h. Organic materials were extracted with dichloromethane three times. The combined extracts were washed with brine, and then dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel (chloroform), and then Kugelrohr distillation gave **2** as a colorless liquid (86 mg, 83%). IR (neat) 1295, 1260, 1230, 1110, 1045, 735, 695 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ: 2.89 (2H, q, J_{HF}=11.6 Hz), 7.33–7.45 (10H, m). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 35.1 (qd, J_{CF}=28 Hz, J_{CP}=23 Hz), 126.6 (qd, J_{CF}=275 Hz, J_{CP}=16 Hz), 128.8 (d, J_{CP}=7 Hz), 129.4, 132.7 (d, J_{CP}=21 Hz), 136.4 (d, J_{CP}=11 Hz). ^{19}F NMR (94 MHz, $CDCl_3$) 103.0 (dt, J_{FP}=15 Hz, J_{FH}=12 Hz) ppm. ^{31}P NMR (202 MHz, $CDCl_3$) −26.9 (q, J_{PF}= 15 Hz) ppm. MS (70 eV) *m/z* (rel. intensity) 268 (M^+; 53), 201 (87), 183 (92), 77 (100). HRMS calcd. for $C_{14}H_{12}F_3P$ 268.0628 (M^+); found 268.0589.

5.2. (2,2-Difluorovinyl)diphenylphosphine (3)

To a solution of potassium *tert*-butoxide (440 mg, 3.92 mmol) in THF (10 ml) was added dropwise diphenyl(2,2,2-trifluoroethyl)phosphine (**2**, 500 mg, 1.87 mmol) in THF (3 ml) at −78°C under an argon atmosphere. After the mixture was stirred for 30 min at −78°C, the reaction was quenched with degassed water. Organic materials were extracted with dichloromethane three times. The combined extracts were washed with brine, and then dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel (chloroform) to give **3** as a colorless solid (346 mg, 75%). m.p. 32–34°C. IR (KBr) 3060, 1695, 1440, 1300, 1150, 955, 740, 695 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ: 4.84 (1H, ddd, J_{HF}=28.0, 5.3 Hz, J_{HP}=3.3 Hz), 7.32–7.42 (10H, m). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 74.8 (ddd, J_{CF} or J_{CP}=21, 16, 10 Hz), 128.6 (d, J_{CP}=6 Hz), 128.9, 132.4 (d, J_{CP}=20 Hz), 137.6 (d, J_{CP}=7 Hz), 160.0 (ddd, J_{CF}=302, 294 Hz, J_{CP}=33 Hz). ^{19}F NMR (470 MHz, $CDCl_3$) 86.9 (1F, ddd, J_{FP}=44 Hz, J_{FH}=28 Hz, J=12 Hz), 96.2 (1F, ddd, J=12 Hz, J_{FP}=7 Hz, J_{FH}=5 Hz) ppm. ^{31}P NMR (202 MHz, $CDCl_3$) −33.3 (dd, J_{PF}=43, 8 Hz) ppm. MS (70 eV) m/z (rel. intensity) 248 (M^+; 52), 164 (63), 122 (100), 91 (53). HRMS calcd. for $C_{14}H_{12}F_3P$ 248.0566 (M^+); found 248.0560.

5.3. (2,2-Difluorovinyl)diphenylphosphine oxide (4)

To a solution of (2,2-difluorovinyl)diphenylphosphine (**3**, 30 mg, 0.12 mmol) in THF (2 ml) was added 30% hydrogen peroxide (0.2 ml) at 0°C. After the mixture was stirred for 10 min at 0°C, the reaction was quenched with water. Organic materials were extracted with dichloromethane three times. The combined extracts were washed with brine, and then dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by thin layer chromatography on silica gel (chloroform–ethyl acetate 1:1) to give **4** as a colorless solid (31 mg, 97%). m.p. 108–110°C. IR (KBr) 2980, 1705, 1440, 1325, 1195, 1120, 970, 795, 755, 720, 695 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ: 5.04 (1H, ddd, J_{HF}=28.4, 5.3 Hz, J_{HP}=5.3 Hz), 7.21–7.60 (6H, m), 7.60–7.88 (4H, m). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 74.4 (ddd, J_{CP}=106 Hz, J_{CF}=18, 13 Hz), 128.8 (d, J_{CP}=13 Hz), 131.0 (d, J_{CP}=10 Hz), 132.3 (d, J_{CP}=3 Hz), 132.4 (dd, J_{CP}=112 Hz, J_{CF}=2 Hz), 160.4 (ddd, J_{CF}=308, 303 Hz, J_{CP}=5 Hz). ^{19}F NMR (94 MHz, $CDCl_3$) 98.9 (1F, ddd, J_{FH}=28 Hz, J=8 Hz, J_{FP}=7 Hz), 102.2 (1F, ddd, J_{FP}=22 Hz, J=8 Hz, J_{FH}=5 Hz) ppm. ^{31}P NMR (202 MHz, $CDCl_3$) 19.3 (dd, J_{PF}=22, 7 Hz) ppm. MS (70 eV) *m/z* (rel. intensity) 264 (M^+; 84), 263 (100), 77 (66), 51 (37). Anal. calcd. for $C_{14}H_{11}F_2OP$: C, 63.64; H, 4.20. Found C, 63.62; H, 4.36.

5.4. (2,2-Difluorovinyl)diphenylphosphine-borane (5)

To a solution of (2,2-difluorovinyl)diphenylphosphine (**3**, 333 mg, 1.34 mmol) in THF (5 ml) was added borane–THF (1.48 ml, 1.0 M in THF, 1.48 mmol) at 0°C. After the mixture was stirred for 15 min at 0°C, the reaction was quenched with phosphate buffer (pH 7). Organic materials were extracted with dichloromethane three times. The

combined extracts were washed with brine, and then dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by thin layer chromatography on silica gel (hexane–ether 5:1) gave **5** as a colorless solid (308 mg, 88%). m.p. 32–34°C. IR (neat) 3070, 2420, 1710, 1490, 1440, 1320, 1175, 1110, 1060, 980, 735, 695 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ: 0.78–1.50 (3H, m), 4.82 (1H, ddd, J_{HF}=28.3, 5.1 Hz, J_{HP}=2.7 Hz), 7.43–7.53 (6H, m), 7.64–7.70 (4H, m). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 70.2 (ddd, J_{CP}=61 Hz, J_{CF}=17, 17 Hz), 128.7 (d, J_{CP}=61 Hz), 129.0 (d, J_{CP}=10 Hz), 131.6 (d, J_{CP}=3 Hz), 132.2 (d, J_{CP}=10 Hz), 159.8 (ddd, J_{CF}=305, 303 Hz, J_{CP}=7 Hz). ^{19}F NMR (470 MHz, $CDCl_3$) 97.9 (1F, br d, J_{FH}=28 Hz), 102.7 (1F, ddd, J_{FP}=9 Hz, J_{FH}=5 Hz, J=5 Hz) ppm. ^{31}P NMR (202 MHz, $CDCl_3$) 9.2 (m) ppm. MS (70 eV) *m/z* (rel. intensity) 248 (M^+–BH_3; 52), 183 (20), 127 (44), 108 (100), 77 (18). HRMS calcd. for $C_{14}H_{11}F_2P$ 248.0565 (M^+–BH_3); found 248.0551.

5.5. (2-Fluorovinyl)diphenylphosphine oxide (6)

To a solution of (2,2-difluorovinyl)diphenylphosphine oxide (**4**, 50 mg, 0.19 mmol) in THF (2 ml) was added $LiAlH(O^tBu)_3$ (0.21 ml, 1.0 M in THF, 0.21 mmol) at −78°C. After the mixture was stirred for 10 min at −78°C, the reaction was quenched with 2 M HCl. Organic materials were extracted with ethyl acetate three times. The combined extracts were washed with brine, and then dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by thin layer chromatography on silica gel (ethyl acetate) to give **6** as a colorless solid (43 mg, 92%, *E*/*Z*=93/7).

(*E*)-**6**: IR (KBr) 1665, 1620, 1440, 1320, 1190, 1120, 1090, 970, 720, 700 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ: 6.02 (1H, ddd, J_{HF}=21.6 Hz, J=11.9 Hz, J_{HP}=11.9 Hz), 7.07 (1H, ddd, J_{HF}=83.2 Hz, J=11.9 Hz, J_{HP}=7.4 Hz), 7.45–7.57 (6H, m), 7.66–7.75 (4H, m). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 104.7 (dd, J_{CP}=104 Hz, J_{CF}= 3 Hz), 128.7 (d, J_{CP}=12 Hz), 131.1 (d, J_{CP}=10 Hz), 132.3 (dd, J_{CP}=110 Hz, J_{CF}=2 Hz), 132.3 (d, J_{CP}=3 Hz), 162.1 (dd, J_{CF}=288 Hz, J_{CP}=18 Hz). ^{19}F NMR (470 MHz, $CDCl_3$) 67.0 (ddd, J_{FH}=83 Hz, J_{FP}=42 Hz, J_{FH}=22 Hz) ppm. ^{31}P NMR (202 MHz, $CDCl_3$) 22.2 (d, J_{PF}=41 Hz) ppm. MS (70 eV) *m/z* 246 (M^+), 245, 105 (base peak), 77. HRMS calcd. for $C_{14}H_{12}FOP$ 246.0609 (M^+); found 246.0604. Anal. calcd. for $C_{14}H_{12}FOP$: C, 68.29; H; 4.91. Found C, 68.14; H, 5.02.

(*Z*)-**6**: m.p. 61–63°C. IR (KBr) 1630, 1440, 1180, 1120, 1025, 720, 700 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ: 5.65 (1H, ddd, J_{HF}=48.3 Hz, J_{HP}=7.1 Hz, J=6.2 Hz), 7.05 (1H, ddd, J_{HF}=83.0 Hz, J_{HP}=24.7 Hz, J=6.2 Hz), 7.46–7.51 (4H, m), 7.53–7.58 (2H, m), 7.68–7.73 (4H, m). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 105.1 (dd, J_{CP}=98 Hz, J_{CF}=5 Hz), 128.6 (d, J_{CP}=12 Hz), 131.0 (d, J_{CP}=11 Hz), 132.1 (d, J_{CP}=3 Hz), 132.8 (d, J_{CP}=110 Hz), 158.9 (dd, J_{CF}=281 Hz, J_{CP}=7 Hz). ^{19}F NMR (470 MHz, $CDCl_3$) 70.6 (ddd, J_{FH}=83, 48 Hz, J_{FP}=9 Hz) ppm. ^{31}P NMR (202 MHz, $CDCl_3$) 19.8 (d, J_{PF}=9 Hz) ppm. MS (70 eV) *m/z* 246 (M^+), 245, 77 (base peak). HRMS calcd. for $C_{14}H_{12}FOP$ 246.0609 (M^+); found 246.0570. Anal. calcd. for $C_{14}H_{12}FOP$: C, 68.29; H, 4.91. Found C, 68.22; H, 5.06.

5.6. (2-Fluorovinyl)diphenylphosphine-borane (7)

To a solution of (2,2-difluorovinyl)diphenylphosphine-borane (58 mg, 0.22 mmol) in THF (2 ml) was added $LiAlH(O^tBu)_3$ (0.33 ml, 1.0 M in THF, 0.33 mmol) at −78°C. After the mixture was stirred for 3.5 h at room temperature, the reaction was quenched with 2 M HCl. Organic materials were extracted with ethyl acetate three times. The combined extracts were washed with brine, and then dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by thin layer chromatography on silica gel (hexane–ethyl acetate 5:1) to give **7** as a colorless solid (47 mg, 87%, *E*/*Z*=68/32).[5]

(*E*)-**7**: m.p. 52–54°C. IR (KBr) 2400, 1625, 1490, 1440, 1320, 1105, 1055, 940, 865, 825, 735, 690 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ: 0.70–1.40 (3H, m), 5.95 (1H, dd, J_{HF}=20.9 Hz, J=11.8 Hz), 7.13 (1H, ddd, J_{HF}=83.2 Hz, J=11.8 Hz, J_{HP}=6.9 Hz), 7.42–7.52 (6H, m), 7.59–7.64 (4H, m). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 101.3 (dd, J_{CP}=60 Hz, J_{CF}=7 Hz), 129.0 (d, J_{CP}=10 Hz), 129.0 (d, J_{CP}=61 Hz), 131.5 (d, J_{CP}=2 Hz), 132.1 (d, J_{CP}=10 Hz), 161.7 (dd, J_{CF}=287 Hz, J_{CP}=28 Hz). ^{19}F NMR (470 MHz, $CDCl_3$) 70.6 (ddd, J_{FH}=83 Hz, J_{FP}=28 Hz, J_{FH}=21 Hz) ppm. MS (70 eV) *m/z* 230 (M^+–BH_3; base peak), 108. HRMS calcd. for $C_{14}H_{12}FP$ 230.0661 (M^+–BH_3); found 230.0682.

(*Z*)-**7**: IR (KBr) 2400, 1635, 1490, 1440, 1110, 1060, 1030, 740, 700 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ: 0.80–1.75 (3H, m), 5.45 (1H, ddd, J_{HF}=47.6 Hz, J_{HP}=8.6 Hz, J=5.9 Hz), 7.07 (1H, ddd, J_{HF}=82.7 Hz, J_{HP}=20.5 Hz, J=5.9 Hz), 7.42–7.52 (6H, m), 7.68–7.73 (4H, m). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 101.2 (dd, J_{CP}=54 Hz, J_{CF}=5 Hz), 128.8 (d, J_{CP}=10 Hz), 128.9 (d, J_{CP}=60 Hz), 131.4 (d, J_{CP}=3 Hz), 132.3 (d, J_{CP}=10 Hz), 158.8 (dd, J_{CF}=280 Hz, J_{CP}=6 Hz). ^{19}F NMR (470 MHz, $CDCl_3$) 70.3 (dd, J_{FH}=83, 47 Hz) ppm. MS (70 eV) *m/z* (rel. intensity) 230 (M^+–BH_3; 58), 183 (43), 152 (18), 127 (19), 108 (100). HRMS calcd. for $C_{14}H_{12}FP$ 230.0661 (M^+–BH_3); found 230.0643.

5.7. (2-Fluoro-2-phenylthiovinyl)diphenylphosphine oxide (8)

To a solution of (2,2-difluorovinyl)diphenylphosphine oxide (**4**, 117 mg, 0.44 mmol) in THF (2 ml) was added lithium benzenthiolate, generated from benzenethiol (46 ml, 0.45 mmol) and butyllithium (0.27 ml, 1.61 M in THF, 0.45 mmol) in THF (1 ml), at −78°C. After the

[5] *E*/*Z* isomerization occurred after quenching the reaction.

mixture was stirred for 2 h at −78°C, the reaction was quenched with phosphate buffer (pH 7). Organic materials were extracted with ethyl acetate three times. The combined extracts were washed with brine, and then dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by thin layer chromatography on silica gel (hexane–ethyl acetate 1:1) to give **8** as a colorless solid (130 mg, 83%, *E*/*Z*=90/10).

(*E*)-**8**: m.p. 89–91°C. IR (KBr) 1610, 1575, 1445, 1210, 1190, 750, 700 cm^{-1}. ^1H NMR (60 MHz, $CDCl_3$) δ: 5.45 (1H, dd, J_{HF}=41.0 Hz, J_{HP}=6.8 Hz), 7.16–7.87 (15H, m). ^{13}C NMR (68 MHz, $CDCl_3$) δ: 100.0 (dd, J_{CP}=98 Hz, J_{CF}=16 Hz), 127.2, 128.5 (d, J_{CP}=12 Hz), 129.9, 130.2, 130.9 (d, J_{CP}=11 Hz), 131.9 (d, J_{CP}=2 Hz), 133.2 (d, J_{CP}=109 Hz), 134.4, 169.3 (dd, J_{CF}=305 Hz, J_{CP}=4 Hz). ^{19}F NMR (94 MHz, $CDCl_3$) 98.5 (dd, J_{FH}=41 Hz, J_{FP}=3 Hz) ppm. ^{31}P NMR (202 MHz, $CDCl_3$) 19.8 (d, J_{PF}=3 Hz) ppm. MS (70 eV) *m*/*z* 354 (M^+; base peak), 261, 201, 77. HRMS calcd. for $C_{20}H_{16}FOPS$ 354.0643 (M^+); found 354.0660. Anal. calcd. for $C_{20}H_{16}FOPS$: C, 67.79; H, 4.55. Found C, 67.96; H, 4.69.

(*Z*)-**8**: ^1H NMR (60 MHz, $CDCl_3$) δ: 6.00 (1H, dd, J_{HF}=17.9 Hz, J_{HP}=11.6 Hz), 7.12–7.97 (15H, m). ^{13}C NMR (68 MHz, $CDCl_3$; selected peaks) δ: 103.3 (dd, J_{CP}=109 Hz, J_{CF}=15 Hz), 168.0 (dd, J_{CF}=326 Hz, J_{CP}=14 Hz). ^{19}F NMR (94 MHz, $CDCl_3$) 109.7 (dd, J_{FP}=29 Hz, J_{FH}=18 Hz) ppm. MS (70 eV) *m*/*z* 354 (M^+), 261, 201, 77 (base peak). HRMS calcd. for $C_{20}H_{16}FOPS$ 354.0643 (M^+); found 354.0635.

5.8. [2,2-Bis(phenylthio)vinyl]diphenylphosphine oxide (**9**)

To a solution of (2,2-difluorovinyl)diphenylphosphine oxide (**4**, 84 mg, 0.32 mmol) in THF (2 ml) was added lithium benzenthiolate, generated from benzenethiol (77 μl, 0.75 mmol) and butyllithium (0.43 ml, 1.62 M in THF, 0.70 mmol) in THF (1 ml), at −78°C. After the mixture was stirred for 1 h at −78°C, the reaction was quenched with phosphate buffer (pH 7). Organic materials were extracted with dichloromethane three times. The combined extracts were washed with brine, and then dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by thin layer chromatography on silica gel (ethyl acetate) to give **9** as a colorless solid (118 mg, 84%). m.p. 145–147°C. IR (KBr) 1520, 1485, 1440, 1190, 1180, 1120, 900, 825, 750, 720, 700 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ: 6.08 (1H, d, J_{HP}=11.6 Hz), 7.17–7.48 (16H, m), 7.65–7.79 (4H, m). ^{13}C NMR (68 MHz, $CDCl_3$) δ: 117.4 (d, J_{CP}=104 Hz), 128.4 (d, J_{CP}=12 Hz), 128.7, 128.7, 128.8, 129.6, 129.6, 130.8, 131.6 (d, J_{CP}=9 Hz), 131.4 (d, J_{CP}=2 Hz), 134.0, 134.4 (d, J_{CP}=107 Hz), 134.8, 159.7. MS (70 eV) *m*/*z* 444 (M^+), 335, 201 (base peak), 77. HRMS calcd. for $C_{26}H_{21}OPS_2$ 444.0772 (M^+); found 444.0796. Anal. calcd. for $C_{26}H_{21}OPS_2$: C, 70.25; H, 4.76. Found C, 70.20; H, 4.96.

5.9. N-tert-butyl(diphenylphosphinoyl)acetamide (**11**)

To a solution of *tert*-butylamine (57 ml, 0.54 mmol) in THF (2 ml) was added (2,2-difluorovinyl)diphenylphosphine oxide (**4**, 48 mg, 0.18 mmol) in THF (1 ml) at 0°C. After the mixture was stirred for 30 min at 0°C, the reaction was quenched with phosphate buffer (pH 7). Organic materials were extracted with ethyl acetate three times. The combined extracts were washed with brine, and then dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by thin layer chromatography on silica gel (ethyl acetate) to give **11** as a colorless solid (48 mg, 85%). m.p. 185–186°C. IR (KBr) 3250, 3070, 2960, 1660, 1565, 1440, 1325, 1225, 1190, 1130, 725, 695 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ: 1.22 (9H, s), 3.29 (2H, d, J_{HP}=12.9 Hz), 7.27 (1H, br s), 7.42–7.58 (6H, m), 7.73–7.84 (4H, m). ^{13}C NMR (68 MHz, $CDCl_3$) δ: 28.4, 39.7 (d, J_{CP}=60 Hz), 51.4, 128.7 (d, J_{CP}=12 Hz), 130.7 (d, J_{CP}=10 Hz), 131.7 (d, J_{CP}=103 Hz), 132.2 (d, J_{CP}=2 Hz), 163.7 (d, J_{CP}=5 Hz). MS (70 eV) *m*/*z* 315 (M^+), 300, 260, 243, 215, 201 (base peak), 77. HRMS calcd. for $C_{18}H_{22}NO_2P$ 315.1388 (M^+); found 315.1415. Anal. calcd. for $C_{18}H_{22}NO_2P$: C, 68.56; H, 7.03; N, 4.44. Found C, 68.64; H, 6.98; N, 4.38.

5.10. 1-(2-Diphenylphosphinoylacetyl)pyrrolidine (**12**)

To a solution of pyrrolidine (56 ml, 0.67 mmol) in THF (2 ml) was added (2,2-difluorovinyl)diphenylphosphine oxide (**4**, 59 mg, 0.22 mmol) in THF (1 ml) at 0°C. After the mixture was stirred for 10 min at 0°C, the reaction was quenched with 1 M NaOH. Organic materials were extracted with ethyl acetate three times. The combined extracts were washed with brine, and then dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by thin layer chromatography on silica gel (ethyl acetate–methanol 10:1) to give **12** as a colorless solid (51 mg, 74%). m.p. 150–152°C. IR (KBr) 1630, 1440, 1205, 720 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ: 1.65–1.83 (4H, m), 3.31 (2H, t, *J*=6.5 Hz), 3.47 (2H, t, *J*=6.6 Hz), 3.52 (2H, d, J_{HP}=15.5 Hz), 7.41–7.57 (6H, m), 7.84–7.95 (4H, m). ^{13}C NMR (68 MHz, $CDCl_3$) δ: 24.3, 25.9, 39.6 (d, J_{CP}=61 Hz), 46.0, 47.7, 128.5 (d, J_{CP}=12 Hz), 131.2 (d, J_{CP}=11 Hz), 132.0 (d, J_{CP}=2 Hz), 132.4 (d, J_{CP}=103 Hz), 163.5 (d, J_{CP}=5 Hz). MS (70 eV) *m*/*z* 313 (M^+), 215 (base peak), 201, 77. HRMS calcd. for $C_{18}H_{20}NO_2P$ 313.1232 (M^+); found 313.1247. Anal. calcd. for $C_{18}H_{20}NO_2P$: C, 68.99; H, 6.43; N, 4.47. Found C, 68.77; H, 6.49; N, 4.40.

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