

Synthesis and reactions of α -fluorovinylphosphonium salts

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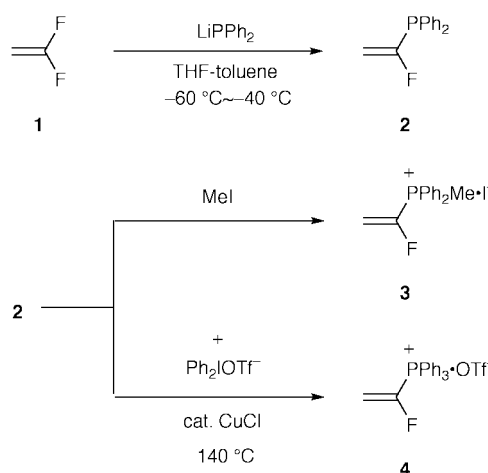
The α -fluorovinyltriphenylphosphonium triflate **4** is prepared in high yields by the diphenylphosphinylation of 1,1-difluoroethylene **1** and subsequent quaternization of the phosphine **2** with diphenyliodonium triflate in the presence of CuCl. The salt **4** then undergoes Michael addition followed by Wittig olefination to give the corresponding monofluoroethylene compounds in good yields. The reaction of **4** with the caesium salts of salicylaldehyde derivatives in DMF at 130 °C affords the corresponding monofluorinated chromenes in a one-pot synthesis. The hydrolysis of **4** in the presence of sodium hydroxide gives triphenylphosphine oxide in quantitative yield.

Introduction

Much effort has been made to introduce fluorine into organic compounds due to its dramatic effects on their structure, stability, reactivity and biological activity.¹ Among them, the preparation of monofluorinated compounds can be divided into two main methods: one is the direct exchange of hydrogen by fluorine,² and the other is the use of monofluorinated building blocks. As the former requires special techniques and equipment, the latter has recently received much attention and has become a significant procedure in this field.³ Vinylphosphonium salts are useful building blocks for the construction of two-carbon-extended olefinic compounds.⁴ Although some substituted vinylphosphonium salts have been synthesized and their reactivities examined,⁵ the syntheses of fluorine-substituted vinylphosphonium salts have been rarely reported.⁶ We have considered the α -fluorovinyltriphenylphosphonium triflate **4** as a promising candidate for the monofluorinated building block which would be stable and easy to handle. We have reported our preliminary findings⁷ and now provide a full account of the work.

Results and discussion

Previously used methods for the preparation of the vinyltriphenylphosphonium salts generally include elimination reactions of the corresponding alkyltriphenylphosphonium salts. Recently, Stang and co-workers have introduced a new method using the palladium-catalyzed vinylation of triphenylphosphine with vinyl triflates.⁸ However, these convenient methods appeared to be not applicable to the salt **4**, which required the development of a new method from us. Our synthetic route for the preparation of the α -fluorovinylphosphonium salts is depicted in Scheme 1. We initially attempted to examine the convenient preparation of α -fluorovinyltriphenylphosphine **2** as the precursor for the salt. Since it is well documented that nucleophilic addition followed by elimination of the fluoride for producing 1,1-difluoroethylene derivatives is easy,⁹ it was therefore anticipated that the reaction of lithium diphenylphosphide¹⁰ and 1,1-difluoroethylene **1** should afford a convenient preparation of **2**. Thus, to a THF solution of lithium diphenylphosphide prepared from lithium and chlorodiphenylphosphine was bubbled 1,1-difluoroethylene at -78 °C and the resulting mixture was stirred for 16 h at the same temperature. After the usual work-up, we obtained **2** in modest yield. In order to improve the yield of **2**, we conducted the reaction at elevated reaction temperatures (-78 – 0 °C); however, the undesirable 1,1-bis(diphenylphosphinyl)ethylene was produced



Scheme 1

as a by-product. We next carefully investigated the reaction conditions and found that when the reaction was conducted over the temperature range of -60 to -40 °C in THF–toluene under a 1,1-difluoroethylene atmosphere, the yield was improved up to 86%. The added co-solvent, toluene, facilitated stirring of the reaction mixture at these low temperatures. The obtained **2** was generally oxidized in air to give the corresponding phosphine oxide.

Quaternization of **2** with iodomethane smoothly proceeded to give the α -fluorovinyl(methyl)diphenylphosphonium iodide **3** in 91% yield. However, the alkyltriphenylphosphonium salts exhibited less performance compared with the corresponding triphenylphosphonium salts;¹¹ therefore, we examined the quaternization of **2** with aryl compounds.¹² The reaction of **2** with aryl halides or aryl triflates did not take place under certain conditions. Kitamura *et al.* have described the direct *S*-arylation of benzo[*b*]thiophenes to produce the 1-arylbenzo[*b*]thiophenium salt.¹³ This prompted us to use the diaryliodonium salts for the *P*-arylation of **2** instead of the *S*-arylation of the sulfides. We attempted to use the method of Kitamura.¹³ Compound **2** was treated with diphenyliodonium triflate in the presence of a catalytic amount of Cu(OAc)₂ at 140 °C for 30 min under an Ar atmosphere. The reaction mixture turned into a brown-black oil. It was difficult to solidify the residual oil after the addition of an excess of diethyl ether to the oil. However, based on the NMR spectra, we confirmed the formation of **4**. After many attempts, we optimized the best reaction conditions. Thus, the α -fluorovinyltriphenylphosphonium triflate

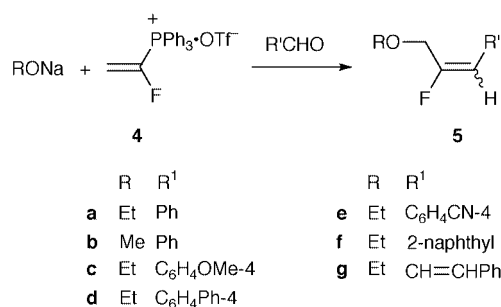
Table 1 Reaction of α -fluorovinylphosphonium salts with various aldehydes

Entry	RONa	R'CHO	Yield (%) ^a	E/Z ^b
1 ^c	MeONa	PhCHO	43	52/48
2			63	40/60
3 ^c	EtONa		52	53/47
4			75	43/57
5		4-MeOC ₆ H ₄ CHO	80	35/65
6		4-PhC ₆ H ₄ CHO	70	47/53
7		4-NCC ₆ H ₄ CHO	69	52/48
8		2-Naphthaldehyde	77	41/59
9		Cinnamaldehyde	82	37/63
10		Hydrocinnamaldehyde	trace	

^a Isolated yield. ^b Determined by capillary GC-MS analysis. ^c Salt **3** was used.

4 was obtained by the reaction of diphenyliodonium triflate in the presence of CuCl in 1,1,2,2-tetrachloroethane at 140 °C in 82% yield. We believe that this *P*-arylation method provides a new route for the synthesis of aryl phosphonium salts.

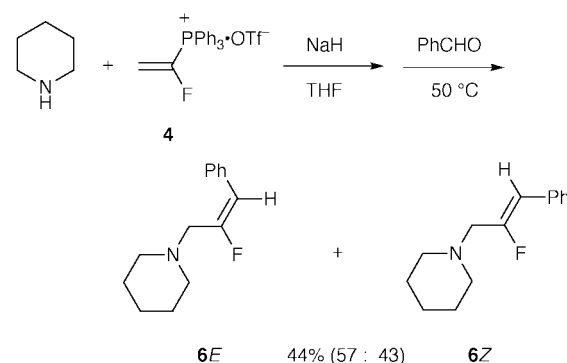
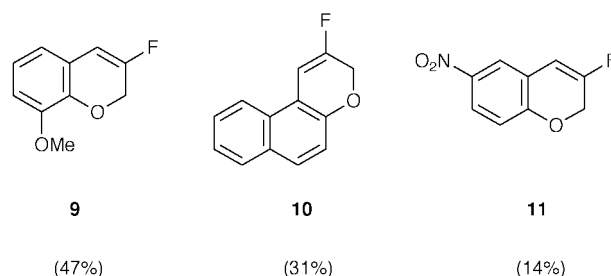
For comparison of the reactivities of the vinylphosphonium bromide (Schweizer's reagent), the reaction of **4** with sodium ethoxide and benzaldehyde was carried out (Scheme 2). The

**Scheme 2**

β -ethoxy- α -fluoroethyltriphenylphosphonium ylide, generated *via* the addition of an ethoxide anion to **4** in ethanol at room temperature, reacted with benzaldehyde to provide 3-ethoxy-2-fluoro-1-phenylpropene **5a** as a 43:57 mixture of *E* and *Z* isomers in 75% yield (Table 1, entry 4). The *E/Z* ratio was determined by capillary GC-MS analysis. The geometrical isomers were separated from each other on a silica gel column and characterized based on their NMR spectra. The coupling constants with fluorine showed a value of 20 Hz for the *E* isomer and 39 Hz for the *Z* isomer. As expected, the reactivity of **4** was much higher than that of **3** as compared with the yields (entries 1 *vs.* 2 and 3 *vs.* 4). Although aromatic aldehydes and an α,β -unsaturated aldehyde gave good results, the aliphatic aldehyde gave poor results. A similar reaction using sodium piperidide as the nucleophile instead of sodium ethoxide in THF at 50 °C gave the corresponding 2-fluoro-1-phenyl-3-piperidinopropene **6** as a mixture of diastereomers in 44% total yield (Scheme 3). Furthermore, no reaction occurred with ketones (cyclohexanone and acetophenone) due to possible steric hindrance in the Wittig reaction.

These results prompted us to utilize **4** for the synthesis of a variety of monofluorinated heterocyclic ring systems, since the synthesis of fluorinated heterocyclic compounds has also become an important area of agrochemical and pharmaceutical studies due to their unique biological properties.¹⁴ Among them, the syntheses of fluorinated chromenes are quite limited,¹⁵ although the chromene nucleus is also encountered in insecticides and natural products.¹⁶

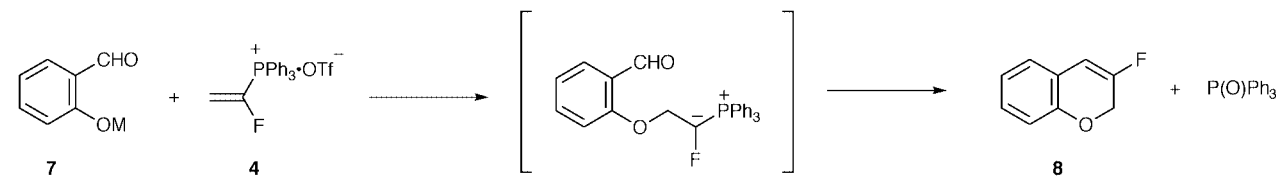
We initially examined the synthesis of 3-fluoro-2*H*-chromene **8** as a model compound based on Schweizer's protocol (Table

**Scheme 3****Chart 1** Monofluorinated chromene derivatives. All reactions were conducted in DMF for 40 h at 130 °C.

2).¹⁷ Contrary to our expectation, the reaction of the sodium salt of salicylaldehyde **7** with **4** in acetonitrile at 70 °C afforded no cyclized product (run 1), presumably due to the influence of the fluorine atom at the α -position of the salt. A further attempt to obtain the desired cyclized product in the above reaction was made by examining the effect of the solvent. However, the lack of satisfactory yield caused us to abandon the use of the sodium salt of the salicylaldehyde. Next, we focused on the effects of varying the cation on the salicylaldehyde and investigated three different bases. Unfortunately, the use of the potassium, magnesium, and lithium salts of the salicylaldehyde resulted in low yields or no reaction (runs 6, 7, and 8, respectively).

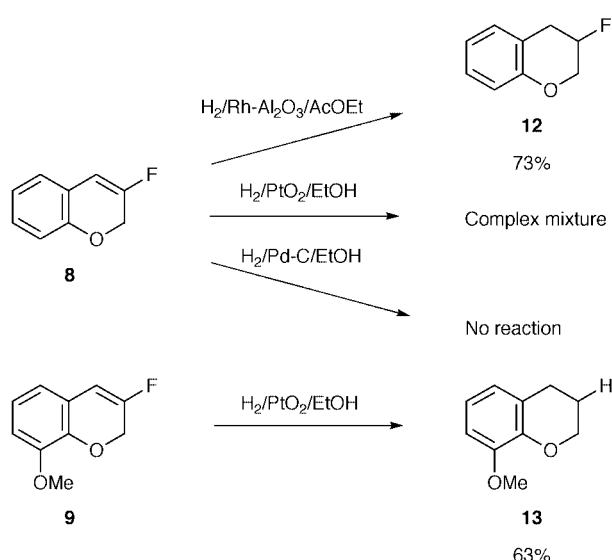
We next turned our attention to the potential of the CsF–Si(OEt)₄ system.¹⁸ Although we examined the above reaction conditions for the cyclization of the salicylaldehyde, no improved yields were obtained. We also investigated the scope and limitations of the *in situ* preparation and reaction of the caesium salts of other salicylaldehyde derivatives. The cyclization of 3-methoxysalicylaldehyde and 2-hydroxy-1-naphthaldehyde proceeded to give the corresponding monofluorinated chromene derivatives **9**, **10** in 47 and 31% yield, respectively (Chart 1). On the other hand, the cyclization of 5-nitrosalicylaldehyde resulted in a low yield (14%) of the product **11**. It is noteworthy that the CsF–Si(OEt)₄ system was effective for the above cyclization, because we confirmed that no cyclization of the sodium salts of 2-hydroxy-1-naphthaldehyde and 5-nitrosalicylaldehyde occurred under the conditions employed for the salicylaldehyde (entry 5 in Table 2). The reaction of the caesium salt of *o*-hydroxyacetophenone with the α -fluorovinyltriphenylphosphonium triflate did not give the anticipated product.

Furthermore, we examined the hydrogenation of the obtained monofluorinated chromenes to produce the corresponding monofluorinated chromanes.¹⁹ We employed three types of catalysts for the hydrogenation of **8**.²⁰ All the reactions were conducted under hydrogen at atmospheric pressure and room temperature. These results are shown in Scheme 4. The Rh/Al₂O₃ catalyst was the most effective for the transformation without any loss of the fluorine atom in the molecule. Thus, 3-fluorochromane **12** was obtained in 73% yield. In the case of **9**, PtO₂-catalyzed hydrogenation gave the corresponding

Table 2 Cyclization of salicylaldehyde under various conditions


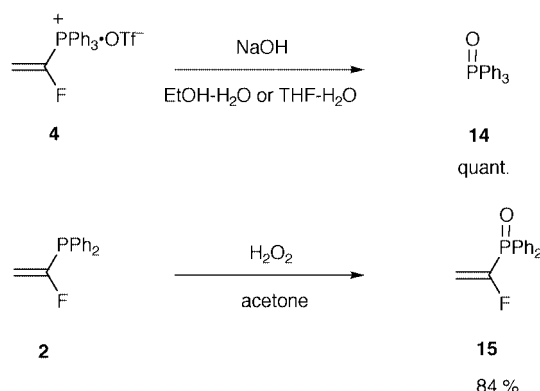
Run	M	Base (mol. equiv.)	Solvent ^a	T/°C	t/h	Yield (%)
1	Na	None	Acetonitrile	70	88	0
2	Na	None	<i>tert</i> -BuOH	80	40	27
3	Na	None	DMSO	120	16	32
4	Na	None	DMF	130	40	20
5	Na	None	DEM-DMF 4:1	80	40	35
6	H	TMSOK (1.0)	THF	50	16	0
7	H	EtMgBr (1.0)	DEM-DMF 4:1	80	16	0
8	H	BuLi (1.0)	DEM-DMF 4:1	80	16	7
9	H	CsF (1.7)/Si(OEt) ₄ (1.3)	DEM-DMF 4:1	80	40	8
10	H	CsF (1.7)/Si(OEt) ₄ (1.3)	DMF	130	40	34

^a DEM: Diethoxymethane.

**Scheme 4**

8-methoxychromane **13** with loss of the fluorine atom in the molecule in 63% yield.

Finally, other reactivities of **4** were examined (Scheme 5).

**Scheme 5**

The hydrolysis of the salt was carried out in aq. alcohols or aq. THF containing excess of sodium hydroxide.²¹ Neither reaction produced the corresponding β -ethoxy- α -fluoroethyl-diphenylphosphine oxide or the corresponding α -fluorovinyl-diphenylphosphine oxide, but they did quantitatively

produce triphenylphosphine oxide **14**. On the other hand, the oxidation of **2** conducted in acetone containing hydrogen peroxide gave the corresponding α -fluorovinyl-diphenylphosphine oxide **15** in 84% yield.

In conclusion, the α -fluorovinyltriphenylphosphonium triflate **4** can be a useful reagent for the synthesis of compounds containing monofluorinated olefinic moieties in one pot. Such systems are not readily available using general methods.

Experimental

Mps were measured with a Yanagimoto micro melting point apparatus MP-S3 and are uncorrected. IR spectra were recorded on a Perkin-Elmer Spectrum 2000. ¹H NMR spectra were measured on a JEOL JNM-GX270. Chemical shifts are given by δ relative to that of internal Me₄Si (TMS). Mass spectra were obtained with a Shimadzu GCMS QP-5000. Fast-atom-bombardment mass spectra (FABMS) were obtained with a JEOL JMS-HX110A. Elemental analyses were performed on a Yanagimoto MT3 CHN corder or were accomplished at the service center of the elementary analysis of organic compounds, Kyushu University. Analytical TLC was performed on silica gel plates (Merck, Kieselgel 60 F254, 20 \times 20 cm, 0.25 mm). All solvents were purified before use: THF and diethoxymethane (DEM) were dried over sodium benzophenone ketyl radical; 1,1,2,2-tetrachloroethane, DMF, DMSO, MeCN and EtOH were distilled from calcium hydride. The procedures for the preparation of **2**, **4** and **5** have already been reported.⁷

α -Fluorovinyl(methyl)diphenylphosphonium iodide **3**

A mixture of α -fluorovinyl-diphenylphosphine **2** (1.50 g, 6.52 mmol) and iodomethane (1.2 mL, 19.3 mmol) in toluene (2.0 mL) was stirred at room temperature in the dark for 16 h. After the addition of diethyl ether (\approx 25 mL) to the mixture, the resulting precipitates were collected by filtration. Recrystallization from hexane-CH₂Cl₂ gave the desired product (2.20 g, 91%), mp 126.4–128.3 °C; ν (KBr)/cm⁻¹ 3103, 3062, 3007, 2959, 2884, 2801, 1636, 1588, 1482, 1435, 1407, 1370, 1322, 1298, 1274, 1186, 1162, 1114, 1070, 1036, 992, 900, 859, 791, 750, 685 and 644; δ _H(CDCl₃) 3.27 (3H, d, *J* 13.7 Hz), 5.79 (1H, ddd, *J* 6.4, 7.3, 49.3 Hz), 6.49 (1H, ddd, *J* 6.4, 21.5, 29.8 Hz), 7.7–8.0 (m, 10 H); FABMS: *m/z* 245 (*M*⁺ - I) (Calc. for C₁₅H₁₅FIP: C, 48.41; H, 4.06. Found: C, 48.19; H, 3.91%).

(*E*)- and (*Z*)-2-Fluoro-3-methoxy-1-phenylpropene **5b**

Total yield 63%. (*E*)-isomer: ν (neat)/cm⁻¹ 3055, 3027, 2986,

2925, 2815, 1680, 1598, 1492, 1400, 1288, 1257, 1217, 1189, 1142, 1097, 954, 917, 750, 699 and 631; $\delta_{\text{H}}(\text{CDCl}_3)$ 3.42 (3H, s), 4.14 (2H, d, J 23.0 Hz), 6.48 (1H, d, J 19.5 Hz), 7.24–7.38 (5H, m); MS m/z 166 (50%, M^+), 151 (42), 135 (41), 133 (62), 115 (82), 109 (100) (Calc. for $\text{C}_{10}\text{H}_{11}\text{FO}$: C, 72.27; H, 6.67. Found: C, 72.10; H, 6.71%).

(*Z*)-isomer: $\nu(\text{neat})/\text{cm}^{-1}$ 3055, 3027, 2986, 2993, 2822, 1693, 1600, 1530, 1495, 1451, 1383, 1349, 1220, 1189, 1165, 1155, 1101, 1091, 958, 917, 879, 753 and 694; $\delta_{\text{H}}(\text{CDCl}_3)$ 3.44 (3H, s), 4.08 (2H, d, J 15.6 Hz), 5.76 (1H, d, J 38.6 Hz), 7.25–7.55 (5H, m); m/z 166 (75%, M^+), 151 (47), 135 (59), 133 (69), 115 (95), 109 (100) (Found: C, 72.56; H, 6.75%).

(*E*)- and (*Z*)-3-Ethoxy-2-fluoro-1-(4'-methoxyphenyl)propene 5c

Total yield 80%. (*E*)-isomer: $\nu(\text{neat})/\text{cm}^{-1}$ 2978, 2932, 2897, 2870, 1683, 1609, 1574, 1515, 1464, 1383, 1295, 1252, 1180, 1142, 1096, 1035, 886, 862, 831, 770 and 715; $\delta_{\text{H}}(\text{CDCl}_3)$ 1.25 (3H, t, J 6.8 Hz), 3.58 (2H, q, J 6.8 Hz), 3.81 (3H, s), 4.17 (2H, d, J 23.4 Hz), 6.40 (1H, d, J 20.5 Hz), 6.88 (2H, d, J 8.8 Hz), 7.20 (2H, d, J 8.8 Hz); m/z 210 (51%, M^+), 166 (31), 165 (100), 139 (68), 133 (35), 121 (32), 115 (37), 91 (30) (Calc. for $\text{C}_{12}\text{H}_{15}\text{FO}_2$: C, 68.55; H, 7.19. Found: C, 68.73; H, 7.37%).

(*Z*)-isomer: $\nu(\text{neat})/\text{cm}^{-1}$ 2978, 2932, 2897, 2836, 1693, 1609, 1574, 1515, 1506, 1346, 1295, 1252, 1179, 1162, 1097, 1036, 879, 859, 821 and 770; $\delta_{\text{H}}(\text{CDCl}_3)$ 1.26 (3H, t, J 6.8 Hz), 3.59 (2H, q, J 6.8 Hz), 3.81 (3H, s), 4.11 (2H, d, J 16.1 Hz), 5.70 (1H, d, J 38.6 Hz), 6.87 (2H, d, J 8.8 Hz), 7.46 (2H, d, J 8.8 Hz); m/z 210 (52%, M^+), 166 (32), 165 (100), 139 (60), 133 (31), 115 (33), 91 (29) (Found: C, 68.65; H, 7.40%).

(*E*)- and (*Z*)-1-(4'-Biphenyl)-3-ethoxy-2-fluoropropene 5d

Total yield 70%. (*E*)-isomer: $\nu(\text{neat})/\text{cm}^{-1}$ 3055, 3027, 2978, 2856, 1683, 1600, 1486, 1445, 1380, 1274, 1257, 1217, 1145, 1096, 1005, 886, 764 and 695; $\delta_{\text{H}}(\text{CDCl}_3)$ 1.27 (3H, t, J 6.8 Hz), 3.60 (2H, q, J 6.8 Hz), 4.23 (2H, d, J 23.4 Hz), 6.48 (1H, d, J 20.0 Hz), 7.33–7.62 (9H, m); m/z 256 (68%, M^+), 196 (43), 191 (53), 185 (100), 179 (38), 178 (56) (Calc. for $\text{C}_{17}\text{H}_{17}\text{FO}$: C, 79.66; H, 6.68. Found: C, 79.40; H, 6.80%).

(*Z*)-isomer: mp 40.0–42.0 °C; $\nu(\text{KBr})/\text{cm}^{-1}$ 2979, 2897, 2869, 1693, 1679, 1594, 1506, 1482, 1444, 1403, 1349, 1328, 1257, 1162, 1083, 1018, 903, 869, 852, 818, 753 and 698; $\delta_{\text{H}}(\text{CDCl}_3)$ 1.28 (3H, t, J 6.8 Hz), 3.62 (2H, q, J 6.8 Hz), 4.15 (2H, d, J 15.1 Hz), 5.81 (1H, d, J 38.6 Hz), 7.25–7.63 (9H, m); m/z 256 (76%, M^+), 211 (33), 196 (46), 191 (57), 185 (100), 179 (36), 178 (55) (Found: C, 79.42; H, 6.70%).

(*E*)- and (*Z*)-1-(4'-Cyanophenyl)-3-ethoxy-2-fluoropropene 5e

Total yield 69%. (*E*)-isomer: $\nu(\text{neat})/\text{cm}^{-1}$ 2964, 2904, 2229, 1684, 1559, 1411, 1259, 1097, 1018, 869, 819 and 703; $\delta_{\text{H}}(\text{CDCl}_3)$ 1.26 (3H, t, J 6.8 Hz), 3.59 (2H, q, J 6.8 Hz), 4.15 (2H, d, J 23.4 Hz), 6.44 (1H, d, J 19.1 Hz), 7.39 (2H, d, J 8.3 Hz), 7.64 (2H, d, J 8.3 Hz); m/z 205 (28%, M^+), 177 (43), 160 (56), 158 (46), 156 (32), 148 (33), 140 (100), 134 (99), 133 (43), 130 (37), 129 (99), 128 (77), 116 (99), 101 (39), 75 (34) (Calc. for $\text{C}_{12}\text{H}_{12}\text{FNO}$: C, 70.23; H, 5.89. Found: C, 70.31; H, 5.99%).

(*Z*)-isomer: $\nu(\text{neat})/\text{cm}^{-1}$ 2964, 2904, 2226, 1559, 1414, 1259, 1098, 1018, 865, 820 and 702; $\delta_{\text{H}}(\text{CDCl}_3)$ 1.28 (3H, t, J 6.8 Hz), 3.62 (2H, q, J 6.8 Hz), 4.14 (2H, d, J 12.7 Hz), 5.82 (1H, d, J 37.6 Hz), 7.58 (2H, d, J 8.8 Hz), 7.62 (2H, d, J 8.8 Hz); m/z 205 (37%, M^+), 177 (44), 161 (26), 160 (64), 158 (45), 148 (31), 140 (100), 134 (93), 133 (40), 130 (35), 129 (89), 128 (66), 116 (91), 101 (35), 75 (31) (Found: C, 69.87; H, 5.99%).

(*E*)- and (*Z*)-3-Ethoxy-2-fluoro-1-(2'-naphthyl)propene 5f

Total yield 77%. (*E*)-isomer: $\nu(\text{neat})/\text{cm}^{-1}$ 3055, 2977, 2871, 1681, 1598, 1557, 1507, 1380, 1273, 1182, 1138, 1097, 1018, 900, 868, 818 and 743; $\delta_{\text{H}}(\text{CDCl}_3)$ 1.25 (3H, t, J 6.8 Hz), 3.60 (2H, q, J 6.8 Hz), 4.25 (2H, d, J 23.4 Hz), 6.60 (1H, d, J 20.0 Hz), 7.36–7.84 (7H, m); m/z 230 (93%, M^+), 201 (38), 186 (39), 185 (59),

184 (31), 183 (95), 170 (38), 165 (100), 159 (86), 153 (93) (Calc. for $\text{C}_{15}\text{H}_{15}\text{FO}$: C, 78.24; H, 6.57. Found: C, 78.31; H, 6.68%).

(*Z*)-isomer: mp 39.0–41.0 °C; $\nu(\text{KBr})/\text{cm}^{-1}$ 3068, 3034, 2977, 2863, 1699, 1676, 1605, 1564, 1489, 1445, 1404, 1377, 1349, 1288, 1261, 1213, 1162, 1099, 1008, 866, 832, 764, 729 and 697; $\delta_{\text{H}}(\text{CDCl}_3)$ 1.29 (3H, t, J 6.8 Hz), 3.64 (2H, q, J 6.8 Hz), 4.18 (2H, d, J 15.1 Hz), 5.93 (1H, d, J 38.6 Hz), 7.40–7.95 (7H, m); m/z 230 (98, M^+), 201 (34), 186 (30), 185 (72), 183 (81), 170 (37), 166 (30), 165 (100), 159 (87), 153 (78) (Found: C, 78.14; H, 6.63%).

(*E*)- and (*Z*)-5-Ethoxy-4-fluoro-1-phenylpenta-1,3-diene 5g

Total yield 82%. These compounds could not be separated. $\nu(\text{neat})/\text{cm}^{-1}$ 3021, 2977, 2870, 1673, 1492, 1448, 1346, 1138, 1097, 968, 886, 750 and 692; $\delta_{\text{H}}(\text{CDCl}_3)$ 1.25 (3H, t, J 6.8 Hz), 1.26 (3H, t, J 6.8 Hz), 3.57 (2H, q, J 6.8 Hz), 3.59 (2H, q, J 6.8 Hz), 4.07 (2H, d, J 15.6 Hz), 4.29 (2H, d, J 20.5 Hz), 5.69 (1H, dd, J 10.7, 34.2 Hz), 6.13 (1H, dd, J 11.2, 18.1 Hz), 6.55 (2H, d, J 16.1 Hz), 6.80 (1H, ddd, J 1.0, 11.2, 16.1 Hz), 7.09 (1H, dd, J 10.7, 16.1 Hz), 7.20–7.45 (10H, m); (*E*)-isomer: m/z 206 (36%, M^+), 159 (35), 147 (49), 146 (75), 142 (38), 141 (40), 129 (100), 128 (55), 115 (77), 91 (53); (*Z*)-isomer: m/z 206 (41%, M^+), 159 (33), 147 (34), 146 (63), 142 (34), 141 (42), 129 (100), 128 (50), 115 (70), 91 (41) [Calc. for $\text{C}_{13}\text{H}_{15}\text{FO}$ (*M*): 206.1096. Found: M^+ , 206.1109].

(*E*)- and (*Z*)-2-Fluoro-1-phenyl-3-piperidinopropene 6

Total yield 44%. (*E*)-isomer: $\nu(\text{neat})/\text{cm}^{-1}$ 2936, 2853, 2777, 1676, 1453, 1302, 1282, 1223, 1133, 1098, 1065, 1039, 997, 882, 860, 787, 750 and 700; $\delta_{\text{H}}(\text{CDCl}_3)$ 1.35–1.50 (2H, m), 1.55–1.70 (4H, m), 2.35–2.55 (4H, m), 3.28 (2H, d, J 22.5 Hz), 6.40 (1H, d, J 21.5 Hz), 7.22–7.36 (5H, m); m/z 219 (82%, M^+), 218 (48), 136 (52), 135 (100), 133 (72), 128 (30), 116 (30), 115 (58), 109 (36), 98 (85), 97 (36), 84 (94), 83 (61) [Calc. for $\text{C}_{14}\text{H}_{19}\text{FN}$ (*M* + *H*): 220.1501. Found: m/z , 220.1469].

(*Z*)-isomer: $\nu(\text{neat})/\text{cm}^{-1}$ 2936, 2855, 2809, 2770, 1689, 1496, 1451, 1398, 1372, 1345, 1301, 1275, 1251, 1111, 1040, 996, 885, 862, 785, 754 and 694; $\delta_{\text{H}}(\text{CDCl}_3)$ 1.35–1.50 (2H, m), 1.55–1.70 (4H, m), 2.40–2.60 (4H, m), 3.18 (2H, d, J 18.1 Hz), 5.65 (1H, d, J 38.6 Hz), 7.15–7.55 (5H, m); m/z 219 (100%, M^+), 218 (51), 136 (22), 135 (82), 133 (33), 115 (73), 98 (42), 84 (86), 83 (27) [Calc. for $\text{C}_{14}\text{H}_{19}\text{FN}$ (*M* + *H*): 220.1501. Found: m/z , 220.1461].

3-Fluoro-2H-chromene 8

To a suspension of CsF (65.5 mg, 0.43 mmol), $\text{Si}(\text{OEt})_4$ (72.0 μL , 0.32 mmol), and salicylaldehyde (26.0 μL , 0.25 mmol) in DMF at room temperature under argon atmosphere was added α -fluorovinyltriphenylphosphonium triflate **4** (114 mg, 0.25 mmol) in one portion. After being heated to 130 °C the reaction mixture was stirred for 40 h at that temperature. After usual work-up, the residual oil was chromatographed on silica gel (hexane as eluent) to give the desired product (12.9 mg, 34%) as a colorless oil, which generally turned yellow on storage under an argon atmosphere: $\nu(\text{neat})/\text{cm}^{-1}$ 3068, 2959, 2849, 1695, 1578, 1489, 1455, 1390, 1274, 1189, 1105, 1047, 1022, 879, 838, 752 and 658; $\delta_{\text{H}}(\text{CDCl}_3)$ 4.81 (1H, d, J 1.0 Hz), 4.82 (1H, d, J 1.5 Hz), 6.04 (1H, dt, J 1.0, 12.2 Hz), 6.81 (1H, dd, J 2.0, 7.8 Hz), 6.87 (1H, dd, J 2.0, 7.8 Hz), 6.94 (1H, dt, J 2.0, 7.8 Hz), 7.07 (1H, dt, J 2.0, 7.8 Hz); m/z 150 (100%, M^+), 131 (26), 121 (28), 101 (38), 96 (33), 75 (34), 74 (24), 63 (21) (Found: M^+ , 150.0467. Calc. for $\text{C}_9\text{H}_7\text{FO}$: *M*, 150.0481).

3-Fluoro-8-methoxy-2H-chromene 9

47% Yield. $\nu(\text{neat})/\text{cm}^{-1}$ 2963, 2836, 1694, 1580, 1483, 1329, 1278, 1204, 1140, 1102, 1078, 1035, 971, 849, 730 and 641; $\delta_{\text{H}}(\text{CDCl}_3)$ 3.87 (3H, s), 4.87 (1H, d, J 1.0 Hz), 4.88 (1H, d, J 1.5 Hz), 6.04 (1H, dt, J 1.0, 10.3 Hz), 6.61 (1H, dd, J 1.5, 7.3 Hz), 6.76 (1H, dd, J 1.5, 8.3 Hz), 6.86 (1H, ddd, J 1.0, 7.3, 8.3 Hz);

m/z 180 (100%, M^+), 179 (78), 149 (22), 137 (75), 109 (52), 101 (21), 89 (21), 83 (71), 75 (21), 63 (46), 62 (21) (Found: M^+ , 180.0587. Calc. for $C_{10}H_9FO$: M , 180.0617).

2-Fluoro-3H-naphtho[2,1-b]pyran 10

31% Yield. Mp 38.1–39.5 °C; $\nu(\text{neat})/\text{cm}^{-1}$ 3034, 2849, 1683, 1631, 1506, 1230, 1185, 1083, 1032, 889, 814 and 749; $\delta_H(\text{CDCl}_3)$ 4.91 (1H, d, J 2.0 Hz), 4.92 (1H, d, J 1.5 Hz), 6.72 (1H, d, J 12.0 Hz), 7.09 (1H, d, J 9.3 Hz), 7.36 (1H, ddd, J 1.0, 6.8, 9.3 Hz), 7.48 (1H, ddd, J 1.0, 6.8, 9.3 Hz), 7.62 (1H, d, J 9.3 Hz), 7.76 (1H, d, J 9.3 Hz), 7.80 (1H, d, J 9.3 Hz); m/z 200 (100%, M^+), 199 (98), 171 (34), 170 (54), 153 (39), 152 (27) (Found: M^+ , 200.0638. Calc. for $C_{13}H_9FO$: M , 200.0637).

3-Fluoro-6-nitro-2H-chromene 11

14% Yield. Mp 129.2–130.5 °C; $\nu(\text{KBr})/\text{cm}^{-1}$ 2917, 1699, 1615, 1583, 1505, 1404, 1338, 1261, 1208, 1154, 1093, 1027, 906, 849, 829, 748, 725, 699 and 625; $\delta_H(\text{CDCl}_3)$ 4.98 (2H, d, J 1.5 Hz), 6.12 (1H, d, J 11.1 Hz), 6.87 (1H, d, J 8.8 Hz), 7.86 (1H, d, J 2.4 Hz), 7.99 (1H, dd, J 2.4, 8.8 Hz); m/z 195 (94%, M^+), 194 (100), 149 (11), 148 (34), 120 (14), 101 (45), 83 (11), 75 (33), 74 (13) [Found: (M^+ + H), 196.0423. Calc. for $C_9H_7FNO_2$: m/z , 196.0410].

3-Fluorochromane 12

To a solution of 23.9 mg of 3-fluoro-2H-chromene **8** (0.159 mmol) in 5 mL of ethyl acetate was added a catalytic amount of 5% Rh– Al_2O_3 . Hydrogenation at atmospheric pressure was conducted for 16 h at room temperature. After usual work-up, the residual oil was chromatographed on silica gel (hexane–diethyl ether 100:1 as eluent) gave the desired product (17.6 mg, 73%), $\nu(\text{neat})/\text{cm}^{-1}$ 2964, 1585, 1491, 1463, 1346, 1302, 1265, 1233, 1183, 1117, 1094, 1063, 1026, 1008, 948, 828, 785 and 756; $\delta_H(\text{CDCl}_3)$ 2.95–3.25 (2H, m), 4.0–4.25 (1H, m), 4.25–4.40 (1H, m), 5.12 (1H, ddq, J 2.0, 47.4, 4.4 Hz), 6.86 (1H, dd, J 1.0, 7.3 Hz), 6.92 (1H, dt, J 1.0, 7.3 Hz), 7.07 (1H, dd, J 1.0, 7.3 Hz), 7.13 (1H, dt, J 1.0, 7.3 Hz); m/z 152 (100%, M^+), 131 (31), 106 (44), 78 (56), 77 (22) (Found: M^+ , 152.0623. Calc. for C_9H_9FO : M , 152.0638).

8-Methoxychromane 13

To a solution of 15.9 mg of 3-fluoro-8-methoxy-2H-chromene **9** (0.088 mmol) in 2 mL of EtOH was added a catalytic amount of PtO_2 . Hydrogenation at atmospheric pressure was conducted for 16 h at room temperature. After usual work-up, the residual oil was chromatographed on silica gel (hexane–diethyl ether 10:1 as eluent) gave the desired product (9.2 mg, 63%), $\nu(\text{neat})/\text{cm}^{-1}$ 2964, 1261, 1094, 1019, 866 and 800; $\delta_H(\text{CDCl}_3)$ 1.97–2.06 (2H, m), 2.79 (2H, t, J 6.3 Hz), 3.86 (3H, s), 4.27 (2H, t, J 5.4 Hz), 6.65–6.82 (3H, m); m/z 164 (100%, M^+), 149 (55), 136 (40), 135 (39), 121 (41), 107 (36), 103 (41), 93 (37), 91 (55), 78 (34), 77 (59), 65 (49) [lit.,²² m/z 164 (100%, M^+), 150 (12), 149 (23), 136 (16), 135 (12), 133 (5), 122 (4), 121 (25), 108 (5), 107 (10), 105 (7), 91 (9), 79 (5), 78 (6.5), 77 (16), 65 (16), 51 (9)].

α -Fluorovinylidiphenylphosphine oxide 15

To a solution of α -fluorovinylidiphenylphosphine **2** (51.8 mg, 0.22 mmol) in acetone (1 mL) was added 30% aq. hydrogen peroxide (0.1 mL) at 0 °C. After the mixture had been stirred for 30 min, the reaction was quenched with aq. NaHSO_3 . The mixture was extracted with diethyl ether, then the ethereal solution was dried over MgSO_4 . After removal of the solvent, the remaining oil was separated by column chromatography (silica gel; hexane–EtOAc 1:1) to give the desired product (46.4 mg, 84%), mp 83.5–84.5 °C; $\nu(\text{KBr})/\text{cm}^{-1}$ 3096, 3055, 3021, 2959, 1632, 1588, 1489, 1435, 1336, 1319, 1203, 1179, 1121, 1097, 998, 913, 801, 757, 729, 712, 689 and 658; $\delta_H(\text{CDCl}_3)$ 5.72 (1H, ddd, J 3.9, 22.0, 23.0 Hz), 5.82 (1H, ddd, J 3.9, 6.4, 51.3 Hz), 7.3–7.9

(m, 10 H); m/z 246 (14%, M^+), 201 (43), 186 (38), 185 (100), 184 (21), 183 (88), 152 (35), 107 (21), 78 (21), 77 (64) (Calc. for $\text{C}_{14}\text{H}_{12}\text{FOP}$: C, 68.29; H, 4.91. Found: C, 68.30; H, 4.91%).

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