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Microwave assisted fluorofunctionalization of phenyl substituted alkenes using selectfluor™

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ABSTRACT

A rapid fluorofunctionalization of alkenes and diene using selectfluor™ has been uncovered. The olefins such as 1-phenyl ethene; 1,1-diphenylethene; (E)-1,2-diphenylethene; (E)-1,2-dinaphthylethene; 1,1,2-triphenylethene; 1,1,2,2-tetraphenylethene and 1,1,4-triphenyl-1,3-butadiene react with selectfluor™ (F-TEDA-BF_4) in water and methanol to give α-fluorohydrins and α-fluoromethoxy compounds respectively under microwave radiations. The electrophilic addition of 'FOH' and 'FOMe' on the double bond occurs regioselectively with excellent yield.

1. Introduction

The importance of organofluorine compounds is well documented [1]. There are fast growing demands of fluorinated building blocks in diverse fields such as medicinal chemistry, biochemistry and material science [2–4]. Approximately 20% of drugs in the market contain fluorine and this number is expected to grow [5]. The presence of fluorine in organic drugs can have a profound influence on their biological activity by altering the metabolic stability, hydrogen bonding capability, lipophilicity, solubility, conformation and overall structure [6]. The ability of fluorine to have a higher bonding affinity to drug receptors than non-fluorine containing molecules has made organofluorine chemistry very important to the pharmaceutical industry [7]. The use of fluorohydrins, in particular vicinal fluorohydrins, is the subject of recent interest in medicinal chemistry [7c,d]. A precise methodology is therefore required for their synthesis [8].

α-Fluorohydrins have been prepared by reducing α-fluoroketones [9], ring opening of epoxide [10] and by fluorofunctionalization of olefins [11–20]. In first two cases, the substrates are not easily accessible due to the use of some hazardous and toxic chemicals for their syntheses. The syntheses of α-fluorohydrins and derivatives are generally carried out by the reaction of electrophilic fluorinating reagents such as selectfluor™ (F-TEDA-BF_4) and accufluor™ (NFTh) with phenyl substituted olefins [12,14,15]. The methodology involves long reaction time using conventional heating to reflux conditions. Moreover, in the case of insoluble alkenes, surfactant such as sodium lauryl ether sulfate has been added to yield good results [12]. Considering the slow rate of fluorofunctionalization and to improve the usefulness of this methodology, we resorted to the use of microwave radiations for the synthesis of α-fluorohydrins and α-fluoromethoxy compounds.

The use of microwaves has played an important role in organofluorine chemistry [21–29]. As the selectfluor™ (F-TEDA-BF_4) is an electrophilic fluorinating reagent, it would give electrophilic substitution/addition reactions. The substrates having high electron density are suitable for such reactions. The fluorination of 1-arylethanones [21], 1,3-dicarbonyl compounds [22], 1-aryl-1-nitromethanes [23] and aromatic compounds [24] are few examples of electrophilic substitution reactions using selectfluor™ (F-TEDA-BF_4). However, the electrophilic addition reactions of fluorine are still awaited using selectfluor™ under microwave radiations. Olefins are considered to be cost effective and versatile electron rich substrates for such reactions. In this backdrop, the fluorofunctionalization of olefins using non-conventional microwaves and selectfluor is unprecedent for the synthesis of α-fluorohydrins and α-fluoromethoxy compounds. Thus, herein we report a rapid synthesis of α-fluorohydrins and their derivatives by the treatment of phenyl substituted olefins with selectfluor™ (F-TEDA-BF_4) in water and methanol under microwave radiations.

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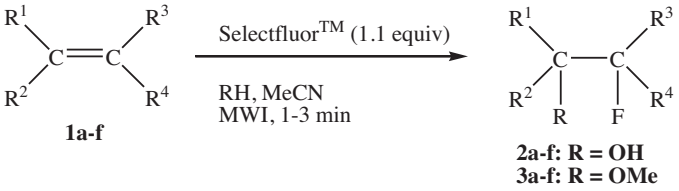


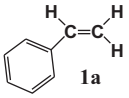
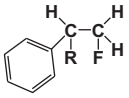
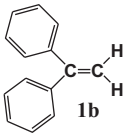
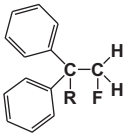
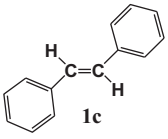
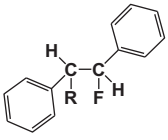
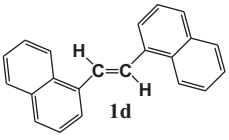
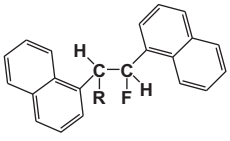
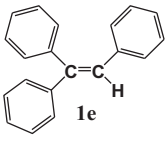
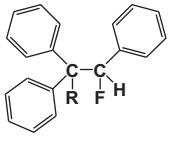
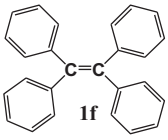
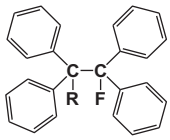
Scheme 1. Fluorofunctionalization of olefins, **1a–f**, using selectfluor™ and microwaves.

2. Results and discussion

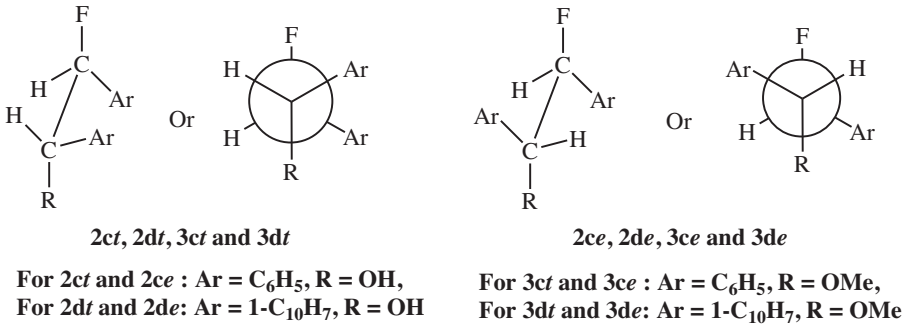
In order to obtain phenyl substituted α-fluorohydrins, phenyl substituted olefin such as styrene (**1a)** in acetonitrile containing selectfluor™ (F-TEDA-BF_4) and water was irradiated under microwave radiations for 2 min (Scheme 1, entry 1). After usual work up, the product was identified as 2-fluoro-1-phenyletnanol (**2a**) on the basis of physical and spectral data [12]. The regioselectivity of the addition was according to Markownikoff's rule [14]. The maximum time period reported for such fluorohydroxylation of styrene was 24 h using selectfluor™ (F-TEDA-BF_4) at 60 °C [12] and N-fluorobis[(perfluoroalkyl) sulfonyl] imide at room temperature [18].

After successful fluorohydroxylation of styrene, other olefins such as 1,1-diphenylethene (**1b**), (E)-1,2-diphenylethene (**1c**), (E)-1,2-dinaphthylethene (**1d**) 1,1,2-triphenylethene (**1e**) and 1,1,2,2-tetraphenylethene (**1f**), in acetonitrile were irradiated in microwave oven for appropriate time period using above conditions to give their corresponding α-fluorohydrins (**2b–f**) (Scheme 1) [12–14,17,18]. Similarly, vicinal fluoromethoxy derivatives (**3a–f**) of olefins (**1a–f**) were obtained by using methanol. The time taken for

Table 1
Reaction time and yield of **2a–f** and **3a–f**.

Entry	Alkene	Product	R	Time (s)	Yield[a] (%)
1	 1a	 **2a**: R=OH, **3a**: R=OMe	OH OMe	120 120	90 92
2	 1b	 **2b**: R=OH, **3b**: R=OMe	OH OMe	60 60	98 97
3	 1c	 **2c**: R=OH, **3c**: R=OMe	OH OMe	90 60	92[b] 95[b]
4	 1d	 **2d**: R=OH, **3d**: R=OMe	OH OMe	120 120	85[b] 82[b]
5	 1e	 **2e**: R=OH, **3e**: R=OMe	OH OMe	120 90	95 94
6	 1f	 **2f**: R=OH, **3f**: R=OMe	OH OMe	180 120	90 90

[a] These are isolated yields of products after flash column chromatography.
[b] DL-Threo (1R*, 2S*) and DL-erythro (1R*, 2R*) isomers were formed in these cases and their ratio was estimated by the integration of vicinal protons coupled with each other in ^{1}H NMR spectra of the mixture.



2c*t*, 2d*t*, 3c*t* and 3d*t* **2c*e*, 2d*e*, 3c*e* and 3d*e***

For 2c*t* and 2c*e* : Ar = C_6H_5, R = OH,
For 2d*t* and 2d*e*: Ar = 1-$C_{10}H_7$, R = OH

For 3c*t* and 3c*e* : Ar = C_6H_5, R = OMe,
For 3d*t* and 3d*e*: Ar = 1-$C_{10}H_7$, R = OMe

Fig. 1. Sawhorse and Newman projections of (1R*, 2S*) and (1R*, 2R*) isomers of **2c**, **2d**, **3c** and **3d** (the italic '*t*' and '*e*' denotes threo and erythro isomer).

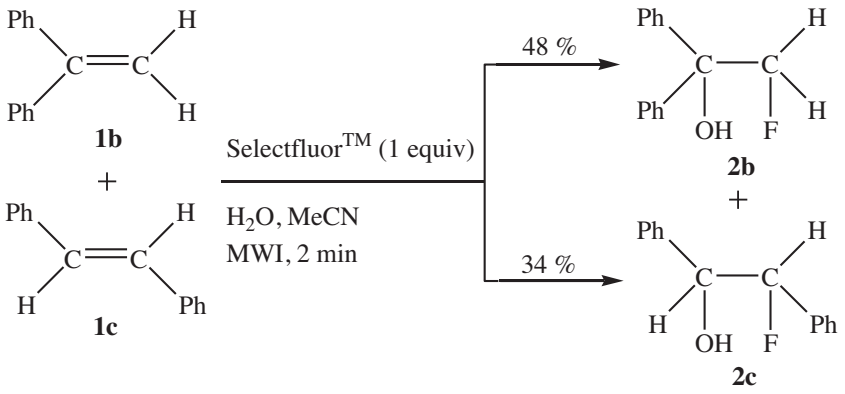
the reaction and yield of isolated products are given in Table 1. Markownikoff type of regioselectivity was also observed in case of fluorofunctionalization of **1b** and **1e**. The relatively lower yields of **2d**, **2f**, **3d** and **3f** were due to the heterogeneity of the reaction mixture because the alkenes **1d** and **1f** were partially insoluble in acetonitrile.

In case of **1c** and **1d**, diastereomers of vicinal fluorohydrins (**2c** and **2d**) and fluoromethoxy (**3c** and **3d**) were obtained (Scheme 1). The formation of DL-erythro (1R*, 2R*) stereoisomer in both cases was found to be predominant. In ^{1}H NMR, the coupling constant for vicinal protons is 4.8–5.2 Hz for (1R*, 2R*) isomers while 7.2–7.5 Hz for (1R*, 2S*) isomers. The presence of two signals as doublet of doublet at different chemical shift values in ^{19}F NMR further confirms the presence of two isomers. These two isomers were separated by flash column chromatography and finally confirmed by their individual physical and spectral data.

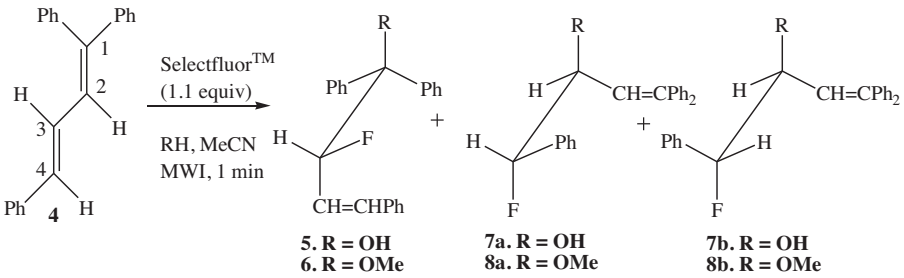
The ratio of two isomers in case of **2c**, **2d**, **3c** and **3d** can be understood from their Sawhorse or Newman projections (Fig. 1). The two aryl rings are syn to each other in threo (1R*, 2S*) isomer. The steric hindrance between the two aryl rings decreases the yield of threo isomer. While the two aryl rings being anti to each other, increases the yield of more stable erythro 1R*2R* isomer. A little more yield in case of **1b** than **1c** reflects the role phenyl group during fluorofunctionalization. The two phenyl rings present at the same carbon in **1b** stabilizes the carbocation effectively and thereby increases the yield. Further to study the effect of phenyl group, a synergistic experiment was carried out. Both **1b** and **1c** in equimolar quantity were irradiated together in microwave oven using one equivalent of selectfluor^{TM} (F-TEDA-BF_4) in water for 2 min (Scheme 2). The yields of their corresponding products **2b** and **2c** are 48% and 34% respectively. More yield in case of **1b** again suggests a crucial role of the phenyl ring.

In order to understand the reactivity pattern of germinal and vicinal phenyl groups on C=C bond; 1,1,4-triphenyl-1,3-butadiene, **4**, was chosen. This diene can be considered as having 1,1-diphenylethene (**1b**) and (E)-1,2-diphenylethene (**1c**) moieties. This will provide a better understanding whether the addition occurs like that of **1b** or **1c** alkene. It is further envisaged that the positive outcome of such reaction would give us an effective methodology to introduce fluorine in aryl substituted 1,3-dienes. Keeping this in view (E)-1,1,4-triphenyl-1,3-butadiene (**4**) was subjected to fluorohydroxylation using selectfluor^{TM} (F-TEDA-BF_4) and water under microwave radiations for 1 min (Scheme 3). The organic compound was extracted with DCM, washed with water, dried over anhydrous Na_2SO_4 and purified by flash column chromatography. It was interesting to note that the fluorohydroxylation of **4** occurred according to both 1,2-addition (as in case of **1b**) and 3,4-addition (as in case of **1c**). By 1,2-addition, 2-fluoro-1,1,4-triphenyl-but-3-en-1-ol (**5**) was formed in 35% yield while (1R*, 2S*)- (**7a**) and (1R*, 2R*)-1-fluoro-2-hydroxy-1-phenyl-2-(1,1-diphenylethylenyl) ethane (**7b**) was obtained by 3,4-addition reaction in 47% yield [30]. The ratio of **7a** and **7b** isomer is 33:67. In this case, both the double bonds of 1,3-diene reacted with the electrophilic fluorine. The facile electrophilic attack on double bond occurs in which a relatively more stable α-fluorocarbocation is formed. The diaryl methyl carbenium ion is formed during 1,2-addition while allylic carbocation is formed in case of 3,4-addition. As the allylic carbocations are more stable than diaryl methyl carbenium ion, the yield of **7a** and **7b** was more than that of 2-fluoro-1,1,4-triphenyl-but-3-en-1-ol (**5**). Similar results were obtained during the reaction of **4** in methanol to obtain **6, 8a** and **8b**. All these compounds were characterized by various spectral data.

In ^{1}H NMR of **5**, C-1 proton appeared as ddd at δ 5.74–5.88. The large coupling constant value ($^2J_{HF}$ = 46.9 Hz) for this proton suggests that fluorine is present on the carbon bearing hydrogen atom i.e. C_2H. The position of fluorine incorporation into **4** was further determined by dept-135, HSQC and by consideration of



Scheme 2. Fluorohydroxylation of equimolar mixture of **1b** and **1c**.



Scheme 3. Products formed from the fluorofunctionalization of **4**, using selectfluor under microwave radiations in the presence of water and methanol.

fluorine couplings in the ^{1}H NMR and ^{13}C NMR spectra. Both the olefinic protons also appeared as ddd at δ 6.12–6.20 and at δ 6.53–6.58 respectively. The coupling constant value for the olefinic protons ($^{3}J_{HH}$ = 16 Hz) suggested that these protons were trans to each other. The double doublet at δ −9.9 in ^{19}F NMR and a doublet for carbon bearing fluorine at δ 95.0 ($^{1}J_{CF}$ = 176 Hz) in ^{13}C NMR further supported the structure formula assigned to **5**. Beside this, the presence of two isomers (**7a** and **7b**) was confirmed by ^{1}H NMR spectral data. In this case, the yield of (1R*, 2R*) isomer (**7b**) was found to be more than that of (1R*, 2S*) isomer (**7a**). The coupling constant value for (1R*, 2S*) isomer is 6.6 Hz while it is 4.2 Hz for the (1R*, 2R*) isomer. Similar observations were recorded for **6**, **8a** and **8b**.

3. Conclusion

A convenient and rapid method for the preparation of α-fluorohydrins and α-fluoromethoxy compounds of phenyl substituted alkenes and diene has been developed. The electrophilic addition of 'FOH' and 'FOMe' on alkene and diene has been accomplished using selectfluor™ (F-TEDA-BF_4) in water and methanol under microwave radiations. The excellent regioselectivity of the addition reaction in case of **1a**, **1b** and **1e** suggests the formation of a stable carbenium ion as an intermediate in fluorofunctionalization.

4. Experimental

4.1. Equipments/chemicals

Microwave oven (BPL, BMC-900T) operated at 1350 W having radiations of 2450 MHz frequency. The IR spectra were recorded on Perkin Elmer IR 1800 spectrophotometer. The ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ on JEOL AL 300 spectrometer operating at 300 MHz and 75 MHz respectively with TMS as an internal standard. ^{19}F NMR spectra were measured on JEOL AL 300 spectrometer operating at 282 MHz. For ^{1}H NMR and ^{13}C NMR spectra, chemical shifts are in parts per million relative to TMS while for ^{19}F NMR spectra, the chemical shift values are relative to hexafluorobenzene which has chemical shift value at δ −164.9 ppm relative to $CFCl_3$. Coupling constants are in hertz (Hz). The ^{1}H NMR and ^{13}C NMR spectra of **5**, **6**, **8a** and **8b** were recorded in $CDCl_3$ on Bruker Avance 400 spectrometer operating at 400 MHz and 100 MHz respectively with TMS as an internal standard. Alkene **1a**, 1,3-diene, **4** and selectfluor™ (F-TEDA-BF_4) were purchased from Sigma–Aldrich. A toluene solution of 1,1-diphenylethanol was heated under reflux in the presence of a catalytic amount of PTSA to obtain alkene **1b**. Similarly, alkene **1e** was prepared from 1,1,2-triphenylethanol. Alkenes **1c** and **1d** were synthesized by McMurry coupling reaction [31]. Alkene **1f** was prepared from dichlorodiphenyl methane [32]. TLC analyses were performed using aluminium backed plates pre-coated with silica gel containing fluorescent material and examining them under UV light (λ = 254 and 355 nm). Flash chromatography was performed by using 40–63 μm silica gel (230–400 mesh) and applying nitrogen pressure from the top of the column.

4.2. General procedure for the fluorofunctionalization of olefins (*1a–f*)

A solution of phenyl substituted olefin, **1a–f** (100 mg, 0.10–0.30 mmol) in acetonitrile (10 mL), F-TEDA-BF_4 (0.11–0.33 mmol, 1.1 equiv.) and water (2 mL) or methanol (2 mL) was taken in a 100 mL erlenmeyer flask. The mixture was irradiated under microwave oven for 1–3 min. After cooling to room temperature the crude product was extracted with DCM. The insoluble material was filtered off. The filtrate was washed with water and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure to give product **2a–f** and **3a–f**. The structure formulae for compounds **2a–f** and **3a–f** have been supported by the spectral data.

4.2.1. 2-Fluoro-1-phenylethanol [12] (*2a*)

Colourless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.86 (s, 1H, OH), 4.53–4.71 (dm, 2H, $^{2}J_{HF}$ = 47.1 Hz), 5.15–5.27 (ddd, 1H, $^{3}J_{HF}$ = 14.1 Hz, $^{3}J_{HH}$ = 8.2 Hz, $^{3}J_{HH}$ = 3.9 Hz), 7.08–7.30 (m, 5H, ArH). ^{19}F NMR ($CDCl_3$, 282 MHz): δ −60.4 (td, $^{2}J_{FH}$ = 47.1 Hz, $^{3}J_{FH}$ = 14.1 Hz).

4.2.2. 2-Fluoro-1,1-diphenylethanol (*2b*)

White solid. Mp 63–64 °C (Lit. [12] mp 65–66.7 °C). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.89 (s, 1H, OH), 4.69 (d, 2H, $^{2}J_{HF}$ = 47.7 Hz), 7.14–7.35 (m, 10H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 77.7 (d, $^{2}J_{CF}$ = 18.5 Hz, C-1), 86.2 (d, $^{1}J_{CF}$ = 178.6 Hz, C-2), 126.7, 127.7, 128.3, 142.4. ^{19}F NMR ($CDCl_3$, 282 MHz): δ −50.9 (t, $^{2}J_{FH}$ = 47.7 Hz).

4.2.3. A mixture of (1R*, 2S*) and (1R*, 2R*)-1-Fluoro-2-hydroxy-1,2-diphenylethane, *2c* [12,20] (separated by flash chromatography, yield 92%, ratio 35:65)

(1R*, 2S*)-1-Fluoro-2-hydroxy-1,2-diphenylethane (2ct). White solid. Mp 96–98 °C (Lit. [20] mp 99 °C). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.8 (s, 1H, OH), 4.93 (dd, 1H, $^{3}J_{HF}$ = 12.7, $^{3}J_{HH}$ = 7.5 Hz), 5.39 (dd, 1H, $^{2}J_{HF}$ = 47.6 Hz, $^{3}J_{HH}$ = 7.5 Hz), 7.10–7.28 (m, 10H, ArH). ^{19}F NMR ($CDCl_3$, 282 MHz): δ −13.1 (dd, $^{2}J_{FH}$ = 47.6 Hz, $^{3}J_{FH}$ = 12.7 Hz).

(1R*, 2R*)-1-Fluoro-2-hydroxy-1,2-diphenylethane (2ce). White solid. Mp 98–99 °C (Lit. [20] mp 99 °C). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.0 (s, 1H, OH), 4.91 (dd, 1H, $^{3}J_{HF}$ = 12.3, $^{3}J_{HH}$ = 5.5 Hz), 5.36 (dd, 1H, $^{2}J_{HF}$ = 45.8 Hz, $^{3}J_{HH}$ = 5.5 Hz), 7.13–7.27 (m, 10H, ArH). ^{19}F NMR ($CDCl_3$, 282 MHz): δ −15.5 (dd, $^{2}J_{FH}$ = 45.8 Hz, $^{3}J_{FH}$ = 12.2 Hz).

4.2.4. A mixture of (1R*, 2S*) and (1R*, 2R*)-1-Fluoro-2-hydroxy-1,2-dinaphthylethane, (*2d*)

Viscous oil. Yield 85%. Ratio 33:67. FT-IR (neat): 3417, 3051, 2977, 2903, 1597, 1513, 1384, 1247.

(1R*, 2S*)-1-Fluoro-2-hydroxy-1,2-dinaphthylethane (2dt). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.0 (s, 1H, OH), 5.95 (dd, 1H, $^{3}J_{HF}$ = 14.4, $^{3}J_{HH}$ = 6.3 Hz), 6.42 (dd, 1H, $^{2}J_{HF}$ = 46.8 Hz,

$^3J_{HH}$ = 6.3 Hz), 7.19–7.54 (m, 14H, ArH). ^{19}F NMR ($CDCl_3$, 282 MHz): δ −15.2 (dd, $^2J_{FH}$ = 47.1 Hz, $^3J_{FH}$ = 13.8 Hz).

(1R*, 2R*)-1-Fluoro-2-hydroxy-1,2-dinaphthylethane (2de). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.8 (s, 1H, OH), 6.08 (dd, 1H, $^3J_{HF}$ = 12.3, $^3J_{HH}$ = 5.4 Hz), 6.54 (dd, 1H, $^2J_{HF}$ = 45.3 Hz, $^3J_{HH}$ = 5.4 Hz), 7.64–7.86 (m, 14H, ArH). ^{19}F NMR ($CDCl_3$, 282 MHz): δ −14.1 (dd, $^2J_{FH}$ = 45.7 Hz, $^3J_{FH}$ = 12.1 Hz).

*4.2.5. 2-Fluoro-1,1,2-triphenylethanol (**2e**)*

White solid. Mp 153–154 °C (Lit. [18] mp 153–155 °C). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.7 (s, 1H, OH), 6.2 (d, 1H, $^2J_{HF}$ = 44.9 Hz), 6.89–6.92 (m, 2H, ArH), 7.10–7.13 (m, 8H, ArH), 7.22–7.32 (m, 3H, ArH), 7.47–7.50 (m, 2H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 77.5 (d, $^2J_{CF}$ = 22.8 Hz, C-1), 94.6 (d, $^1J_{CF}$ = 181.7 Hz, C-2), 126.5, 127.3, 127.5, 127.8, 128.1, 128.7, 139.0, 141.7. ^{19}F NMR ($CDCl_3$, 282 MHz): δ −12.4 (d, $^2J_{FH}$ = 44.9 Hz).

*4.2.6. 2-Fluoro-1,1,2,2-tetraphenylethanol (**2f**)*

White solid. Mp 180–181 °C (Lit. [18] mp 180 °C). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.86 (s, 1H, OH), 7.02–7.11 (m, 12H, ArH), 7.18–7.2 (m, 8H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 81.5 (d, $^2J_{CF}$ = 26 Hz, C-1), 100.4 (d, $^1J_{CF}$ = 186.0 Hz, C-2), 126.8, 127.2, 127.5, 127.9, 128.0, 128.1, 140.9, 143.5. ^{19}F NMR ($CDCl_3$, 282 MHz): δ 25.3 (s).

*4.2.7. 1-Fluoro-2-methoxy-1-phenylethane[15] (**3a**)*

Colourless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.29 (s, 3H, OCH_3), 4.50–4.68 (dm, 2H, $^2J_{HF}$ = 46.8 Hz), 5.12–5.26 (ddd, 1H, $^3J_{HF}$ = 14.4 Hz, $^3J_{HH}$ = 8.1 Hz, $^3J_{HH}$ = 4.2 Hz), 7.18–7.28 (m, 5H, ArH). ^{19}F NMR ($CDCl_3$, 282 MHz): δ −59.6 (td, $^2J_{FH}$ = 46.8 Hz, $^3J_{FH}$ = 14.4 Hz).

*4.2.8. 1-Fluoro-2-methoxy-1,1-diphenylethane[15] (**3b**)*

Colourless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.21 (d, 3H, $^5J_{HF}$ = 1.2 Hz, OCH_3), 4.80 (d, 2H, $^2J_{HF}$ = 47.7 Hz), 7.13–7.27 (m, 10H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 52.6 (d, $^4J_{CF}$ = 3.7 Hz), 82.3 (d, $^2J_{CF}$ = 16.7 Hz, C-1), 85.5 (d, $^1J_{CF}$ = 182.3 Hz, C-2), 127.7, 127.8, 128.2, 141.3. ^{19}F NMR ($CDCl_3$, 282 MHz): δ −51.5 (t, $^2J_{FH}$ = 47.7 Hz).

4.2.9. A mixture of (1R, 2S*) and (1R*, 2R*)-1-Fluoro-2-methoxy-1,2-diphenylethane, **3c** [13,19] (separated by flash chromatography, yield 95%, ratio 33:67)*

(1R*, 2S*)-1-Fluoro-2-methoxy-1,2-diphenylethane (3ct). Colourless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.26 (s, 3H, OCH_3), 4.36–4.42 (dd, 1H, $^3J_{HF}$ = 12.9, $^3J_{HH}$ = 7.2 Hz), 5.31–5.49 (dd, 1H, $^2J_{HF}$ = 47.1 Hz, $^3J_{HH}$ = 7.2 Hz), 7.04–7.25 (m, 10H, ArH). ^{19}F NMR ($CDCl_3$, 282 MHz): δ −12.5 (dd, $^2J_{FH}$ = 47.1 Hz, $^3J_{FH}$ = 12.9 Hz).

(1R*, 2R*)-1-Fluoro-2-methoxy-1,2-diphenylethane (3ce). White solid. Mp 50–51 °C (Lit. [19] mp 51–52 °C). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.17 (s, 3H, OCH_3), 4.33–4.39 (dd, 1H, $^3J_{HF}$ = 14.1, $^3J_{HH}$ = 5.4 Hz), 5.36–5.53 (dd, 1H, $^2J_{HF}$ = 45.9 Hz, $^3J_{HH}$ = 5.4 Hz), 7.12–7.31 (m, 10H, ArH). ^{19}F NMR ($CDCl_3$, 282 MHz): δ −16.4 (dd, $^2J_{FH}$ = 45.9 Hz, $^3J_{FH}$ = 14.1 Hz).

4.2.10. A mixture of (1R, 2S*) and (1R*, 2R*)-1-Fluoro-2-methoxy-1,2-dinaphthylethane, **3d** (separated by flash chromatography, yield 82%, ratio 30:70)*

(1R*, 2S*)-1-Fluoro-2-methoxy-1,2-dinaphthylethane (3dt). Colourless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.30 (s, 3H, OCH_3), 5.41 (dd, 1H, $^3J_{HF}$ = 13.2 Hz, $^3J_{HH}$ = 7.2 Hz, C_1–H), 6.36 (dd, 1H, $^2J_{HF}$ = 46.8 Hz, $^3J_{HH}$ = 7.2 Hz, C_2H), 7.14–7.30 (m, 8H, ArH), 7.52–7.63 (m, 4H, ArH), 7.65 (d, 1H, J = 8.7 Hz, ArH), 7.99 (d, 1H, J = 8.4 Hz, ArH). ^{13}C NMR ($CDCl_3$, 75.53 MHz): δ 57.3, 84.3 (d, $^2J_{CF}$ = 24.9 Hz, C–O), 94.0 (d, $^1J_{CF}$ = 182.4 Hz, C–F), 123.3, 124.5 (d), 125.3, 125.5, 125.6, 125.7, 125.8 (d), 126.5, 126.8, 128.5 (d), 128.8, 129.0, 130.4 (d), 131.6, 132.2 (d), 132.4, 133.3 (d). ^{19}F NMR ($CDCl_3$, 282 MHz): δ −12.1 (dd, $^2J_{FH}$ = 47.1 Hz, $^3J_{FH}$ = 13.7 Hz). Anal. calcd. for $C_{23}H_{19}FO$: C, 83.61; H, 5.80. Found: C, 83.64; H, 5.79.

(1R*, 2S*)-1-Fluoro-2-methoxy-1,2-dinaphthylethane (3de). White solid. Mp 107–108 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.16 (s, 3H, OCH_3), 5.38 (dd, 1H, $^3J_{HF}$ = 15.0 Hz, $^3J_{HH}$ = 4.8 Hz, C_1–H), 6.46 (dd, 1H, $^2J_{HF}$ = 45.6 Hz, $^3J_{HH}$ = 4.8 Hz, C_2H), 7.21–7.38 (m, 8H, ArH), 7.64–7.85 (m, 6H, ArH). ^{13}C NMR ($CDCl_3$, 75.53 MHz): δ 57.3, 82.9 (d, $^2J_{CF}$ = 24.9 Hz, C-1), 92.7 (d, $^1J_{CF}$ = 178.7 Hz, C-1), 122.9 (d), 123.5, 124.5, 124.9, 125.1, 125.3, 125.4, 125.5, 125.8, 126.1, 126.5, 128.7, 130.6, 132.1 (d), 132.5, 133.3 (d). ^{19}F NMR ($CDCl_3$, 282 MHz): δ −15.5 (dd, $^2J_{FH}$ = 45.9 Hz, $^3J_{FH}$ = 15.1 Hz). Anal. Calcd. for $C_{23}H_{19}FO$: C, 83.61; H, 5.80. Found: C, 83.66; H, 5.84.

*4.2.11. 1-Fluoro-2-methoxy-1,1,2-triphenylethane (**3e**)*

White solid. Mp 60–61 °C (Lit. [16] mp 61–62 °C). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.16 (d, 3H, $^5J_{HF}$ = 1.2 Hz OCH_3), 6.16 (d, 1H, $^2J_{HF}$ = 44.7 Hz), 6.73–6.75 (m, 2H, ArH), 6.99–7.09 (m, 3H, ArH), 7.14–7.17 (m, 10H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 53.1 (d, $^4J_{CF}$ = 3.6 Hz) 84.6 (d, $^2J_{CF}$ = 22.8 Hz, C-1), 94.5 (d, $^1J_{CF}$ = 184.2 Hz, C-2), 124.4, 127.5, 127.9, 128.8, 129.3, 136.0, 140.0, 141.4. ^{19}F NMR ($CDCl_3$, 282 MHz): δ −12.5 (d, $^2J_{FH}$ = 44.7 Hz).

*4.2.12. 1-Fluoro-2-methoxy-1,1,2,2-tetraphenylethane (**3f**)*

White solid. Mp 150–151 °C (Lit. [16] mp 152.9–153.5 °C). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.16 (d, 3H, $^5J_{HF}$ = 1.1 Hz OCH_3),7.04–7.44 (m, 20H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 53.1 (d, $^4J_{CF}$ = 1.8 Hz), 90.1 (d, $^2J_{CF}$ = 30.3 Hz, C-1), 99.0 (d, $^1J_{CF}$ = 184.2 Hz, C-2), 126.6, 126.7, 126.9, 127.1, 127.3, 131.1, 138.8, 143.2. ^{19}F NMR ($CDCl_3$, 282 MHz): δ 15.7 (s).

*4.3. General procedure for the fluorofunctionalization of (E)-1,1,4-triphenyl-1,3-butadiene (**4**)*

A solution 1,3-diene, **4** (100 mg, 0.35 mmol) in acetonitrile (10 mL), F-TEDA-BF_4 (1.1 equiv) and water (2 mL) or methanol (2 mL) was taken in a 100 mL erlenmeyer flask. The mixture was irradiated under microwave radiations for 1 min. After cooling to room temperature the crude product was extracted with DCM. The insoluble material was filtered off. The filtrate was washed with water and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure to give the yellowish oil product, which was purified by flash column chromatography to yield **5**, **6**, **7a** + **7b** and **8a** + **8b**.

*4.3.1. 2-Fluoro-1,1,4-triphenyl-but-3-en-1-ol (**5**)*

Yield 35%. White solid. Mp 118–119 °C. IR (KBr): 3569, 3058, 3024, 1597, 1493, 1447, 1174, 1064, 1033, 966, 748, 699 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.76 (d, 1H, 3 J_{HH} = 1.7 Hz, OH), 5.74–5.88 (ddd, 1H, $^2J_{HF}$ = 46.9 Hz, $^3J_{HH}$ = 6.8 Hz, $^4J_{HH}$ = 1.0 Hz, C_2H), 6.12–6.20 (ddd, 1H, $^3J_{HH}$ = 16 Hz, $^3J_{HF}$ = 12.5 Hz, $^3J_{HH}$ = 6.8 Hz, C_3H), 6.53–6.58 (ddd, 1H, $^3J_{HH}$ = 16 Hz, $^4J_{HF}$ = 3.9 Hz, $^3J_{HH}$ = 1.0 Hz, C_4H), 7.13–7.24 (m, 9H, ArH), 7.28–7.36 (m, 4H, ArH), 7.51–7.54 (m, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 79.2 (d, $^2J_{CF}$ = 22.1 Hz, C-1), 95.0 (d, $^1J_{CF}$ = 177.6 Hz, C-2), 122.6 (d, $^2J_{CF}$ = 18.2 Hz, C-3), 126.3, 126.8 (d), 127.4 (d), 128.2, 128.3, 135.8 (d, $^3J_{CF}$ = 12.4 Hz, C-4), 142.6 (d), 143.9. ^{19}F NMR ($CDCl_3$, 282 MHz): δ −9.9 (dd, $^2J_{FH}$ = 45.6 Hz, $^3J_{FH}$ = 12.2 Hz). Anal. Calcd. for $C_{22}H_{19}FO$: C, 82.99; H, 6.02. Found: C, 83.02; H, 5.98.

4.3.2. A mixture of (1R, 2S*) and (1R*, 2R*)-1-Fluoro-2-hydroxy-1-phenyl-2-(1,1-diphenylethylenyl) ethane (light yellowish oil, yield 47%, ratio 33:67)*

(1R*, 2S*)-1-Fluoro-2-hydroxy-1-phenyl-2-(1,1-diphenylethylenyl) ethane (7a). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.27 (s, 1H, OH), 4.36 (m 1H, C_2H), 5.22 (dd, 1H, $^2J_{HF}$ = 47.1 Hz, $^3J_{HH}$ = 6.6 Hz, C_1H), 5.91 (d, 1H, $^3J_{HH}$ = 9.9 Hz, C_3H), 6.71–7.29 (m, 15H, ArH). ^{19}F NMR ($CDCl_3$, 282 MHz): δ −27.1 (dd, $^2J_{FH}$ = 47.1 Hz, $^3J_{FH}$ = 13.5 Hz).

(1R*, 2R*)-1-Fluoro-2-hydroxy-1-phenyl-2-(1,1-diphenylethylenyl) ethane (7b). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.88 (d, 1H, $^4J_{HH}$ = 1.4 Hz, OH), 4.32 (m 1H, C_2H), 5.34 (dd, 1H, $^2J_{HF}$ = 46.8 Hz, $^3J_{HH}$ = 4.2 Hz, C_1H), 5.99 (d, 1H, $^3J_{HH}$ = 9.9 Hz, C_3H), 6.84–7.29 (m, 15H, ArH). ^{19}F NMR ($CDCl_3$, 282 MHz): δ −22.2 (dd, $^2J_{FH}$ = 46.8 Hz, $^3J_{FH}$ = 16.9 Hz).

*4.3.3. 3-Fluoro-4-methoxy-1,4,4-triphenylbut-1-ene (**6**)*

Yield 34%. Light yellowish oil. IR (KBr): 3057, 3028, 1591, 1497, 1444, 1176, 1067, 1033 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.17 (d, 3H, $^5J_{HH}$ = 1.8 Hz, OCH_3), 5.74–5.88 (ddd, 1H, $^2J_{HF}$ = 47.2 Hz, $^3J_{HH}$ = 6.6 Hz, $^4J_{HH}$ = 0.9 Hz, C_3H), 6.04–6.13 (ddd, 1H, $^3J_{HH}$ = 16 Hz, $^3J_{HF}$ = 12.2 Hz, $^3J_{HH}$ = 6.6 Hz, C_2H), 6.43–6.48 (ddd, 1H, $^3J_{HH}$ = 16 Hz, $^4J_{HF}$ = 3.8 Hz, $^3J_{HH}$ = 0.9 Hz, C_1H), 7.13–7.16 (m, 3H, ArH), 7.17–7.26 (m, 12H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 55.8 (d, $^4J_{CF}$ = 4 Hz, OCH_3), 84.2 (d, $^2J_{CF}$ = 21 Hz, C-4), 95.3 (d, $^1J_{CF}$ = 181 Hz, C-3), 123.4 (d, $^2J_{CF}$ = 17 Hz, C-2), 126.7 (d), 127.4, 127.5, 127.8, 127.9, 128.1, 128.5, 128.7 (d) 134.7 (d, $^3J_{CF}$ = 12 Hz, C-1), 136.3 (d), 140.6, 141.5 (d). ^{19}F NMR ($CDCl_3$, 282 MHz): δ −8.03 (dd, $^2J_{FH}$ = 47.1 Hz, $^3J_{FH}$ = 12.1 Hz). Anal. calcd. for $C_{23}H_{21}FO$: C, 83.10; H, 6.37. Found: C, 83.11; H, 6.36.

4.3.4. A mixture of (1R, 2S*) and (1R*, 2R*)-1-Fluoro-2-methoxy-1-phenyl-2-(1,1-diphenylethylenyl) ethane (A light yellowish oil, yield 47%, ratio 35:65)*

(1R*, 2S*)-1-fluoro-2-methoxy-1-phenyl-2-(1,1-diphenylethylenyl) ethane (8a). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.24 (s, 3H, OCH_3), 3.96 (ddd, 1H, $^3J_{HF}$ = 16.6 Hz, $^3J_{HH}$ = 9.8 Hz, $^3J_{HH}$ = 6.6 Hz, C_3H), 5.37 (dd, 1H, $^2J_{HF}$ = 46.7 Hz, $^3J_{HH}$ = 6.6 Hz, C_4H), 5.82 (d, 1H, $^3J_{HH}$ = 9.8 Hz, C_2H), 7.04–7.08 (m, 2H, ArH), 7.23–7.44 (m, 13H, ArH). ^{19}F NMR ($CDCl_3$, 282 MHz): δ −27.1 (dd, $^2J_{FH}$ = 47.1 Hz, $^3J_{FH}$ = 13.5 Hz).

(1R*, 2R*)-1-fluoro-2-methoxy-1-phenyl-2-(1,1-diphenylethylenyl) ethane (8b). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.16 (s, 3H, OCH_3), 3.86 (ddd, 1H, $^3J_{HF}$ = 18.4 Hz, $^3J_{HH}$ = 9.8 Hz, $^3J_{HH}$ = 3.9 Hz, C_3H), 5.48 (dd, 1H, $^2J_{HF}$ = 46.8 Hz, $^3J_{HH}$ = 3.9 Hz, C_4H), 6.04 (d, 1H, $^3J_{HH}$ = 9.8 Hz, C_2H), 6.06–6.64 (m, 2H, ArH), 7.10–7.21 (m, 13H, ArH). ^{19}F NMR ($CDCl_3$, 282 MHz): δ −22.0 (dd, $^2J_{FH}$ = 47.1 Hz, $^3J_{FH}$ = 18.3 Hz).

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