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The Addition of Dibromodifluoromethane to (Trimethylsilyl)acetylene and Transformation of the Products

Feng-Ling Qing,* and Dong-Peng Wan

Laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Lu, Shanghai 200032, P. R. China

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Abstract: Reaction of dibromodifluoromethane (1) with (trimethylsilyl)acetylene (2) initiated by ammonium persulfate/sodium formate ($(NH_4)_2S_2O_8/HCO_2Na$) yield the addition-reduction product (3a), tribromide compound (3b) and the non-fluorinated compound (4) which could be separated by careful distillation. The reaction appears to be initiated by $CO_2^{\bullet-}$. Indium mediated coupling of 3a with aldehydes gave the corresponding gem-difluorohomoallyl alcohols bearing a trimethylsilyl group 8 in high yields. In the presence of indium, 3b reacted with aldehydes to afford the coupling-reduction product gem-difluorohomoallyl alcohols 9. The regiochemistry of this reaction and the retention of the configuration of double bond could be rationalized in terms of the more nucleophilic α -carbon of the gem-difluoroallyl intermediate. © 1998 Elsevier Science Ltd. All rights reserved.

INTRODUCTION

The synthesis of compounds containing difluoromethylene (CF_2) group has been an area of active interest, as many of these compounds have been found to be biologically active.¹ A well-tried approach involves the transformation of a ketonic carbonyl group directly using (diethylamino)sulfur trifluoride (DAST).^{2,3} However, in complex molecules the installation of the appropriate carbonyl precursor to the CF₂ group may be far from straightforward. There may be additional limitations imposed by the nature of the mechanism of the DAST fluorination reaction. An alternative strategy uses fluorinated building blocks, and methods involving these are being reported for the synthesis of functionalized, difluoromethyl-substituted compounds.⁴,⁵ Of the two strategies, the building block approach is potentially more versatile.

Readily available dibromodifluoromethane (CF_2Br_2) is frequently used as a starting material for the synthesis of difluoromethylene -containing building blocks, in which three type reactions are involved. CF_2Br_2

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reacts with nucleophiles such as phenoxides, thiophenoxides, carbanions or enamines in an apparent nucleophilic displacement reaction, which usually involves a radical or carbene mechanism;⁶ Reaction of CF2Br2 with alkenes in the presence of zinc or base afforded gem-difluorocyclopropanes,⁷ The majority of reactions proceed by the free-radical addition of CF2Br2 across alkenes.⁸ Difluoromethylene radicals are very promising intermediates for the preparation of complex fluorinated molecules under mild conditions. They are usually more reactive than the corresponding non-fluorinated radicals in carbon-carbon bond forming reactions, because of the σ -nature of the radical and the increased strength of the bond formed.⁹ Diffuoromethylene radicals are generally considered as strongly electrophilic.¹⁰ The addition of CF₂Br₂ involving difluoromethylene radical to alkenes initiated by dibenzoyl peroxide,¹¹ copper(I) chloride,¹² or UV light in the case of electron rich alkenes,¹³ has been well studied. New initiators for this reaction have also been reported: triethylborane/oxygen at room temperature;¹⁴ a chromium trichloride/iron bimetal redox system;¹⁵ and a manganese mediated electrochemical initiation.¹⁶ To the best of our knowledge, however, the free-radical addition of CF₂Br₂ to the alkynes rarely appeared. The only two examples have been hitherto the addition of CF_2Br_2 across acetylene¹⁷ and 1-dodecyne¹⁴ to form the 1:1 adducts. This paper is devoted to the addition of dibromodifluoromethane to (trimethylsily)acetylene initiated by a redox pair for the preparation of highly functionalized difluoromethylene -containing building blocks and their further transformation.

RESULTS AND DISCUSSION

We found that, when initiated by a redox pair, dibromodifluoromethane (CF₂Br₂ 1)can add to alkynes. In the presence of an equimolar mixture of $(NH_4)_2S_2O_8$ and $HCO_2Na.2H_2O$, the addition of 1 to (trimethylsilyl)acetylene (2) proceeded smoothly in DMF suspension at 50°C to yield the mixture of E-isomer of addition-reduction product (3a), tribromide compound (3b) and the non-fluorinated compound 4 which could be separated by careful distillation (Scheme 1). The ratio of 3a : 3b : 4 is 4 : 12 : 3 as determined by ¹H NMR spectra. The structures of 3a, 3b and 4 were readily determined by their ¹H NMR spectra, ¹³C-NMR spectra, MS and elemental analysis. The configuration of double bond in 3a was assigned by the coupling constant of the two vinyl protons ($3a J_{H,H}$ = 19.0 Hz). The 1:1 adduct product 5 and the Z-isomer of additionreduction product 6 were not detected. The addition did not occur below 40°C. This reaction was quite solvent sensitive. In aqueous CH₃CN, no reaction occurred. The results described here represent the first example of the addition of perfluoroalkyl halides like R_fX (X=I, Br) to alkynes to give the stereo-specific additionreduction products in one step.



Ammonium persulfate is a one-electron oxidant that spontaneously decomposes to SO_4^{\bullet} . When $(NH_4)_2S_2O_8$ and HCO₂Na are mixed together, CO₂^{\bullet} is formed.¹⁸ Experiments showed that the presence of both $(NH_4)_2S_2O_8$ and HCO₂Na.2H₂O was necessary for the addition to occur. It thus seems likely that the reaction is initiated by the transfer of a single electron to CF₂Br₂ from CO₂^{\bullet} rather than from SO₄^{\bullet}. The transfer of a single electron to CF₂Br₂ from CO₂^{\bullet} produced BrCF₂ \bullet and Br \bullet in two different reaction routes. The intermediate BrCF₂ \bullet added to alkyne 2 to form BrCF₂CH=C[•]Si(CH₃)₃. Because trimethylsilyl group can stabilize the carboradical and is sterically bulky, ^{19,20} BrCF₂CH=C[•]Si(CH₃)₃ abstracted a hydrogen presumably from the solvent to stereo-specifically form **3a**. The self-coupling of Br \bullet formed Br₂, then addition of Br₂ across alkyne **2** afforded **4**. The addition of BrCF₂ \bullet to **4**, followed by abstracting a bromine produced BrCF₂CHBrCBr₂Si(CH₃)₃, this compound was unstable and subsequently eliminated (CH₃)₃SiBr⁻²¹ to give **3b**. A tentative mechanism for this reaction was shown in Scheme 2.

 $S_{2}O_{8}^{2^{*}} \rightarrow 2 \text{ SO}_{4}^{*^{*}}$ $SO_{4}^{*^{*}} + HCO_{2}^{*} \rightarrow HSO_{4}^{*} + CO_{2}^{*^{*}}$ $CF_{2}Br_{2} + CO_{2}^{*^{*}} \rightarrow BrCF_{2}^{\bullet} + CO_{2} + Br^{\bullet} \text{ and}$ $CF_{2}Br_{2} + CO_{2}^{*^{*}} \rightarrow BrCF_{2}^{\bullet} + CO_{2} + Br^{\bullet}$ $BrCF_{2}^{\bullet} + HC \equiv CSi(CH_{3})_{3} \rightarrow BrCF_{2}CH \equiv C^{*}Si(CH_{3})_{3} \rightarrow BrCF_{2}CH \equiv CHSi(CH_{3})_{3}$ a $2 Br^{\bullet} \rightarrow Br_{2}$ $Br_{2} + HC \equiv CSi(CH_{3})_{3} \rightarrow BrCH = CBrSi(CH_{3})_{3}$ a $BrCF_{2}^{\bullet} + BrCH \equiv CBrSi(CH_{3})_{3} \rightarrow BrCF_{2}CHBr C^{*}BrSi(CH_{3})_{3} \rightarrow BrCF_{2}CHBrCBr_{2}Si(CH_{3})_{3}$ \downarrow $BrCF_{2}CH \equiv CBrSi(CH_{3})_{3} \rightarrow BrCF_{2}CHBr C^{*}BrSi(CH_{3})_{3} \rightarrow BrCF_{2}CHBrCBr_{2}Si(CH_{3})_{3}$ \downarrow $BrCF_{2}CH \equiv CBrSi(CH_{3})_{3} \rightarrow BrCF_{2}CHBr C^{*}BrSi(CH_{3})_{3} \rightarrow BrCF_{2}CHBrCBr_{2}Si(CH_{3})_{3}$

The coupling of aldehydes to allylic and allenic indium reagents is currently an active area of research.²² The allylic reagents can be readily generated form allylic halides and indium metal and they are relatively nontoxic. Unlike their more reactive counterparts, allylic Grignard and lithium reagents, they are compatible with protic solvents and can easily be generated in water and combinations of water and miscible organic solvents. They also show no tendency to give dimeric hydrocarbons as byproducts of their formation from bromides. The most used allylic halides in these coupling are allyl bromide.²³ α -(bromomethyl)acrylic acid ²⁴ and its ester.²⁵ Coupling involving fluorinated allylic halides has rarely appeared. Only indium-mediated allylation of aldehydes with 1,1,1-trifluoro-4-bromobut-2-ene ²⁶ and 3-bromo-3,3-difluoropropene ²⁷ were reported. 3a and 3b are a valuable building block in the synthesis of compounds containing the difluoromethyl group because three functional groups are present: the C-Br bond, the C=C bond, and the trimethylsilyl group. To demonstrate the synthetic utilities of **3a** and **3b**, the indium mediated coupling of aldehydes with **3a** and **3b** was investigated. The indium mediated coupling of benzaldehyde (7a) with 3a was used as model reaction to enable us to explore the reaction conditions. Initially we attempted to carry out this model reaction in water under vigorously stirring, but no reaction occurred. In THF or 1:1 mixture of THF and water, no reaction was observed too. When the coupling reaction was conducted in DMF at 50°C for 24 h, only 50% of 3a was converted into the allylated product 8a. Finally we found, in the presence of an equimolar mixture of indium and lithium iodide, the coupling of benzaldehyde (7a) with 3a proceeded smoothly in DMF at room temperature for 8 h to yield 8a in 71% isolated yield. The accelerating effect of lithium iodide may be due to the exchange of bromine-carbon bond in 3a to a carbon- iodide bond. Based on these reaction conditions, reaction of 3a with other aldehydes formed corresponding allylated product in high yield in all cases, and several characteristic features were observed (Scheme 3 and Table 1). (1). the reaction was α -regioselective, these results are in agreement with previous experimental results ^{27, 28} and Tonachini theoretical description, ²⁹ in which the negative charge is shown to reside at the α -carbon in the gem-difluoroallyl anion (CF₂ site). (2). The configuration of double bonds remained intact. These results are in contrast with (Z)-1trimethylsilylpropenylbromide in the indium-mediated allylation, ³⁰ where the coupling product was a mixture of E- and Z-vinylsilanes. (3). The reaction with the α,β -unsaturated aldehyde 7e gave the 1,2-adduct 8e exclusively.



(Scheme 3)



Table 1. Allylation reaction of aldehydes with 3a*

" All reactions were carried out on a 1.0-1.5 mmol scale, see Experimental Section. " Yield of purified product.

After the successful coupling reaction of 3a with aldehydes, we then extended the reaction conditions to 3b. However, in the presence of indium and lithium iodide, the reaction of 3b with aldehydes in DMF did not occur at room temperature. When the reaction mixture was warmed to 50°C, the coupling reaction took place and the coupling-reduction products gem-difluorohomoallyl alcohols 9 were isolated in high yields (Scheme 4 and Table 2). This success suggested that the reaction temperature was important for the coupling of 3b with aldehydes. It should be noted that under these reaction conditions the vinyl carbon-bromine bonds (3b) were totally reduced, whereas the aryl-bromine bond (7f) was tolerated.



Aldehyde	Product	Yield (%) ^b
H 7a		72
CH30 7b		74
H 7c OMe		71
H 7d OH		78
CH=CHCHO 7e		77
CHO Br		66

Table 2. Allylation reaction of aldehydes with 3b^{*}

To account for the above observations, we propose in broad terms the following mechanism for the indium mediated coupling of 3a and 3b with aldehydes (Scheme 5). First, an allyl indium species 10 was formed which did not exist in equilibrium with its regioisomer 11, because the the pyramidal structure of the *gem*-difluorohomoallyl intermediate is more stable than the planar structure and the negative charge in the intermediate resides at the α -carbon (CF₂ site). Thus, the α -regioselectivity of these coupling reactions can be rationalized in terms of attack of the more nucleophilic α -carbon of the *gem*-difluorohomoallyl intermediate. Furthermore, there was no regioisomer 12. Thus, the stereochemistry of the double bond in the allylic indium species 10 can not be isomerised so that the configuration of double bonds remained intact. In the coupling with aldehyde, the reaction presumably proceeded the cyclic transition state 13. In case where the R1 and R2

^a All reactions were carried out on a 1.0-1.5 mmol scale, see Experimental Section. ^b Yield of purified product.

were bromine (3b), the reduction of carbon-bromine bond initiated by indium was further carried out and coupling-reduction product 9 was obtained.



In summary, a convenient method for the preparation of new difluoromethylene-containing building blocks (**3a** and **3b**) has been developed. Indium mediated the coupling of **3a** and **3b** with aldehydes provided a variety of *gem*-difluorohomoallyl alcohols (**8** and **9**). These reactions offered a new method for the introduction of the difluoromethylene functionality into organic compounds under mild conditions.

EXPERIMENTAL SECTION

Boiling points are uncorrected. ¹⁹F NMR spectra (56.4 Hz) were recorded with Varian EM-360L instrument using CF₃CO₂H as an external standard, upfield positive. ¹H NMR and ¹³C NMR spectra were recorded on a 300 MHz spectrometer with tetramethylsilane as the internal standard. All chemical shifts are expressed in ppm. Light petroleum ether refers to the fraction with distillation range 60-90°C.

General procedure for the addition of dibromodifluoromethane to (trimethylsilyl)acetylene

A 500ml, three-necked, round-bottomed flask was equipped with an efficient magnetic stirring bar, a thermometer and a dry ice-acetone condenser. To this flask were added (trimethylsilyl)acetylene (9.82g, 0.1 mol), DMF (100 ml), $(NH_4)_2S_2O_8$ (22.8g, 0.1 mol), HCO₂Na.2H₂O (10.4g, 0.1 mol) and CF₂Br₂ (14 ml, 0.15 mol). After the mixture was stirred at 50°C for 2 h, the mixture was cooled to room temperature , and $(NH_4)_2S_2O_8$ (22.8g, 0.1 mol), HCO₂Na.2H₂O (10.4g, 0.1 mol) and CF₂Br₂ (14 ml, 0.15 mol) were added. The resulting mixture was still stirred at 50°C overnight. The stirred reaction mixture was then diluted with 150 ml

of ethyl ether. The suspension was filtered through an Buchner funnel fitted with two filter papers and the solid was washed with three 50 ml portions of ethyl ether. The filtrate was washed with three 100 ml portions of water and twice with 100 ml of brine. The organic solution was dried over anhydrous magnesium sulfate. The solvent was removed by rotary evaporation using a water aspirator. The same scale reaction was repeated three times. The combined crude material was fractionally distilled through spinning band fractionating colume to afford 3a (6.1g), 3b (24.6g) and 4 (5.1g).

(E)-(3-Bromo-3,3-difluoro-1-propenyl)trimethylsilane (3a)

colorless liquid; bp 33-34°C / 15mmHg. ¹⁹F NMR (CDCl₃): -30.0(d, J= 9.0 Hz); ¹H NMR (CDCl₃): 0.01 (s, 9H), 6.05(dt, J= 19.0, 9.0 Hz, 1H), 6.25 (dt, J= 19.0, 2.0 Hz, 1H); ¹³C NMR (CDCl₃): -2.1, 117.3 (t, J= 300 Hz), 135.9 (t, J= 5 Hz), 138.7(t, J= 24 Hz); IR (film) 2961, 1810, 1606, 1253, 1207, 1097, 927, 866 and 844cm⁻¹; MS m/z (EI) 215 (M⁺-CH₃, 30.6), 213 (M⁺-CH₃, 29.6), 143 (24.9), 141 (24.1), 81 (58.4), 77 (63.9), 53 (100.0); HRMS calcd for C₁₂ H₈ Br⁷⁹F₂ Si (M⁺-CH₃) 212.9546, Found: 212.9519; HRMS calcd for C₁₂ H₈ Br⁸¹F₂ Si (M⁺-CH₃) 214.9526, Found: 214.9517.

1, 1, 3-Tribromo-3,3-difluoro-1-propene (3b)

pale-yellow liquid; bp 45-46°C / 12mmHg. ¹⁹F NMR (CD_3COCD_3): -33.3(d, J= 9.0 Hz); ¹H NMR (CD_3COCD_3): 7.50 (t, J= 9.0 Hz); ¹³C NMR (CD_3COCD_3): 101.4 (t, J= 8 Hz), 115.7 (t, J= 299 Hz), 134.9 (t, J= 29 Hz); 1R (film) 3057, 1605, 1203, 1110, 859, 835, 688, and 563 cm⁻¹; MS *m/z* (El) 237 (M⁺-Br, 57.9), 235 (M⁺-Br, 100.0), 233(M⁺-Br, 49.5), 75 (21.0); Anal. Calcd for $C_3HBr_3F_2$: C, 11.45; H, 0.32; Br, 76.16. Found: C, 11.48; H, 0.43; Br, 74.84.

(1,2-Dibromoethenyl)trimethylsilane (4)³¹

colorless liquid; b.p. 62° C / 12mmHg. ¹H NMR (CD₃COCD₃): 0.37 (s, 9H), 7.43 (s, 1H); ¹³C NMR (CD₃COCD₃): 0.1, 116.0, 128.4; MS *m*/*z* (EI) 260 (M⁺, 8.8), 258 (M⁺, 16.5), 256(M⁺, 8.3), 245 (18.5), 243 (32.9), 241 (16.5), 139 (100.0), 137 (86.8). This date was consistent with that reported in the literature.

General Procedure for the indium mediated coupling of 3a and 3b with aldehydes.

A mixture of **3a** or **3b** (**3a**, 0.34g; **3b**, 0.47g, 1.5 mmol), indium powder (0.17g, 15 mmol), lithium iodide (0.38g, 2.0 mmol) and aldehyde **5** (1.0 mmol) in anhydrous DMF (2 ml) was stirred vigorously at room temperature (for **3b**, at 50°C) for 8 h. Then, saturated aqueous ammonium chloride (10 ml) and ethyl acetate (10 ml) was introduced, and the aqueous phase was extracted with ethyl acetate ($2 \times 10 \text{ ml}$). The combined organic solutions were washed with water ($3 \times 10 \text{ ml}$) and brine ($2 \times 10 \text{ ml}$), and then dried over anhydrous magnesium sulfate. After evaporation of the solvents, the residue was subjected to flash chromatography on silica gel (elution with 10:1 petroleum ether/ ethyl acetate) to afford **8** or **9**.

(E)-2,2-Difluoro-1-phenyl-4-trimethylsilyl-3-buten-1-ol (8a)

colorless liquid; ¹⁹F NMR (CDCl₃): 31.3(d, J=9.0 Hz); ¹H NMR (CDCl₃): 0.08 (s, 9H), 2.53 (br, 1H), 4.89 (t, J= 9.0 Hz, 1H), 5.92(dt, J= 19.0, 9.0 Hz, 1H), 6.22 (dt, J=19.0, 2.0 Hz, 1H), 7.32-7.40 (m, 5H); IR (film) 3435, 2959, 1497, 1456, 1336, 1251, 1054, 990, 867, 742, 699 and 598 cm⁻¹; MS m/z (EI) 257 (M⁺+1, 5.8), 179 (21.6), 147 (11.2), 127 (30.7) 105 (100.0); Anal. Calcd for C₁₃H₁₈F₂OSi : C, 60.94; H, 7.10; F, 14.84. Found: C, 60.98; H, 6.96; F, 14.81.

(E)-2,2-Difluoro-1-(4-methoxy-phenyl)-4-trimethylsilyl-3-buten-1-ol (8b)

colorless oil; ¹⁹F NMR (CDCl₃): 31.3(d, J= 9.0 Hz); ¹H NMR (CDCl₃): 0.06 (s, 9H), 2.53 (br, 1H), 3.80 (s, 3H), 4.81 (t, J= 9.0 Hz, 1H), 5.96(dt, J= 19.0, 9.0 Hz, 1H), 6.21 (dt, J=19.0, 2.0 Hz, 1H), 6.86 (d, J=9.0 Hz, 2H), 7.32 (d, J=9.0 Hz, 2H); IR (film) 3450, 2958, 1614, 1516, 1252,1177, 1036, 866, 843 and 579 cm⁻¹; MS m/z (EI) 286 (M⁺, 0.8), 269 (24.0), 137 (100.0), 109 (33.7), 77 (24.3); Anal. Calcd for C₁₄H₂₀F₂O₂Si : C, 58.71; H, 7.04; F, 13.27. Found: C, 57.80; H, 7.19; F, 13.33.

(E)-2,2-Difluoro-1-(2-methoxy-phenyl)-4-trimethylsilyl-3-buten-1-ol (8c)

colorless oil; ¹⁹F NMR (CDCl₃): 32.6(d, J= 9.0 Hz); ¹H NMR (CDCl₃): 0.06 (s, 9H), 3.02 (br, 1H), 3.84 (s, 3H), 5.19 (t, J= 9.0 Hz, 1H), 6.02(dt, J= 19.0, 9.0 Hz, 1H), 6.25 (dt, J=19.0, 2.0 Hz, 1H), 6.88-6.98 (m, 2H), 7.26-7.37 (m, 2H); IR (film) 3450, 2957, 2841, 1604, 1495, 1466, 1249, 1050, 867, 756 and 695 cm⁻¹; MS $m_{\cdot}z$ (EI) 286 (M⁺, 0.8), 269 (1.5), 137 (100.0), 107 (37.0), 77 (16.0); Anal. Calcd for C₁₄H₂₀F₂O₂Si : C, 58.71; H, 7.04; F, 13.27. Found: C, 57.40; H, 7.06; F, 13.36.

(E)-2,2-Difluoro-1-(2-hydroxy-phenyl)-4-trimethylsilyl-3-buten-1-ol (8d)

colorless oil; ¹⁹F NMR (CDCl₃): 32.0(d, J= 9.0 Hz); ¹H NMR (CDCl₃): 0.06 (s, 9H), 4.09 (br, 1H), 5.02 (t, J= 9.0 Hz, 1H), 6.01(dt, J= 19.0, 9.0 Hz, 1H), 6.28 (dt, J=19.0, 2.0 Hz, 1H), 6.82-6.93 (m, 2H), 7.01-7.05 (m, 1H), 7.19-7.39 (m, 1H), 7.83 (br, 1H); IR (film) 3362, 2958, 2901, 1614, 1591, 1493, 1460, 1251, 1033, 989, 867, 755 and 609 cm⁻¹; MS m/z (EI) 199 (M⁺-TMS, 1.3), 179 (35.8), 124 (10.7), 123 (100.0), 95 (22.2); Anal. Calcd for C₁₃H₁₈F₂O₂Si : C, 57.32; H, 6.66; F, 13.95. Found: C, 57.42; H, 6.32; F, 13.82.

(5 E)-4, 4 -Difluoro-1-phenyl-6-trimethylsilyl-1,5-hexadien-3-ol (8e)

colorless oil; ¹⁹F NMR (CDCl₃): 30.6 (dd, J= 112, 9.0 Hz); ¹H NMR (CDCl₃): 0.10 (s, 9 H), 4.49 (t, J= 9.0 Hz, 1H), 6.14(dt, J= 19.0, 9.0 Hz, 1H), 6.20 (d, J= 16.0 Hz, 1H), 6.45 (dt, J=19.0, 2.0 Hz, 1H), 6.74 (dt, J= 19.0, 9.0 Hz, 1H), 7.27-7.57 (m, 5H); IR (film) 3341, 2957, 1668, 1498, 1451, 1250, 1129, 1050, 972, 868, 749 and 691 cm⁻¹; MS m/z (EI) 245 (2.4), 133 (100.0), 115 (20.6), 77 (16.9); Anal. Calcd for $C_{15}H_{20}F_2OSi : C, 63.80;$ H, 7.14. Found: C, 63.71; H, 6.84.

2, 2-Difluoro-1-phenyl-3-buten-1-ol (9a)²⁸

colorless liquid; ¹⁹F NMR (CDCl₃): 30.9 (d, J= 30.0 Hz); ¹H NMR (CDCl₃): 2.46 (br, 1H), 4.84 (t, J= 11.0 Hz, 1H), 5.40 (d, J= 11.0 Hz, 1H), 5.49-5.57 (m, 1H), 5.74-5.84 (m, 1H), 7.23-7.46 (m, 5H); MS m/z (EI) 164 (M^{*}- HF, 1.1), 108 (14.4), 107 (100.0), 79 (75.6), 77 (45.3). This date was consistent with that reported in the literature.

2,2-Difluoro-1-(4-methoxy-phenyl)-3-buten-1-ol (9b)

colorless oil; ¹⁹F NMR (CDCl₃): 30.2 (d, J= 30.0 Hz); ¹H NMR (CDCl₃): 2.63 (br, 1H), 3.80 (s, 3H), 4.84(t, J= 11.0 Hz, 1H), 5.45(d, J= 11.0 Hz, 1H), 5.55-5.62(m, 1H), 5.77-5.94 (m, 1H), 6.88 (d, J= 9.0Hz, 2H), 7.30 (d, J= 9.0Hz, 2H); IR (film) 3553, 2927, 1614, 1516, 1421, 1253, 1177, 1069, 994, 954 and 801 cm⁻¹; MS m/z (EI) 214 (M⁺, 1.7), 138 (10.6), 137 (100.0), 77 (29.1); Anal. Calcd for C₁₁H₁₂F₂O₂ : C, 61.68; H, 5.65; F, 17.74. Found: C, 61.37; H, 5.62; F, 17.47.

2,2-Difluoro-1-(2-methoxy-phenyl)-3-buten-1-ol (9c)

colorless oil; ¹⁹F NMR (CDCl₃): 32.2 (s); ¹H NMR (CDCl₃): 3.20(br, 1H), 3.84 (s, 3H), 5.33(t, J= 11.0 Hz, 1H), 5.44(d, J= 11.0 Hz, 1H), 5.57-5.65(m, 1H), 5.86-6.04(m, 1H), 6.89-7.02 (m, 2H), 7.29-7.39 (m, 2H); IR (film) 3445, 2943, 1604, 1495, 1466, 1248, 1052, 994, 854, 757 and 701cm⁻¹; MS m/z (EI) 214 (M⁺, 0.2), 138 (13.3), 137 (100.0), 107 (58.2), 77 (29.1); Anal. Calcd for C₁₁H₁₂F₂O₂ : C, 61.68; H, 5.65; F, 17.74. Found: C, 61.46; H, 5.62; F, 18.04.

2,2-Difluoro-1-(2-hydroxy-phenyl)-3-buten-1-ol (9d)

colorless oil; ¹⁹F NMR (CDCl₃): 32.2 (d, J= 20.0 Hz); ¹H NMR (CDCl₃): 3.92 (br, 1H), 5.04(t, J= 11.0 Hz, 1H), 5.51(d, J= 9.0 Hz, 1H), 5.65(d, J=19.0 Hz, 1H), 5.81-5.99 (m, 1H), 6.85-6.89(m, 2H), 7.06-7.13 (m, 1H), 7.20-7.28 (m, 1H), 7.72(s, 1H); IR (film) 3351, 2925, 1613, 1590, 1494, 1421, 1242, 1032, 995, 877, 757, 699 and 644 cm⁻¹; MS m/z (EI) 201 (M⁺ + 1, 2.0), 200(M⁺, 6.3), 183 (10.3), 129 (11.5), 123 (100.0), 77 (45.8); Anal. Calcd for C₁₀H₁₀F₂O₂ : C, 60.00; H, 5.04; F, 18.98. Found: C, 59.77; H, 5.09; F, 18.87.

4, 4 -Difluoro-1-phenyl-1,5-hexadien-3-ol (9e)²⁸

colorless oil; ¹⁹F NMR (CDCl₃): 31.5 (d, J= 80.0 Hz); ¹H NMR (CDCl₃): 2.27(br, 1H), 4.53 (t, J= 9.0 Hz, 1H), 5.57 (d, J= 9.0 Hz, 1H), 5.72-5.79 (m, 1H), 5.93-6.06 (m, 1 H), 6.09-6.24 (m, 1 H), 6.78 (d, J= 16.0 Hz, 1 H), 7.27-7.43 (m, 5H); MS m/z (EI) 210 (M⁺, 1.1), 170 (9.2), 134 (19.6), 133 (100.0), 115 (42.2), 103 (15.0), 77 (23.4). This date was consistent with that reported in the literature.

2,2-Difluoro-1-(2-bromo-phenyl)-3-buten-1-ol (9f)

colorless oil; ¹⁹F NMR (CD₃COCD₃): 32.5(s); ¹H NMR (CD₃COCD₃): 5.39(t, J= 11.0 Hz, 1H), 5.49-5.56 (m, 2H), 5.59(s, 1H), 6.03-6.19 (m, 1H), 7.22-7.28 (m, 1H), 7.33-7.41(m, 1H), 7.55-7.65 (m, 2H); **IR** (film) 3412, 2930, 1593, 1570, 1474, 1421, 1194, 1069, 995, 849, 753 and 680 cm⁻¹; MS m/z (EI) 187 (

100.0), 185 (83.3), 159 (17.6), 157 (19.5), 77 (59.1); Anal. Calcd for $C_{10}H_9BrF_2O$: C, 45.65; H, 3.45. Found: C, 45.58; H, 3.59.

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