A convenient synthesis of bromodifluoromethyl-substituted alkenes

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Abstract

Various functionalized bromodifluoromethyl-substituted alkenes have been prepared by addition of dibromodifluoromethane to functionalized alkenes promoted by a $CrCl_3$/Fe bimetal redox system, followed by dehydrobromination with KF/Al_2O_3.

Introduction

In our continuing studies on the application of redox system in organofluorine chemistry and on the synthetic utility of dibromodifluoromethane, we have found that the bimetal redox system $CrCl_3$/Fe can efficiently promote the addition of dibromodifluoromethane to electron-deficient alkenes to form hydrobromodifluoromethylation products [1]. Subsequent investigation showed that this redox system could also promote the addition of dibromodifluoromethane to electron-rich alkenes to produce 1,3-dibromo-1,1-difluoroalkanes as 1:1 adducts. Later, we found that KF/Al_2O_3 was an efficient dehydrobrominating agent which eliminated hydrobromide from such 1,3-dibromo-1,1-difluoroalkanes [2]. Thus the preparation of bromodifluoromethyl-substituted alkenes becomes feasible by utilizing dibromodifluoromethane as the source of the bromodifluoromethyl unit. On dehydrobromination with KF/Al_2O_3, 1,3-dibromo-1,1-difluoroalkanes gave the corresponding bromodifluoromethyl-substituted alkenes which are useful building blocks for the introduction of the allylic difluoromethylene fragment into organic molecules [3, 4]. Here, we report the detailed results of such synthetic utility of dibromodifluoromethane and some unexpected reactions.

Results and discussion

Many initiators, for example, benzoyl peroxide, azobisisobutyronitrile, UV light, CuCl/2-ethanolamine, $AlMe_3$, BEt_3, $(NH_4)_2S_2O_8/HCO_2NH_4$, etc. have been reported as promoting the addition of dibromodifluoromethane (**1**) to electron-rich alkenes **2**, giving 1,3-dibromo-1,1-difluoroalkanes **3** as the 1:1 adduct. Of these initiators, the redox system has distinct advantages when compared with other initiation techniques [5]. In fact, in the presence of the $CrCl_3$/Fe redox system, alkenes **2** bearing various functional groups such as alkyl, alkenyl, ester, carbonyl and ether groups provide suitable substrates for obtaining 1:1 adducts **3** in good yield. The results are summarized in Table 1. In the case of allyl acetate (**2g**), some telomerized product was detected, and the yield of the 1:1 adduct was low (Run 7). Diallyl ether (**2h**) gave the tetrahydrofuran derivative **3h** in 78% yield. This result implies that the reaction proceeds via a radical addition pathway. In addition, certain known 1,3-dibromides **3i–k** have been synthesized according to the reported procedure [6]. Compound **3l** was obtained in 82% yield by the $Na_2S_2O_4$/$NaHCO_3$ promoted addition of dibromodifluoromethane to diethyl allylmalonate.

$$\underset{(1)}{CF_2Br_2} + \underset{(2)}{CH_2{=}CHR} \xrightarrow[60\text{–}70\ ^\circ C]{CrCl_3/Fe/EtOH} \underset{(3)}{BrCF_2CH_2CH(Br)R}$$

$$\underset{(1)}{CF_2Br_2} \longrightarrow BrCF_2SO_2Br \xrightarrow{\text{alkenes or alkynes}} \underset{(3i\text{–}k)}{BrCF_2\text{–}\overset{\cdot}{C}\text{–}\overset{\cdot}{C}\text{–}R}$$

$$CF_2Br_2 + CH_2{=}CHCH_2CH(CO_2Et)_2 \xrightarrow[CH_3CN/H_2O]{Na_2S_2O_4/NaHCO_3} \underset{(3)\ (82\%)}{BrCF_2CH_2CHBrCH_2CH(CO_2Et)_2}$$

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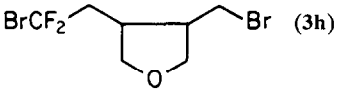
TABLE 1. Addition of CF_2Br_2 (**1**) to alkenes **2**[a]

Run No.	Alkene **2**	Product **3**	Yield (%)[b]
1	$CH_2=CHC_4H_9$ (**2a**)	$BrCF_2CH_2CHBrC_4H_9$ (**3a**)	96
2	$CH_2=CHC_6H_{13}$ (**2b**)	$BrCF_2CH_2CHBrC_6H_{13}$ (**3b**)	84
3	$CH_2=CHC_2H_4CH=CH_2$ (**2c**)	$BrCF_2CH_2CHBrC_2H_4CH=CH_2$ (**3c**)	72
4	$CH_2=CHC_2H_4COCH_3$ (**2d**)	$BrCF_2CH_2CHBrC_2H_4COCH_3$ (**3d**)	64
5	$CH_2=CH(CH_2)_8CO_2Me$ (**2e**)	$BrCF_2CH_2CHBr(CH_2)_8CO_2Me$ (**3e**)	64
6	cyclohexene (**2f**)	2-bromo-1-bromodifluoromethylhexane (**3f**)	74
7	$CH_2=CHCH_2OAc$ (**2g**)	$BrCF_2CH_2CHBrCH_2OAc$ (**3g**)	30[c]
8	$(CH_2=CHCH_2)_2O$ (**2h**)	 (**3h**)	78
9	$CH_2=CHCH_2Cl$ (**2i**)	$BrCF_2CH_2CHBrCH_2Cl$ (**3i**)	64[d]
10	$CH_2=CHPh$ (**2j**)	$BrCF_2CH_2CHBrPh$ (**3j**)	67[d]
11	$HC\equiv CPh$ (**2k**)	$BrCF_2CH=CBrPh$ (**3k**)	65[d]

[a]Molar ratio of **1**/**2**/$CrCl_3$/Fe = 1.2–1.5:1:0.2:1.5. Reactions were carried out at 60–70 °C for *c.* 12 h.
[b]Isolated yields based on alkene **2**.
[c]Telomerized product was also obtained.
[d]See ref. 6.

On treatment with KF/Al_2O_3 [7] (*c.* 2.5 equiv. KF) in acetonitrile or *N,N*-dimethylformamide with stirring at 40–50 °C for several hours, these 1,3-dibromides **3** gave the corresponding dehydrobrominated products, i.e. 1-bromodifluoromethyl-alk-1-enes **4**. The results are summarized in Table 2.

$$\underset{(3)}{BrCF_2CH_2CHBrR} \xrightarrow[CH_3CN,\ 40\text{–}50\ ^\circ C]{KF/Al_2O_3} \underset{(4)}{BrCF_2CH=CHR}$$

Dehydrobromination proceeded smoothly to give the corresponding alkenes **4** in good yield. These products were a mixture of *E* and *Z* isomers, with the former predominating. Thus, treatment of 1,3-dibromo-1,1-difluoromethylheptane (**3a**) with KF/Al_2O_3 gave such a mixture, the δ_{CF_2} signal of the *E* isomer appearing at −39 ppm in the ^{19}F NMR while the δ_{CF_2} spectrum of the *Z* isomer appeared at −35 ppm. The *E*/*Z* ratio agreed well with the result obtained by GC analysis.

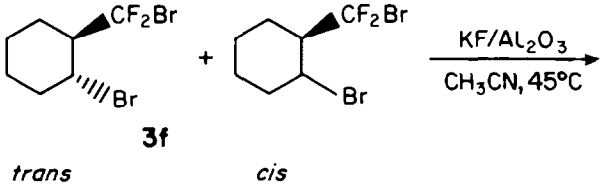
In contrast with the procedure using refluxing triethylamine as the dehydrobrominating agent, the KF/Al_2O_3-promoted dehydrobromination reaction proceeded under much milder conditions and the yields were excellent. Furthermore, the *E*/*Z* ratio of the products obtained was high (Run Nos. 1–3).

TABLE 2. Dehydrobromination of 1,3-dibromides **3** with KF/Al_2O_3[a]

Run No.	1,3-Dibromides **3**	Reaction time (h)	Product **4**	*E*/*Z*[b]	Yield (%)[c]
1	$CF_2BrCH_2CHBrC_4H_9$ (**3a**)	4	$CF_2BrCH=CHC_4H_9$ (**4a**)	95:5	87
2	**3a**	4	$CF_2BrCH=CHC_4H_9$ (**4a**)	94:6	94[d]
3	**3a**	28	$CF_2BrCH=CHC_4H_9$ (**4a**)	1:1	70[e]
4	$CF_2BrCH_2CHBrC_6H_{13}$ (**3b**)	4	$CF_2BrCH=CHC_6H_{13}$ (**4b**)	92:8	84
5	$CF_2BrCH_2CHBrC_2H_4CH=CH_2$ (**3c**)	4	$CF_2BrCH=CHC_2H_4CH=CH_2$ (**4c**)	88:12	55
6	$CF_2BrCH_2CHBrC_2H_4Ac$ (**3d**)	4	$CF_2BrCH=CHC_2H_4Ac$ (**4d**)	84:16	74
7	$CF_2BrCH_2CHBr(CH_2)_8CO_2Me$ (**3e**)	6	$CF_2BrCH=CH(CH_2)_8CO_2Me$ (**4e**)	88:12	90
8	2-bromo-1-bromodifluoromethylcyclohexane (**3f**)	8	1-bromodifluoromethylcyclohexene (**4f**)	–	40
9	$CF_2BrCH_2CHBrCH_2OAc$ (**3g**)	4	$CF_2BrCH=CHCH_2OAc$ (**4g**)	95:5	65
10	$CF_2BrCH_2CHBrCH_2Cl$ (**3i**)	5	$CF_2BrCH=CHCH_2Cl$ (**4i**)	–	74
11	$CF_2BrCHCHC_4H_9$ (**9**) (Br Br)	4	$CF_2BrCBr=CHC_4H_9$ (**10**)	58:42	87

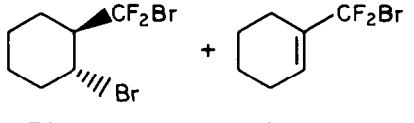
[a]All reactions were carried out in CH_3CN at 40–50 °C with 2.5 equiv. of KF/Al_2O_3 unless otherwise indicated.
[b]Estimated by ^{19}F NMR spectroscopy.
[c]Isolated yields.
[d]*N,N*-Dimethylformamide was used as the solvent.
[e]Reaction carried out in refluxing triethylamine.

Functionalities such as the ester, carbonyl, alkenyl and chloromethyl group could tolerate such conditions and did not affect the elimination reaction. For 1-bromodifluoromethyl-2-bromocyclohexane (**3f**), only the *cis* isomer was dehydrobrominated, while the *trans* isomer was unaffected even at 70 °C after 5 h.



3f

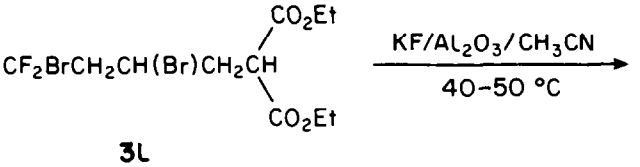
trans *cis*



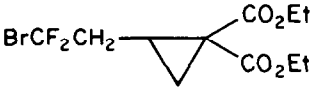
3f **4f**

trans

When **3l** was dehydrobrominated with KF/Al_2O_3, an unexpected product, i.e. diethyl bromodifluoromethyl-methyl-1,1-cyclopropanecarboxylate (**5**), was obtained in 92% isolated yield. The structure of compound **5** was confirmed from its ^1H and ^{13}C NMR spectra. The signal from the methylene group of the cyclopropane ring appeared as a doublet at 1.5 ppm ($J=8$ Hz) and integrated for two protons. Under such conditions, the ethyl ester group remained intact. It was interesting to note that no $BrCF_2$-substituted alkene could be detected. This result shows that the acidity of the methinic proton in $CH(CO_2Et)_2$ is stronger than that of the methinic proton adjacent to the CF_2 group. The carbanion formed underwent nucleophilic reaction with the CHBr to give the corresponding cyclopropane derivative **5**.



3L



5

As the bromine atom in bromodifluoromethyl-substituted alkenes is in the allylic position, it is relatively labile under certain conditions. For example, when 1,3-dibromo-1,1-difluoro-3-phenyl-propane (**3j**) was treated with KF/Al_2O_3, the α,β-unsaturated carboxylic acid **6** was formed in nearly quantative yield. (α,β-Unsaturated carboxylic fluoride **7** is considered to be the intermediate.) Compound **7** was not isolated but its presence could be deduced spectroscopically ($\delta_F/CDCl_3 = -90$ ppm/CF_3CO_2H; $\nu_{max} = 1800$ (vs) cm^{-1}). The same result was obtained with the $BrCF_2$-substituted vinyl bromide **3k**. However, the bromodifluoromethyl-substituted alkyne could not be obtained in this way.

$$\underset{\textbf{(3j)}}{PhCHBrCH_2CF_2Br} \xrightarrow[40\text{–}50\ ^\circ C]{KF/Al_2O_3/CH_3CN} [PhCH{=}CHCF_2Br] \longrightarrow [PhCH{=}C{=}CF_2] \longrightarrow \underset{\textbf{(7)}}{[PhCH{=}CHCOF]} \longrightarrow \underset{\textbf{(6)}}{PhCH{=}CHCO_2H}$$

$$\underset{\textbf{(3k)}}{PhCBr{=}CHCF_2Br} \xrightarrow[40\text{–}50\ ^\circ C]{KF/Al_2O_3/CH_3CN} \underset{\textbf{(8)}}{PhC{\equiv}CCO_2H}$$

These bromodifluoromethyl-substituted alkenes react with bromine to give 1,2,3-tribromides in near-quantative yield under UV irradiation. For example, **4a** reacted with bromine giving the 1,2,3-tribromide **9**, and compound **9** could be further dehydrobrominated to the 1,2-dibromo-2-alkene **10** which could not be further dehydrobrominated under these conditions.

$$\underset{\textbf{(4a)}}{CF_2BrCH{=}CHC_4H_9} + Br_2 \xrightarrow{h\nu} \underset{\textbf{(9)}}{BrCF_2CHBrCHBrC_4H_9} \xrightarrow[CH_3CN,\ 45\ ^\circ C]{KF/Al_2O_3} \underset{\textbf{(10)}}{CF_2BrC(Br){=}C_4H_9}$$

In summary, although there are some exceptions, KF supported on alumina in acetonitrile or *N,N*-dimethylformamide has been shown to be a mild dehydrobrominating agent. The simplicity of the experimental procedure, the ready availability of the base and the good yields make this approach a useful route for synthesizing various bromodifluoromethyl-substituted alkenes. Furthermore, such functionalized alkenes bearing an allyl bromine atom are potential CF_2-introducing building blocks in organic synthesis.

Experimental

All boiling points are uncorrected. ^1H NMR spectra were obtained in CCl_4 or $CDCl_3$ on an EM-360A (60 MHz) or a Bruker AC-300 (300 MHz) spectrometer. ^{19}F NMR spectra were recorded on a Varian EM-360L (56.4 MHz) spectrometer in CCl_4 or $CDCl_3$ using CF_3CO_2H (TFA) as external standard. Chemical shifts in ppm were positive for upfield shifts. ^{13}C NMR spectra

were recorded on an FX-90Q (22.6 MHz) spectrometer in $CDCl_3$. Infrared spectra were obtained from neat liquids on a Shimadzu IR-440 spectrometer. MS spectra were measured on a Finnigan MS-4021 spectrometer. All reagents and solvents were used directly without further purification. In the preparations described below, the product was new where no literature reference is given.

Addition of CF_2Br_2 (1) to alkenes 2. General procedure

The procedure was based on that reported in the literature [1]. A mixture of 50 mmol of CF_2Br_2 (**1**), 60 mmol of alkene (**2**), 10 mmol of $CrCl_3 \cdot 6H_2O$ and 75 mmol of iron powder in 100 ml of ethanol was stirred at 60–70 °C for the required time. The reaction was monitored by ^{19}F NMR spectroscopy. After reaction wa complete, the resulting mixture was poured into 50 ml of dilute hydrochloric acid (1 N) and extracted with diethyl ether (3×30 ml). The combined extract was successively washed with HCl (1 N), water, brine and then dried over Na_2SO_4. After removal of the solvent, the residue was purified by distillation under reduced pressure to give the pure products **3**.

The preparation of compounds **3i–k** was based on the method described previously [6]. Compound **3l** was prepared as follows [7]. A mixture of diethyl allylmalonate (10 mmol, 2 g), CF_2Br_2 (12 mmol, 2.5 g), $Na_2S_2O_4$ (12 mmol, 2 g), $NaHCO_3$ (12 mmol, 1 g) in 50 ml of a mixed solvent consisting of CH_3CN and water (3:7) was stirred at 40 °C for *c.* 1.5 h. The reaction was monitored by ^{19}F NMR spectroscopy. The purifying procedure followed was as described above.

1,3-Dibromo-1,1-difluoroheptane (**3a**) [6]: Colourless oil, b.p. 95–98 °C/45 mmHg. ^{19}F NMR δ: −34.5 (s, CF_2Br) ppm. ^1H NMR δ: 4.3 (m, 1H, CHBr); 3.05 (m, 2H, CF_2CH_2); 2.2–1.0 (m, 9H, C_4H_9) ppm.

1,3-Dibromo-1,1-difluorononane (**3b**) [6]: Colourless oil, b.p. 108–110 °C/10 mmHg. ^{19}F NMR δ: −35 (s, CF_2Br) ppm. ^1H NMR δ: 4.1 (m, 1H, CHBr); 3.2–2.6 (m, 2H, CF_2CH_2); 1.8–1.0 (m, 10H, 5×CH_2); 0.8 (t, $^3J_{HH}$=2 Hz, 3H, CH_3) ppm. IR $\nu_{max.}$ (cm^{-1}): 2900 (s, C–H); 1100 (s, C–F); 670 (s, C–Br).

1,3-Dibromo-1,1-difluorohept-6-ene (**3c**): Colourless oil, b.p. 108–110 °C/10 mmHg. ^{19}F NMR δ: −35 (s, CF_2Br) ppm. ^1H NMR δ: 6.1–5.7 (m, 1H, CH=CH_2); 5.3–4.9 (m, 2H, CH=CH_2); 4.2 (m, 1H, CHBr); 3.4–2.7 (m, 2H, CF_2CH_2); 2.5–1.8 (m, 4H, CH_2CH_2) ppm. IR $\nu_{max.}$ (cm^{-1}): 1640 (m, C=C); 1200, 1100 (s, C–F). MS *m/z* (%): 211 (M^+ − Br, 9.75); 213 (M^+ − Br, 10.62); 191 (13.16); 193 (13.66); 131 (52.55); 121 (100); 111 (47.37); 81 (34.72). Analysis: Calc. for $C_7H_{10}Br_2F_2$ (FW 292): C, 28.77; H, 3.42; F, 13.01; Br, 54.79%. Found: C, 28.74; H, 3.62; F, 13.20; Br, 54.80%.

1,3-Dibromo-1,1-difluoroheptan-6-one (**3d**): b.p. 82–86 °C/2 mmHg, light yellow oil (turns slowly deep brown at room temperature). ^{19}F NMR δ: −35.5 (s, CF_2Br) ppm. ^1H NMR δ: 4.2 (m, 1H, CHBr); 3.4–2.0 (m, 9H, others) ppm. IR $\nu_{max.}$ (cm^{-1}): 1720 (s, C=O); 1200, 1170 (s, C–F); 640, 540 (s, C–Br). MS *m/z* (%): 306 (M^+, 0.29); 308 (M^+, 0.75); 310 (M^+, 0.53); 58 (51.10); 43 (Ac^+, 100). Analysis: Calc. for $C_7H_{10}Br_2F_2O$ (FW 308): c, 27.27; H, 3.25; F, 12.34; Br, 51.95%. Found: C, 27.30; H, 3.27; F, 12.19; Br, 51.75%.

Methyl 10,12-dibromo-12,12-difluorotridecanoate (**3e**): Colourless oil, b.p. 150 °C/1 mmHg. ^{19}F NMR δ: −35 (s, CF_2Br) ppm. ^1H NMR δ: 4.1 (m, 1H, CHBr); 3.65 (s, 3H, OMe); 3.15–2.6 (m, 2H, CF_2CH_2); 2.20 (t, $^3J_{HH}$=3.5 Hz, 2H, CH_2CO); 1.8–1.2 (m, 14H, 7×CH_2) ppm. IR $\nu_{max.}$ (cm^{-1}): 2900 (s, C–H); 1740 (s, C=O); 1220, 1180 (s, C–F); 660 (s, C–Br). MS *m/z* (%): 74 ($C_4H_7F^+$, 100); 55 ($C_4H_7^+$, 87.96). Analysis: Calc. for $C_{13}H_{22}Br_2F_2O_2$ (FW 408): C, 38.24; H, 5.39%. Found: C, 38.25; H, 5.48%.

1-Bromodifluoromethyl-2-bromocyclohexane (**3f**) [6]: Colourless oil, b.p. 108–110 °C/40 mmHg. ^{19}F NMR δ: −23.5, −32 (AB, CF_2Br, *cis* isomer); −35 (s, CF_2Br, *trans* isomer) ppm. ^1H NMR δ: 4.8–3.7 (m, 1H, CHBr); 3.05 (m, 1H, $CHCF_2$); 1.9–1.1 (m, 8H, 4×CH_2) ppm.

2,4-Dibromo-4,4-difluorobutyl acetate (**3g**): Colourless oil, b.p. 115–118 °C/10 mmHg. ^{19}F NMR δ: −34.8 (s, CF_2Br) ppm. ^1H NMR δ: 4.3 (m, 3H, $CH(Br)CH_2O$); 3.8–2.8 (m, 2H, CH_2); 2.0 (s, 3H, Ac) ppm. IR $\nu_{max.}$ (cm^{-1}) 1750: (s, C=O); 1240 (s, C–F); 930, 910 (m, C–Br). MS *m/z* (%): 309 (M^+ +1, 21.99); 311 (M^+ +1, 47.58); 313 (M^+ +1, 30.98); 249 (M^+ − OAc, 15.82); 251 (M^+ − OAc, 28.59); 253 (M^+ − OAc, 13.32); 229 (M^+ − Br, 27.07); 231 (M^+ − Br, 33.79); 169 (100); 171 (82.81); 43 (98.44). Analysis: Calc. for $C_6H_8Br_2F_2O_2$ (FW 310): C, 23.24; H, 2.58; F, 12.26; Br, 51.61%. Found: C, 23.43; H, 2.49; F, 12.22; Br, 51.47%.

3-Bromomethyl-4-(2′-bromo-2′,2′-difluoroethyl)tetrahydrofuran (**3h**): Colourless oil, b.p. 118–120 °C/20 mmHg. ^{19}F NMR δ: −35.0 (s, CF_2Br) ppm. ^1H NMR δ: 4.30–2.30 (m) ppm. Analysis: Calc. for $C_7H_{10}Br_2F_2O$ (FW 308): C, 27.27; H, 3.25; F, 12.34; Br, 51.95%. Found: C, 27.86; H, 3.25; F, 12.47; Br, 51.72%.

1,3-Dibromo-4-chloro-1,1-difluoropentane (**3i**) [6]: Colourless oil, b.p. 84–85 °C/20 mmHg. ^{19}F NMR δ: −34.5 (s, CF_2Br) ppm. ^1H NMR δ: 4.3 (m, 1H, CHBr); 3.8 (m, CH_2Cl); 3.3–1.8 (m, 2H, CH_2) ppm. IR $\nu_{max.}$ (cm^{-1}): 1195 (s, C–F); 730 (m, C–Cl).

1,3-Dibromo-1,1-difluoro-3-phenylpropane (**3j**) [6]: ^{19}F NMR δ: −33.2 (s, CF_2Br) ppm. ^1H NMR δ: 6.93 (s, 5H, Ph); 5.10–4.80 (m, 1H, CHBr); 3.30–2.90 (m, 2H, CH_2CF_2) ppm.

1,3-Dibromo-1,1-difluoro-3-phenylprop-2-ene (**3k**) [6]: ^{19}F NMR δ: −36 (s, CF_2Br) ppm. ^1H NMR δ: 7.65 (s, 5H, Ph); 7.30–7.00 (m, 1H, CH) ppm.

Diethyl 2,4-dibromo-4,4-difluorobutylmanolate (**3l**): Colourless oil, b.p. 128 °C/1 mmHg. ^{19}F NMR δ: −35.0 (s, CF_2Br) ppm. ^{1}H NMR δ: 4.20 (q, $^3J_{HH}$=7 Hz, 4H, 2×OEt); 3.8–1.8 (m, 6H, others); 1.36 (t, $^3J_{HH}$=7 Hz, 6H, 2×OEt) ppm. IR $\nu_{max.}$ (cm^{-1}): 1760, 1740 (s, C=O); 1200 (vs, C–F). MS *m/z* (%): 411 (M^++1, 100); 413 (M^++1, 73.67); 331 (50.34); 333 (21.47). Analysis: Calc. for $C_{11}H_{16}Br_2F_2O_4$ (FW 410): C, 32.20; H, 3.90; F, 9.27%. Found: C, 32.45; H, 3.86; F, 9.87%.

Preparation of KF/Al_2O_3 [8]

To 250 ml of water was added 20 g of KF (or 34 g of KF·$2H_2O$) and 30 g of natural alumina. The water was removed on a rotary evaporator at 50–70 °C, and the solid was then dried at 50 °C on a vacuum pump for 2 h until it became powdery. This KF/Al_2O_3 corresponded to 7 mmol F/1 g powder.

Dehydrobromination of 1,3-dibromides in the presence of KF/Al_2O_3. General procedure

A suspension consisting of 20 ml of acetonitrile or DMF (both commercial samples), 10 mmol of a 1,3-dibromide and 25 mmol of the above KF/Al_2O_3 powder was stirred at 40–50 °C for several hours. After the ^{19}F NMR and GC spectra showed that the 1,3-dibromide had been completely consumed, the mixture was filtered off. The filtrate was poured into water and extracted with diethyl ether (3×15 ml). The combined ethereal extracts were washed successively with saturated aq. $NaHSO_3$ solution, water and brine, and then dried over Na_2SO_4. After removal of diethyl ether, the residue was distilled under reduced pressure to give the pure products.

1-Bromo-1,1-difluorohept-2-ene (**4a**): Volatile colourless oil, b.p. 78–87 °C/60 mmHg. ^{19}F NMR δ: −39 (s, 2F×5%, CF_2Br, *E* isomer); −33.5 (s, 2F×95%, CF_2Br, *Z* isomer) ppm. ^{1}H NMR δ: 6.8–6.6 (m, 2H, CH=CH); 2.6–2.4 (m, 2H, CH_2CH=); 1.8–0.8 (m, 7H, C_3H_7) ppm. IR $\nu_{max.}$ (cm^{-1}): 2950 (s, C–H); 1650 (m, C=C); 1180 (s, C–F). MS *m/z* (%): 212 (M^+, 0.95); 214 (M^+, 0.95); 133 (M^+−Br, 37.61); 83 (CF_2Br^+, 11.08); 77 (CF_2CH=CH^+, 100); 57 ($C_4H_9^+$, 11); 53 ($C_3H_5^+$, 42.41). Analysis: Calc. for $C_7H_{11}BrF_2$ (FW 213): C, 39.44; H, 5.16; f, 17.84; Br, 37.56%. Found: C, 39.49; H, 5.17; F, 17.28; Br, 37.60%.

1-Bromo-1,1-difluorononon-2-ene (**4b**) [6]: Volatile colourless oil, b.p. 92–95 °C/60 mmHg. ^{19}F NMR δ: −40 (s, 2F×9%, CF_2Br, *Z* isomer); −35 (s, 2F×91%, CF_2Br, *E* isomer) ppm. ^{1}H NMR δ: 6.6–5.4 (m, 2H, CH=CH); 2.1 (m, CH_2C=); 1.8–0.8 (m, 11H, C_5H_{11}) ppm.

1-Bromo-1,1-difluorohept-2,6-diene (**4c**): Volatile colourless oil, b.p. 58–62 °C/30 mmHg. ^{19}F NMR δ: −39 (s, 2F×16%, CF_2Br, *E* isomer); −34 (s, 2F×84%, CF_2Br, *Z* isomer) ppm. ^{1}H NMR δ: 6.3 (m, 2H, CH=CH); 5.1–5.0 (m, 3H, CH=CH_2); 2.3–2.2 (m, 4H, CH_2CH_2) ppm. IR $\nu_{max.}$ (cm^{-1}): 1680, 1660 (w, C=C); 1200 (s, C–F). MS *m/z* (%): 211 (M^++1, 7.03); 213 (M^++1, 6.21); 131 (M^+−Br, 100). Analysis: Calc. for $C_7H_9BrF_2$ (FW 211): HRMS: 211.9833. Found: HRMS: 211.9876.

1-Bromo-1,1-difluorohept-2-en-6-one (**4d**): Volatile colourless oil, b.p. 78–87 °C/60 mmHg. ^{19}F NMR δ: −36 (s, 2F×12%, CF_2Br, *E* isomer); −34 (s, 2F×88%, CF_2Br, *Z* isomer) ppm. ^{1}H NMR δ: 6.5–5.9 (m, 2H, CH=CH); 3.2–1.8 (m, 7H, others) ppm. IR $\nu_{max.}$ (cm^{-1}): 1720, 1700 (s, C=O); 1660 (m, C=C); 1120, 1160 (s, C–F). MS *m/z* (%): 227 (M^++1, 6.34); 229 (M^++1, 6.67); 226 (M^+, 2.55); 228 (M^+, 2.2); 211 (3.77); 213 (3.66); 183 (M^+−Ac, 1.34); 185 (M^+−Ac, 1.28); 147 (M^+−Br, 21.57); 103 (13.38); 43 (100). Analysis: Calc. for $C_7H_9BrF_2O$ (FW 227): HRMS: 226.9880 (^{79}Br); 228.9860 (^{81}Br). Found: HRMS: 226.9850 (^{79}Br); 228.9860 (^{81}Br).

Methyl 11-bromodifluoroundecenoate (**4e**): Colourless oil, b.p. 123–125 °C/1 mmHg. ^{19}F NMR δ: −39 (s, 2F×12%, CF_2Br, *E* isomer); −33.5 (s, 2F×88%, CF_2Br, *Z* isomer) ppm. ^{1}H NMR δ: 6.25–6.15 (m, 1H, CH=CH); 5.90–5.80 (m, 1H, CH=CH); 3.65 (s, 3H, OMe); 2.3 (t, $^3J_{HH}$=3.5 Hz, 2H, CH_2CO); 2.15 (dt, J_{HH}=6 Hz, 2H, CH_2CH=CH); 1.5–1.0 (m, 12H, 6×CH_2) ppm. IR $\nu_{max.}$ (cm^{-1}): 2900 (s, C–H); 1740 (s, C=O); 1660 (s, C=C); 1220, 1180 (s, C–F); 660 (s, C–Br). MS *m/z* (%): 327 (M^++1, 1.35); 329 (M^++1, 1.66); 295 (M^+−OMe, 1.81); 297 (M^+−OMe, 1.43); 307 (7.98); 309 (8.43); 247 (34.61); 175 (46.89); 55 (100). Analysis: Calc. for $C_{13}H_{21}BrF_2O_2$ (FW 327): C, 47.71; H, 6.42; F, 11.62%. Found: C, 47.62; H, 6.45; F, 11.98%.

Bromodifluoromethylcyclohex-1-ene (**4f**): Volatile colourless oil, b.p. 78–80 °C/60 mmHg. ^{19}F NMR δ: −29.5 (s, CF_2Br) ppm. ^{1}H NMR δ: 7.2 (s, 1H, CH=); 2.10 (m, 4H, CH_2CH=CCH_2); 1.7 (t, $^3J_{HH}$=2 Hz, 4H, CH_2CH_2) ppm. IR $\nu_{max.}$ (cm^{-1}): 1640 (s, C=C); 1280 (s, C–F). Analysis: Calc. for $C_7H_9BrF_2$ (FW 211): C, 39.81; H, 4.27; Br, 37.91%. Found: C, 39.94; H, 4.55; Br, 36.60%.

Bromodifluoromethylallyl acetate (**4g**): Volatile colourless oil, b.p. 77–79 °C/60 mmHg. ^{19}F NMR δ: −36 (s, 2F×5%, CF_2Br, *E* isomer); −33.5 (s, 2F×95%, CF_2Br, *Z* isomer) ppm. ^{1}H NMR δ: 6.3 (m, 1H, CH=); 5.3–4.2 (m, 3H, CH_2CH=); 2.0 (s, 3H, Ac) ppm. IR $\nu_{max.}$ (cm^{-1}): 1750 (s, C=O); 1710 (w, C=C); 1220 (s, C–F). MS *m/z* (%): 229 (M^++1, 2.14); 231 (M^++1, 1.79); 169 (M^+−OAc, 16.23); 171 (M^+−OAc, 15.30); 90 (13.03); 44 (100). Analysis: Calc. for $C_5H_7BrF_2O_2$ (FW 229): C, 31.44; H, 3.06; F, 16.59%. Found: C, 31.52; H, 3.08; F, 16.66%.

1-Bromo-1,1-difluoro-4-chlorobut-2-ene (**4i**): Volatile colourless oil, b.p. 110–115 °C. ^{19}F NMR δ: −31.5 (s, 2F, CF_2Br) ppm. ^{1}H NMR δ: 6.25 (m, 2H, CH=CH);

4.15 (m, 2H, CH_2Cl) ppm. IR $\nu_{max.}$ (cm^{-1}): 1720 (s, C=C); 1220 (s, C–F); 740 (s, C–Cl); 660 (s, C–Br). MS *m/z* (%): 204 (M^+, 1.51); 169 ($M^+ - Cl$, 12.36); 171 ($M^+ - Cl$, 10.91); 125 (100); 127 (33.21).

Diethyl 2-bromodifluoromethylmethyl-1,1-cyclopropanedicarboxylate (**5**): Colourless oil, b.p. 120–125 °C/5 mmHg. ^{19}F NMR δ: −34 (s, CF_2Br) ppm. ^1H NMR δ: 4.2 (q, $^3J_{HH}=7$ Hz, 4H, 2×OEt); 2.8–2.1 (m, 3H, CF_2CH_2CH); 1.50 (d, $^3J_{HH}=8$ Hz, 2H, cyclo-CH_2); 1.26 (t, $^3J_{HH}=7$ Hz, 6H, 2×OEt) ppm. ^{13}C NMR δ: 168–167 (s, C=O); 121 (t, $^2J_{FC}=300$ Hz, CF_2); 61 (OCH_2); 42.7 (t, $^3J_{FC}=22$ Hz, CF_2CH_2); 32 (s, cyclo-C); 21.5 (t, $^4J_{FC}=5$ Hz, cyclo-CH); 19.6 (cyclo-CH_2); 13.7 (CH_3) ppm. IR $\nu_{max.}$ (cm^{-1}): 1740, 1720 (s, C=O); 1280, 1220 (s, C–F). MS *m/z* (%): 329 ($M^+ + 1$, 100); 331 ($M^+ + 1$, 88.42); 283 ($M^+ - OEt$, 42.70); 285 ($M^+ - OEt$, 49.37); 250 (5.09). Analysis: Calc. for $C_{11}H_{15}BrF_2O_4$ (FW 328): C, 40.24; H, 4.57; F, 11.59; Br, 24.39%. Found: C, 39.88; H, 4.60; F, 11.97; Br, 24.71%.

1,2,3-Tribromo-1,1-difluoroheptane (**9**): Colourless oil, b.p. 115–117 °C/4 mmHg. ^{19}F NMR δ: −33.0 (AB, $J=200$ Hz, CF_2Br) ppm. ^1H NMR δ: 5.2–3.8 (m, 2H, CHBrCHBr); 2.3–0.8 (m, 9H, C_4H_9) ppm. IR $\nu_{max.}$ (cm^{-1}): 1080 (s, C–F); 690, 680, 655 (m, C–Br). MS *m/z* (%): 290 (2.10); 211 (23.2); 213 (21.5); 131 (100). Analysis: Calc. for $C_7H_{11}Br_3F_2$ (FW 373): C, 22.52; H, 2.95; F, 10.19; Br, 66.34%. Found: C, 22.49; H, 2.85; F, 9.98; Br, 66.61%.

1,2-Dibromo-1,1-difluorohept-2-ene (**10**). Volatile colourless oil, b.p. 83–84 °C/15 mmHg. ^{19}F NMR δ: −38 (s, 2F×42%, CF_2Br, *E* isomer); −32 (s, 2F×58%, CF_2Br, *Z* isomer) ppm. ^1H NMR δ: 1.6 (t, $^3J_{HH}=7.5$ Hz, 1H, CH=); 2.4 (m, 2H, CH_2C=); 1.8–0.9 (m, 4H, CH_2CH_2); 0.8 (t, $^3J_{HH}=2$ Hz, 3H, CH_3) ppm. IR $\nu_{max.}$ (cm^{-1}): 1630 (m, C=C); 1100 (s, C–F); 695 (s, C=C). MS *m/z* (%): 290 (M^+, 2.15); 292 (M^+, 3.99); 294 (M^+, 2.12); 211 (24); 213 (20.8); 131 (100). Analysis: Calc. for $C_7H_{10}Br_2F_2$ (FW 292): C, 28.77; H, 3.42; F13.01%. Found: C, 28.85; H, 3.35; F, 12.95%.

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