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Journal of Fluorine Chemistry 86 (1997) 89–97

JOURNAL OF FLUORINE CHEMISTRY

$Na_2S_2O_4/NaHCO_3$-system promoted addition–cyclization of per(poly)fluoroalkyl iodides or perhaloalkanes with 1,6-heptadienes

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Received 12 November 1996; accepted 19 May 1997

Abstract

An efficient and practical synthetic method for the preparation of five-membered ring compounds is reported. Carbocyclic and heterocyclic five-membered ring compounds bearing polyfluoroalkyl groups were obtained using $Na_2S_2O_4/NaHCO_3$ promoted addition–cyclization of per(poly)fluoroalkyl iodides or perhaloalkanes with 1,6-heptadienes. The stereochemistry of hydrodehalogenation products (**5**, **6**, **8**, **9**) was determined based on their ^{1}H-NMR spectra. γ-Lactams and γ-lactones bearing fluoroalkyl groups were obtained using the same system promoted per(poly)fluoroalkylation reaction with *N*-allyl acrylamides (**10**) and allyl propiolate (**15**) under similar reaction conditions. © 1997 Elsevier Science S.A.

Keywords: Sodium dithionate; Perhaloalkylation; Fluoroalkylated five-membered ring compound

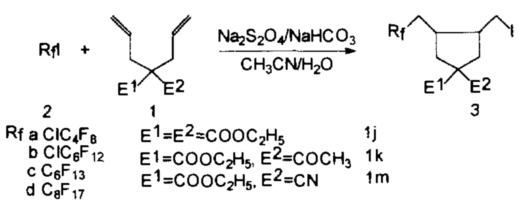
1. Introduction

The development of radical reactions for synthetic purposes has been an area of active research since the early eighties [1]. Synthetic applications of radical addition–cyclization of 1,6-dienes to give cyclopentylmethyl radicals as reactive intermediates have received much attention in recent years [1,2]. Brace reported the radical cyclization of hepta-1,6-diene with perfluoroalkyl iodides (R_fI) to produce five-membered ring compounds using azoisobutylonitrile (AIBN) as initiator [3]. In the course of our research on radical addition of per(poly)fluoroalkyl iodides to alkenes using $Na_2S_2O_4/NaHCO_3$ [4], we found that the reagent system could initiate effectively addition reactions of per(poly)fluoroalkyl iodides or perhalogenated alkanes to 1,6-heptadiene. The reaction shows good stereo- and regioselectivity of adducts and provides a useful route to five-membered ring compounds containing perhalogenated alkyl groups.

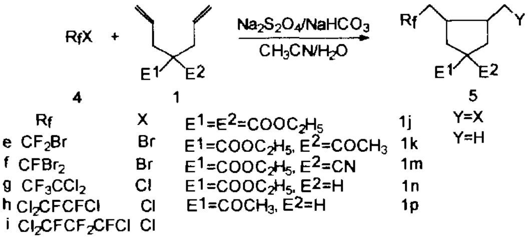
2. Results and discussions

Initially, we studied the reactions of per(poly)fluoroalkyl iodides (R_fI) with diallylmalonates and related compounds in the presence of a stoichiometric amount of $Na_2S_2O_4$ and $NaHCO_3$ and showed that the corresponding addition–cyclization products were obtained exclusively under mild conditions (Schemes 1 and 2).

Thus, addition reactions of diethyl diallylmalonate (**1j**) and related compound **1m** with per(poly)fluoroalkyl iodides (**2**) in the presence of the $Na_2S_2O_4/NaHCO_3$ system in aqueous CH_3CN at 20–40 °C takes place smoothly in 30 min to 1 h. The results are shown in Table 1. The per(poly)fluoroalkylmethyl cyclopentanes (**3**) are formed in good yields. The products are purified by distillation. Neither bis-addition



Scheme 1.



Scheme 2.

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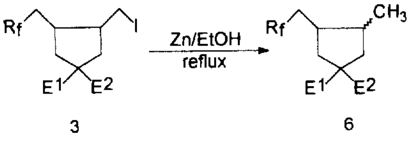
PII S0022-1139(97)00067-5

Table 1
$Na_2S_2O_4$/$NaHCO_3$ promoted addition–cyclization of R_fX (**2**,**4**) to 1,6-heptadiene (**1**)

Entry No.	Hepta-1,6-diene	R_fX	Temp./Time (°C)/(h)	Isolated yield (%)	6(5)-cis :6(5)-trans
1	**1j**	**2a**	25/0.5	**3aj**, 88; **6aj**, 82	11.0 : 1 [a]
2	**1j**	**2b**	25/1.0	**3bj**, 86; **6bj**, 81	10.0 : 1 [a]
3	**1j**	**2c**	25/1.0	**3cj**, 85; **6cj**, 84	10.6 : 1 [a]
4	**1m**	**2a**	25/0.5	**3am**, 85; **6am**, 83	8.5 : 1 [a]
5	**1m**	**2b**	25/1.0	**3bm**, 82; **6bm**, 82	5.6 : 1 [a]
6	**1j**	**4e**	0–5/20	**5ej**, 81	– [a]
7	**1m**	**4e**	0–5/20	**5em**, 78	– [a]
8	**1n**	**4e**	0–5/20	**5en**, 75	– [a]
9	**1j**	**4f**	40/20	**5fj**, 51	– [b]
10	**1m**	**4f**	40/20	**5fm**, 62	– [b]
11	**1n**	**4f**	40/20	**5fn**, 58	– [b]
12	**1k**	**4g**	30/18	**5gk**, 79	5.0 : 1 [c]
13	**1m**	**4g**	30/18	**5gm**, 82	6.0 : 1 [c]
14	**1p**	**4g**	30/18	**5gp**, 76	6.0 : 1 [c]
15	**1j**	**4h**	30/15	**5hj**, 55	7.5 : 1 [c]
16	**1m**	**4h**	30/15	**5hm**, 50	8.0 : 1 [c]
17	**1j**	**4i**	30/15	**5ij**, 41	3.0 : 1 [c]
18	**1m**	**4i**	30/15	**5im**, 43	4.0 : 1 [c]

[a] Volume ratio $CH_3CN : H_2O = 1 : 1$.
[b] Volume ratio $CH_3CN : H_2O = 10 : 1$.
[c] Volume ratio $DMF : H_2O = 5 : 1$.

nor telomers are obtained under these conditions. Only a small amount of R_fSO_2Na is formed as a by-product. The ratio of organic solvent and water could be varied from 1 : 1 to 10 : 1. The reaction could also be accelerated by using a slight excess of $Na_2S_2O_4$. The structure of product **3** is assigned on the basis of the ^1H-NMR spectra of **6** which are produced in good yields by reductive deiodination of product **3** with zinc powder in EtOH (Eq. (1)). As expected, the cis isomer predominates. Little change is observed in the stereoselectivity by changing the chain length of the perfluoroalkyl group and the volume ratio of CH_3CN/H_2O.



(1)

For example, the configuration of the major isomer of **6cj** is established by application of a series of ^1H-NMR selective decoupling experiments and two-dimensional ^1H-NMR measurements. The 2D NOESY ^1H-NMR spectrum clearly showed a cross diagonal peak between the Ha and Hb to prove that the major isomer possesses a cis-configuration (Fig. 1). The other cyclization products show ^1H-NMR spectra similar to that of **6cj**.

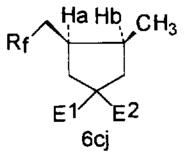
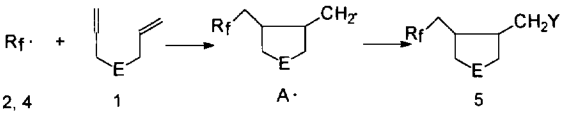


Fig. 1. The configuration of the major isomer of product **6cj**.

In a similar way, reactions of perhaloalkanes **4** with **1** give products in moderate to good yields using an excess of **1** at 0–40 °C (Scheme 1). Interestingly, the reaction of **1** with **4g**, **4h**, **4i** gave the hydrodechlorination product **5** (Y = H), however, with **2**, **4e**, **4f** yielded the normal adducts **5** (Y = I,Br). These results are in agreement with the known fact that the intermediate radical, A, would attack the R_f–X bond (X = I, Br) to give the normal chain transfer products, **5** (Y = I, Br). But a similar chain transfer reaction did not occur in the case of perfluorochloro compounds, due to a higher bond strength of R_f–Cl as compared with that of R_f–Br and R_f–I, so the intermediate radical, A, was eventually reduced further by SO_2^- to the corresponding anion, a$^-$, which then picked up a proton from the reaction medium to give the hydrodechlorination product, **5** (Y = H).



(2)

We also prepared heterocyclic compounds, namely pyrrolidine derivatives, by the reaction of **7** with **2** or **4** in the presence of $Na_2S_2O_4$/$NaHCO_3$ at 0–40 °C (Scheme 3) and the results are shown in Table 2.

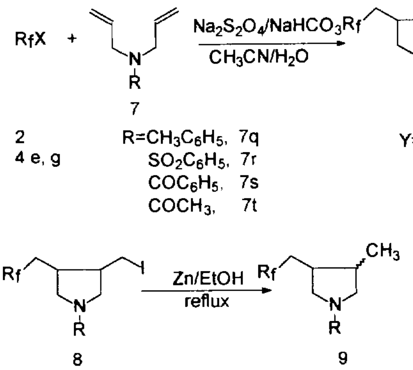
The mono-adducts are obtained in moderate yields. The reaction time is longer than that of the cyclopentane derivatives and we find that the resulting iodides or bromides are not very stable at room temperature. The structures of the products are determined by ^1H NMR similar to that of the above carbocyclic compounds. But, the cis/trans ratio of **9** decreases to 3 : 1 (cf. Scheme 3).

We then studied the addition–cyclization reaction of per(poly)fluoroalkyl iodides **2** to *N*-allyl acrylamides **10** or

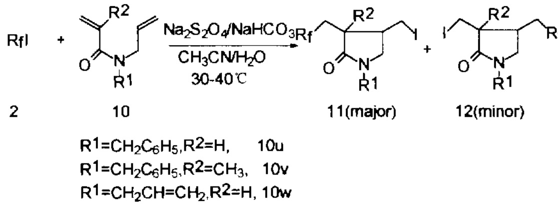
Table 2
$Na_2S_2O_4/NaHCO_3$ promoted addition–cyclization of R_fX (**2**, **4**) to 1,6-heptadiene (**7**) and the reduction of **8** with zinc powder in EtOH to give **9**

Entry No.	Hepta-1,6-diene	R_fX	Temp./Time (°C)/(h)	Isolated yield (%)	6(5)-cis :6(5)-trans
1	**7t**	**2a**	0–40/3.0	**8at**, 68; **9at**, 76	3.1 : 1 [a]
2	**7q**	**2c**	0–40/3.0	**8cq**, 59; **9cq**, 71	3.0 : 1 [a]
3	**7r**	**2c**	0–40/3.0	**8cr**, 57; **9cr**, 74	3.0 : 1 [a]
4	**7r**	**4e**	0–5/20	**8er**, 62	– [b]
5	**7s**	**4e**	0–5/20	**8es**, 72	– [b]
6	**7q**	**4g**	30/18	**8gq**, 68	7.0 : 1 [c]
7	**7r**	**4g**	30/18	**8gr**, 76	7.0 : 1 [c]
8	**7s**	**4g**	30/18	**8gs**, 75	7.0 : 1 [c]

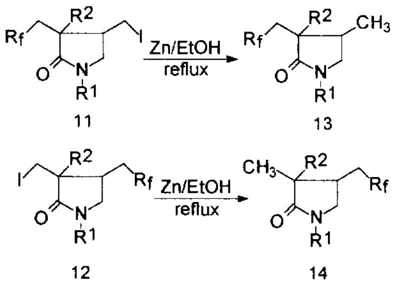
[a] Volume ratio $CH_3CN : H_2O = 5 : 1$.
[b] Volume ratio $CH_3CN : H_2O = 1 : 1$.
[c] Volume ratio $DMF : H_2O = 5 : 1$.



Scheme 3.



Scheme 4.



Scheme 5.

allyl propiolate (**15**) which gave per(poly)fluoroalkylmethyl–γ-lactams or –γ-lactones respectively in good yields. Thus, treatment of a mixture of *N*-allyl acrylamides **10** (1 eq) and per(poly)fluoroalkyl iodides **2** (1.5 eq) with sodium dithionite (1.2 eq) and sodium bicarbonate (1.2 eq) at 30–40 °C in aqueous acetonitrile furnished polyfluoroalkylated γ-lactams (Scheme 4). The detailed results are shown in Table 3.

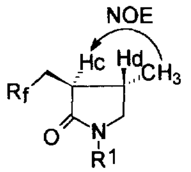
In most cases, a mixture of γ-lactams **11** (major) and **12** (minor) is obtained within minutes in good yield, except that the reaction of **10v** with **2** yields **11** exclusively. The pyrrolidinones **11** and **12** could be separated by flash column chromatography using ethyl acetate–petroleum ether as eluent. Reductive deiodination of **11** or **12** using zinc powder in EtOH under reflux lead to the corresponding lactams **13** or **14** in good yields (Scheme 5).

It is worth mentioning that, in the present case, the electrophilic per(poly)fluoroalkyl radical attacks preferentially the electron deficient acrylic double bond rather than the electron-rich allylic one, apparently due to the stabilization of the intermediate free radical conjugated to a carbonyl group through spin delocalization. The assignment of the configurations of **11**, **12**, **13** and **14** is based on a series of ^1H-NMR

Table 3
$Na_2S_2O_4/NaHCO_3$ initiated addition–cyclization of R_fI (**2**) to 1,6-heptadiene (**10**) or 1,6-heptayne-ene (**15**) and reduction of the product using zinc powder in EtOH

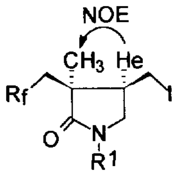
Entry no.	Hepta-1,6-diene Hepta-1,6-yne-ene	R_fI	Isolated yield (%)	Isolated yield (%) (cis : trans)
1 [a]	**10u**	**2a**	**11au**, 72; **12au**, 3.5	**13au**, 94(1 : 6); **14au**, 93(5.8 : 1)
2 [a]	**10u**	**2c**	**11cu**, 84; **12cu**, 3.1	**13cu**, 95(1 : 7); **14cu**, 94(6.2 : 1)
3 [b]	**10v**	**2c**	**11cv**, 58	**13cv**, 92(100 : 0)
4 [b]	**10w**	**2a**	**11aw**, 78; **12aw**, 7.4	**13aw**, 92(1 : 18); **14aw**, 91(8.0 : 1)
5 [b]	**15**	**2a**	**16a**, 41.5; **17a**, 42	
6 [b]	**15**	**2c**	**16c**, 40; **17c**, 41	

[a] Volume ratio $CH_3CN : H_2O = 5 : 1$.
[b] Volume ratio $CH_3CN : H_2O = 10 : 1$.



13av

Fig. 2. The configuration of compound **13av**.

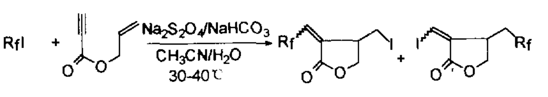


11bv

Fig. 3. The configuration of compound **11bv**.

selective decoupling experiments and two-dimensional ^1H–^1H NOESY measurements (Figs. 2 and 3).

Finally, we examined the reaction of per(poly)fluoroalkyl iodides **2** with allyl propynonate **15** under similar reaction conditions (Eq. (3)). The results are listed in Table 3. It is interesting to point out that some of our present work touches common ground with that recently reported in the literature [5], in which a moderate yield of compound **17** from the reaction of compound **15** with R_fI in the presence of $Na_2S_2O_4$ and $NaHCO_3$ was recorded. However, we are able to show that under similar reaction conditions, per(poly)fluoroalkyl radical attacks both the reactive sites of substrate **15** to form γ-lactones **16** and **17** in a ratio of about 1 : 1 (Table 3).



(3)

2 15 16 17

In summary, we have developed an efficient and practical synthetic method for the preparation of carbocyclic and heterocyclic five-membered-ring compounds as well as γ-lactams, γ-lactones bearing fluoroalkyl groups using the $Na_2S_2O_4/NaHCO_3$ system promoting a per(poly)fluoroalkylation reaction under mild conditions.

3. Experimental

All melting points and boiling points were uncorrected. IR spectra were measured with a Shimadzu IR-440 spectrometer using liquid films and KBr pellets for solids. ^1H-NMR spectra were recorded on Varian EM-360A, FX-90Q, AM-200 and AMX-600 spectrometers using TMS as internal standard. ^{19}F-NMR spectra were recorded on an EM-360L spectrometer at 56.4 MHz using TFA as external standard. In ^{19}F-NMR spectra, chemical shifts (ppm) were positive for upfield shifts. Mass and HRMS spectra were taken on a Finnigan GC-MS-4021 Spectrometer. Elemental analysis data were obtained by the Elemental Analysis Group of SIOC.

3.1. General procedure

A mixture of 1,6-diene (**1**, **7**, **10**, **15**) (10 mmol), R_fX (**2**, **4**) (12 mmol), $Na_2S_2O_4$ (1.0 g), $NaHCO_3$ (0.5 g), organic solvent (such as CH_3CN, CH_2Cl_2, DMF) and water ($V_{\text{organic solvent}}/V_{H2O}$ = 1 : 1–10 : 1) was stirred at 0–49 °C for 0.5–24 h. After the completion of the reaction, the mixture was extracted with ether (3×30 ml), and the organic layer was washed with brine, then dried over Na_2SO_4. After the removal of ether, the crude product was purified by column chromatography or distillation under reduced pressure to give pure product. Then a mixture of the above products (5 mmol), Zn dust (6 mmol) and 20 ml EtOH was stirred under reflux for 6–12 h and worked-up to yield reductive dehalogenation products.

*3.1.1. Compound **3aj**: colourless oil, bp 98–100 °C/ 0.01 mmHg*

γ_{max} (cm^{-1}): 1730, 1720 (s, C=O), 1250 and 1100 (C–F); ^1H-NMR ($CDCl_3$), δH 1.25 (t, $^3J_{HH}$=7.0, 6H), 2.0–2.8 (m, 8H), 3.1 (dt, $^3J_{HH}$=8, $^2J_{HH}$=16.0, 1H), 3.3 (dd, $^3J_{HH}$=4, $^2J_{HH}$=16.0, 1H) and 4.2 (q, $^3J_{HH}$=7.0, 4H); ^{19}F-NMR (CCl_4), δF −9.0 (s, 2F), 38.5 (s, 2F) and 44.5 (s, 2F); MS (*m/z*) 603 (M^++1, 100%) and 474 (M^+–HI, 5.70); Elemental Analysis (for $C_{17}H_{20}ClF_8IO_4$): Found: C 33.70; H 3.40; Cl 5.79; F 25.11; I 22.80%; Calcd: C 33.88, H 3.34; F 25.22; Cl 5.88; I 21.06%.

*3.1.2. Compound **3bj**: colourless oil, bp 120–124 °C/ 0.01 mmHg*

γ_{max} (cm^{-1}) 1730, 1720 (s, C=O), 1250 and 1200 (C–F); ^1H-NMR ($CDCl_3$), δH 1.25 (t, $^3J_{HH}$=7.0, 6H), 2.0–2.8 (m, 8H), 3.1 (dt, $^3J_{HH}$=8, $^2J_{HH}$=16.0, 1H), 3.3 (dd, $^3J_{HH}$=4, $^2J_{HH}$=16.0, 1H) and 4.2 (q, $^3J_{HH}$=7.0, 4H); ^{19}F-NMR (CCl_4), δF −8.5 (s, 2F), 37.0 (m, 2F) and 43.5–47.5 (m, 8F); MS (*m/z*) 703 (M^++1, 100%) and 474 (M^+–C_2F_4–HI, 1.65); Elemental Analysis (for $C_{19}H_{20}ClF_{12}IO_4$): Found: C 33.68; H 3.12; Cl 5.10; F 32.09; I 17.91%; Calcd: C 32.48, H 2.87; F 32.44; Cl 5.05; I 18.05%

*3.1.3. Compound **3cj**: colourless oil, bp 125–126 °C/ 0.01 mmHg*

γ_{max} (cm^{-1}) 1730, 1720 (s, C=O); ^1H-NMR ($CDCl_3$), δH 1.25 (t, $^3J_{HH}$=7.0, 6H), 2.0–2.8 (m, 8H), 3.1 (dt, $^3J_{HH}$=8, $^2J_{HH}$=16.0, 1H), 3.3 (dd, $^3J_{HH}$=4, $^2J_{HH}$=16.0, 1H) and 4.2 (q, $^3J_{HH}$=7.0, 4H); ^{19}F-NMR (CCl_4), δF 4.5 (s, 3F), 38.0 (m, 2F) and 44.0–48.0 (m, 8F); MS (*m/z*) 784 (M^+, 100%) and 638 (M^+-$2C_2H_5$, 5.63); Elemental Analysis (for $C_{21}H_{20}F_{17}IO_4$): Found: C 32.18; H 2.46; F 42.32; I 16.10%; Calcd: C 32.08, H 2.56; F 41.08; I 16.14%

*3.1.4. Compound **3am**: waxy solid*

γ_{max} (cm^{-1}) 2250, 1720 (s, C=O); ^1H-NMR ($CDCl_3$), δH 1.25 (t, $^3J_{HH}$=7.0, 3H), 2.0–2.8 (m, 8H), 3.2–3.5 (m, 2H) and 4.2 (q, $^3J_{HH}$=7.0, 2H); ^{19}F-NMR (CCl_4), δF −9.5 (s, 2F), 37.5 (m, 2F), 38.5 (s, 2F) and 44.5 (s, 2F); MS (*m*/*z*) 543 (M^+, 100%) and 514 (M^+–C_2H_5, 67); HRMS (for $C_{15}H_{15}ClF_8INO_2$): Found: 543.6185; Calcd: 543.6190.

3.1.5. Compound **3bm**: colourless oil, bp 98 °C/0.01 mmHg

γmax (cm^{-1}) 2250, 1720 (s, C=O); ^{1}H-NMR ($CDCl_3$), δH 1.25 (t, $^3J_{HH}$ = 7.0, 3H), 2.02.8 (m, 8H), 3.2–3.5 (m, 2H) and 4.2 (q, $^3J_{HH}$ = 7.0, 2H); ^{19}F-NMR (CCl_4), δF −8.5 (s, 2F), 38.0 (m, 2F) and 44.0–48.0 (m, 8F); MS (*m*/*z*) 608 (M^+, 100%) and 579 (M^+–C_2H_5, 46); HRMS (for $C_{17}H_{15}NClF_{12}IO_2$): Found: 608.1809; Calcd: 608.1805

3.1.6. Compound **5ej**: colourless oil

γmax (cm^{-1}): 1740 (s, C=O), 1200, ^{1}H-NMR ($CDCl_3$), δH (ppm): 1.30 (t, $^3J_{HH}$ = 7.0 Hz, 6H), 2.3–2.7 (m, 8H), 3.3 (m, 2H); 4.3 (q, $^3J_{HH}$ = 7.0 Hz, 4H); ^{19}F-NMR ($CDCl_3$), δF (ppm): −36.2 (dd, 2F); MS (*m*/*z*): 451 (M^+ + 1, 13.75); 173 (100); HRMS ($C_{14}H_{20}O_4Br_2F_2$): Found: 447.9665; Calcd: 447.9996;

3.1.7. Compound **5em**: colourless oil

γmax (cm^{-1}): 2400, 1740 (s, C=O), 1200, ^{1}H-NMR ($CDCl_3$), δH (ppm): 1.40 (t, $^3J_{HH}$ = 7.0 Hz, 3H); 2.2–2.8 (m, 8H), 3.4 (m, 2H); 4.3 (q, $^3J_{HH}$ = 7.0 Hz, 2H); ^{19}F-NMR ($CDCl_3$), δF (ppm): −36.6 (dd, 2F); MS (*m*/*z*): 404 (M^+ + 1, 6.72), 331 (M^+–CO2Et + 1, 66.07), 150 (100); HRMS ($C_{12}H_{15}F_2Br_2O_2N$): Found: 400.9461; Calcd: 400.9438;

3.1.8. Compound **5en**: colourless oil

γmax (cm^{-1}): 1740 (s, C=O), 1200; ^{1}H-NMR ($CDCl_3$), δH (ppm): 1.20 (t, $^3J_{HH}$ = 7.0 Hz, 3H), 1.7–2.9 (m, 9H), 3.3 (dm, 2H); 4.1 (q, . $^3J_{HH}$ = 7.0 Hz, 2H); ^{19}F-NMR ($CDCl_3$), δF (ppm): −37.3 (dd, 2F); MS (*m*/*z*): 379 ($M^{\pm}1$, 56.16); 300 (M^+–Br, 25.7); HRMS: (for $C_{11}H_{16}O_2F_2Br_2$): Found: 379.9435; Calcd: 379.9444.

3.1.9. Compound **5fj**: colourless oil

γmax (cm^{-1}): 1740 (s, C=O), 1200, ^{1}H-NMR ($CDCl_3$), δH (ppm): 1.3 (t, $^3J_{HH}$ = 7.0 Hz, 6H); 1.8–2.2 (m, 4H), 2.5–2.9 (m, 5H), 4.3 (q. $^3J_{HH}$ = 7.0 Hz, 4H); ^{19}F-NMR ($CDCl_3$), δF (ppm): −32.0 (dd, 2F); MS (*m*/*z*): 509 (M^+ + 1, 3.48), 387 (M^+–Br, 7.86), 173 (100); HRMS: (for $C_{14}H_{20}O_4FBr_3$): Found: 511.8856; Calcd: 511.8855.

3.1.10. Compound **5fm**: colourless oil

γmax (cm^{-1}): 2420, 1740 (s, C=O), 1200; ^{1}H-NMR ($CDCl_3$), δH (ppm): 1.3 (t, $^3J_{HH}$ = 7.0 Hz, 3H); 2.3–3.0 (m, 8H), 3.4 (m, 2H); 4.3 (q, $^3J_{HH}$ = 7.0 Hz, 2H); ^{19}F-NMR ($CDCl_3$), δF (ppm): −33.0 (dd, 2F); MS (*m*/*z*)): 461 (M^+, 10.15), 384 (M^+–Br + 1, 97.81), 106 (100); HRMS (for $C_{12}H_{15}NO_2FBr_3$): Found: 460.8686; Calcd: 460.8636.

3.1.11. Compound **5fn**: colourless oil

γmax (cm^{-1}): 1740 (s, C=O), 1200, ^{1}H-NMR ($CDCl_3$), δH (ppm): 1.3 (t, $^3J_{HH}$ = 7.0 Hz, 3H); 1.8–22 (m, 4H), 2.5–2.9 (m, 5H), 4.2 (q, $^3J_{HH}$ = 7.0 Hz, 2H); ^{19}F-NMR ($CDCl_3$), δH (ppm): −32.0 (dd, 2F); MS (*m*/*z*): 439 (M^+–1, 3.00), 359 (M^+–Br, 58.1), 79 (100); HRMS: (for $C_{11}H_{16}O_2FBr_3$): Found: 439.8637; Calcd: 439.8643.

3.1.12. Compound **5gk**: colourless oil

γmax (cm^{-1}): 1740, 1700, 1200; ^{1}H-NMR ($CDCl_3$), δH (ppm): 0.84 (d, ^{12}J = 6.8 Hz), 0.98 (d, ^{12}J = 6.1 Hz) (3H); 1.25 (t, $^3J_{HH}$ = 7.0 Hz, 3H); 2.1–2.9 (m, 11H); 4.15 (q, $^3J_{HH}$ = 7.0 Hz, 2H); ^{19}F-NMR ($CDCl_3$), δH (ppm): 1.8 (s, 3F); MS (*m*/*z*): 363 (M^+ + 1, 13.39), 320 (M^+–OC_2H_5, 100); HRMS ($C_{14}H_{19}F_3Cl_2O_3$): Found: 362.0707; Calcd: 362.0663;

3.1.13. Compound **5gm**: colourless oil

γmax (cm^{-1}): 2400, 1740 (s, C=O), 1100; ^{1}H-NMR ($CDCl_3$), δH (ppm): 0.9 (d, ^3J = 7.0 Hz), 1.2 (d, ^3J = 6.1 Hz) (3H), 1.35 (t, $^3J_{HH}$ = 7.0 Hz, 3H); 2.1–2.7 (m, 8H); 4.3 (q, $^3J_{HH}$ = 7.0 Hz, 2H); ^{19}F-NMR ($CDCl_3$), δF (ppm): 2.0 (s, 3F); MS (*m*/*z*): 346 (M^+, 10.38), 273 (M^+–2Cl + 1, 67.06), 238 (100); HRMS ($C_{13}H_{16}F_3Cl_2O_2N$–OC_2H_5): Found: 317.0170; Calcd: 317.0197;

3.1.14. Compound **5gp**: colourless oil

γmax (cm^{-1}): 1700 (s, C=O), 1200; ^{1}H-NMR ($CDCl_3$), δH (ppm): 0.81 (d, ^{12}J = 7.0 Hz), 1.0 (d, ^{12}J = 6.5 Hz) (3H); 1.7–2.7 (m, 12H); 3.0 (m, 2H); ^{19}F-NMR ($CDCl_3$), δF (ppm): 1.8 (s, 3F); MS (*m*/*z*): 291 (M^+ + 1, 17.96), 43 (100): HRMS ($C_{11}H_{17}F_3Cl_2O$): Found: 290.0495; Calcd: 290.0452;

3.1.15. Compound **5hj**: colourless oil

γmax (cm^{-1}): 1730 (s, C=O), 1250, 1150; ^{1}H-NMR ($CDCl_3$), δH (ppm): 0.8 (d, ^{12}J = 7.0 Hz), 1.0 (d, ^{12}J = 6.2 Hz) (3H); 1.2 (t, $^3J_{HH}$ = 7.0 Hz, 6H); 1.9–2.5 (m, 8H); 4.15 (q, $^3J_{HH}$ = 7.0 Hz, 4H); ^{19}F-NMR ($CDCl_3$), δF (ppm): −11.0 (d, $^3J_{FF}$ = 56 Hz, 1F), 37.5 (m, 1F); MS (*m*/*z*): 410 (M^+ + 1, 18.61), 363 (M^+–OEt-1, 17.82) Elemental Analysis: (for $C_{15}H_{21}F_2Cl_3O_4$): Found: C: 43.85, H: 5.15, F: 10.03%; Calcd: C: 43.98, H: 5.17, F: 9.27%.

3.1.16. Compound **5hm**: colourless oil

γmax (cm^{-1}): 1740 (s, C=O), 1220; ^{1}H-NMR ($CDCl_3$), δH (ppm): 0.8 (d, ^{12}J = 7.0 Hz), 1.0 (d, ^{12}J = 6.1 Hz) (3H); 1.3 (t, $^3J_{HH}$ = 7.1 Hz, 3H); 2.1–2.9 (m, 8H); 4.3 (q, $^3J_{HH}$ = 7.1 Hz, 2H); ^{19}F-NMR (CDl_3), δF (ppm): −11.0 (d, $^3J_{FF}$ = 56 Hz, 1F), 38.0 (m, 1F); MS (*m*/*z*): 365 (M^+, 12.90), 289 (M^+–Cl–OC_2H_5, 44.70) Elemental Analysis (for $C_{13}H_{16}F_2Cl_3O_2N$): Found: C: 43.32, H: 4.48, N: 3.78, F: 10.60%; Calcd: C: 43.06, H: 4.45, N: 3.86, F: 10.48%.

3.1.17. Compound **5ij**: colourless oil

γmax (cm^{-1}): 1730 (s, C=O), 1180; ^{1}H-NMR ($CDCl_3$), δH (ppm): 0.8 (d, ^{12}J = 7.0 Hz), 1.0 (d, ^{12}J = 6.2 Hz) (3H); 1.2 (t, $^3J_{HH}$ = 7.0 Hz, 6H); 2.0–2.6 (m, 8H); 4.15 (q, $^3J_{HH}$ = 7.0 Hz, 4H); ^{19}F-NMR ($CDCl_3$), δF (ppm): −11.0 (s, 1F), 33.1 (s, 2F), 38.1 (m, 1F); MS (*m*/*z*): 462

($M^{+}+2$, 2.44), 173 (100); Elemental Analysis (for $C_{16}H_{21}F_{4}Cl_{3}O_{4}$): Found: C: 41.75, H: 4.62; Calcd: C: 41.81, H: 4.60.

3.1.18. *Compound* ***5im****: colourless oil*

γmax (cm^{-1}): 1780, 1210; ^{1}H-NMR ($CDCl_3$), δH (ppm): 0.8 (d, ^{12}J=7.0 Hz), 1.0 (d, ^{12}J=6.2 Hz) (3H); 1.35 (t, $^{3}J_{HH}$=7.0 Hz, 3H); 2.0–2.9 (m, 8H); 4.25 (q, $^{3}J_{HH}$=7.0 Hz, 2H); ^{19}F-NMR ($CDCl_3$), δF (ppm): −11.0 (s, 1F), 33.0 (s, 2F), 38.5 (m, 1F); MS (*m/z*):414 (M^{+}-1, 5.71), 339 (M^{+}-CN-Cl-Me+1, 18.75), 304 (M^{+}-CN-2Cl-Me^{+}1, 65.37), 95 (100); Elemental Analysis (for $C_{14}H_{16}F_{4}Cl_{3}O_{2}N$): Found: C: 40.94, H:3.90, N: 3.29; Calcd: C: 40.75, H: 3.91, N: 3.39.

3.1.19. *Compound* ***6aj****: colourless oil, bp 96 °C/0.1 mmHg*

γmax (cm^{-1}) 1730, 1720 (s, C=O), 1250 and 1100 (C–F); ^{1}H-NMR ($CDCl_3$), δH 0.95 (d, $^{3}J_{HH}$=7.1 Hz), 1.02 (d, $^{3}J_{HH}$=6.3 Hz) (3H), 1.25 (t, $^{3}J_{HH}$=7.0 Hz, 6H), 1.99 (td, $^{3}J_{HF}$=22.9, $^{2}J_{HH}$=15.0, $^{3}J_{HH}$=5.71 Hz, 1H), 2.06 (ABX, $^{2}J_{HH}$=13.3, $^{3}J_{HH}$=10.4, $^{3}J_{HH}$=2.94 Hz, 1H), 2.13 (ABX, $^{2}J_{HH}$=13.33, $^{3}J_{HH}$=10.04, $^{3}J_{HH}$=2.94 Hz, 1H) 2.20 (m, $^{3}J_{HF}$=21.8, $^{2}J_{HH}$=15.0, $^{3}J_{HH}$=6.4 Hz, 1H), 2.50 (ABX, $^{2}J_{HH}$=14.0, $^{3}J_{HH}$=7.3, $^{3}J_{HH}$=6.7 Hz, 2H) and 4.2 (q, $^{3}J_{HH}$=7.0, 4H); ^{19}F-NMR (CCl_4), δF 9.5 (s, 2F), 38.0 (m, 2F), 44.0 (s, 2F) and 46.0 (s, 2F); MS (*m/z*) 475 (M^{+}-1, 60) and 241 (M^{+}-$ClC_{4}F_{8}$, 100); Elemental Analysis (for $C_{17}H_{21}ClF_{8}O_{4}$): Found: C 43.09; H 4.41; Cl 7.73; F 31.87%; Calcd: C 42.83, H 4.44; F 31.88; Cl 7.44%.

3.1.20. *Compound* ***6bj****: colourless oil, bp 128 °C/0.15 mmHg*

γmax (cm^{-1}) 1725, 1720 (s, C=O), 1250 and 1200 (C–F); ^{1}H-NMR ($CDCl_3$), δH 0.95 (d, $^{3}J_{HH}$=7.1 Hz), 1.02 (d, $^{3}J_{HH}$=6.3 Hz) (3H), 1.25 (t, $^{3}J_{HH}$=7.0 Hz, 6H), 1.99 (td, $^{3}J_{HF}$=22.9, $^{2}J_{HH}$=15.0, $^{3}J_{HH}$=5.71 Hz, 1H), 2.06 (ABX, $^{2}J_{HH}$=13.3, $^{3}J_{HH}$=10.4, $^{3}J_{HH}$=2.94 Hz, 1H), 2.13 (ABX, $^{2}J_{HH}$=13.33, $^{3}J_{HH}$=10.04, $^{3}J_{HH}$=2.94 Hz, 1H) 2.20 (m, $^{3}J_{HF}$=21.8, $^{2}J_{HH}$=15.0, $^{3}J_{HH}$=6.4 Hz, 1H), 2.50 (ABX, $^{2}J_{HH}$=14.0, $^{3}J_{HH}$=7.3, $^{3}J_{HH}$=6.7 Hz, 2H) and 4.2 (q, $^{3}J_{HH}$=7.0 Hz, 4H); ^{19}F-NMR (CCl_4), δF 8.20 (s, 2F), 38.2 (m, 2F), 44.0–46.0 (m, 6F); MS (*m/z*) 576 (M^{+}, 56%) and 242 (M^{+}-$ClC_{6}F_{12}$+1, 100); Elemental Analysis (for $C_{19}H_{21}ClF_{12}O_{4}$): Found: C 39.68; H 3.78; Cl 6.40; F 40.10%; Calcd: C 39.56, H 3.67; F 39.52; Cl 6.15%.

3.1.21. *Compound* ***6cj****: colourless oil, bp 104 °C/0.1 mmHg*

γmax (cm^{-1}) 1730, 1720 (s, C=O), 1250 and 1100 (C–F); ^{1}H-NMR ($CDCl_3$), δH 0.95 (d, $^{3}J_{HH}$=7.1 Hz), 1.02 (d, $^{3}J_{HH}$=6.3 Hz) (3H), 1.25 (t, $^{3}J_{HH}$=7.0 Hz, 6H), 1.99 (td, $^{3}J_{HF}$=22.9, $^{2}J_{HH}$=15.0, $^{3}J_{HH}$=5.71 Hz, 1H), 2.06 (ABX, $^{2}J_{HH}$=13.3, $^{3}J_{HH}$=10.4, $^{3}J_{HH}$=2.94 Hz, 1H), 2.13 (ABX, $^{2}J_{HH}$=13.33, $^{3}J_{HH}$=10.04, $^{3}J_{HH}$=2.94 Hz, 1 H) 2.20 (m, $^{3}J_{HF}$=21.8, $^{2}J_{HH}$=15.0, $^{3}J_{HH}$=6.4 Hz, 1H), 2.50 (ABX, $^{2}J_{HH}$=14.0, $^{3}J_{HH}$=7.3, $^{3}J_{HH}$=6.7 Hz, 2H) and 4.2 (q, $^{3}J_{HH}$=7.0 Hz, 4H); ^{19}F-NMR (CCl_4), δF 5.5 (s, 2F), 38.0 (m, 2F), 43.0–48.0 (m, 6F); MS (*m/z*) 658 (M^{+}-2, 100%) and 242 (M^{+}-2XCO_{2}Et-1, 90); Elemental Analysis (for $C_{21}H_{21}F_{17}O_{4}$): Found: C 37.86; H 3.14; F 47.86%; Calcd: C 38.20, H 3.21; F 48.91%.

3.1.22. *Compound* ***6am****: colourless oil, bp 118–119 °C/ 0.15 mmHg*

γmax (cm^{-1}) 2250, 1720 (s, C=O), 1200 and 1100 (C–F); ^{1}H-NMR ($CDCl_3$), δH 0.85 (d, $^{3}J_{HH}$=7.1 Hz), 0.88 (d, $^{3}J_{HH}$=6.3 Hz) (3H), 0.96 (d, $^{3}J_{HH}$=7.1 Hz), 1.0 (d, $^{3}J_{HH}$=6.4 Hz), 1.05 (d, $^{3}J_{HH}$=7.1 Hz), 1.15 (d, $^{3}J_{HH}$=6.4 Hz) (3H); 1.25 (t, $^{3}J_{HH}$=7.0 Hz, 3H), 2.05–2.70 (m, 8H) and 4.25 (q, $^{3}J_{HH}$=7.0 Hz, 2H); ^{19}F-NMR (CCl_4), δF −9.8 (s, 2F), 30.0 (s, 2F), 35 (s, 2F) and 38 (s, 2F); MS (*m/z*) 430 (M^{+}+1, 8.07) and 357 (100); Elemental Analysis (for $C_{15}H_{16}F_{8}ClO_{2}N$): Found: C 40.98; H 3.84; Cl 8.38, F 35.40%; Calcd: C 41.91, H 3.73; Cl 8.26, F 35.38%.

3.1.23. *Compound* ***6bm****: colourless oil, bp 130–132 °C/ 0.15 mmHg*

γmax (cm^{-1}) 2250, 1720 (s, C=O), 1200 and 1100 (C–F); ^{1}H-NMR ($CDCl_3$), δH 0.85 (d, $^{3}J_{HH}$=7.1 Hz), 0.88 (d, $^{3}J_{HH}$=6.3 Hz) (3H), 0.96 (d, $^{3}J_{HH}$=7.1 Hz), 1.0 (d, $^{3}J_{HH}$=6.4 Hz), 1.05 (d, $^{3}J_{HH}$=7.1 Hz), 1.15 (d, $^{3}J_{HH}$=6.4 Hz) (3H); 1.25 (t, $^{3}J_{HH}$=7.0 Hz, 3H), 2.05–2.70 (m, 8H) and 4.25 (q, $^{3}J_{HH}$=7.0 Hz, 2H); ^{19}F-NMR (CCl_4), δF −8.2 (s, 2F), 37.0 (s, 2F), 43.5–47.5 (m, 8F); MS (*m/z*) 529 (M^{+}, 10) and 413 (100); Elemental Analysis (for $C_{17}H_{16}F_{12}ClO_{2}N$): Found: C 38.64; H 3.29 Cl 6.86, F 42.78%; Calcd: C 38.53, H 3.02; Cl 6.70, F 43.05%.

3.1.24. *Compound* ***8at****: colourless oil, 108–110 °C/ 0.12 mmHg*

γmax (cm^{-1}) 1650 (s, C=O), 1200 and 1100 (C–F); ^{1}H-NMR ($CDCl_3$), δH 1.98 (s, 3H), 2.00–3.45 (m, 6H), 3.50–4.50 (m, 4H); ^{19}F-NMR (CCl_4), δF −8.2 (s, 2F), 37.0 (s, 2F), 43.5–47.5 (m, 8F); MS (*m/z*) 601 (M^{+}, 100), 458 (64) and 43 (73).

3.1.25. *Compound* ***8cq****: colourless oil, bp 110–114 °C/ 0.1 mmHg*

γmax (cm^{-1}) 1600 (s, C=O), 1200 and 1100 (C–F); ^{1}H-NMR ($CDCl_3$), δH 1.80–3.50 (m, 6H), 3.5–4.50 (m, 6H), 7.3 (m, 5H); ^{19}F-NMR (CCl_4), δF 4.2 (s, 3F), 38.0 (m, 2F), 44–48.5 (m, 6F), 50 (s, 2F); MS (*m/z*) 633 (M^{+}, 100) and 91 (54); Elemental Analysis (for $C_{19}H_{17}F_{13}IN$): Found: C 36.02; H 2.68, N 2.21, F 39.02%; Calcd: C 36.21, H 2.71; N 2.25, F 39.13%.

3.1.26. *Compound* ***8cr****: waxy solid*

γmax (cm^{-1}) 1580 (s, C=O), 1250 and 1100 (C–F); ^{1}H-NMR ($CDCl_3$), δH 1.80–4.20 (m, 10H), 7.45 (m, 3H), 7.79 (m, 2H); ^{19}F-NMR (CCl_4), δF 4.2 (s, 3F), 38.0 (m, 2F), 44–48.5 (m, 6F), 50 (s, 2F); MS (*m/z*) 683 (M^{+}, 100) and 141 (67); Elemental Analysis (for $C_{18}H_{15}F_{13}INSO_{2}$): Found: C 36.02; H 2.68, N 2.21, F 39.02%; Calcd: C 36.21, H 2.71; N 2.25, F 39.13%.

*3.1.27. Compound **8er**: colourless oil*

γmax (cm^{-1}): 1620 (s, C=O), 1200; ^{1}H-NMR (CDCl$_3$), δH (ppm): 2.3–2.9 (m, 6H); 3.2 (m, 2H); 3.4 (m, 2H); 7.6 (m, 3H); 7.8 (m, 2H); ^{19}F-NMR (CDCl$_3$), δF (ppm): −36.0 (dd, 2F); MS (*m/z*): 447 (M$^+$, 4.57), 368 (M$^+$−Br+1, 95.16); HRMS ($C_{13}H_{15}O_2NSBr_2F_2$): Found: 444.9168; Calcd: 444.9158;

*3.1.28. Compound **8es**: colourless oil*

γmax (cm^{-1}): 1580 (s, C=O), 1200, 1150; ^{1}H-NMR (CDCl$_3$), δH (ppm): 2.4–2.9 (m, 8H); 3.6 (m, 2H); 7.5 (m, 5H); ^{19}F-NMR (CDCl$_3$), δF (ppm): −33.7 (dd, 2F); MS (*m/z*): 409 (M$^+$, 2.69); 105 (100); HRMS ($C_{14}H_{15}ONBr_2F_2$): Found: 408.9422; Calcd: 408.9488.

*3.1.29. Compound **8gq**: colourless oil*

γmax (cm^{-1}): 1600 (s, C=O), 1260, 1150; ^{1}H-NMR (CDCl$_3$), δH (ppm): 0.9 (d, ^{12}J=6.7 Hz), 1.2 (d, ^{12}J= 6.0 Hz) (3H); 2.1–2.8 (m, 4H), 3.7 (m, 4H); 7.3 (m, 5H); ^{19}F-NMR (CDCl$_3$), δF (ppm): 2.0 (s, 3F); MS (*m/z*): 338 (M$^+$, 17.12), 91 (100); HRMS ($C_{14}H_{16}F_3Cl_2N$): Found: 339.0751; Calcd: 339.0769.

*3.1.30. Compound **8gr**: colourless oil*

γmax (cm^{-1}): 1580 (s, C=O), 1200; ^{1}H-NMR (CDCl$_3$), δH (ppm): 0.8 (d, ^{12}J=7.0 Hz), 0.9 (d, ^{12}J=6.3 Hz) (3H); 2.1–2.6 (m, 4H); 3.5 (m, 4H); 7.6 (m, 3H); 7.9 (m, 2H); ^{19}F-NMR (CDCl$_3$), δF (ppm): 2.0 (s, 3F); MS (*m/z*): 390 (M$^+$, 16.72), 77 (100); HRMS ($C_{14}H_{16}F_3Cl_2NSO_2$): Found: 389.0248; Calcd: 389.0231.

*3.1.31. Compound **8gs**: colourless oil*

γmax (cm^{-1}): 1590 (s, C=O), 1260, 1150; ^{1}H-NMR (CDCl$_3$), δH (ppm): 0.9 (d, ^{12}J=7.0 Hz), 1.2 (d, ^{12}J= 6.3 Hz) (3H); 2.2 (m, 4H); 3.6 (m, 4H); 7.5 (m, 5H); ^{19}F-NMR (CDCl$_3$), δF (ppm): 2.0 (s, 3F); MS (*m/z*): 353 (M$^+$, 11.75), 188 (42.18, M$^+$-COPh–CF$_3$–CH$_3$), 105 (100); HRMS ($C_{15}H_{16}F_3Cl_2NO$): Found: 353.0530; Calcd: 353.0561.

*3.1.32. Compound **9at**: colourless oil, 120 °C/2.0 mmHg*

γmax (cm^{-1}) 1580 (s, C=O), 1250 and 1100 (C–F); ^{1}H-NMR (CDC13), δH 0.98 (d, $^{3}J_{HH}$=7.0 Hz), 0.90 (d, $^{3}J_{HH}$=6.4 Hz) (3H), 1.95 (s, 3H), 2.00–3.00 (m, 4H), 3.05–4.20 (m, 4H); ^{19}F-NMR (CCl$_4$), δF −9.5 (s, 2F), 36.0 (m, 2F), 38 (s, 2F), 45 (s, 2F); MS (*m/z*) 375 (M$^+$, 62) and 43 (100); Elemental Analysis (for $C_{12}H_{14}F_8ClNO$): Found: C 38.43; H 3.48, N 3.77, F 40.52%; Calcd: C 38.37, H 3.76; N 3.73, F 40.46%.

*3.1.33. Compound **9cq**: colourless oil*

γmax (cm^{-1}) 1580 (s, C=O), 1250 and 1100 (C–F); ^{1}H-NMR (CDCl$_3$), δH 1.05 (d, $^{3}J_{HH}$=7.0 Hz), 0.950 (d, $^{3}J_{HH}$=6.3 Hz) (3H), 1.90–3.00 (m, 4H), 3.0–3.90 (m, 4H), 4.45 (dd, $^{2}J_{HH}$=14.5 Hz, 2H), 7.35 (m, 5H); ^{19}F-NMR (CCl$_4$), δF 4.2 (s, 3F), 38.0 (m, 2F), 43–48 (m, 6F), 55 (s, 2F); MS (*m/z*) 507 (M$^+$, 26) and 91 (100); HRMS (for $C_{19}H_{18}F_{13}N$): Found: 507.3368; Calcd: 507.3371.

*3.1.34. Compound **9cr**: colourless oil*

γmax (cm^{-1}) 1580 (s, C=O), 1250 and 1100 (C–F); ^{1}H-NMR (CDCl$_3$), δH 1.30 (d, $^{3}J_{HH}$=6.6 Hz, 3H), 2.00–4.00 (m, 5H), 7.5 (m, 3H), 7.8 (m, 2H); ^{19}F-NMR (CCl$_4$), δF 4.1 (s, 3F), 38.0 (m, 2F), 43–48 (m, 6F), 50 (s, 2F); MS (*m/z*) 557 (M$^+$, 10) and 77 (100); Elemental Analysis (for $C_{18}H_{16}F_{13}NSO_2$): Found: C 36.02, H 2.68, N 2.21, F 39.02%; Calcd: C 36.21, H 2.71, N 2.25, F 39.13%.

*3.1.35. Compound **11au**: white solid. mp: 75 °C*

γmax (cm^{-1}) 1680 (s, C=O), 1200 and 1100 (C–F); ^{1}H-NMR (CDCl$_3$), δH 2.16 (m, 1H), 2.36 (m, 1H), 2.67 (m, 1H), 3.0 (dd, $^{3}J_{HH}$=2.5, $^{3}J_{HH}$=11.4 Hz, 1H), 3.2 (dd, $^{3}J_{HH}$=1.5, $^{3}J_{HH}$=8.6 Hz, 1H), 3.44 (d, $^{3}J_{HH}$=1.6, $^{3}J_{HH}$= 8.5 Hz, 1H), 3.5 (dd, $^{3}J_{HH}$=3.5, $^{3}J_{HH}$=10.2 Hz, 1H), 4.53 (dd, $^{2}J_{HH}$=14.6 Hz, 2H), 7.35 (m, 5H); ^{19}F-NMR (CCl$_4$), δF −9.0 (s, 2F), 36.0 (m, 2F), 43.0 (s, 2F), 48 (s, 2F); MS (*m/z*) 563 (M$^+$, 29.5) and 91 (100); HRMS (for $C_{17}H_{15}ClF_8INO$): Found: 562.9715, Calcd: 562.9759.

*3.1.36. Compound **11cu**: white solid. mp: 68 °C*

γmax (cm^{-1}) 1680 (s, C=O), 1200 and 1100 (C–F); ^{1}H-NMR (CDCl$_3$), δH 2.16 (m, 1H), 2.36 (m, 1H), 2.67 (m, 1H), 3.0 (dd, $^{3}J_{HH}$=2.5, $^{3}J_{HH}$=11.4 Hz, 1H), 3.2 (dd, $^{3}J_{HH}$=1.5, $^{3}J_{HH}$=8.6 Hz, 1H), 3.44 (d, $^{3}J_{HH}$=1.6, $^{3}J_{HH}$= 8.5 Hz, 1H), 3.5 (dd, $^{3}J_{HH}$=3.5, $^{3}J_{HH}$=10.2 Hz, 1H), 4.53 (dd, $^{2}J_{HH}$=14.6 Hz, 2H), 7.35 (m, 5H); ^{19}F-NMR (CCl$_4$), δF 3.5 (s, 2F), 34.0 (s, 2F), 45.0–47 (m, 6F), 48 (s, 2F); MS (*m/z*) 647 (M$^+$, 47.8) and 91 (100); HRMS (for $C_{19}H_{15}F_{13}INO$): Found: 646.9994, Calcd: 646.9998.

*3.1.37. Compound **11cv**: white solid. mp: 84–86 °C*

γmax (cm^{-1}) 1680 (s, C=O), 1200 and 1100 (C–F); ^{1}H-NMR (CDCl$_3$), δH 1.35 (d, $^{4}J_{HH}$=2.7 Hz, 1H), 2.35 (t, $^{3}J_{HH}$=16.5 Hz), 2.50 (m, 1H), 2.6 (t, $^{3}J_{HH}$=16.5 Hz, 1H), 2.95 (t, $^{3}J_{HH}$=10.3 Hz, 1H), 3.15 (dd, $^{3}J_{HH}$=2.4, $^{3}J_{HH}$= 10.7 Hz, 1H), 3.45 (dd, $^{3}J_{HH}$=4.2, $^{3}J_{HH}$=6.5 Hz, 1H), 4.45 (d, $^{2}J_{HH}$=14.5 Hz, 1H), 4.61 (d, $^{2}J_{HH}$=14.5 Hz, 1H), 7.35 (m, 5H); ^{19}F-NMR (CCl$_4$), δF 3.5 (s, 2F), 34.0 (s, 2F), 45.0–47 (m, 6F), 48 (s, 2F); MS (*m/z*) 661 (M$^+$, 43.4) and 91 (100); HRMS (for $C_{20}H_{17}F_{13}INO$): Found: 661.2524, Calcd: 661.2519.

*3.1.38. Compound **12au**: white solid. mp: 72–73 °C*

γmax (cm^{-1}) 1680 (s, C=O), 1200 and 1100 (C–F); ^{1}H-NMR (CDCl$_3$), δH 2.16 (m, 1H), 2.36 (m, 1H), 2.96 (t, $^{3}J_{HH}$=16.5 Hz, 1H), 3.03 (dd, $^{3}J_{HH}$=9.8, $^{3}J_{HH}$=10 Hz, 1H), 3.2 (dd, $^{3}J_{HH}$=8.9, $^{3}J_{HH}$=9.8 Hz, 1H), 3.48 (dd, $^{3}J_{HH}$=3.1, $^{3}J_{HH}$=10.2 Hz, 1H), 4.50 (dd, $^{2}J_{HH}$=13.6 Hz, 2H), 7.22–7.35 (m, 5H); ^{19}F-NMR (CCl$_4$), δF −9.5 (s, 2F), 35.0 (m, 2F), 45.0 (s, 2F), 48 (s, 2F); MS (*m/z*) 563 (M$^+$, 73.2) and 91 (100); HRMS (for $C_{17}H_{15}ClF_8INO$): Found: 562.9715, Calcd: 562.9759.

*3.1.39. Compound **11aw**: waxy solid*

γmax (cm^{-1}) 1680 (s, C=O), 1640, 1200 and 1100 (C–F); ^{1}H-NMR (CDCl$_3$), δH 1.95 (m, 1H), 2.35 (m, 1H), 2.65 (m, 1H), 2.8 (m. 1H), 2.98 (m, 1H), 3.18 (m, 1H), 3.42 (m, 1H), 3.52 (m, 1H), 3.87 (d, $^{3}J_{HH}=6.3$ Hz, 2H), 5.11 (m, 2H), 5.56–5.87 (m, 1H); ^{19}F-NMR (CCl$_4$), δF -9.5 (s, 2F), 34.0 (m, 2F), 45.0 (s, 2F), 48 (s, 2F); MS (*m/z*) 513 (M$^+$, 47.5); HRMS (for C$_{13}$H$_{13}$ClF$_8$INO): Found: 513.5968, Calcd: 513.5961.

*3.1.40. Compound **12aw**: waxy solid*

γmax (cm^{-1}) 1680 (s, C=O), 1640, 1200 and 1100 (C–F); ^{1}H-NMR (CDCl$_3$), δH 1.98 (m, 1H), 2.40 (m, 1H), 2.85 (m, 1H), 2.8 (m. 1H), 3.10 (m, 1H), 3.23 (m, 1H), 3.49 (m, 1H), 3.55 (m, 1H), 3.90 (d, $^{3}J_{HH}=6.3$ Hz, 2H), 5.1 (m, 2H), 5.55–5.87 (m, 1H); ^{19}F-NMR (CCl$_4$), δF -9.0 (s, 2F), 33.0 (m, 2F), 44.0 (s, 2F), 48 (s, 2F); MS (*m/z*) 513 (M$^+$); HRMS (for C$_{13}$H$_{13}$ClF$_8$INO): Found: 513.5957, Calcd: 513.5961.

*3.1.41. Compound **13au**: colourless oil*

γmax (cm^{-1}) 1680 (s, C=O), 1200 and 1100 (C–F); ^{1}H-NMR (CDCl$_3$), δH 0.92 (d, $^{3}J_{HH}=7.2$ Hz, cis-CH$_3$), 1.17 (d, $^{3}J_{HH}=6.6$ Hz, trans-CH$_3$) (3H), 2.05 (m, 1H), 2.20 (m, 1H), 2.45–2.55 (m, 1H), 2.84 (dd, $^{3}J_{HH}=4.8$ Hz, $^{3}J_{HH}=9.6$ Hz, 1H), 2.93 (m, 1H), 3.35 (dd, $^{3}J_{HH}=$ 1.2 Hz, $^{3}J_{HH}=8.4$ Hz, 1H), 4.47 (dd, $^{2}J_{HH}=14.6$ Hz, 2H), 7.22–7.35 (m, 5H); ^{19}F-NMR (CCl$_4$), δF -9.5 (s, 2F), 36.5 (m, 2F), 44.0 (s, 2F), 48.5 (s, 2F); MS (*m/z*) 437 (M$^+$, 68) and 91 (100); Elemental Analysis (for C$_{17}$H$_{16}$ClF$_8$NO): Found: C 46.64, H 3.68, N 3.20, F 56.42%; Calcd: C 46.71, H 3.73, N 3.25, F 56.10%.

*3.1.42. Compound **13cu**: colourless oil*

γmax (cm^{-1}) 1680 (s, C=O), 1200 and 1100 (C–F); ^{1}H-NMR (CDCl$_3$), δH 0.92 (d, $^{3}J_{HH}=7.2$ Hz, cis-CH$_3$), 1.17 (d, $^{3}J_{HH}=6.6$ Hz, trans-CH$_3$) (3H), 2.05 (m, 1H), 2.20 (m, 1H), 2.45–2.55 (m, 1H), 2.84 (dd, $^{3}J_{HH}=4.8$ Hz, $^{3}J_{HH}=9.6$ Hz, 1H), 2.93 (m, 1H), 3.35 (dd, $^{3}J_{HH}=$ 1.2 Hz, $^{3}J_{HH}=8.4$ Hz, 1H), 4.47 (dd, $^{2}J_{HH}=14.6$ Hz, 2H), 7.22–7.35 (m, 5H); ^{19}F-NMR (CCl$_4$), δF 3.5 (s, 3F), 34.5 (s, 2F), 44.5 (m, 6F), 48.5 (s, 2F); MS (*m/z*) 521 (M$^+$, 52) and 91 (100); Elemental Analysis (for C$_{19}$H$_{16}$F$_{13}$NO): Found: C 43.78, H 3.09, N 2.69, F 47.38%; Calcd: C 43.82, H 3.06, N 2.75, F 47.44%.

*3.1.43. Compound **13cv**: colourless oil*

γmax (cm^{-1}) 1680 (s, C=O), 1250 and 1100 (C–F); ^{1}H-NMR (CDCl$_3$), δH 0.95 (d, $^{3}J_{HH}=7.1$ Hz, cis-CH$_3$, 3H), 1.32 (d, $^{3}J_{HH}=2.90$ Hz, 3H), 2.25 (m, 1H), 2.45–2.65 (m, 2H), 2.75 (dd, $^{3}J_{HH}=1.3$ Hz, $^{3}J_{HH}=10.1$ Hz, 1H), 3.45 (dd, $^{3}J_{HH}=6.24$, $^{3}J_{HH}=10.0$ Hz, 1H), 4.45 (dd, $^{2}J_{HH}=14.5$ Hz, 2H), 7.30 (m, 5H); 19F-NMR (CCl4), δF 3.5 (s, 3F), 34.0 (s, 2F), 45.05 (m, 6F), 48.0 (s, 2F); MS (*m/z*) 535 (M$^+$, 57.9) and 91 (100); HRMS (for C$_{20}$H$_{18}$F$_{13}$NO): Found: 535.3418; Calcd: 535.3422.

*3.1.44. Compound **13aw**: colourless oil*

γmax (cm^{-1}) 1680 (s, C=O), 1250 and 1100 (C–F); ^{1}H-NMR (CDCl$_3$), δH 0.99 (d, $^{3}J_{HH}=7.0$ Hz, cis-CH$_3$), 1.22 (d, $^{3}J_{HH}=6.6$ Hz, trans-CH$_3$) (CH), 2.0–2.3 (m, 2H), 2.45 (m, 1H), 2.8–3.0 (m, 2H), 3.45 (m, 1H), 3.9 (m, 2H), 5.15 (m, 2H), 5.7 (m, 1H); ^{19}F-NMR (CCl$_4$), δF -9.5 (s, 3F), 34.0 (s, 2F), 44.0 (s, 2F), 48.0 (s, 2F); MS (*m/z*) 387 (M$^+$, 100) and 41 (72.5); HRMS (for C$_{13}$H$_{14}$F$_8$ClNO): Found: 387.6998; Calcd: 387.6995.

*3.1.45. Compound **14au**: colourless oil*

γmax (cm^{-1}) 1680 (s, C=O), 1200 and 1100 (C–F); ^{1}H-NMR (CDCl$_3$), δH 0.90 (d, $^{3}J_{HH}=7.1$ Hz, cis-CH$_3$), 1.15 (d, $^{3}J_{HH}=6.5$ Hz, trans-CH$_3$) (3H), 2.20 (m, 1H), 2.55 (m, 1H), 2.60–2.95 (m, 3H), 3.45 (dd, $^{3}J_{HH}=5.9$, $^{3}J_{HH}=$ 10.0 Hz, 1H), 4.50 (dd, $^{2}J_{HH}=14.6$ Hz, 2H), 7.2–7.40 (m, 5H); ^{19}F-NMR (CCl$_4$), δF -9.5 (s, 2F), 36.5 (m, 2F), 44.0 (s, 2F), 48.5 (s, 2F); MS (*m/z*) 437 (M$^+$, 35) and 91 (100); HRMS (for C$_{17}$H$_{16}$ClF$_8$NO): Found: 437.7511 Calcd: 437.7597.

*3.1.46. Compound **14cu**: colourless oil*

γmax (cm^{-1}) 1680 (s, C=O), 1200 and 1100 (C–F); ^{1}H-NMR (CDCl$_3$), δH 0.92 (d, $^{3}J_{HH}=7.2$ Hz, cis-CH$_3$, 1.17 (d, $^{3}J_{HH}=6.6$ Hz, trans-CH$_3$) (3H), 2.05 (m, 1H), 2.20 (m, 1H), 2.45–2.55 (m, 1H), 2.84 (dd, $^{3}J_{HH}=4.8$ Hz, $^{3}J_{HH}=$ 9.6 Hz, 1H), 2.93 (m, 1H), 3.35 (dd, $^{3}J_{HH}=1$, 2, $^{3}J_{HH}=$ 8.4 Hz, 1H), 4.47 (dd, $^{2}J_{HH}=14.6$ Hz, 2H), 7.22–7.35 (m, 5H); ^{19}F-NMR (CCl$_4$), δF 4.2 (s, 3F), 34.5 (s, 2F), 36–44 (m, 2F), 48.5 (s, 2F); MS (*m/z*) 521 (M$^+$, 47) and 91 (100); Elemental Analysis (for C$_{19}$H$_{16}$F$_{13}$NO): Found: C 43.78, H 3.09, N 2.69, F 47.38%; Calcd: C 43.75, H 3.12, N 2.78, F 47.33%.

*3.1.47. Compound **14aw**: colourless oil*

γmax (cm^{-1}) 1680 (s, C=O), 1250 and 1100 (C–F); ^{1}H-NMR (CDCl$_3$), δH 1.0 (d, $^{3}J_{HH}=7.1$ Hz, cis-CH$_3$), 1.25 (d, $^{3}J_{HH}=6.5$ Hz, trans-CH$_3$) (3H), 2.1–2.3 (m, 1H), 2.6–2.9 (m, 4H), 3.5 (m, 1 H), 3.85 (m, 1H), 4.0 (m, 1H), 5.2 (m, 2H), 5.7 (m, 1H); ^{19}F-NMR (CCl$_4$), δF -9.0 (s, 3F), 33.0 (s, 2F), 44.0 (s, 2F), 48.0 (s, 2F); MS (*m/z*) 387 (M$^+$, 48) and 41 (100); HRMS (for C$_{13}$H$_{14}$F$_8$ClNO): Found: 387.6990; Calcd: 387.6995.

*3.1.48. Compound **16a**: colourless oil*

γmax (cm^{-1}) 1760 (s, C=O), 1380 and 1120 (C–F); ^{1}H-NMR (CDCl$_3$), δH 2.5 (m, 1H), 2.8–3.2 (m, 2H), 4.3 (dd, $^{3}J_{HH}=6.2$ Hz, $^{3}J_{HH}=10.0$ Hz, 1H), 4.6 (dd, $^{3}J_{HH}=$ 3.2 Hz, $^{3}J_{HH}=10.2$ Hz, 1H), 6.8 (t, $^{3}J_{HH}=15.5$ Hz), 7.25 (t, $^{3}J_{HH}=15.5$ Hz) (1H); ^{19}F-NMR (CCl$_4$), δF -9.0 (s, 2F), 32.0 (d, $^{3}J_{HF}=15.5$ Hz, 0.33F), 38 (d, $^{3}J_{HF}=15.5$ Hz, 0.67F), 44.0 (s, 2F), 46 (s, 2F); MS (*m/z*) 472 (M$^+$, 100); HRMS (for C$_{10}$H$_6$F$_8$IClO$_2$): Found: 471.8965 Calcd: 471.8973.

3.1.49. Compound ***17a****: colourless oil*

γmax (cm^{-1}) 1760 (s, C=O), 1380 and 1120 (C–F); ^{1}H-NMR (CDCl$_3$), δH 2.4 (m, 1H), 2.7 (m, 1H), 3.55 (m, 1H), 4.05 (dd, $^{3}J_{\mathrm{HH}}=5.1$ Hz, $^{3}J_{\mathrm{HH}}=11.7$ Hz, 0.48H, Z-isomer), 4.2 (dd, $^{3}J_{\mathrm{HH}}=6.1$ Hz, $^{3}J_{\mathrm{HH}}=10.2$ Hz, 0.52H, E-isomer), 4.4 (dd, $^{3}J_{\mathrm{HH}}=2.0$ Hz, $^{3}J_{\mathrm{HH}}=9.8$ Hz, 0.52H, E-isomer) 4.5 (dd, $^{3}J_{\mathrm{HH}}=8.2$, $^{3}J_{\mathrm{HH}}=10.0$ Hz, 0.48H, Z-isomer), 7.5 (d, $^{4}J_{\mathrm{HH}}=2.1$ Hz, 0.48H, Z-isomer), 8.0 (d, $^{4}J_{\mathrm{HH}}=2.1$ Hz, 0.52H, E-isomer); ^{19}F-NMR (CCl$_4$), δF −9.0 (s, 2F), 36.0 (m, 2F), 43.0 (s, 2F), 47 (s, 2F); MS (*m/z*) 472 (M$^+$, 100); HRMS (for $C_{10}H_6F_8ClIO_2$): Found: 471.8939 Calcd: 471.8973.

3.1.50. Compound ***16c****: colourless oil*

γmax (cm^{-1}) 1760 (s, C=O), 1250 and 1120 (C–F); ^{1}H-NMR (CDCl$_3$), δH 2.5 (m, 1H), 2.8–3.2 (m, 2H), 4.3 (dd, $^{3}J_{\mathrm{HH}}=6.2$ Hz, $^{3}J_{\mathrm{HH}}=10.0$ Hz, 1H), 4.6 (dd, $^{3}J_{\mathrm{HH}}=3.2$ Hz, $^{3}J_{\mathrm{HH}}=10.2$ Hz, 1H), 6.8 (t, $^{3}J_{\mathrm{HH}}=15.5$ Hz), 7.25 (t, $^{3}J_{\mathrm{HH}}=15.5$ Hz) (1H); ^{19}F-NMR (CCl$_4$), δF 4.2 (s, 3F), 33.0 (d, $^{3}J_{\mathrm{HF}}=15.5$ Hz, 0.25F), 38 (d, $^{3}J_{\mathrm{HF}}=15.5$, 0.75F), 44.0 (s, 2F), 46 (s, 2F); MS (*m/z*) 556 (M$^+$, 100); HRMS (for $C_{12}H_6F_{13}IO_2$): Found: 556.0623 Calcd: 556.0619.

3.1.51. Compound ***17c****: colourless oil*

γmax (cm^{-1}) 1760 (s, C=O), 1250 and 1120 (C–F); ^{1}H-NMR (CDCl$_3$), δH 2.4 (m, 1H), 2.7 (m, 1H), 3.55 (m, 1H), 4.05 (dd, $^{3}J_{\mathrm{HH}}=5.1$ Hz, $^{3}J_{\mathrm{HH}}=11.7$ Hz, 0.45H, Z-isomer), 4.2 (dd, $^{3}J_{\mathrm{HH}}=6.1$ Hz, $^{3}J_{\mathrm{HH}}=10.2$ Hz, 0.55H, E-isomer), 4.4 (dd, $^{3}J_{\mathrm{HH}}=2.0$ Hz, $^{3}J_{\mathrm{HH}}=9.8$ Hz, 0.55H, E-isomer) 4.5 (dd, $^{3}J_{\mathrm{HH}}=8.2$, $^{3}J_{\mathrm{HH}}=10.0$ Hz, 0.45H, Z-isomer), 7.5 (d, $^{4}J_{\mathrm{HH}}=2.1$ Hz, 0.45H, Z-isomer), 8.0 (d, $^{4}J_{\mathrm{HH}}=2.1$ Hz, 0.55H, E-isomer); ^{19}F-NMR (CCl$_4$), δF −9.0 (s, 2F), 33–36.0 (m, 2F), 43.0 (s, 2F), 47 (s, 2F); MS (*m/z*) 556 (M$^+$, 100), 388 (65), 372 (34); HRMS (for $C_{12}H_6F_{13}IO_2$): Found: 556.0614 Calcd: 556.0619.

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