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Synthesis of *ortho*-perfluoroalkyl phenones from hemifluorinated enones as key building blocks

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Abstract—The title compounds are prepared by cycloaddition of perfluoroalkenyl ketones and 1,3-dienes, with a subsequent aromatization by basic dehydrofluorination. The perfluoroalkenyl ketones were prepared by the reaction of perfluoroorganometallic reagents with acylsilanes. The transformation may be performed more efficiently in a simplified process without purification of the intermediate cycloadducts. The overall methodology is an interesting entry to *ortho*-perfluoroalkyl phenones with the possibility to vary the substitution at the acyl and on the ring moiety.

1. Introduction

In recent years, the synthesis of fluorinated organic compounds has become an important field in organic chemistry due to the unique properties of the fluorine atom able to significantly modify their physico-chemical and biological properties.[1] Substitution of a hydrogen atom by a fluorine or introduction of a trifluoromethyl group may improve the pharmacodynamic and the pharmacokinetic profiles of a bioactive molecule by concomitant alteration of its electronic, steric, lipophilic, or metabolic characteristics. In particular, considerable efforts have been devoted to the introduction of a trifluoromethyl group into organic molecules.[2]

Among these fluorinated molecules, fluorinated aromatics and especially trifluoromethylated ones have been extensively developed in the pharmaceutical and agrochemical fields.[3] Structures of some examples of such molecules are presented in Figure 1.

Aromatics bearing a longer *F*-alkyl chain have also been extensively studied for their applications as amphiphilic molecules or as fluorous catalysts in asymmetric catalysis.[4]

We have recently reported an exploratory study of the [4+2] cycloaddition reactions with hemifluorinated enones.[5] These substrates, in contrast to simple fluorovinylic derivatives,[6] behave as excellent dienophiles in normal electron-demand Diels–Alder reactions, due to the additive withdrawing

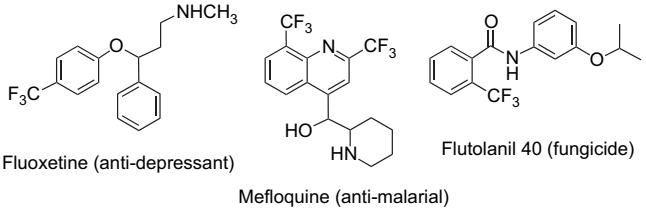

Figure 1. Some selected trifluoromethyl aromatic compounds with biological activities.

effects of the vicinal perfluoroalkyl and acyl groups. Recently, the application of vinyl fluorides in cycloadditions has been reviewed.[7] The polyfluorinated dienophiles used in this work were of variable structure (aromatic, aliphatic, carbohydrate-derived) and were prepared by our general method starting from acylsilanes and perfluoroorganometallic reagents.[8] This methodology was carried out with various dienes such as cyclopentadienes or buta-1,3-dienes and gave access to polyfluorinated norbornenes and cyclohexenes.[5] The polyfluorinated cycloalkenes thus obtained are original compounds, which deserved to be considered as elaborated intermediates for further transformations. In particular, one could expect an easy aromatization under basic conditions owing to the vicinal difluoro pattern present in their structures. Thus, hemifluorinated enones should be building blocks of choice toward *ortho*-perfluoroalkyl phenones.

We report here the synthesis of polysubstituted *ortho*-perfluoroalkyl phenones in a simple two-step process: a [4+2] cycloaddition between a diene and a hemifluorinated enone followed by a double HF elimination under basic conditions as shown in the following retrosynthetic scheme (Scheme 1).

Keywords: Organofluorine compounds; Aromatics; Enones; Diels–Alder reactions; Fluorinated phenones.
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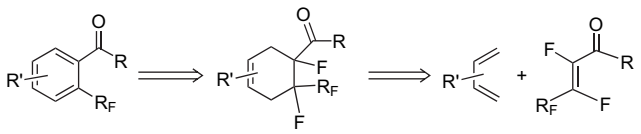


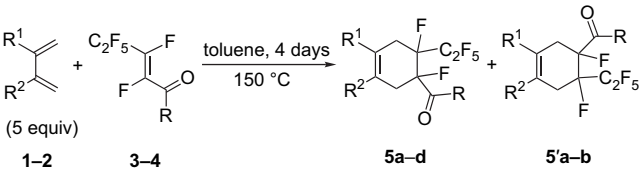
Scheme 1.

2. Results and discussion

As previously reported, the cyclohexenes were prepared in 64–77% isolated yields by heating for several days the dienes **1** and **2** and the enones **3** and **4** in toluene at 150 °C in a sealed tube (Table 1).[5] The reaction with isoprene gave a mixture of isomers in the ratio 60/40. The poor regioselectivity observed could be attributed to a weak polarization of the enone due to the presence of an electron withdrawing group at each carbon of the double bond (CO group and *F*-alkyl chain). The regioisomers were not separated and the assignment of their structure was deduced from the subsequent aromatic derivatives.

Treatment of these cycloadducts by potassium hydroxide in methanol induced the double elimination of hydrogen fluoride[9] and led to the expected *ortho*-perfluoroalkylated phenones **6** in 66–82% isolated yields (Table 2). Compounds **5** and **5′** were converted into the corresponding phenones **6** and **6′** with a similar regioisomeric ratio.

Table 1. Diels–Alder reactions of buta-1,3-dienes and hemifluorinated enones

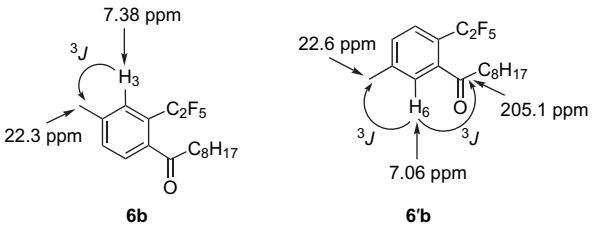


(5 equiv)

1–2 **3–4** **5a–d** **5′a–b**

Entry[a]	Diene	R^1	R^2	Enone	R	Product	Ratio **5/5′**[b]	Yield (%)
1	**1**	Me H	H Me	**3**	Ph	**5a** **5′a**	62/38	64
2	**1**	Me H	H Me	**4**	C_8H_{17}	**5b** **5′b**	51/49	65
3	**2**	Me	Me	**3**	Ph	**5c**	—	76
4	**2**	Me	Me	**4**	C_8H_{17}	**5d**	—	77

[a] Reaction conditions: 5.0 equiv of diene, toluene 10 mL at 150 °C (oil bath) in a sealed tube.
[b] Determined by ^{19}F NMR.



6b **6′b**

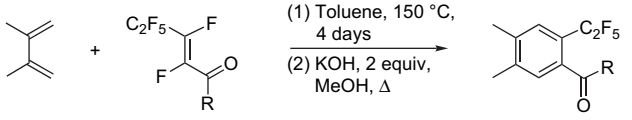
Figure 2. Determination of the structures of the aromatic regioisomers.

Although the compounds were not separated, the determination of the structure of the two regioisomers **6b** and **6′b** was performed using a ^1H–^{13}C HMBC NMR sequence. The two singlets corresponding to H-3 for the regioisomer **6b** and H-6 for the regioisomer **6′b** were attributed according to long-distance coupling constants ^3J between these two hydrogen atoms, the carbonyl group, and the methyl group as shown in Figure 2.

The same result was obtained with the regioisomers **6a** and **6′a**.

Interestingly, synthesis of the aromatic compounds can be readily achieved in a 'one-pot' sequence without isolation of the intermediate cycloadducts. After completion of the Diels–Alder reaction (GC monitoring), toluene was evaporated and the crude mixture dissolved in methanol with subsequent addition of potassium hydroxide. This process allowed a significant improvement of the yields (91–95%) of the fluorinated aromatics (Table 3).

Table 3. 'One-pot' synthesis of the *ortho*-perfluoroalkyl phenones



2 **3–4** **6c–d**

Entry	Enone	R	Product	Yield (%)
1	**3**	Ph	**6c**	91
2	**4**	C_8H_{17}	**6d**	95

Table 2. Synthesis of the *ortho*-perfluoroalkyl phenones

5a–d **5′a–b** **6a–d** **6′a–b**

Entry	Cycloadduct	R^1	R^2	R	Product	Ratio **6/6′**[b]	Yield (%)
1	**5a** **5′a**	Me H	H Me	Ph	**6a** **6′a**	62/38	66[a]
2	**5b** **5′b**	Me H	H Me	C_8H_{17}	**6b** **6′b**	51/49	75[a]
3	**5c**	Me	Me	Ph	**6c**	—	75
4	**5d**	Me	Me	C_8H_{17}	**6d**	—	82

[a] Obtained as a mixture of non-separated regioisomers.
[b] Determined by ^{19}F NMR.

3. Conclusion

Hemifluorinated enones proved to be good dienophiles for [4+2] cycloaddition reactions with buta-1,3-dienes. Basic treatment of the cycloadducts leads to the formation of *ortho*-(perfluoroethyl)phenones with good yields. These fluorinated aromatic compounds were also synthesized without isolation of the intermediate cyclohexene derivatives. Although it is limited to a few examples exhibiting the feasibility of the transformation, this paper discloses a potentially versatile methodology allowing to introduce structural diversity at the acyl moiety (structure of the starting acylsilane) and at the aryl substitution pattern (structure of the diene and length of the perfluoroalkyl chain).

4. Experimental

4.1. General methods

All air- and moisture-sensitive reactions were carried out under an argon atmosphere. Diethyl ether was distilled over Na/benzophenone before use. All reported NMR spectra were recorded with a Bruker AC 250. Chemical shifts are reported as δ values relative to $CHCl_3$ peak defined at δ=7.27 (^{1}H NMR) or δ=77.0 (^{13}C NMR). IR spectra were recorded using NaCl film or KBr pellets on an Avatar 320 FT-IR (Nicolet) spectrometer. Mass spectra (MS) were obtained on a Thermoquest Trace GC 2000 Series instrument. Elementary analyses were taken on a Perkin–Elmer CHN 2400 elementary analysis instrument. Analytical TLC was performed on Merck 60 PF_{254} silica gel pre-coated plates. Preparative flash silica gel chromatography was performed using Merck Kieselgel 60 (40–63 μm). Petroleum ether refers to the fraction with bp 40–65 °C.

All commercially available chemicals were used as received unless otherwise noted. Hemifluorinated enones **3** and **4** were obtained as previously described.[8]

4.2. General procedure for the synthesis of cycloadducts 5 and 5′

A solution of the dienes **1** and **2** (5 mmol) and the hemifluorinated enones **3** and **4** (1 mmol) was warmed in toluene (15 mL) in an oil bath at 150 °C in a sealed tube. After completion of the reaction (4 days), the reaction mixture was cooled to room temperature and toluene was evaporated. The crude mixture was purified by flash chromatography over silica gel (petroleum ether/EtOAc 99:1) to afford pure cycloadducts.

4.2.1. Mixture of non-separated regioisomers 5a/5′a (59/41). Orange oil. Yield: 65%. IR (film) ν_{max} cm^{-1}: 2925, 2858, 1698 (CO), 1579, 1448, 1383; EIMS *m/z* (%): 354 (M$^+$, 1), 334 (M−20), 295, 257, 237, 215, 137, 105 (100). Anal. Calcd for $C_{16}H_{13}F_7O$: C, 54.25; H, 3.70. Found: C, 54.33; H, 3.82.

4.2.1.1. 1-(1,6-Difluoro-4-methyl-6-pentafluoroethyl-cyclohex-3-enyl)-phenone 5a. ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.74 (s, 3H, CH_3), 2.36–2.61 (m, 2H, H-5, H-2), 2.90–3.10 (m, 2H, H-5′, H-2′), 5.37 (br s, 1H, H-3), 7.37 (t, 2H, *J*=7.6 Hz, H-arom. *meta*), 7.49 (t, 1H, *J*=7.6 Hz, H-arom. *para*), 7.89 (d, 2H, *J*=7.6 Hz, H-arom. *ortho*); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 22.6 (CH_3), 34.7 (C-2), 35.0 (C-5), 115.8 (C-4), 128.2–129.8 (CH-arom.), 129.9 (C-3), 133.1 (C_q-arom.), 192.8 (CO); ^{19}F NMR (235.4 MHz, $CDCl_3$): δ −79.8 (d, 3F, *J*=13.3 Hz, CF_3), −117.1 (ddd, 1F, $^2J_{F,F}$=284.2 Hz, *J*=17.1, 11.4 Hz, CF_2), −119.1 (dd, 1F, $^2J_{F,F}$=284.2 Hz, *J*=19.1 Hz, CF_2), −166.2 (dt, 1F, *J*=38.2, 19.1 Hz, F-6), −171.9 (m, 1F, F-1).

4.2.1.2. 1-(1,6-Difluoro-3-methyl-6-pentafluoroethyl-cyclohex-3-enyl)-phenone 5′a. ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.70 (s, 3H, CH_3), 2.71–2.90 (m, 2H, H-5′, H-2′), 5.33 (br s, 1H, H-4); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 22.3 (CH_3), 33.8 (C-2), 33.9 (C-5), 114.1 (C-4), 128.2–129.8 (CH-arom.), 129.7 (C-3), 133.1 (C_q-arom.), 192.9 (CO); ^{19}F NMR (235.4 MHz, $CDCl_3$): δ −79.9 (d, 3F, *J*=13.3 Hz, CF_3), −117.1 (ddd, 1F, $^2J_{F,F}$=284.2 Hz, *J*=19.1, 11.4 Hz, CF_2), −119.2 (dd, 1F, $^2J_{F,F}$=284.2 Hz, *J*=19.1 Hz, CF_2), −165.0 (dt, 1F, *J*=38.2, 19.1 Hz, F-6), −173.4 (m, 1F, F-1).

4.2.2. Mixture of non-separated regioisomers 5b/5′b (62/38). Orange oil. Yield: 64%. IR (film) ν_{max} cm^{-1}: 2928, 2857, 1732 (CO), 1445, 1205; EIMS *m/z* (%): 390 (M$^+$, 18), 370, 350, 280, 272, 230 (100). Anal. Calcd for $C_{18}H_{25}F_7O$: C, 56.38; H, 6.45. Found: C, 56.46; H, 6.60.

4.2.2.1. (1,6-Difluoro-4-methyl-6-pentafluoroethyl-cyclohex-3-enyl)-nonan-1-one 5b. ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.88 (t, 3H, *J*=6.9 Hz, CH_3), 1.23–1.33 (m, 10H, CH_2), 1.60 (m, 2H, CH_2), 1.77 (s, 3H, CH_3), 2.10–2.98 (m, 6H, CH_2CO, H-2, H-2′, H-5, H-5′), 5.39 (br s, 1H, H-3); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 14.0 (CH_3), 22.3 (CH_3), 22.6 (CH_2), 22.9 (CH_2), 28.9 (CH_2), 29.1 (CH_2), 29.3 (CH_2), 32.0 (CH_2), 34.8 (C-2), 35.2 (C-5), 38.3 (CH_2CO), 114.3 (C-4), 130.5 (C-3), 204.2 (CO); ^{19}F NMR (235.4 MHz, $CDCl_3$): δ −79.7 (d, 3F, *J*=11.4 Hz, CF_3), −118.5 (dm, 1F, $^2J_{F,F}$=284.2 Hz, CF_2), −120.3 (dd, 1F, $^2J_{F,F}$=284.2 Hz, *J*=21.0 Hz, CF_2), −170.5 (dt, 1F, *J*=38.2, 19.1 Hz, F-6), −174.1 (dt, 1F, *J*=26.6, 13.3 Hz, F-1).

4.2.2.2. (1,6-Difluoro-3-methyl-6-pentafluoroethyl-cyclohex-3-enyl)-nonan-1-one 5′b. ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.74 (s, 3H, CH_3), 5.34 (br s, 1H, H-4); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 31.8 (CH_2), 34.9 (C-2), 35.1 (C-5), 38.4 (CH_2CO), 116.0 (C-4), 129.9 (C-3), 204.4 (CO); ^{19}F NMR (235.4 MHz, $CDCl_3$): δ −79.8 (d, 3F, *J*=13.3 Hz, CF_3), −118.5 (d, 1F, $^2J_{F,F}$=284.2 Hz, CF_2), −120.5 (dd, 1F, $^2J_{F,F}$=284.2 Hz, *J*=22.9 Hz, CF_2), −169.3 (dt, 1F, *J*=38.2, 19.1 Hz, F-6), −175.6 (dt, 1F, *J*=26.6, 13.3 Hz, F-1).

4.2.3. (1,6-Difluoro-3,4-dimethyl-6-pentafluoroethyl-cyclohex-3-enyl)-phenone 5c. Yellow oil. Yield: 76%. IR (film) ν_{max} cm^{-1}: 2922, 2865, 1688 (CO), 1598, 1579, 1448, 1421, 1387, 1203, 748, 691; ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.71 (s, 3H, CH_3), 1.74 (s, 3H, CH_3), 2.42–2.57 (m, 2H, H-5, H-2), 2.77–3.17 (m, 2H, H-5′, H-2′), 7.44 (t, 2H, *J*=7.6 Hz, H-arom. *meta*), 7.56 (t, 1H, *J*=7.6 Hz, H-arom. *para*), 7.96 (d, 2H, *J*=7.6 Hz, H-arom. *ortho*); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 18.1 (CH_3), 18.3 (CH_3), 33.0 (dd, $^2J_{C,F}$=21.7 Hz, $^3J_{C,F}$=2.4 Hz, C-2 or C-5), 38.6

(dd, $^2J_{C,F}$=21.7 Hz, $^3J_{C,F}$=2.4 Hz, C-2 or C-5), 93.6 (dm, $^1J_{C,F}$=196.3 Hz, C-6), 97.2 (dd, $^1J_{C,F}$=196.4 Hz, $^2J_{C,F}$= 22.9 Hz, C-1), 117.6 (C-4), 118.4 (tq, $^1J_{C,F}$=288.3 Hz, $^2J_{C,F}$=34.5 Hz, CF_3), 119.3 (C-3), 126.3–127.9 (CH-arom.), 133.7 (C_q-arom.), 195.6 (d, $^2J_{C,F}$=27.3 Hz, CO); ^{19}F NMR (235.4 MHz, $CDCl_3$): δ −79.9 (d, 3F, J=13.3 Hz, CF_3), −117.3 (ddd, 1F, $^2J_{F,F}$=284.2 Hz, J=11.4, 7.6 Hz, CF_2), −119.5 (dd, 1F, $^2J_{F,F}$=284.2 Hz, J=17.2 Hz, CF_2), −165.2 (dt, 1F, J=38.1, 19.1 Hz, F-6), −172.2 (ddtt,1F, J=38.1, 13.3, 5.7 Hz, F-1); EIMS m/z (%): 368 (M^+, 2), 348 (M−20, 100), 328, 295, 271, 251, 229. Anal. Calcd for $C_{17}H_{15}F_7O$: C, 55.44; H, 4.11. Found: C, 55.59; H, 4.12.

4.2.4. 1-(1,6-Difluoro-3,4-dimethyl-6-pentafluoroethyl-cyclohex-3-enyl)-nonan-1-one 5d. Yellow oil. Yield: 77%. IR (film) ν_{max} cm^{-1}: 2927, 2858, 1733 (CO), 1460, 1421, 1221; ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.89 (t, 3H, J=6.9 Hz, CH_3), 1.23–1.35 (m, 10H, CH_2), 1.61 (quint., 2H, CH_2), 1.68 (s, 3H, CH_3), 1.71 (s, 3H, CH_3), 2.12–2.50 (m, 2H, H-2, H-5), 2.59–2.99 (m, 4H, CH_2CO, H-2′, H-5′); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 14.0 (CH_3), 18.1 (CH_3), 18.3 (CH_3), 22.6 (CH_2), 22.8 (CH_2), 22.9 (CH_2), 28.9 (CH_2), 29.1 (CH_2), 29.3 (CH_2), 31.8 (CH_2), 34.6 (dm, $^2J_{C,F}$=21.7 Hz, C-5), 38.4 (dd, $^2J_{C,F}$=21.7 Hz, $^3J_{C,F}$= 2.0 Hz, C-2), 38.5 (d, $^3J_{C,F}$=3.2 Hz, CH_2CO), 119.2 (C-4), 121.0 (C-3), 206.6 (d, $^2J_{C,F}$=29.3 Hz, CO); ^{19}F NMR (235.4 MHz, $CDCl_3$): δ −79.8 (d, 3F, J=11.4 Hz, CF_3), −118.6 (ddd, 1F, $^2J_{F,F}$=284.2 Hz, $^3J_{F,F}$=11.4, 5.7 Hz, CF_2), −120.4 (dd, 1F, $^2J_{F,F}$=284.2 Hz, J=22.9 Hz, CF_2), −169.5 (dt, 1F, J=40.0, 19.0 Hz, F-6), −174.4 (dt, 1F, J=40.0, 13.3 Hz, F-1); EIMS m/z (%): 404 (M^+, 4), 384, 364, 314, 286, 229. Anal. Calcd for $C_{19}H_{27}F_7O$: C, 56.43; H, 6.73. Found: C, 56.58; H, 6.81.

4.3. General procedure for the synthesis of *ortho*-perfluoroalkyl phenones 6 and 6′

Method A: to a solution of the fluorinated cycloadduct **5** or the mixture of cycloadducts **5**–**5′** (1 mmol) in methanol (5 mL) was added potassium hydroxide (2 mmol). The solution was refluxed for 24 h. After completion of the reaction, the reaction mixture was cooled to room temperature and methanol was evaporated. The crude mixture was dissolved in diethyl ether (50 mL) and extracted twice with a saturated NaCl solution. The organic layer was then dried over $MgSO_4$ and the organic solvent was evaporated. The crude mixture was purified by flash chromatography over silica gel (petroleum ether/EtOAc 99:1) to afford pure aromatic compounds.

Method B: to a solution of the dienes **1** and **2** (5 mmol) and the hemifluorinated enones **3** and **4** (1 mmol) in toluene (15 mL) in an oil bath at 150 °C in a sealed tube. After completion of the reaction (4 days), the reaction mixture was cooled to room temperature and toluene was evaporated. The crude residue was dissolved in methanol and potassium hydroxide (2 mmol) was added. After completion of the reaction (24 h), the reaction mixture was cooled to room temperature and methanol was evaporated. The crude mixture was dissolved in diethyl ether (50 mL) and extracted twice with brine. The organic layer was then dried over $MgSO_4$ and the organic solvent was evaporated. The crude mixture was purified by flash chromatography over silica gel (petroleum ether/EtOAc 99:1) to afford pure aromatic compounds.

4.3.1. Mixture of non-separated regioisomers 6a/6′a (61/39). Yellow oil. Yield: 75%. IR (film) ν_{max} cm^{-1}: 2969, 1681 (CO), 1597, 1450, 1332, 1212, 1082, 998.

4.3.1.1. (4′-Methyl-2′-pentafluoroethyl)phenyl-phenone 6a. ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.40 (s, 3H, CH_3), 7.15 (d, 1H, J=7.9 Hz, H-6′), 7.32–7.40 (m, 3H, H-arom. *meta*, H-3′, H-5′), 7.48 (t, 1H, J=7.6 Hz, H-arom. *para*), 7.65 (d, 2H, J=7.6 Hz, H-arom. *ortho*); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 21.0 (CH_3), 124.0 (t, $^2J_{C,F}$=30.0 Hz, C-2′), 126.6 (C-6′), 128.4–130.1 (C-3′, CH-arom.), 132.0 (C-5′), 133.2 (C_q-arom.), 139.7 (C-4′), 139.9 (C-1′), 195.9 (CO); ^{19}F NMR (235.4 MHz, $CDCl_3$): δ −83.8 (s, 3F, CF_3), −107.7 (s, 2F, CF_2).

4.3.1.2. (5′-Methyl-2′-pentafluoroethyl)phenyl-phenone 6′a. ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.43 (s, 3H, CH_3), 7.07 (s, 1H, H-6′), 7.32–7.40 (m, 3H, H-arom. *meta*, H-3′, H-4′), 7.48 (t, 1H, J=7.6 Hz, H-arom. *para*), 7.65 (d, 2H, J=7.6 Hz, H-arom. *ortho*); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 21.2 (CH_3), 121.7 (t, $^2J_{C,F}$=30.0 Hz, C-2′), 126.9 (C-6′), 128.4–130.1 (C-3′, CH-arom.), 133.3 (C_q-arom.), 135.7 (C-4′), 144.0 (C-1′), 144.2 (C-5′), 196.1 (CO); ^{19}F NMR (235.4 MHz, $CDCl_3$): δ −84.0 (s, 3F, CF_3), −107.7 (s, 2F, CF_2).

4.3.2. Mixture of non-separated regioisomers 6b/6′b (60/40). Yellow oil. Yield: 66%. IR (film) ν_{max} cm^{-1}: 2958, 2928, 2857, 1713 (CO), 1612, 1572, 1459, 1333, 1205, 1086, 857; EIMS m/z (%): 350 (M^+, 8), 330, 302, 252, 237 (100), 219, 164, 159.

4.3.2.1. 1-(4′-Methyl-6′-pentafluoroethyl)phenyl-nonan-1-one 6b. ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.88 (t, 3H, J=6.9 Hz, CH_3), 1.23–1.33 (m, 10H, CH_2), 1.68 (quint., 2H, J=6.9 Hz, CH_2), 2.43 (s, 3H, CH_3), 2.76 (t, 2H, J= 6.9 Hz, CH_2), 7.17 (d, 1H, J=8.3 Hz, H-6′), 7.38 (s, 1H, H-3′), 7.39 (d, 1H, J=8.3 Hz, H-5′); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 14.0 (CH_3), 22.6 (CH_2), 23.5 (CH_3), 23.6 (CH_2), 29.0 (CH_2), 29.1 (CH_2), 29.3 (CH_2), 31.8 (CH_2), 44.0 (CH_2), 124.5 (t, $^2J_{C,F}$=29.0 Hz, C-2′), 126.5 (C-6′), 129.8 (C-3′), 132.4 (C-5′), 139.6 (C-4′), 139.8 (C-1′), 205.1 (CO); ^{19}F NMR (235.4 MHz, $CDCl_3$): δ −83.6 (s, 3F, CF_3), −107.8 (s, 2F, CF_2).

4.3.2.2. 1-(4′-Methyl-2′-pentafluoroethyl)phenyl-nonan-1-one 6′b. ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.88 (t, 3H, J=6.9 Hz, CH_3), 1.23–1.33 (m, 10H, CH_2), 1.68 (quint., 2H, J=6.9 Hz, CH_2), 2.42 (s, 3H, CH_3), 2.78 (t, 2H, J=6.9 Hz, CH_2), 7.06 (s, 1H, H-6′), 7.31 (d, 1H, J= 8.0 Hz, H-4′), 7.47 (d, 1H, J=8.0 Hz, H-3′); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 14.0 (CH_3), 22.6 (CH_2), 23.4 (CH_3), 23.6 (CH_2), 29.0 (CH_2), 29.1 (CH_2), 29.3 (CH_2), 31.9 (CH_2), 44.2 (CH_2), 121.4 (t, $^2J_{C,F}$=30.0 Hz, C-2′), 126.8 (C-6′), 128.6 (C-3′), 142.6 (C-1′), 142.9 (C-5′), 205.3 (CO); ^{19}F NMR (235.4 MHz, $CDCl_3$): δ −83.9 (s, 3F, CF_3), −107.8 (s, 2F, CF_2).

4.3.3. 1-(4′,5′-Dimethyl-2′-pentafluoroethyl)phenyl-phenone 6c. Yellow oil. Yields: 75% (Method A), 95% (Method B). IR (film) ν_{max} cm^{-1}: 2920, 2865, 1685 (CO), 1598, 1575, 1442, 1420, 1387, 1203, 748, 691; ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.25 (s, 3H, CH_3), 2.31 (s, 3H, CH_3), 7.00 (s,

1H, H-3′), 7.35 (t, 3H, J=7.4 Hz, H-arom. *meta*, H-6′), 7.49 (t, 1H, J=7.4 Hz, H-arom. *para*), 7.67 (d, 2H, J=7.4 Hz, H-arom. *ortho*); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 19.6 (CH_3), 19.7 (CH_3), 127.3 (C-3), 128.4 (CH-arom.), 129.0 (CH-arom.), 129.4 (C-6), 130.1 (CH-arom.), 133.5 (CH-arom.), 136.8 (C_q-arom.), 138.4 (C-4 or C-5), 140.8 (C-4 or C-5), 196.0 (CO); ^{19}F NMR (235.4 MHz, $CDCl_3$): δ −83.9 (s, 3F, CF_3), −107.6 (s, 2F, CF_2); EIMS m/z (%): 328 (M^+, 31), 309, 251, 201, 173, 133, 105 (100). Anal. Calcd for $C_{17}H_{13}F_5O$: C, 62.20; H, 3.99. Found: C, 62.47; H, 4.21.

4.3.4. 1-(4′,5′-Dimethyl-2′-pentafluoroethyl)phenyl-nonan-1-one 6d. Yellow oil. Yields: 82% (Method A), 91% (Method B). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.88 (t, 3H, J=6.9 Hz, CH_3), 1.23–1.35 (m, 10H, CH_2), 1.68 (quint., 2H, J=7.2 Hz, CH_2), 2.32 (br s, 6H, $2CH_3$), 2.75 (t, 2H, J=7.4 Hz, CH_2), 7.01 (s, 1H, H-3), 7.32 (s, 1H, H-6); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 14.0 (CH_3), 19.5 (CH_3), 19.6 (CH_3), 22.6 (CH_2), 23.6 (CH_2), 29.0 (CH_2), 29.1 (CH_2), 29.3 (CH_2), 31.8 (CH_2), 44.8 (CH_2), 127.5 (C-3), 129.0 (C-6), 138.2 (C-4 or C-5), 141.1 (C-4 or C-5), 205.3 (CO); ^{19}F NMR (235.4 MHz, $CDCl_3$): δ −83.8 (s, 3F, CF_3), −107.6 (s, 2F, CF_2); EIMS m/z (%): 364 (M^+, 8), 349, 308, 279, 251 (100), 237, 223, 177. Anal. Calcd for $C_{19}H_{25}F_5O$: C, 62.63; H, 6.91. Found: C, 62.94; H, 6.99.

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