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Supporting Information

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„Fluorinating-cleavage“ – The first fluorinating cleavable linker for combinatorial solid-phase synthesis

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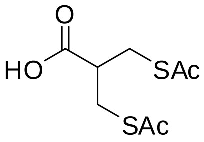
Instrumentation and reagents: ^{1}H NMR spectra were recorded on *Bruker* AM 250 (250 MHz), *Bruker* AM 400 (400 MHz) and *Bruker* AM 500 (500 MHz) spectrometers. Chemical shifts are expressed in parts per million (ppm, δ) downfield from tetramethylsilane (TMS) and are referenced to $CHCl_3$ (7.26 ppm) or acetone[d_6] (2.09 ppm) as internal standard. All couplings constants are absolute values and *J* values are expressed in Hertz (Hz). The description of signals include: s = singlet, d = doublet, bd = broad doublet, t = triplet, dd = doublet of doublets, dt doublet of triplets, m = multiplet. The spectra were analyzed according to first order. ^{13}C NMR spectra were recorded on *Bruker* AM 250 (62.5 MHz), *Bruker* AM 400 (100 MHz) and *Bruker* AM 500 (125 MHz) spectrometers. Chemical shifts are expressed in parts per million (ppm, δ) downfield from tetramethylsilane (TMS) and are referenced to $CHCl_3$ (77.4 ppm) or acetone[d_6] (30.6 ppm) as internal standard. For measurement of ^{13}C-NMR-Gel-Spectra, 60-100 mg of the resin were swollen in a NMR-tube with the appropriate amount of $CDCl_3$). The NMR-spectrometer was run with pulse program zgpg30 (Relaxation delay D1 = 0.2 seconds, linebroadening LB = 9.0 Hz, 5120 scans). MS (EI) (electron impact mass spectrometry): *Finnigan* MAT 90 (70 eV). The molecular fragments are quoted as the relation between mass and charge (*m/z*), the intensities as a percentage value relative to the intensity of the base signal (100%). The abbreviation [M^+] refers to the molecule ion. IR (infrared spectroscopy): FTIR *Bruker* IFS 88. IR spectra of solids were recorded in KBr, and as thin films on KBr for oils and liquids. The deposit of the absorption band was given in wave numbers in cm^{-1}. The forms and intensities of the bands were characterized as follows: m = medium 40–70% T, w = weak 70–90% T, vw = very weak 90–100% T. Routine monitoring of reactions were performed using Silica gel coated aluminium plates (Merck, silica gel 60, F_{254}) which were analyzed under UV-light at 254 nm and/or dipped into a solution of molybdato phosphate (5% phosphor molybdic acid in ethanol, dipping solution) and heated with a heat gun. Solvent mixtures are understood as volume/volume. Solid materials were powdered. Solvents, reagents and chemicals were purchased from Aldrich, Fluka and Acros. Tetrahydrofuran was distilled from sodium/benzophenone under argon prior use. Dichloromethane, ethyl acetate and diethyl ether were distilled from calcium hydride. All reactions involving moisture sensitive reactants were executed under an argon atmosphere using oven dried and/or flame dried glassware, all other solvents, reagents and chemicals were used as purchased unless stated otherwise. Aminomethyl Resin was purchased from Polymer Laboratories (PL-AMS Resin, 2.06 mmol/g, 75-150 µm, AMS 118). As not stated otherwise, vials from Macherey-Nagel were used for all reactions beyond room temperature (size 20-20 und 20-10, in combination with N20 oA and N20 TB/oA-M septa).

General washing procedure for resins: (GP 1):

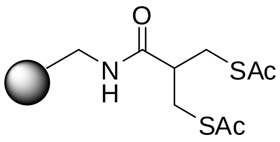
Method 1 (GP 1a): The resins were washed with the following solvents (1 ml per 100 mg resin): 1. dichloromethane/methanol/dichloromethane/methanol/dichloromethane; 2. methanol/water/methanol/ water/methanol; 3. dichloromethane/methanol/dichloromethane/methanol/dichloromethane. Finally, the resins were washed three times with dichloromethane and dried for 24 h under high vacuum.

Method 2 (GP 1b): The resins were washed with the following solvents (1 ml per 100 mg resin): 1. DMF/methanol/water/DMF/methanol/DMF; 2. methanol/dichloromethane/methanol/dichloromethane/ methanol; 3. di-chloromethane/pentane/dichloromethane/pentane/dichloromethane. Finally, the resins were washed three times with dichloromethane and dried for 24 h under high vacuum.

Synthesis of the dithiole linker 7:

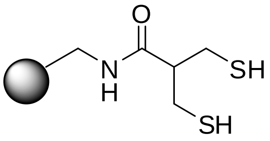


3-(Acetylthio)-2-(acetylthiomethyl)propanoic acid (**4**): A solution of 5.50 g (52.0 mmol) Na_2CO_3 in 20 ml water was added in small portions to a suspension of 4.95 g (30.0 mmol) 2-(bromomethyl)acrylic acid (**3**) in 100 ml water at 0 °C. Then 2.33 g (30.5 mmol) thioacetic acid was added slowly and the mixture was stirred for 30 minutes. pH 1 was adjusted using diluted HCl solution. The mixture was extracted three times with ethyl acetate, the combined organic phases were dried over $MgSO_4$ and the solvent was removed under reduced pressure to yield 4.79 g (29.8 mmol) 2-(acetylthiomethyl)acrylic acid as a white solid. The acid was dissolved in 50 ml ethyl acetate. 3.43 g (45.0 mmol) of thioacetic acid were added and the reaction mixture was stirred for 24 h. The mixture was concentrated at reduced pressure removing the solvent and the excess of thioacetic acid as well to give 7.01 g (29.7 mmol, 99%) of the product as an orange oil. – ^{1}H-NMR (400 MHz, $CDCl_3$): $\delta = 2.31$ (s, 6 H, each $COCH_3$), 2.88 (quin, 1 H, $^3J_{HH} = 6.5$ Hz, $CH(CH_2)_2$), 3.17 (m, 4 H, each CH_2S), 10.81 (s, 1 H, OH) ppm. – ^{13}C-NMR (100 MHz, $CDCl_3$): $\delta = 29.1$ (each CH_2S), 30.5 (each $COCH_3$), 45.0 (CH), 177.8 ($COOH$), 195.6 (each $COCH_3$) ppm. – IR (KBr): $\nu = 2991$ (m, υ(OH)), 2927 (m), 2651 (w), 1695 (s, υ(CO)), 1423 (m), 1355 (m), 1305 (w), 1244 (m), 1133 (s), 958 (m), 852 (w), 806 (w), 688 (vw), 625 (m) cm^{-1}. – MS (EI): *m/z* (%): 236 (1) [M^+], 219 (20) [M^+–OH], 193 (30) [M^+–$COCH_3$], 176 (52) [M^+–$C_2H_4O_2$], 133 (60) [M^+–$C_4H_7O_3$], 43 (100) [$C_2H_3O^+$]. – HRMS ($C_8H_{12}O_4S_2$): calc. 236.0177, found 236.0180. – $C_8H_{12}O_4S_2$ (236.02): calc. C 40.66, H 5.12, S 27.14; found C 40.43, H 5.35, S 27.89.



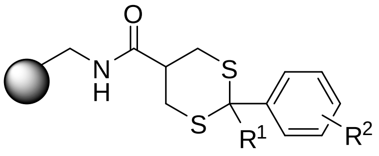
3-(Acetylthio)-2-(acetylthiomethyl))-N-methylpolystyrylpropanamide (**6**): 5.00 g (10.3 mmol) of aminomethyl polystyrene resin (**5**, loading: 2.06 mmol/g) were covered with 50 ml dry dichloromethane and shaken for 30 minutes. Then 7.29 g (30.9 mmol) of thioester **4** were dissolved in 25 ml dry dichloromethane and added to the resin. Afterwards 9.60 g (20.6 mmol) PyBrOP and 4.80 ml (30.9 mmol) DIPEA were added and the mixture was shaken at room temperature. After 48 h, the reaction mixture was filtered off, washed following GP 1a and dried under high vacuum to give 6.96 g of white resin **6**. The yield and the loading of were **6** determined using sulfur elemental analysis (87% yield, loading 1.23 mmol/g). – ^{13}C-NMR (100 MHz, CDCl$_3$): δ = 23.4 (*C*H$_2$S), 30.6 (*C*H$_3$), 53.5 (CO*C*H), 171.5 (NH*C*O), 195.7 (S*C*OCH$_3$) ppm. – IR (KBr): ν = 3564 (w), 3415 (m), 3336 (m), 3115 (w), 2979 (w), 2935 (w), 2784 (vw), 2688 (vw), 2305 (w), 1973 (w), 1894 (w), 1698 (υ(CO), s), 1504 (m), 1469 (m), 1427 (m), 1406 (m), 1352 (m), 1232 (m), 1164 (m), 1132 (m), 1103 (m), 1039 (m), 995 (m), 954 (m), 856 (w).– $C_{44}H_{48}NS_2O_3$: calc. C 75.21, H 6.88, N 1.99, S 9.11; found C 74.92, H 6.22, N 2.09, S 7.90.

3-Mercapto-2-(mercaptomethyl)-N-methylpolystyrylpropanamide (**7**): To 1.00 g (1.23 mmol) of resin **6** in 20 ml chloroform were added 10 ml HCl (1.25 M in methanol, 12.5 mmol) under argon. After shaking for 24 h at 50 °C, the volatile compounds were removed under reduced pressure and the resin was dried 3 h under high vacuum and stored under argon atmosphere. 890 mg of white resin **5** were obtained (loading 1.40 mmol/g). – ^{13}C-NMR (100 MHz, CDCl$_3$): δ = 26.1 (*C*H$_2$SH), 54.7 (CO*C*H), 171.7 (NH*C*O) ppm. – IR (KBr): ν = 3408 (w), 3338 (w), 3024 (vw), 2925 (vw), 2562 (w, υ(SH)), 1731 (w), 1695 (m, υ(CO)), 1525 (w), 1407 (w), 1236 (w), 1172 (w), 1132 (w), 1089 (w), 1040 (w), 995 (w), 929 (w), 730 (w), 647 (w), 538 (vw). – $C_{40}H_{42}NS_2O$: calc. C 77.66, H 6.84, N 2.26, S 10.33; found C 76.87, H 6.78, N 2.36, S 8.95.



General procedure for the attachment of aldehydes and ketones to the dithiole linker 7 (GP 2):

1 equivalent of resin **7** (loading: 1.40 mmol/g) was covered with chloroform (10 ml per 1.00 g resin) under argon atmosphere and shaken for 30 minutes. After cooling to 0 °C, 5 equivalents of the carbonyl compound **8** dissolved in 5 ml chloroform and 5 equivalents BF$_3$·Et$_2$O were added, the vial was sealed and the mixture was shaken for 24 h at 40 °C. Finally, the reaction mixture was filtered off, washed following GP 1a and dried under high vacuum to give resin **9**. ^{13}C-NMR-gelphase spectra were measured for qualititative reaction control. All ^{13}C-NMR signals are given except of those that derive from the polystyrene resin or from the linker molecule. Some of the expected signals of the attached molecules are superimposed by the polystyrene core and can therefore not be detected.



9a: R^1= H, R^2= 4-*t*Bu: Reaction of 300 mg (0.42 mmol) resin with 4-*tert*-butylbenzaldehyde (**8a**) gave 335 mg of bright brown resin **9a**. – ^{13}C-NMR (100 MHz, CDCl$_3$): δ = 31.7 (C(*C*H$_3$)$_3$), 34.5 (*C*(CH$_3$)$_3$), 145.4 (*C*$_{\mathrm{Ar}}$C(CH$_3$)$_3$) ppm.

9b: R^1= Me, R^2= 4-NO$_2$: Reaction of 300 mg (0.42 mmol) resin with 4-nitroacetophenone (**8b**) gave 360 mg of yellow resin **9b**. – ^{13}C-NMR (100 MHz, CDCl$_3$): δ = 29.9 (*C*H$_3$) ppm.

9c: R^1= *p*-Tol, R^2= 4-Me: Reaction of 300 mg (0.42 mmol) resin with 4,4`-dimethylbenzophenone (**8c**) gave 355 mg of bright brown resin **9c**. – ^{13}C-NMR (100 MHz, $CDCl_3$): $\delta = 21.2$ (*C*H_3) ppm.

9d: R^1= Ph, R^2= 4-*t*Bu: Reaction of 300 mg (0.42 mmol) resin with 4-*tert*-butylbenzophenone (**8d**) gave 372 mg of bright brown resin **9d**. – ^{13}C-NMR (100 MHz, $CDCl_3$): $\delta = 31.4$ ($C(CH_3)_3$), 34.5 ($C(CH_3)_3$) ppm.

9e: R^1= Me, R^2= 3-I-5-CO_2Me: Reaction of 300 mg (0.42 mmol) resin with 3-iodo-5-carboxymethyl-acetophenone (**8e**) gave 440 mg of bright brown resin **9e**. – ^{13}C-NMR (100 MHz, $CDCl_3$): $\delta = 27.9$ (*C*H_3), 53.6 (O*C*H_3), 94.4 (C_{Ar}I), 140.7 ($C_{Ar}C_{Ar}$I), 165.3 (*C*OOMe) ppm.

9f: R^1= Me, R^2= 4-NH_2: Reaction of 1.00 g (1.40 mmol) resin with 4-aminoacetophenone (**8f**) gave 1.17 g of bright brown resin **9f**. – ^{13}C-NMR (100 MHz, $CDCl_3$): $\delta = 30.1$ (*C*H_3) 118.2 ($C_{Ar}C_{Ar}NH_2$) ppm.

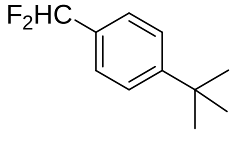
9g: R^1= Me, R^2= 4-I: Reaction of 1.00 g (1.40 mmol) resin with 4-iodoacetophenone (**8g**) gave 1.24 g bright brown resin **9g**. – ^{13}C-NMR (100 MHz, $CDCl_3$): $\delta = 30.1$ (*C*H_3), 92.4 (C_{Ar}I), 137.9 ($C_{Ar}C_{Ar}$I) ppm.

9h: R^1= Me, R^2= 4-Ac: Reaction of 1.00 g (1.40 mmol) resin with 1,4-diacetylbenzene (**8h**) gave 1.19 g of orange resin **9h**. – ^{13}C-NMR (100 MHz, $CDCl_3$): $\delta = 30.2$ (*C*H_3), 195.5 (*C*OCH_3) ppm.

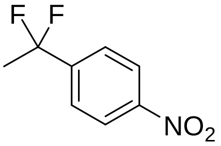
General procedure for the fluorinating cleavage of the compounds from the resin (GP 3):

The cleavage reactions were performed under argon atmosphere in 100 ml Teflon-coated flasks. 4 equivalents of *N*-iodosuccinimide were suspended in 10 ml dry dichloromethane. After cooling to −78 °C, 40 equivalents of HF (70% in pyridine) were added and the mixture was stirred for 10 minutes. Then 1 equivalent of resin **9** was swollen in the twofold volume dry dichloromethane and transferred into the flask. The reaction was stirred for 3 h while warming up to 0 °C. 20 ml dichloromethane were added, followed by 10 ml 5% $NaHSO_3$ solution. After the red colour disappeared, pH 10 was adjusted using $NaHCO_3$/NaOH (20:1) solution. The resin was filtered off, the layers were separated and the water phase was extracted two times with dichloromethane. The combined organic phases were washed with diluted HCl solution (pH 2), dried over $MgSO_4$ and the solvent was removed under reduced pressure to yield the crude products which were purified by flash column chromatography on silica gel.

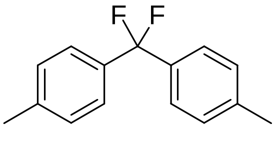
The yields of the products are in all cases given in relation to the stable linker precursor **6** because the determination of the loading by sulphur elemental analysis of **6** is more precise than the calculation by gravimetric measurements after subsequent steps. Therefore the given yields are yields over 3 or 4 steps, respectively.



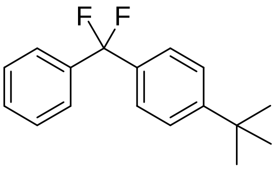
1-tert-Butyl-4-(difluoromethyl)benzene (**10a**): After cleavage from resin **9a** 22 mg (0.12 mmol, 29% over 3 steps) of a bright yellow oil were obtained (pentane/diethylether 40:1, R_f = 0.7). – ^{1}H-NMR (250 MHz, CDCl$_3$): δ = 1.26 (s, 9 H, C(C*H*$_3$)$_3$), 6.55 (t, $^{2}J_{\mathrm{HF}}$ = 56.6 Hz, 1 H, C*H*F$_2$), 7.51 (d, ^{3}J = 8.3 Hz, 2 H, Ar-*H*), 7.74 (d, ^{3}J = 8.3 Hz, 2 H, Ar-*H*) ppm. – ^{13}C-NMR (100 MHz, CDCl$_3$): δ = 28.7 (C(*C*H$_3$)$_3$), 33.9 (*C*(CH$_3$)$_3$), 113.9 (t, $^{1}J_{\mathrm{CF}}$ = 237.9 Hz, *C*HF$_2$), 125.4 (*C*$_{\mathrm{Ar}}$), 125.9 (*C*$_{\mathrm{Ar}}$), 127.4 (t, $^{2}J_{\mathrm{CF}}$ = 23.1 Hz, *C*$_{\mathrm{Ar}}$CF$_2$), 153.0 (*C*$_{\mathrm{Ar}}$C(CH$_3$)$_3$) ppm. – ^{19}F-NMR (376 MHz, H-decoupled, CDCl$_3$): δ = –109.8 ppm. – MS (EI): *m/z* (%): 184 (30) [M$^+$], 169 (100) [M$^+$–CH$_3$]. – HRMS (+Na) ($C_{11}H_{14}F_2Na$): calc. 207.0961; found 207.0958.



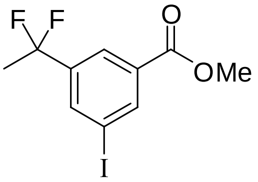
1-(1,1-Difluoroethyl)-4-nitrobenzene (**10b**): After cleavage from resin **9b** 45 mg (0.24 mmol, 57% over 3 steps) of a yellow oil were obtained (pentane/diethylether 10:1, R_f = 0.5). – ^{1}H-NMR (250 MHz, CDCl$_3$): δ = 1.89 (t, $^{3}J_{\mathrm{HF}}$ = 18.2 Hz, 3 H, C*H*$_3$CF$_2$), 7.65 (d, ^{3}J = 8.3 Hz, 2 H, Ar-*H*), 8.18 (d, ^{3}J = 8.3 Hz, 2 H, Ar-*H*) ppm. – ^{13}C-NMR (100 MHz, CDCl$_3$): δ = 24.9 (t, $^{2}J_{\mathrm{CF}}$ = 29.2 Hz, *C*H$_3$CF$_2$), 119.8 (t, $^{1}J_{\mathrm{CF}}$ = 240.5 Hz, *C*F$_2$), 125.0 (*C*$_{\mathrm{Ar}}$), 128.3 (*C*$_{\mathrm{Ar}}$), 143.2 (t, $^{2}J_{\mathrm{CF}}$ = 23.5 Hz, *C*$_{\mathrm{Ar}}$CF$_2$), 148.0 (*C*$_{\mathrm{Ar}}$NO$_2$) ppm. – ^{19}F-NMR (376 MHz, H-coupled, CDCl$_3$): δ = –89.9 (q, $^{3}J_{\mathrm{HF}}$ = 18.2 Hz) ppm. – MS (EI): *m/z* (%): 187 (100) [M$^+$], 172 (46) [M$^+$–CH$_3$], 141 (84) [M$^+$–NO$_2$]. – HRMS ($C_8H_7F_2NO_2$): calc. 187.0445; found 187.0443.



Difluoro-di-para-tolylmethane (**10c**): After cleavage from resin **9c** 28 mg (0.12 mmol, 30% over 3 steps) of a bright yellow oil were obtained (pentane, R_f = 0.9). – ^{1}H-NMR (250 MHz, CDCl$_3$): δ = 2.31 (s, 6 H, each C*H*$_3$), 7.23 (d, ^{3}J = 8.3 Hz, 4 H, Ar-*H*), 7.44 (d, ^{3}J = 8.3 Hz, 4 H, Ar-*H*) ppm. – ^{13}C-NMR (100 MHz, CDCl$_3$): δ = 21.9 (*C*H$_3$), 113.8 (t, $^{1}J_{\mathrm{CF}}$ = 246.5 Hz, *C*F$_2$), 119.0 (t, $^{2}J_{\mathrm{CF}}$ = 23.5 Hz, *C*$_{\mathrm{Ar}}$CF$_2$), 124.0 (*C*$_{\mathrm{Ar}}$), 128.8 (*C*$_{\mathrm{Ar}}$), 138.6 (*C*$_{\mathrm{Ar}}$CH$_3$) ppm. – ^{19}F-NMR (376 MHz, H-decoupled, CDCl$_3$): δ = –87.5 ppm. – MS (EI): *m/z* (%): 232 (20) [M$^+$], 217 (100) [M$^+$–CH$_3$], 141 (9) [M$^+$–C$_6$H$_4$CH$_3$], 91 (40) [C$_6$H$_4$CH$_3$$^+$]. – HRMS ($C_{15}H_{14}F_2$): calc. 232.1064; found 232.1067.

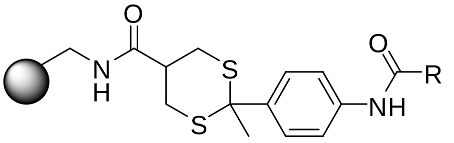


1-tert-Butyl-4-(difluoro(phenyl)methyl)benzene (**10d**): After cleavage from resin **9d** 59 mg (0.23 mmol, 54% over 3 steps) of a bright yellow oil were obtained (pentane/diethylether 40:1, R_f = 0.7). – ^{1}H-NMR (250 MHz, CDCl$_3$): δ = 1.25 (s, 9 H, C(C*H*$_3$)$_3$), 7.28–7.50 (m, 7 H, Ar-*H*), 7.72 (m, 2 H, Ar-*H*). – ^{13}C-NMR (100 MHz, CDCl$_3$): δ = 29.9 (C(*C*H$_3$)$_3$), 33.7 (*C*(CH$_3$)$_3$), 119.8 (t, $^{1}J_{\mathrm{CF}}$ = 241.0 Hz, *C*F$_2$), 124.3, 124.5, 124.8, 127.5, 128.3 (all *C*$_{\mathrm{Ar}}$), 133.8 (t, $^{2}J_{\mathrm{CF}}$ = 28.5 Hz, *C*$_{\mathrm{Ar}}$CF$_2$), 136.8 (t, $^{2}J_{\mathrm{CF}}$ = 28.5 Hz, *C*$_{\mathrm{Ar}}$CF$_2$), 152.0 (*C*$_{\mathrm{Ar}}$C(CH$_3$)$_3$) ppm. – ^{19}F-NMR (376 MHz, H-decoupled, CDCl$_3$): δ = –88.1 ppm. – MS (EI): *m/z* (%): 260 (26) [M$^+$], 245 (100) [M$^+$–CH$_3$], 133 (3) [C$_6$H$_4$C$_4$H$_9$$^+$], 127 (20) [M$^+$–C$_6H_4C_4H_9$$^+$]. – HRMS ($C_{17}H_{18}F_2$): calc. 260.1377; found 260.1378.

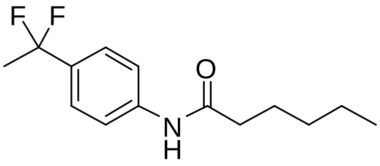


Methyl-3-(1,1-difluoroethyl)-5-iodobenzoate (**10e**): After cleavage from resin **9e** 110 mg (0.34 mmol, 81% over 3 steps) of a bright solid were obtained (cyclohexane/ethyl acetate 10:1, R_f = 0.6). – ^{1}H-NMR (250 MHz, $CDCl_3$): δ = 1.84 (t, $^3J_{HF}$ = 18.2 Hz, 3 H, CH_3CF_2), 3.85 (s, 3 H, OCH_3), 7.92 (s, 1 H, Ar-*H*), 8.06 (s, 1 H, Ar-*H*), 8.36 (s, 1 H, Ar-*H*) ppm. – ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 25.8 (t, $^2J_{CF}$ = 29.1 Hz, CH_3CF_2), 52.7 (OCH_3), 93.7 (C_{Ar}I), 120.4 (t, $^1J_{CF}$ = 240.5 Hz, CF_2), 125.3 (C_{Ar}), 132.2 (C_{Ar}), 137.9 (C_{Ar}), 139.8 (C_{Ar}), 140.4 (t, $^2J_{CF}$ = 23.5 Hz, $C_{Ar}CF_2$), 164.9 (*C*O) ppm. – ^{19}F-NMR (376 MHz, H-decoupled, $CDCl_3$): δ = –88.6 ppm. – MS (EI): *m/z* (%): 326 (100) [M^+], 295 (92) [$M^+–OCH_3$], 267 (18) [$M^+–CO_2CH_3$]. – HRMS ($C_{10}H_9F_2IO_2$): calc. 325.9615; found 325.9613.

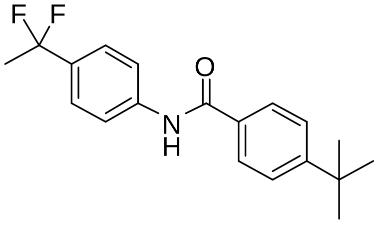
General procedure for the synthesis of the *gem*-difluorinated amides (GP 4):



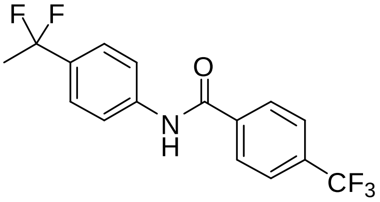
Resin **9f** was divided in 3 portions of 390 mg (0.46 mmol) each. Then the resins were covered with 10 ml dry dichloromethane in a vial and shaken for 30 minutes. After adding 5 equivalents of acid chloride **11** and 5 equivalents triethylamine, the mixture was shaken at room temperature for 24 h. The reaction mixture was filtered off and washed following GP 1a. Due to the excess of acid chloride, double acylation of the N-atom was partially observed via ^{13}C-NMR-gelphase spectra. In order to obtain exclusively the monoacylated compounds, the resins were shaken in 20 ml methanol at 60 °C for 24 h. The resin was filtered off, washed following GP 1a and dried under high vacuum. ^{13}C-NMR-gelphase spectra were measured for qualititative reaction control. Finally, the amides were cleaved from the resin following GP 3 to give the fluorinated compounds **12**.



N-(4-(1,1-Difluorethyl)phenyl)hexanamide (**12a**): R= *n*-pentyl: Reaction of **9f** with hexanoyl chloride (**11a**) gave 429 mg bright orange resin. – ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 14.1 (CH_3CH_2), 22.5 (CH_2), 24.6 (CH_2), 25.4 (CH_2), 31.3 (CH_3), 37.6 (CH_2CO), 52.5 (S*C*S), 119.0 ($C_{Ar}C_{Ar}NH$), 172.4 (NH*C*O) ppm. After the cleavage 46 mg (0.18 mmol, 40% over 4 steps) of a white solid were obtained (cyclohexane/ethyl acetate 5:1, R_f = 0.5). – ^{1}H-NMR (250 MHz, $CDCl_3$): δ = 0.89 (t, ^3J = 6.9 Hz, 3 H, CH_2CH_3), 1.35 (m, 4 H, $CH_2CH_2CH_3$), 1.74 (m, 2 H, $COCH_2CH_2$), 1.91 (t, $^3J_{HF}$ = 18.2 Hz, 3 H, CH_3CF_2), 2.38 (t, ^3J = 6.9 Hz, 2 H, $COCH_2$), 7.35 (s, 1 H, N*H*), 7.46 (d, ^3J = 8.3 Hz, 2 H, Ar-*H*), 7.58 (d, ^3J = 8.3 Hz, 2 H, Ar-*H*) ppm. – ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 13.9 (CH_2CH_3), 22.4 (CH_2CH_3), 25.2 ($COCH_2CH_2$), 25.5 (t, $^2J_{CF}$ = 29.2 Hz, CH_3CF_2), 31.4 ($CH_2CH_2CH_3$), 37.8 ($COCH_2$), 119.4 (C_{Ar}), 121.7 (t, $^1J_{CF}$ = 240.5 Hz, CF_2), 125.5 (C_{Ar}), 135.4 (t, $^2J_{CF}$ = 26.9 Hz, $C_{Ar}CF_2$), 139.2 ($C_{Ar}NH$), 171.6 (*C*O) ppm. – ^{19}F-NMR (376 MHz, H-decoupled, $CDCl_3$): δ = –86.6 ppm. – MS (EI): *m/z* (%): 255 (28) [M^+], 157 (100) [$CH_3CF_2C_6H_4NH_2$]. – HRMS ($C_{14}H_{19}F_2NO$): calc. 255.1435; found 255.1432.

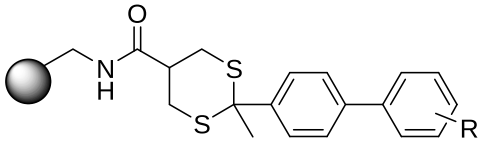


4-tert-Butyl-N-(4-(1,1-difluoroethyl)phenyl)benzamide (**12b**): R= 4-*t*Bu-C$_6$H$_4$: Reaction of **9f** with 4-*tert*-butylbenzoyl chloride (**11b**) gave 454 mg bright orange resin. – ^{13}C-NMR (100 MHz, CDCl$_3$): δ = 31.2 (C(*C*H$_3$)$_3$), 31.7 (*C*H$_3$), 35.1 (*C*(CH$_3$)$_3$), 52.5 (S*C*S), 120.3 (*C$_{Ar}$*), 166.4 (NH*C*O) ppm. After the cleavage 89 mg (0.28 mmol, 60% over 4 steps) of a bright yellow solid were obtained (cyclohexane/ethyl acetate 5:1, R_f = 0.4). – ^{1}H-NMR (250 MHz, CDCl$_3$): δ = 1.25 (s, 9 H, C(C*H*$_3$)$_3$), 1.88 (t, $^3J_{\mathrm{HF}}$ = 18.2 Hz, 3 H, C*H*$_3$CF$_2$), 7.43 (d, ^3J = 8.3 Hz, 2 H, Ar-*H*), 7.46 (d, ^3J = 8.3 Hz, 2 H, Ar-*H*), 7.65 (d, ^3J = 8.3 Hz, 2 H, Ar-*H*), 7.78 (d, ^3J = 8.3 Hz, 2 H, Ar-*H*), 8.01 (s, 1 H, N*H*),ppm. – ^{13}C-NMR (100 MHz, CDCl$_3$): δ = 25.9 (t, $^2J_{\mathrm{CF}}$ = 29.2 Hz, *C*H$_3$CF$_2$), 31.0 (C(*C*H$_3$)$_3$), 35.0 (*C*(CH$_3$)$_3$), 119.8 (t, $^1J_{\mathrm{CF}}$ = 240.5 Hz, *C*F$_2$), 119.8 (*C*$_{\mathrm{Ar}}$), 125.5 (*C*$_{\mathrm{Ar}}$), 125.7 (t, $^2J_{\mathrm{CF}}$ = 26.9 Hz, *C*$_{\mathrm{Ar}}$CF$_2$), 126.7 (*C*$_{\mathrm{Ar}}$), 126.9 (*C*$_{\mathrm{Ar}}$), 130.5 (*C*$_{\mathrm{Ar}}$), 131.8 (*C*$_{\mathrm{Ar}}$NH), 155.4 (*C*$_{\mathrm{Ar}}$C(CH$_3$)$_3$), 166.5 (*C*O) ppm. – ^{19}F-NMR (376 MHz, H-decoupled, CDCl$_3$): δ = –86.9 ppm. – MS (EI): *m/z* (%): 317 (60) [M$^+$], 161 (100) [COC$_6$H$_4$C(CH$_3$)$_3$]. – HRMS (C$_{19}$H$_{21}$F$_2$NO): calc. 317.1591; found 317.1593.



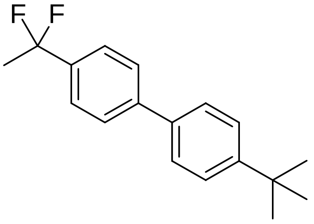
N-(4-(1,1-Difluoroethyl)phenyl)-4-(trifluoromethyl)benzamide (**12c**): R= 4-CF$_3$-C$_6$H$_4$: Reaction of **9f** with 4-trifluoromethylbenzoyl chloride (**11c**) gave 456 mg orange resin. – ^{13}C-NMR (100 MHz, CDCl$_3$): δ = 31.7 (*C*H$_3$), 52.2 (S*C*S), 122.1 (*C*$_{\mathrm{Ar}}$), 133.9 (*C*$_{\mathrm{Ar}}$), 137.6 (*C*$_{\mathrm{Ar}}$), 171.9 (NH*C*O) ppm. After the cleavage 90 mg (0.27 mmol, 58% over 4 steps) of a white solid were obtained (cyclohexane/ethyl acetate 5:1, R_f = 0.5). – ^{1}H-NMR (250 MHz, CDCl$_3$): δ = 1.97 (t, $^3J_{\mathrm{HF}}$ = 18.2 Hz, 3 H, C*H*$_3$CF$_2$), 7.58 (d, ^3J = 8.3 Hz, 2 H, Ar-*H*), 7.89 (d, ^3J = 8.3 Hz, 2 H, Ar-*H*), 7.92 (d, ^3J = 8.3 Hz, 2 H, Ar-*H*), 8.18 (d, ^3J = 8.3 Hz, 2 H, Ar-*H*), 10.65 (s, 1 H, N*H*) ppm. – ^{13}C-NMR (100 MHz, CDCl$_3$): δ = 25.0 (t, $^2J_{\mathrm{CF}}$ = 29.2 Hz, *C*H$_3$CF$_2$), 31.0 (C(*C*H$_3$)$_3$), 35.0 (*C*(CH$_3$)$_3$), 120.0 (*C*$_{\mathrm{Ar}}$), 122.2 (t, $^1J_{\mathrm{CF}}$ = 241.2 Hz, *C*F$_2$), 124.6 (q, $^1J_{\mathrm{CF}}$ = 243.2 Hz, *C*F$_3$), 125.2 (*C*$_{\mathrm{Ar}}$), 125.9 (*C*$_{\mathrm{Ar}}$), 128.6 (*C*$_{\mathrm{Ar}}$), 131.6 (q, $^2J_{\mathrm{CF}}$ = 29.2 Hz, *C*$_{\mathrm{Ar}}$CF$_3$), 132.7 (t, $^2J_{\mathrm{CF}}$ = 29.1 Hz, *C*$_{\mathrm{Ar}}$CF$_2$), 138.4 (*C*$_{\mathrm{Ar}}$NH), 140.3 (*C*$_{\mathrm{Ar}}$CO), 164.6 (*C*O) ppm. – ^{19}F-NMR (376 MHz, H-decoupled, CDCl$_3$): δ = –61.7 (CF$_3$), –84.2 (CF$_2$) ppm. – MS (EI): *m/z* (%): 329 (36) [M$^+$], 173 (100) [COC$_6$H$_4$C(CF$_3$)$_3$]. – HRMS (C$_{16}$H$_{12}$F$_5$NO): calc. 329.0839; found 329.0842.

General procedure for the synthesis of the cross coupling reactions (GP 5):

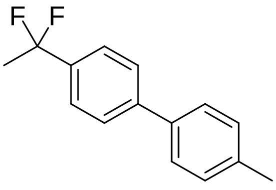


Suzuki coupling (GP 5a): Resin **9g** was divided in 3 portions of 410 mg (0.46 mmol) each. Then the resins were covered with 10 ml dry DMF in a vial under argon and shaken for 30 minutes. After addition of 5 equivalents of boronic acid **13**, 5 equivalents K$_3$PO$_4$ (dissolved in 1 ml water) and 0.1 equivalents Pd(PPh$_3$)$_4$, the vial was sealed and shaken at 100 °C for 48 h. The resin was filtered off, washed following GP 1b and dried under high vacuum. ^{13}C-NMR-gelphase spectra were measured for qualititative reaction control. Finally, the biphenyls were cleaved from the solid support following GP 3 to give the fluorinated compounds **14**.

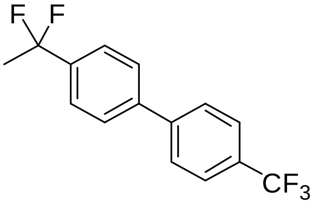
4-tert-Butyl-4´-(1,1-difluoroethyl)biphenyl (**14a**): R= 4-*t*Bu: Reaction of **9g** with 4-*tert*-butylphenylboronic acid (**13a**) gave 419 mg brown resin. – ^{13}C-NMR (100 MHz, CDCl$_3$): δ = 30.9 (CH$_3$), 31.6 (C(CH$_3$)$_3$), 34.7 (C(CH$_3$)$_3$) ppm. After the cleavage 43 mg (0.16 mmol, 34% over 4 steps) of a white solid were obtained (pentane, R_f = 0.8). – ^{1}H-NMR (250 MHz, CDCl$_3$): δ = 1.29 (s, 9 H, C(CH_3)$_3$), 1.90 (t, $^3J_{\mathrm{HF}}$ = 18.2 Hz, 3 H, CH_3CF$_2$), 7.38–7.62 (m, 8 H, Ar-H) ppm. – ^{13}C-NMR (100 MHz, CDCl$_3$): δ = 24.9 (t, $^2J_{\mathrm{CF}}$ = 29.2 Hz, CH$_3$CF$_2$), 30.3 (C(CH$_3$)$_3$), 33.6 (C(CH$_3$)$_3$), 118.0 (t, $^1J_{\mathrm{CF}}$ = 240.0 Hz, CF$_2$), 123.8 (C_{Ar}), 124.8 (C_{Ar}), 125.9 (C_{Ar}), 127.4 (C_{Ar}), 130.5 (C_{Ar}), 136.3 (t, $^2J_{\mathrm{CF}}$ = 26.9 Hz, C_{Ar}CF$_2$), 141.4 (C_{Ar}), 150.4 (C_{Ar}C(CH$_3$)$_3$) ppm. – ^{19}F-NMR (376 MHz, H-coupled, CDCl$_3$): δ = –87.2 (q, $^3J_{\mathrm{HF}}$ = 18.2 Hz) ppm. – MS (EI): *m/z* (%): 274 (38) [M$^+$], 259 (100) [M$^+$–CH$_3$]. – HRMS (C$_{18}$H$_{20}$F$_2$): calc. 274.1533; found 274.1536.



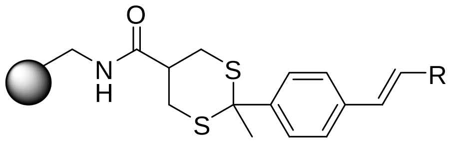
4-(1,1-Difluoroethyl)-4`-methylbiphenyl (**14b**): R= 4-Me: Reaction of **9g** with 4-methylphenylboronic acid (**13b**) gave 400 mg brown resin. – ^{13}C-NMR (100 MHz, CDCl$_3$): δ = 21.3 (C$_{\mathrm{Ar}}$-CH$_3$), 31.6 (CH$_3$) ppm. After the cleavage 32 mg (0.14 mmol, 30% over 4 steps) of a colorless solid were obtained (pentane, R_f = 0.8). – ^{1}H-NMR (250 MHz, CDCl$_3$): δ = 1.88 (t, $^3J_{\mathrm{HF}}$ = 18.2 Hz, 3 H, CH_3CF$_2$), 2.32 (s, 3 H, C$_{\mathrm{Ar}}$CH_3), 7.18 (d, ^3J = 8.1 Hz, 2 H, Ar-H), 7.42 (d, ^3J = 8.1 Hz, 2 H, Ar-H), 7.48 (d, ^3J = 8.3 Hz, 2 H, Ar-H), 7.54 (d, ^3J = 8.3 Hz, 2 H, Ar-H) ppm. – ^{13}C-NMR (100 MHz, CDCl$_3$): δ = 20.0 (C$_{\mathrm{Ar}}$$CH_3$), 24.8 (t, $^2J_{\mathrm{CF}}$ = 29.4 Hz, CH$_3$CF$_2$), 120.8 (t, $^1J_{\mathrm{CF}}$ = 239.8 Hz, CF$_2$), 124.7 (C_{Ar}), 126.0 (C_{Ar}), 126.1 (C_{Ar}), 128.4 (C_{Ar}), 135.7 (t, $^2J_{\mathrm{CF}}$ = 26.9 Hz, C_{Ar}CF$_2$), 136.4 (C_{Ar}), 136.5 (C_{Ar}), 141.6 (C_{Ar}CH$_3$) ppm. – ^{19}F-NMR (376 MHz, H-coupled, CDCl$_3$): δ = –87.2 (q, $^3J_{\mathrm{HF}}$ = 18.2 Hz) ppm. – MS (EI): *m/z* (%): 232 (100) [M$^+$], 217 (84) [M$^+$–CH$_3$]. – HRMS (C$_{15}$H$_{14}$F$_2$): calc. 232.1063; found 232.1060.



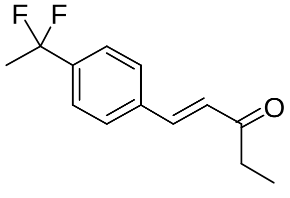
4-(1,1-Difluoroethyl)-4`-(trifluoromethyl)biphenyl (**14c**): R= 4-CF$_3$: Reaction of **9g** with 4-trifluoromethylphenylboronic acid (**13c**) gave 407 mg dark brown resin. – ^{13}C-NMR (100 MHz, CDCl$_3$): δ = 31.6 (CH$_3$) ppm. After the cleavage 24 mg (0.09 mmol, 19% over 4 steps) of a colorless oil were obtained (pentane, R_f = 0.7). – ^{1}H-NMR (250 MHz, CDCl$_3$): δ = 1.82 (t, $^3J_{\mathrm{HF}}$ = 18.1 Hz, 3 H, CH_3CF$_2$), 7.01–7.52 (m, 8 H, Ar-H) ppm. – ^{19}F-NMR (376 MHz, H-decoupled, CDCl$_3$): δ = –62.5 (CF$_3$), –87.5 (CF$_2$) ppm. – MS (EI): *m/z* (%): 286 (66) [M$^+$], 271 (100) [M$^+$–CH$_3$]. – HRMS (C$_{15}$H$_{11}$F$_5$): calc. 286.0781; found 286.0778.



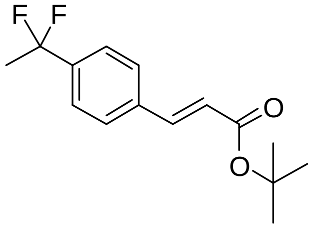
Heck coupling (GP 5b): Portions of 410 mg (0.46 mmol) resin **9g** each were transformed. The resins were covered with 10 ml dry DMF in a vial under argon and shaken for 30 minutes. After addition of 5 equivalents of the olefin **15** or **17**, respectively, 1 equivalent triethylamine, 0.1 equivalents $Pd(OAc)_2$ and 0.5 equivalents PPh_3, the vial was sealed and shaken at 100 °C for 48 h. The resin was filtered off and washed following GP 1b and dried under high vacuum. ^{13}C-NMR-gelphase spectra were measured for qualititative reaction control. Finally, the compounds were cleaved from the solid support following GP 3 to give the fluorinated molecules **16** or **18**, respectively.

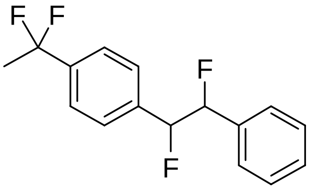


(E)-1-(4-(1,1-Difluoroethyl)phenyl)pent-1-en-3-one (**16a**): R= COEt: Reaction of **9g** with pent-1-en-3-on (**15a**) gave 398 mg black resin. – ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 8.4 (CH_3CH_2), 30.3 (CH_3), 34.2 (CH_3CH_2), 198.1 (CO) ppm. After the cleavage 21 mg (0.10 mmol, 21% over 4 steps) of a colorless oil were obtained (pentane/diethylether 50:1, R_f = 0.8). – ^{1}H-NMR (250 MHz, $CDCl_3$): δ = 1.10 (t, ^3J = 8.3 Hz, 3 H, CH_2CH_3), 1.88 (t, $^3J_{HF}$ = 18.2 Hz, 3 H, CH_3CF_2), 2.65 (q, ^3J = 8.3 Hz, 2 H, CH_2CH_3), 6.72 (d, ^3J = 16.2 Hz, 1 H, $CHCO$), 7.46 (d, ^3J= 8.4 Hz, 2 H, Ar-H), 7.50 (d, ^3J= 8.4 Hz, 2 H, Ar-H), 7.54 (d, ^3J = 16.2 Hz, 1 H, CHC_{Ar}) ppm. – ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 9.1 (CH_3CH_2), 24.2 (t, $^2J_{CF}$ = 29.2 Hz, CH_3CF_2), 33.4 (CH_3CH_2), 119.6 (t, $^1J_{CF}$ = 240.0 Hz, CF_2), 121.5 ($CHCO$), 125.5 (C_{Ar}), 129.1 (C_{Ar}), 135.0 ($C_{Ar}CH$), 137.1 (t, $^2J_{CF}$ = 26.9 Hz, $C_{Ar}CF_2$), 141.3 ($C_{Ar}CH$), 199.3 (CO) ppm. – ^{19}F-NMR (376 MHz, H-decoupled, $CDCl_3$): δ = –88.7 ppm. – MS (EI): *m/z* (%): 224 (22) [M^+], 195 (100) [$M^+–CH_2CH_3$]. – HRMS ($C_{13}H_{14}F_2O$): calc. 224.1013; found 224.1016.



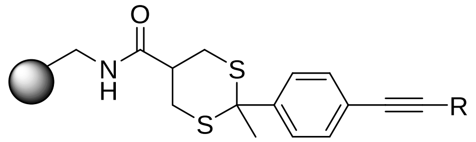
(E)-tert-Butyl-3-(4-(1,1-difluoroethyl)phenyl)acrylate (**16b**): R= CO_2tBu: Reaction of **9g** with *tert*-butyl acrylate (**15b**) gave 410 mg brown resin. – ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 28.3 ($OC(CH_3)_3$), 30.1 (CH_3), 81.1 ($OC(CH_3)_3$), 167.2 (COO) ppm. After the cleavage 18 mg (0.07 mmol, 15% over 4 steps) of a bright yellow oil were obtained (pentane/diethylether 5:1, R_f= 0.6). – ^{1}H-NMR (250 MHz, $CDCl_3$): δ = 1.46 (s, 9 H, $C(CH_3)_3$), 1.87 (t, $^3J_{HF}$ = 18.2 Hz, 3 H, CH_3CF_2), 6.34 (d, ^3J = 16.0 Hz, 1 H, $CHCO$), 7.44 (d, ^3J = 8.4 Hz, 2 H, Ar-H), 7.50 (d, ^3J = 8.4 Hz, 2 H, Ar-H), 7.52 (d, ^3J = 16.0 Hz, 1 H, CHC_{Ar}) ppm. – ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 24.8 (t, $^2J_{CF}$ = 29.2 Hz, CH_3CF_2), 27.7 ($OC(CH_3)_3$), 79.8 ($OC(CH_3)_3$), 120.4 (t, $^1J_{CF}$ = 240.0 Hz, CF_2), 120.5 ($CHCO$), 124.9 (C_{Ar}), 127.0 (C_{Ar}), 135.0 ($C_{Ar}CH$), 138.4 (t, $^2J_{CF}$ = 26.9 Hz, $C_{Ar}CF_2$), 141.3 (CHC_{Ar}), 165.0 (CO) ppm. – ^{19}F-NMR (376 MHz, H-decoupled, $CDCl_3$): δ = –87.7 ppm. – MS (EI): *m/z* (%): 268 (24) [M^+], 212 (100) [$M^++H–C(CH_3)_3$], 195 (60) [$M^+–OC(CH_3)_3$]. – HRMS ($C_{15}H_{18}F_2O_2$): calc. 268.1275; found 268.1272.

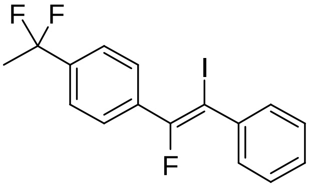




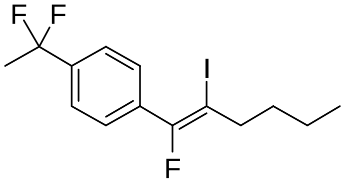
1-(1,2-Difluoroethyl-2-phenylethyl)-4-(1,1-difluoroethyl)benzene (**18**): R= Ph: Reaction of **9g** with styrene (**17**) gave 392 mg black resin. – ^{13}C-NMR (100 MHz, CDCl$_3$): δ = 30.2 (CH$_3$) ppm. After the cleavage 26 mg (0.09 mmol, 20% over 4 steps) of a colorless oil were obtained (pentane/diethylether 40:1, R_f = 0.8). – ^{1}H-NMR (250 MHz, CDCl$_3$): δ = 1.85 (t, $^3J_{HF}$ = 18.2 Hz, 3 H, CH_3CF$_2$), 5.62 (ddd, $^2J_{HF}$ = 60.4 Hz, $^3J_{HF}$ = 31.4 Hz, $^3J_{HH}$ = 4.2 Hz, 2 H, each CHF), 7.10 (m, 2 H, Ar-H), 7.20 (d, ^3J = 8.4 Hz, 2 H, Ar-H), 7.29 (m, 3 H, Ar-H), 7.43 (d, ^3J = 8.4 Hz, 2 H, Ar-H) ppm. – ^{13}C-NMR (100 MHz, CDCl$_3$): δ = 25.9 (t, $^2J_{CF}$ = 29.6 Hz, CH$_3$CF$_2$), 94.0 (dd, $^1J_{CF}$ = 180.0 Hz, $^2J_{CF}$ = 26.6 Hz, each CHF), 120.1 (t, $^1J_{CF}$ = 240.0 Hz, CF$_2$), 124.5 (C_{Ar}), 126.7 (C_{Ar}), 128.3(C_{Ar}), 129.4 (C_{Ar}), 134.4 (d, $^2J_{CF}$ = 27.3 Hz, C_{Ar}CHF), 136.1 (d, $^2J_{CF}$ = 27.3 Hz, C_{Ar}CHF), 138.7 (t, $^2J_{CF}$ = 27.3 Hz, C_{Ar}CF$_2$) ppm. – ^{19}F-NMR (376 MHz, H-decoupled, CDCl$_3$): δ = −87.7 (CF_2), −186.8 (CFH), −187.7 (CFH) ppm. – MS (EI): *m/z* (%): 282 (20) [M$^+$], 263 (12) [M$^+$–F], 173 (24) [M$^+$–C$_6$H$_5$CHF], 109 (100) [C$_6$H$_5$CHF]. – HRMS (C$_{16}$H$_{14}$F$_4$): calc. 282.1032; found 282.1033.

Sonogashira coupling (GP 5c): Portions of 410 mg (0.46 mmol) resin **9g** each were transformed. The resins were covered with 10 ml dry DMF in a vial under argon and shaken for 30 minutes. After addition of 5 equivalents of the acetylene **19**, 1 equivalent triethylamine, 0.5 equivalents CuI and 0.01 equivalents Pd(PPh$_3$)$_4$, the vial was sealed and shaken at 80 °C for 48 h. The resin was filtered off and washed following GP 1b and dried under high vacuum. ^{13}C-NMR-gelphase spectra were measured for qualititative reaction control. Finally, the compounds were cleaved from the solid support following GP 3 to give the fluorinated molecules **20.**



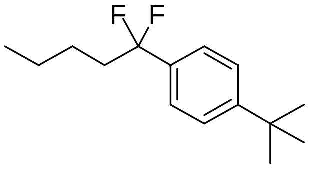


(E)-1-(1,1-Difluoroethyl)-4-(1-fluoro-2-iodo-2-phenylvinyl)benzene (**20a**): R= Ph: Reaction of **9g** with phenylacetylene (**19a**) gave 395 mg brown resin. – ^{13}C-NMR (100 MHz, CDCl$_3$): δ = 30.2 (CH$_3$), 95.2 (C$_{Ar}$$CCC_{Ar}$), 131.9 ($C_{Ar}C_{Ar}$C) ppm. After the cleavage 22 mg (0.06 mmol, 13% over 4 steps) of a colorless solid were obtained (pentane/diethylether 40:1, R_f = 0.8). Only slight impurities by the fluorinated iodide derived from the incomplete coupling reaction could not be removed. – ^{1}H-NMR (250 MHz, CDCl$_3$): δ = 1.83 (t, $^3J_{HF}$ = 18.2 Hz, 3 H, CH_3CF$_2$), 7.38 (d, ^3J = 8.4 Hz, 2 H, Ar-H), 7.30 – 7.55 (m, 5 H, Ar-H), 7.72 (d, ^3J = 8.4 Hz, 2 H, Ar-H) ppm. – ^{13}C-NMR (100 MHz, CDCl$_3$): δ = 23.9 (t, $^2J_{CF}$ = 29.6 Hz, CH$_3$CF$_2$), 68.0 (d, $^2J_{CF}$ = 27.5 Hz, CI), 116.1 (t, $^1J_{CF}$ = 240.0 Hz, CF$_2$), 124.5 (C_{Ar}), 128.1 (C_{Ar}), 128.4 (C_{Ar}), 129.6 (C_{Ar}), 130.2 (C_{Ar}), 131.7 (C_{Ar}), 164.1 (d, $^1J_{CF}$ = 254 Hz, CF) ppm. – ^{19}F-NMR (376 MHz, H-decoupled, CDCl$_3$): δ = –75.7 (CF), –87.6 (CF_2) ppm. – MS (EI): *m/z* (%): 388 (18) [M$^+$], 140 (100) [M$^+$–C$_6$H$_5$CICFH]. – HRMS (C$_{16}$H$_{12}$F$_3$I): calc. 387.9936; found 388.9937.

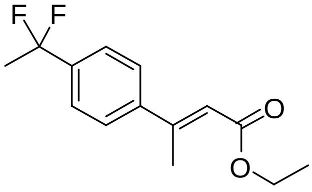


(E)-1-(1,1-Difluoroethyl)-4-(1-fluoro-2-iodohex-1-enyl)benzene (**20b**): R= *n*Bu: Reaction of **9g** with hex-1-ine (**19b**) gave 385 mg black resin. – ^{13}C-NMR (100 MHz, CDCl$_3$): δ = 13.9 (CH$_2$*C*H$_3$), 19.3 (C*C*H$_2$), 22.1 (*C*H$_2$CH$_3$), 30.2 (*C*H$_3$), 30.9 (*C*H$_2$CH$_2$CH$_3$) ppm. After the cleavage 20 mg (0.055 mmol, 12% over 4 steps) of a colorless solid were obtained (pentane/diethylether 20:1, R_f = 0.8). – ^{1}H-NMR (250 MHz, CDCl$_3$): δ = 0.92 (t, ^3J = 7.4 Hz, 3 H, C*H*$_3$), 1.35 (sext, ^3J = 7.4 Hz, 2 H, C*H*$_2$CH$_3$), 1.51 (quin, ^3J = 7.4 Hz, 2 H, C*H*$_2$CH$_2$CH$_3$), 1.88 (t, $^3J_{\mathrm{HF}}$ = 18.2 Hz, 3 H, C*H*$_3$CF$_2$), 2.67 (m, 2 H, ClCH$_2$), 7.42 (d, ^3J = 8.4 Hz, 2 H, Ar-*H*), 7.62 (d, ^3J = 8.4 Hz, 2 H, Ar-*H*) ppm. – ^{13}C-NMR (100 MHz, CDCl$_3$): δ = 13.9 (CH$_2$*C*H$_3$), 21.6 (*C*H$_2$), 25.8 (t, $^2J_{\mathrm{CF}}$ = 29.6 Hz, *C*H$_3$CF$_2$), 31.9 (CH$_2$), 36.2 (*C*H$_2$), 85.2 (d, $^2J_{\mathrm{CF}}$ = 27.5 Hz, *C*I), 121.5 (t, $^1J_{\mathrm{CF}}$ = 240.0 Hz, *C*F$_2$), 124.3 (*C*$_{\mathrm{Ar}}$), 126.5 (*C*$_{\mathrm{Ar}}$), 129.6 (*C*$_{\mathrm{Ar}}$), 134.6 (d, $^2J_{\mathrm{CF}}$ = 27.5 Hz, *C*$_{\mathrm{Ar}}$CF), 153.6 (d, $^1J_{\mathrm{CF}}$ = 254 Hz, *C*F) ppm. – ^{19}F-NMR (376 MHz, H-decoupled, CDCl$_3$): δ = –82.6 (C*F*), –87.8 (C*F*$_2$) ppm. – MS (EI): *m/z* (%): 368 (100) [M$^+$], 349 (10) [M$^+$–F]. – HRMS ($C_{14}H_{16}F_3I$): calc. 368.0249; found 368.0251.

Umpolung and Horner-Wadsorth-Emmons-reaction:



1-tert-Butyl-4-(1,1-difluoropentyl)benzene (**22**): 335 mg (0.42 mmol) of resin **9a** were covered with dry THF in a vial under argon and shaken for 30 minutes. After cooling at –50 °C, 0.5 ml *n*-butyllithium (2.5 M in hexane, 1.2 mmol) were added and shaken for 4 h under warming to –20°C. The mixture was cooled again at –50 °C. *n*-Butyl bromide was added and the reaction was allowed to warm slowly to 0 °C over 15 h. The resin was filtered off, washed three times with THF and then following GP 1b and dried under high vacuum to yield 350 mg brown resin. – ^{13}C-NMR (100 MHz, CDCl$_3$): δ = 14.2 (CH$_2$*C*H$_3$), 22.0 (*C*H$_2$CH$_3$), 22.6 (*C*H$_2$CH$_2$CH$_3$), 31.5 (C(*C*H$_3$)$_3$), 34.5 (*C*(CH$_3$)$_3$) ppm. Cleavage from the solid support following GP 3 gave 16 mg (0.07 mmol, 16% over 4 steps) of a bright yellow oil (pentane/diethylether 40:1, R_f = 0.8). – ^{1}H-NMR (250 MHz, CDCl$_3$): δ = 0.97 (t, ^3J = 7.4 Hz, 3 H, C*H*$_3$), 1.26 (s, 9 H, C(C*H*$_3$)$_3$), 1.33 (sext, ^3J = 7.4 Hz, 2 H, C*H*$_2$CH$_3$), 1.66 (m, 2 H, CH$_2$C*H*$_2$CH$_3$), 2.78 (m, 2 H, C*H*$_2$CF$_2$), 7.21 (d, ^3J = 8.3 Hz, 2 H, Ar-*H*), 7.48 (d, ^3J = 8.3 Hz, 2 H, Ar-*H*) ppm. – ^{13}C-NMR (100 MHz, CDCl$_3$): δ = 13.9 (CH$_2$*C*H$_3$), 23.5 (*C*H$_2$), 24.7 (*C*H$_2$), 31.3 (C(*C*H$_3$)$_3$), 34.4 (t, $^2J_{\mathrm{CF}}$ = 27.7 Hz, *C*H$_2$CF$_2$), 35.2 (*C*(CH$_3$)$_3$), 123.4 (t, $^1J_{\mathrm{CF}}$ = 241.5 Hz, *C*F$_2$), 125.0 (*C*$_{\mathrm{Ar}}$), 128.7 (*C*$_{\mathrm{Ar}}$), 134.9 (t, $^2J_{\mathrm{CF}}$ = 26.9 Hz, *C*$_{\mathrm{Ar}}$CF$_2$), 149.9 (*C*$_{\mathrm{Ar}}$C(CH$_3$)$_3$) ppm. – ^{19}F-NMR (376 MHz, H-decoupled, CDCl$_3$): δ = –94.1 ppm. – MS (EI): *m/z* (%): 240 (14) [M$^+$], 225 (100) [M$^+$–CH$_3$]. – HRMS ($C_{15}H_{22}F_2$): calc. 240.1690; found 240.1693.



E-Ethyl-3-(4-(1,1-difluoroethyl)phenyl)but-2-enoate (**24**): In a vial 85 mg (3.5 mmol) triethylphosphono acetate (**23**) und 920 mg (3.5 mmol) 18-crown-6 were dissolved in 5 ml dry THF and cooled to –78 °C. Then 7 ml of a KHMDS solution (0.5M in toluene, 3.5 mmol) were added and the mixture was allowed to warm to room temperature within 1 h. 600 mg (0.7 mmol) of resin **9h** were swollen in dry THF and transferred to the reaction mixture. After shaking for 15 h at 40 °C, the resin was filtered off, washed three times with THF and then following GP 1a and dried under high vacuum to yield 645 mg brown resin. – ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 14.5 ($\mathit{C}H_3CH_2$), 18.0 ($\mathit{C}H_3$), 30.4 ($\mathit{C}H_3$), 62.0 ($O\mathit{C}H_2$), 166.2 ($\mathit{C}OO$) ppm. Cleavage from the solid support following GP 3 yielded 37 mg (0.15 mmol, 21% over 4 steps) of a white solid (pentane/diethylether 10:1, R_f = 0.8). Slight impurities by the *Z*-isomere could not be removed completely. – ^{1}H-NMR (250 MHz, $CDCl_3$): δ = 1.23 (t, ^3J = 7.2 Hz,3 H, $CH_2C\mathit{H}_3$), 1.85 (t, $^3J_{HF}$ = 18.2 Hz, 3 H, $C\mathit{H}_3CF_2$), 2.50 (s, 3 H, CH_3), 4.14 (q, ^3J = 7.2 Hz, 2 H, $C\mathit{H}_2CH_3$), 6.09 (s, 1 H, $C\mathit{H}CO$), 7.45 (m, 2 H, Ar-*H*), 7.68 (m, 2 H, Ar-*H*) ppm. – ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 10.1 ($\mathit{C}H_3CH_2$), 18.3 ($\mathit{C}H_3$), 24.6 (t, $^2J_{CF}$ = 29.2 Hz, $\mathit{C}H_3CF_2$), 61.0 ($O\mathit{C}H_2$), 118.8 ($\mathit{C}HCO$), 121.2 (t, $^1J_{CF}$ = 240.0 Hz, $\mathit{C}F_2$), 125.9 (C_{Ar}), 128.0 (C_{Ar}), 138.1 (t, $^2J_{CF}$ = 26.9 Hz, $\mathit{C}_{Ar}CF_2$), 143.0 ($\mathit{C}_{Ar}CCHCO$), 154.1 ($C_{Ar}\mathit{C}CHCO$), 166.7 ($\mathit{C}O$) ppm. – ^{19}F-NMR (376 MHz, H-decoupled, $CDCl_3$): δ = –87.8 ppm. – MS (EI): *m/z* (%): 254 (80) [M^+], 225 (40) [M^+–CH_2CH_3], 209 (100) [M^+–OCH_2CH_3]. – HRMS ($C_{14}H_{16}F_2O_2$): calc. 254.1118; found 254.1115.