

## **Extended Supplementary Information for:**

### **Catalytic formation of C(sp<sup>3</sup>)-F bonds via decarboxylative fluorination with mechanochemically-prepared Ag<sub>2</sub>O/TiO<sub>2</sub> heterogeneous catalysts**

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## 1. Experimental procedure for catalyst preparation and characterisation.

### Synthesis of 1% Ag/TiO<sub>2</sub> via sol immobilisation (1Ag/TiO<sub>2(SI)</sub>)

Ag supported on TiO<sub>2</sub> was prepared via sol immobilisation. 31.5 mg of AgNO<sub>3</sub> (20 mg of Ag) were dissolved in 800 mL of deionised water. Under vigorous stirring, 1.3 mL of an aqueous PVA solution (1 g/10 mL) and 9.26 mL of an aqueous NaBH<sub>4</sub> solution (37.8 mg /10 mL) were added to solution, which suddenly turned yellow. After 30 minutes, 990 mg of TiO<sub>2</sub> were added to the brown-orange solution, then acidified with few drops of sulphuric acid to achieve a pH = 1. After 2 hours the solid was filtrated and washed with 2 L of H<sub>2</sub>O and dried at 110 °C for 16 hours. Then, the purple catalyst obtained was grinded and calcined at various temperatures, with a ramp rate of 5 °C/min for 3 hours in static air, to oxidise the metallic Ag, giving a white powder.

### Physical mixture Ag<sub>2</sub>O/TiO<sub>2</sub> (1Ag<sub>2</sub>O/TiO<sub>2(PM)</sub>)

Physical mixtures of Ag<sub>2</sub>O/TiO<sub>2</sub> were prepared by grinding 21.5 mg of Ag<sub>2</sub>O (20 mg of Ag) and 1.980g of TiO<sub>2</sub> in a mortar for 20 min by hand.

### Mechanochemical mixture Ag<sub>2</sub>O/TiO<sub>2</sub> (1Ag<sub>2</sub>O/TiO<sub>2(MM)</sub>)

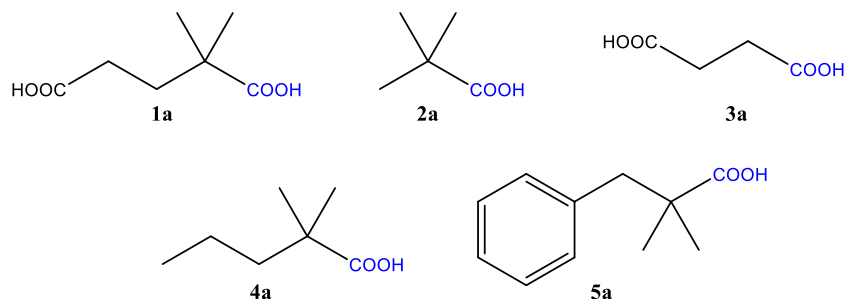
Mechanochemical mixtures of Ag<sub>2</sub>O/TiO<sub>2</sub> were prepared mixing 21.5 mg of Ag<sub>2</sub>O (20 mg of Ag) with 1.980g of TiO<sub>2</sub> in a Retsch Ball Mill model MM 400 for 20 min with a frequency of 15 Hz, using stainless steel 25mL Jars and 10mm stainless steel balls.

### Catalyst preparation

A PANalytical X'PertPRO X-ray diffractometer was employed for powder XRD analysis. A CuKα radiation source (40 kV and 30 mA) was utilised. Diffraction patterns were recorded between 10-80° 2θ. XPS spectra were recorded on a Kratos Axis Ultra DLD spectrometer using a monochromatic Al Kα source. TPR measurements were performed on a Thermo Scientific TPDRO 1100 instrument. Analysis conditions 10% H<sub>2</sub>/Ar at 20 ml min<sup>-1</sup>, Temperature ramp rate 5°C min<sup>-1</sup>.

## 2. General procedure for fluorination reaction.

### Substrates



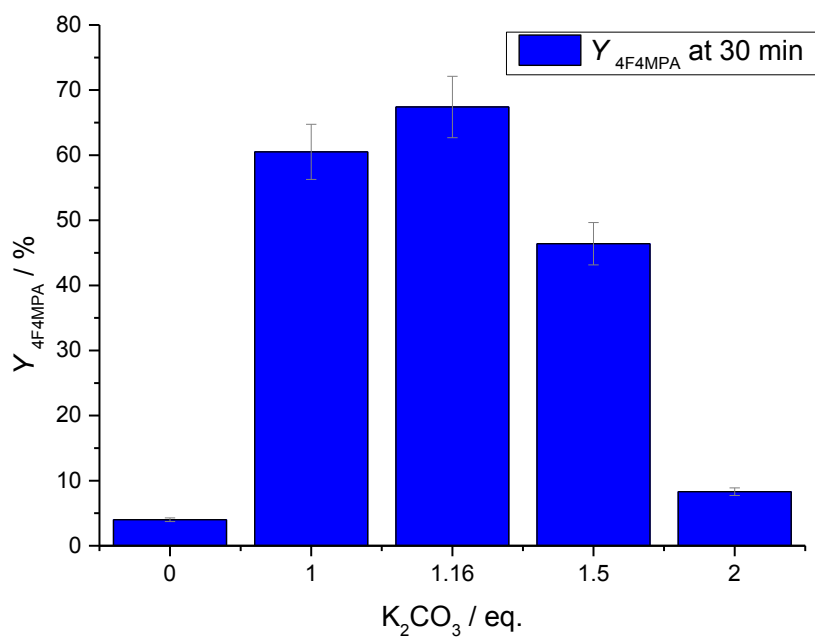
#### General procedure for decarboxylative fluorination reactions

Fluorination reactions were performed at room temperature using a single neck 10 mL round bottom flask filled with 141.7 mg (0.4 mmol) of Selectfluor®, 1.0 mg (0.0093 mmol) of silver from various Ag-containing catalyst and 32.0 mg (0.23 mmol) of  $K_2CO_3$ . For all reactions,  $N_2$  was fluxed into the flask for 5 min, and 4 mL of an aqueous solution of the carboxylic acid 0.05 M were then added into the flask with a syringe.

To perform the kinetic studies when 2,2-dimethylglutaric acid (**1a**) was employed as substrate, during the reaction, samples were regularly withdrawn using a syringe, filtered and analysed into an HPLC, Agilent 1220 Infinity LC System, using a MetaCarb 87H column 250 x 4.6 mm, an aqueous solution of phosphoric acid 0.1 M as mobile phase and succinic acid as external standard. The concentration of 2,2-dimethylglutaric acid and 4-fluoro-4-methylpentanoic acid were obtained *via* previous HPLC calibration with respective standards.

When substrate **3-5a** were used, to measure the product yield, 4 mL of a standard solution of  $\alpha,\alpha,\alpha$ -trifluorotoluene in  $(CH_3)_2CO$  was added to the reaction mixture, the sample was centrifuged to remove the solid catalyst and  $^{19}F$  NMR spectra of the solution was run. Kinetics for pivalic acid were determined by HPLC analysis.

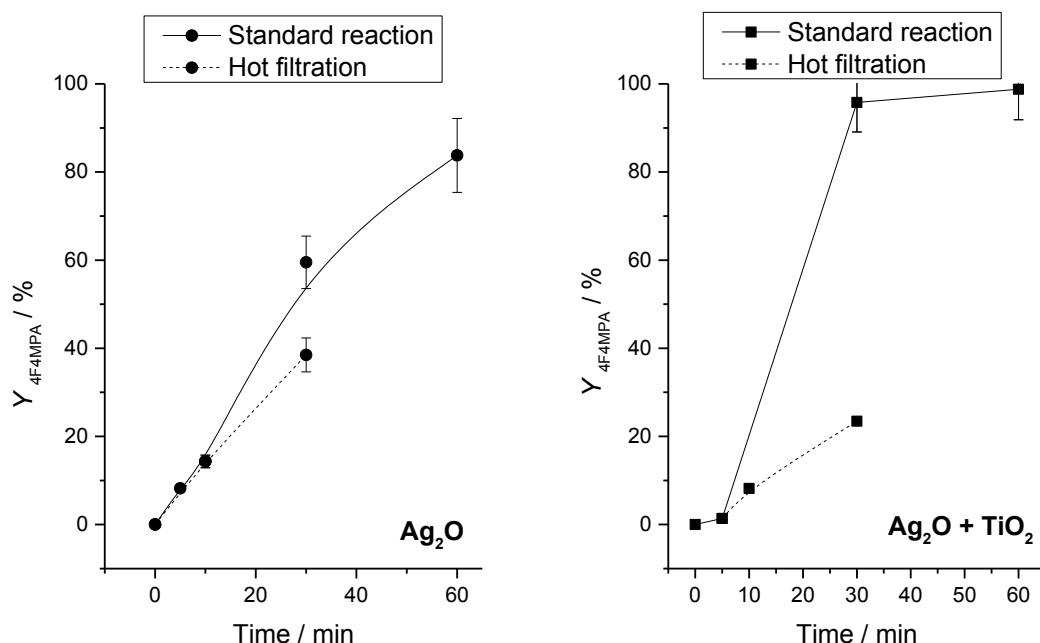
### 3. Base loading optimisation



**Figure S1** Yield of 4F4MPA (**1b**) at 30 min with different K<sub>2</sub>CO<sub>3</sub> loadings. Reaction conditions: 0.2 mmol of **1a**, 0.4 mmol of Selectfluor®, 100 mg of 1Ag/TiO<sub>2</sub>(Si350) (0.0093 mmol of Ag), 4 mL H<sub>2</sub>O, various amount of K<sub>2</sub>CO<sub>3</sub> (equivalents respect to substrate), N<sub>2</sub> atmosphere, 25°C.

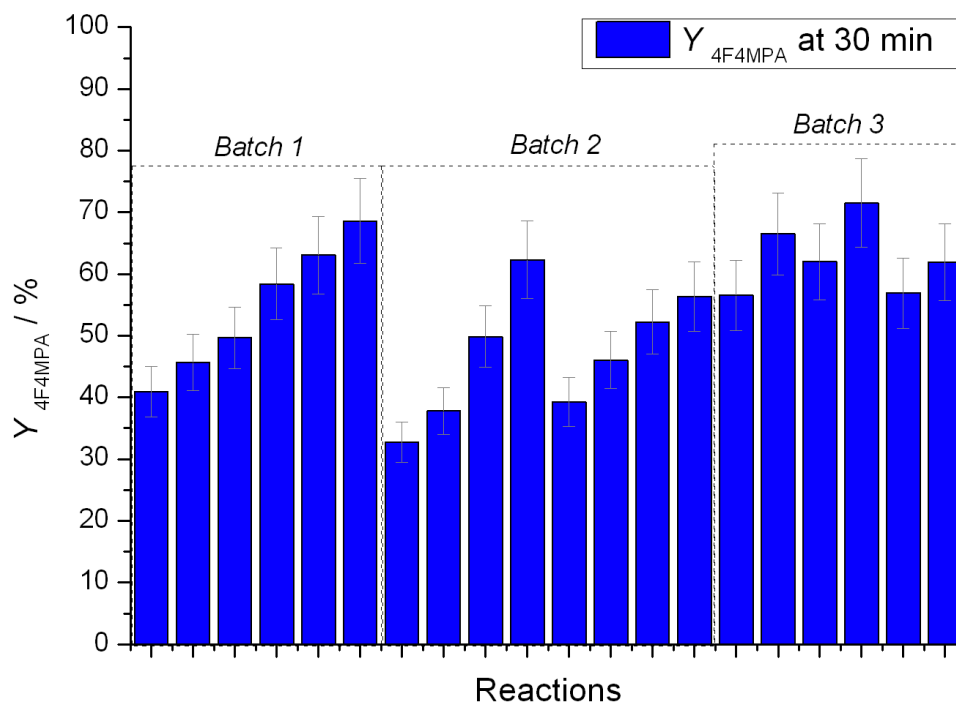
#### 4. Hot filtration of $\text{Ag}_2\text{O}$ and $\text{Ag}_2\text{O}/\text{TiO}_2$ .

Hot filtration of the catalysts was performed filtering the reaction mixture (hence removing the solid catalyst) at 10 min and analysing the variation of **1a** concentration of the filtered solution at 30 min.



**Figure S2 (Left)** Solid line, time on line of **1b** yield without filtering the catalyst. Dashed line, catalytic activity of the reaction solution filtered at 10 min. Reaction conditions: 0.23 mmol of **1a**, 0.4 mmol of Selectfluor®, 1.1 mg of  $\text{Ag}_2\text{O}$  (0.0093 mmol of Ag), 4 mL  $\text{H}_2\text{O}$ , 0.23 mmol of  $\text{K}_2\text{CO}_3$ ,  $\text{N}_2$  atmosphere, 25°C. **Figure S3 (Right)** Solid line, time on line of **1b** yield without filtering the catalyst. Dashed line, catalytic activity of the reaction solution filtered at 10 min. Reaction conditions: 0.23 mmol of **1a**, 0.4 mmol of Selectfluor®, 1.1 mg of  $\text{Ag}_2\text{O}$  (0.0093 mmol of Ag), 99 mg of  $\text{TiO}_2$ , 4 mL  $\text{H}_2\text{O}$ , 0.23 mmol of  $\text{K}_2\text{CO}_3$ ,  $\text{N}_2$  atmosphere, 25°C.

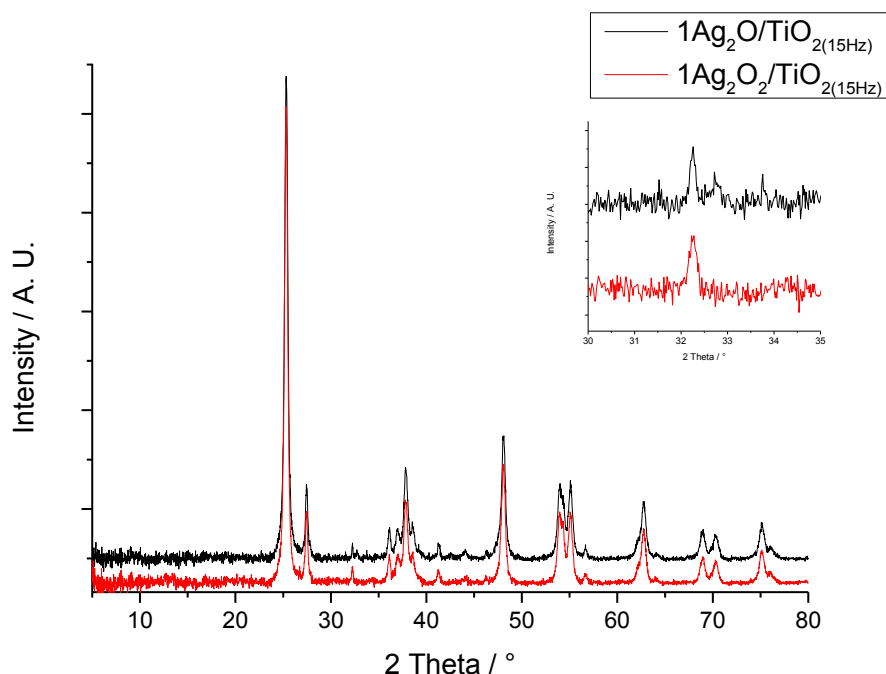
## 5. Reproducibility of 1Ag<sub>2</sub>O/TiO<sub>2</sub>(PM)



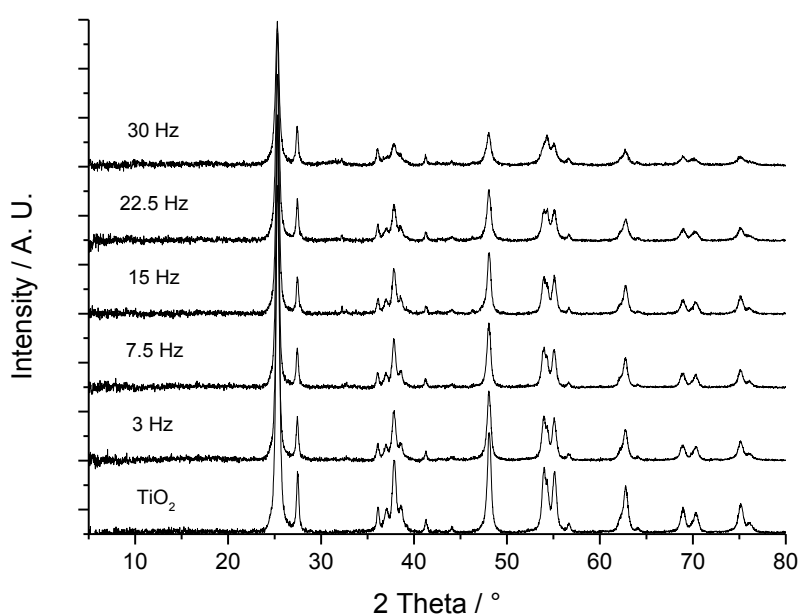
**Figure S3** Activity and reproducibility of different batches of 1Ag<sub>2</sub>O/TiO<sub>2</sub>(PM). Reaction conditions : 0.2 mmol of **1a**, 0.4 mmol of Selectfluor®, 100 mg of 1Ag/TiO<sub>2</sub>(PM) (0.0093 mmol of Ag), 4 mL H<sub>2</sub>O, 0.23 mmol of K<sub>2</sub>CO<sub>3</sub>, N<sub>2</sub> atmosphere, 25°C.

## 6. Powder X-Ray Diffraction (pXRD) patterns

Powder X-ray diffraction was performed on a PANalytical X'PertPRO X-ray diffractometer (PANalytical, Almelo, the Netherlands), using a CuK $\alpha$  radiation source (40 kV and 30 mA), with diffraction patterns recorded between 5° and 80°.



**Figure S4** Powder X-Ray Diffraction (pXRD) pattern of  $1\text{Ag}_2\text{O}_2/\text{TiO}_2(15\text{Hz})$  (red line) and  $1\text{Ag}_2\text{O}/\text{TiO}_2(15\text{Hz})$  (black line).



**Figure S5** Full Powder X-Ray Diffraction (pXRD) pattern of pure  $\text{TiO}_2$  (P25) and  $1\text{Ag}_2\text{O}/\text{TiO}_2(\text{MM})$  prepared at different milling frequency (3-30 Hz).

## 7. Surface area analysis (N<sub>2</sub> physisorption)

Surface area analysis was performed using a Quantachrome Quadrasorb ASiQ - Two station. Surface area analysis was performed at 120 °C. Surface areas were calculated using BET theory over the range  $P/P_0 = 0-1$ .

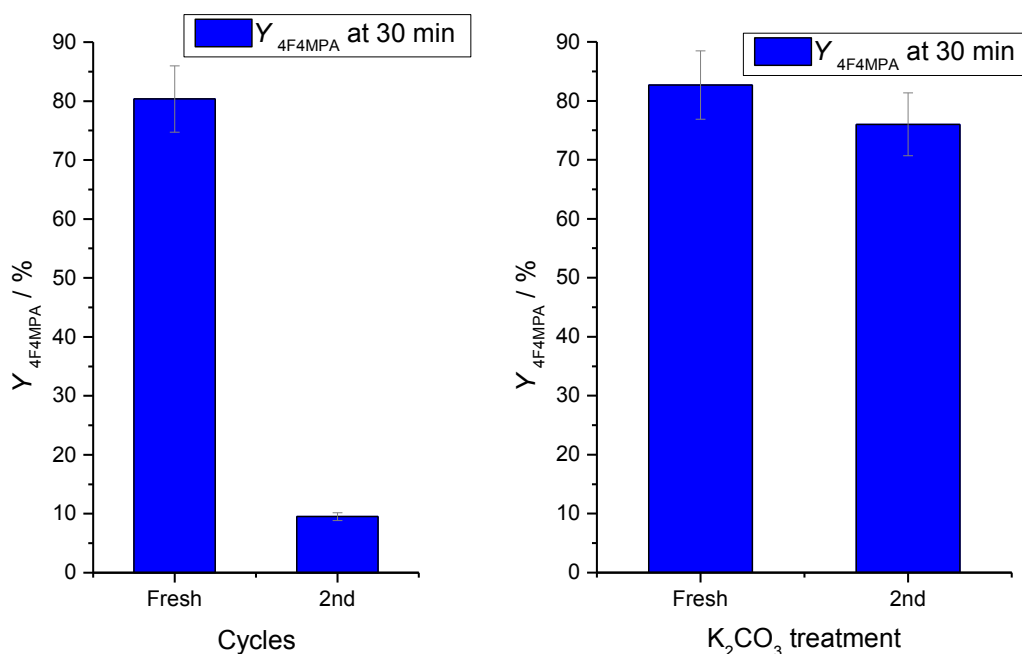
Catalyst	BET Surface area (m <sup>2</sup> g <sup>-1</sup> )
1Ag <sub>2</sub> O/TiO <sub>2</sub> (7.5 Hz)	11.6553
1Ag <sub>2</sub> O/TiO <sub>2</sub> (15 Hz)	23.1909
1Ag <sub>2</sub> O/TiO <sub>2</sub> (30 Hz)	47.8575

**Table S1** BET analysis of 1Ag<sub>2</sub>O/TiO<sub>2</sub> (MM) prepared at different milling frequency.

## 8. Reusability performances of 1% Ag<sub>2</sub>O/TiO<sub>2</sub>(MM) with 2,2-dimethylglutaric acid (1a).

Each reusability test, without intermediate base regeneration of the catalyst, was performed filtering the catalyst and the end of the reaction, washing the catalyst with 20 mL of H<sub>2</sub>O and drying it in an oven at 100°C for 30 min.

For K<sub>2</sub>CO<sub>3</sub> treatment, the used catalyst was previously stirred into 4mL of an aqueous solution of K<sub>2</sub>CO<sub>3</sub> 0.0575M for 1h and dried in an oven at 100°C for 30 min.

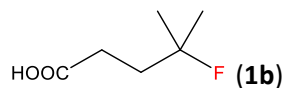


**Figure S6 (Left)** Reusability performances of the used catalyst washed with H<sub>2</sub>O. **Figure S5 (Right)** Reusability performances the used catalyst treated with an aqueous K<sub>2</sub>CO<sub>3</sub> solution. Reaction conditions: 0.2 mmol of DMGA, 0.4 mmol of Selectfluor®, 100 mg of 1% Ag/TiO<sub>2</sub> (0.0093 mmol of Ag), 4 mL H<sub>2</sub>O, 0.23 mmol of K<sub>2</sub>CO<sub>3</sub>, N<sub>2</sub> atmosphere, 30°C.

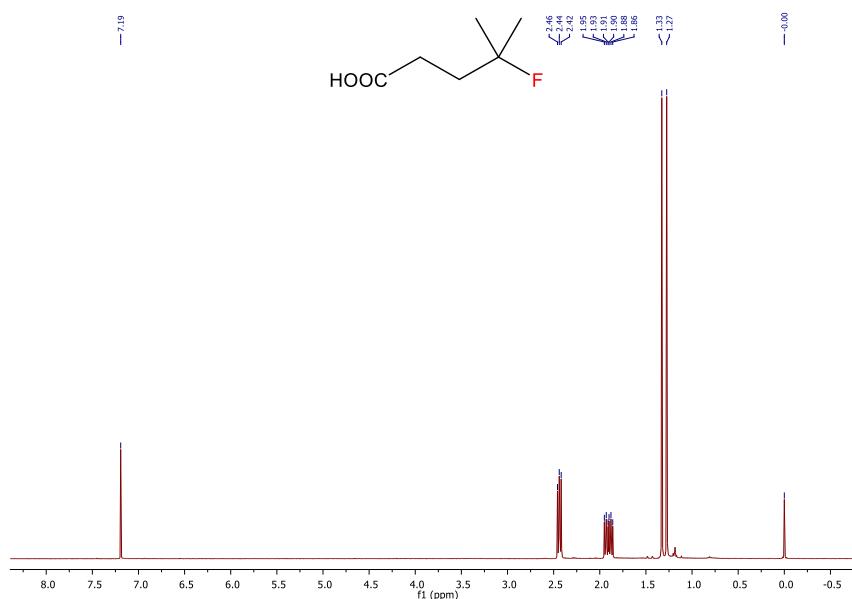


## 9. $^{19}\text{F}$ NMR Spectra of Products.

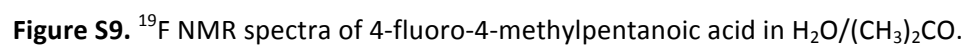
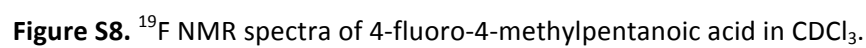
$^{19}\text{F}$  spectra were run on a JEOL Eclipse (+) 300M Hz equipped with a 5mm autotunable BBO probe and on a 400 MHz Bruker UltraShieldTM using  $\alpha,\alpha,\alpha$ -trifluorotoluene as reference ( $\delta=-63.72$  ppm),  $^1\text{H}$  of pure 4-fluoro-4-methylpentanoic acid was run on a 400 MHz Bruker UltraShieldTM spectrometer using TMS as reference ( $\delta=0$  ppm).

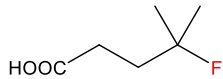


**4-fluoro-4-methylpentanoic acid (1b), 4F4MPA.** Prepared from 2,2-dimethylglutaric acid (**1a**) according to the general procedure.  $^{19}\text{F}$  NMR ( $\text{CDCl}_3$ , 283 MHz):  $\delta$  -141.29 (m, 1F).  $^{19}\text{F}$  NMR ( $\text{H}_2\text{O}/(\text{CH}_3)_2\text{CO}$ , 283 MHz): -135.19 (m, 1F).  $^{19}\text{F}$  NMR ( $\text{D}_2\text{O}$ , 283 MHz)  $\delta$  -137.21 (m, 1F). In good agreement with the value found in literature.<sup>1</sup>

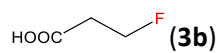


**Figure S7.**  $^1\text{H}$  NMR spectra of 4-fluoro-4-methylpentanoic acid in  $\text{CDCl}_3$ .

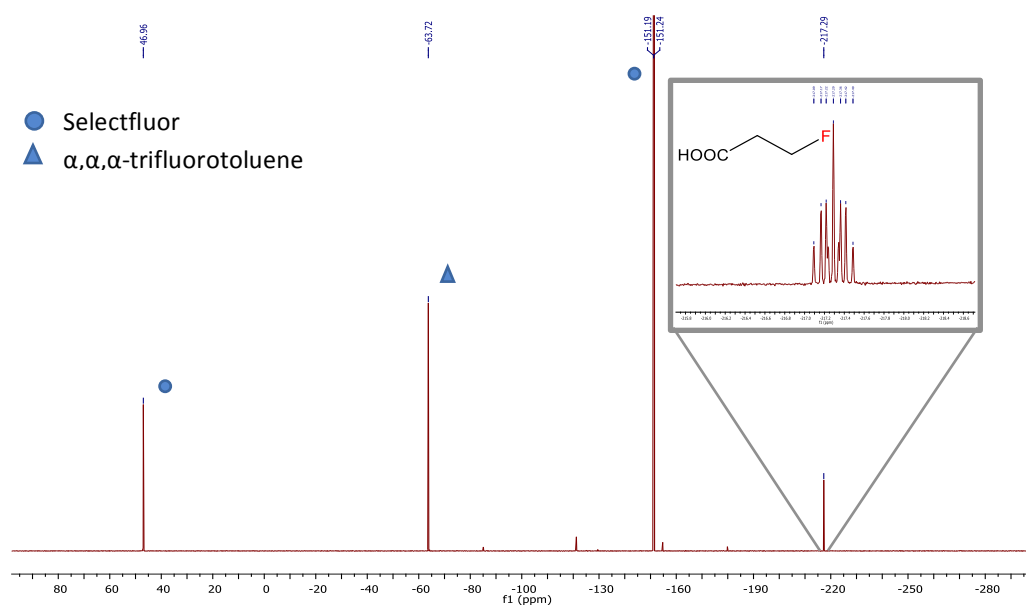




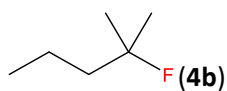
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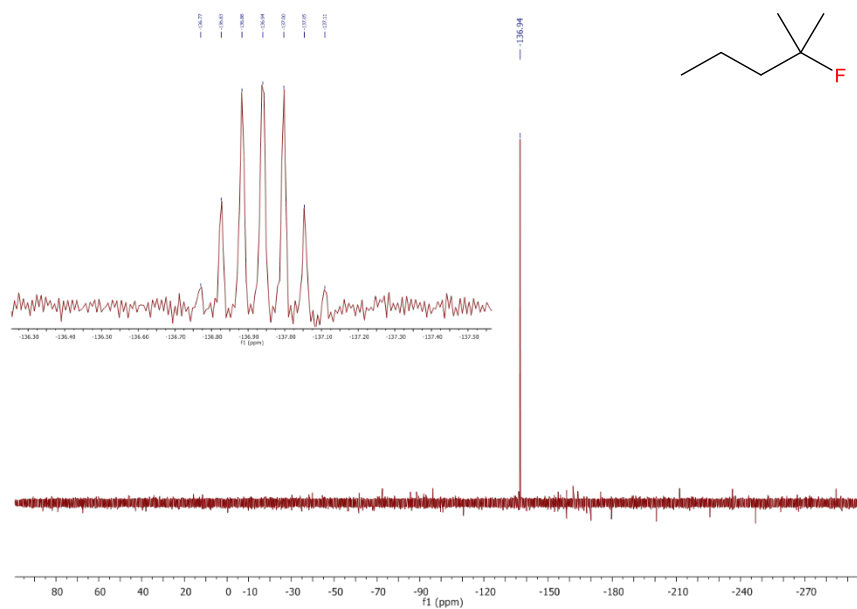
**3-Fluoropropanoic acid (3b).** Prepared from succinic acid (**3a**) according to the general procedure.  $^{19}\text{F}$  NMR (no solvent, 376 MHz):  $\delta$  -217.29 (m, 1F). In good agreement with the value found in literature.<sup>2</sup>



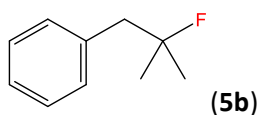
**Figure S11.**  $^{19}\text{F}$  NMR spectra of crude reaction using succinic acid as substrate.



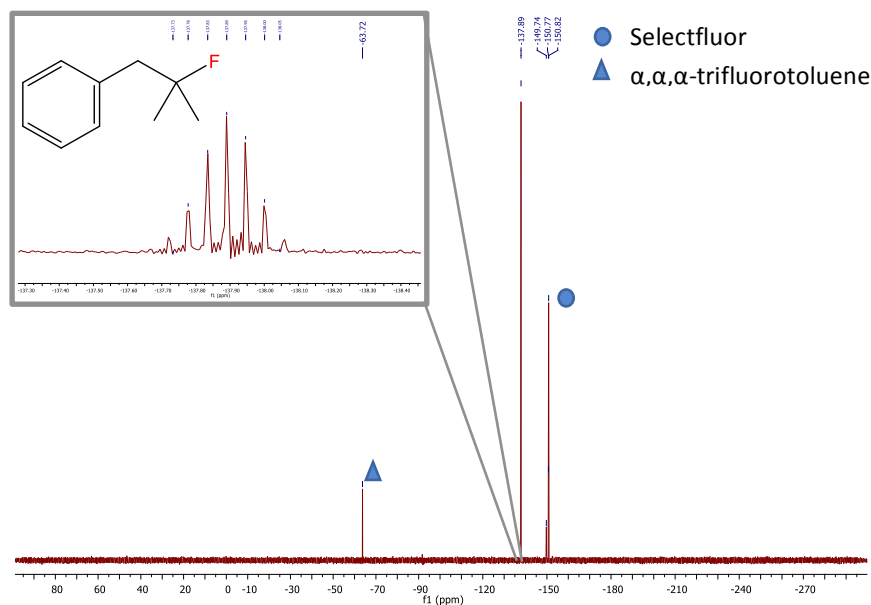
**2-Fluoro-2-methylpentane (4b).** Prepared from 2,2-dimethylvaleric acid (**4a**) according to the general procedure.  $^{19}\text{F}$  NMR ( $\text{CDCl}_3$ , 376 MHz):  $\delta$  –136.94 (m, 1F). In good agreement with the value present in literature.<sup>3</sup>



**Figure S12.**  $^{19}\text{F}$  NMR spectra of 2-fluoro-2-methylpentane in  $\text{CDCl}_3$ .



**(2-fluoro-2-methylpropyl)benzene (5b).** Prepared from 2,2-dimethyl-3-phenylpropionic acid (**5a**) according to the general procedure.  $^{19}\text{F}$  NMR (no solvent, 376 MHz)  $\delta$  -137.89 (m, 1F). In good agreement with the value found in literature.<sup>2</sup>



**Figure S13.**  $^{19}\text{F}$  NMR spectra of crude reaction with 2,2-dimethyl-3-phenylpropionic acid as substrate.

## 10. References for known compounds

All the substrates used were commercially purchased in high purity and used without further purifications.

1. N. R. Patel and R. A. Flowers. *J. Org. Chem.* 2015, **80**, 5834.
2. J.-B. Xia, C. Zhu, and C. Chen *Chem. Commun.*, 2014, **50**, 11701.
3. a) WSS: Wolfgang Robien / University of Vienna (Spectral Data were obtained from Wiley Subscription Services, Inc. (US)); b) F. J. Weigert, *J. Org. Chem.* 1980, 45 (17), 3476.