

# Cu-catalyzed Photoredox Chlorotrifluoromethylation of Polysubstituted Alkenes and Pharmacological Evaluation Supporting Information

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## 1. General informations

Photoredox reactions were performed with HepatoChem lamps into cardboard box with a distance of 8 cm between the lamps and reactions and a stirring at 1000 rpm. All reactions were carried out using an oven-dried 5 mL borosilicate flask and magnetic stirring under air unless otherwise stated. When needed, reactions were heated with a sand bath. Column chromatographies were carried out using silica gel (40-63  $\mu\text{m}$ ) supplied by VWR or Merck PTLC on silica gel 60 F254, 2 mm. Analytical thin layer chromatographies were performed on pre-coated silica gel aluminum plates with F-254 indicator (from Merck) and visualized by UV light (254 nm) and/or chemical stained with a  $\text{KMnO}_4$  solution.  $^1\text{H}$  (300 MHz),  $^{13}\text{C}$  (75 MHz) and  $^{19}\text{F}$  (282 MHz) NMR spectra were recorded on a Bruker DXP 300 MHz spectrometer in  $\text{CDCl}_3$  unless otherwise noted. Chemical shifts ( $\delta$ ) are quoted in ppm relative to the residual solvent peak for  $\text{CDCl}_3$  ( $^1\text{H}$ :  $\delta_{\text{H}} = 7.26$  ppm and  $^{13}\text{C}$ :  $\delta_{\text{C}} = 77.16$  ppm) and relative to the external standard  $\text{CFCl}_3$  ( $^{19}\text{F}$ :  $\delta_{\text{F}} = 0.00$  ppm).  $^1\text{H}$  (400 MHz),  $^{13}\text{C}$  (101 MHz) and  $^{19}\text{F}$  (377 MHz) NMR spectra were recorded on a Bruker Avance III 400 MHz spectrometer in  $\text{CDCl}_3$  or  $(\text{CD}_3)_2\text{SO}$  unless otherwise noted. Chemical shifts ( $\delta$ ) are quoted in ppm relative to the residual solvent peak for  $\text{CDCl}_3$  ( $^1\text{H}$ :  $\delta_{\text{H}} = 7.26$  ppm and  $^{13}\text{C}$ :  $\delta_{\text{C}} = 77.16$  ppm) or  $(\text{CD}_3)_2\text{SO}$  ( $^1\text{H}$ :  $\delta_{\text{H}} = 2.50$  and  $^{13}\text{C}$ :  $\delta_{\text{C}} = 39.52$  ppm). Coupling constants ( $J$ ) are quoted in Hz. The following abbreviations were used to show multiplicities: s = singlet, d = doublet, t = triplet, m = multiplet, q = quarter, p = pentet, dd = doublet of doublets, dt = doublet of triplets, dq = doublet of quartets, tt = triplet of triplets, brs = broad singlet. High-resolution mass (HRMS) were carried out on a Waters LCP Premier XR spectrometer with a TOF analyzer or were acquired on a maXis 3G (ESI-QqTOF) orthogonal mass spectrometer from Bruker Daltonik (Bremen, Germany) using electrospray ionization in positive (or negative) ion mode. Each compound was dissolved in dichloromethane (or methanol) then diluted 10-fold in methanol and infused individually into the ESI-QqTOFMS using a syringe pump at a flow rate of  $5\mu\text{L}/\text{min}$ . Mass spectra were recorded in the range  $m/z$  50–1200 and external calibration was performed using a sodium formate 0.5 mM solution. IR spectra were recorded on a PerkinElmer FT-IR Spectrum 100 (ATR), the wave numbers ( $\nu$ ) of recorded IR-signals (ATR) are quoted in  $\text{cm}^{-1}$ .

The copper complex  $[\text{Cu}(\text{dap})_2]\text{Cl}$  was prepared according to literature.<sup>[1]</sup>

The minor diastereoisomer was characterized only when it could be isolated and the diastereoisomeric ratio was determined by  $^{19}\text{F}$  NMR on crude product, before any treatment or purification.

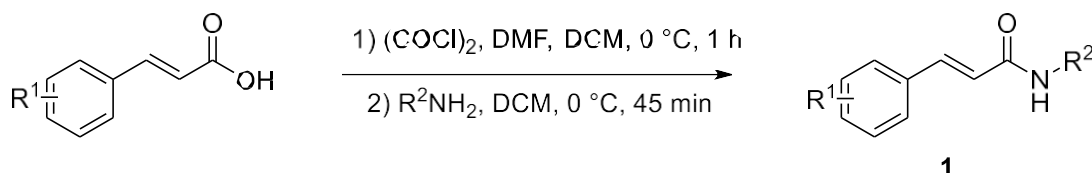
## 2. Materials

Anhydrous acetonitrile (MeCN), anhydrous acetone ((Me)<sub>2</sub>CO), methanol (MeOH), ethanol (EtOH), dimethyl sulfoxide (DMSO) and *N,N*-dimethylformamide (DMF) were purchased from Acros Organics (Solvents Extra Dry Over Molecular Sieve, AcroSeal®). Dichloromethane (DCM) was purified by distillation over CaH<sub>2</sub>. Tetrahydrofuran (THF) was distilled over sodium/benzophenone prior to use.

Cinnamic acid, cinnamic acid derivatives, oxalyl chloride, aniline, benzylamine, methylamine, *tert*-butylamine, aqueous ammonia, phenylacetaldehyde, phenylacetaldehyde derivatives, malonic acid, triethylamine (TEA), 1-3-dimethylaminopropyl-3-ethylcarbodiimide hydrochloride (EDCI), hexafluorophosphate azabenzotriazole tetramethyl uronium (HATU), *N,N*-diisopropylethylamine (DIPEA), benzaldehyde, benzaldehyde derivatives, vinylmagnesium bromide, triethyl orthoacetate (MeC(OEt)<sub>3</sub>), phenol (PhOH), 1,1'-carbonyldiimidazole (CDI), glycine methyl ester hydrochloride, trifluoromethanesulfonyl chloride (F<sub>3</sub>CSO<sub>2</sub>Cl) were purchased from Fisher Scientific, Sigma Aldrich, aaBlocks, Combiblock and were used without any purification steps.

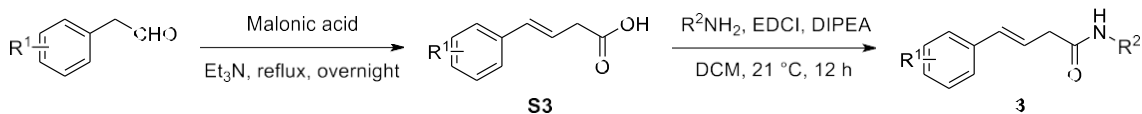
## 3. General procedures

### a. General procedure A for synthesis of amides 1



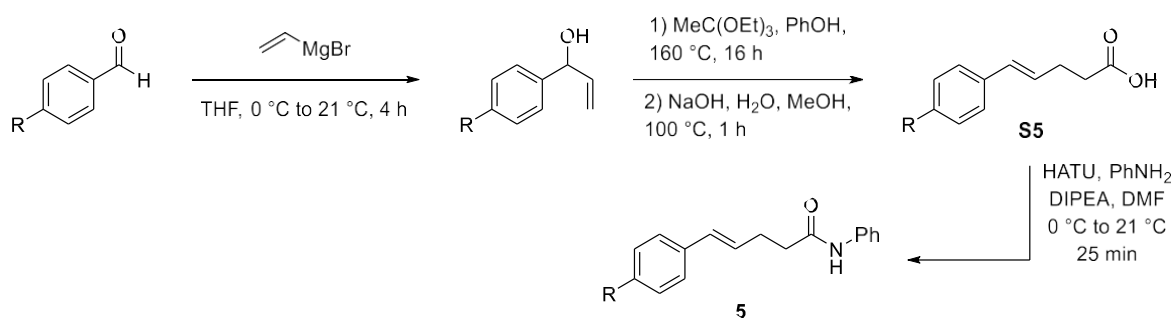
According to literature procedure<sup>[2]</sup> An anhydrous DCM (50 mM) solution of oxalyl chloride (7.80 mmol, 1.3 equiv.) was added slowly to a DCM (150 mM) solution of the appropriate carboxylic acid (6.00 mmol, 1.0 equiv.) and DMF (0.90 mmol, 0.1 equiv.) at 0 °C. The reaction mixture was stirred at 0 °C for 1 h, and the solvent was then evaporated under reduced pressure to give the corresponding cinnamoyl chloride. In a round-bottom flask was placed the corresponding amine in DCM (1 M). The solution was cooled to 0 °C and then cinnamoyl chloride was added in portion while stirring. After addition, the mixture was stirred for 45 min at room temperature and then water was added. The solution was extracted 3 times with DCM. The organic layers were collected together, dried over MgSO<sub>4</sub>, and concentrated under reduced pressure. The crude product was recrystallized from DCM/Pentane.

## b. General procedure B for synthesis of amides 3



Benzaldehyde (7.45 mmol, 1.0 equiv.) and malonic acid (8.20 mmol, 1.1 equiv.) were dissolved in Et<sub>3</sub>N (4 M). The reaction mixture was refluxed for 4 h and then cooled to room temperature. Then, diethyl ether was added to the reaction mixture, and acidified with 10% HCl to pH = 1, the organic layer was separated and washed with 5% NaOH solution, the aqueous layer was extracted with diethyl ether and the organic layer was discarded (to remove the organic impurities). The aqueous layer was acidified again with 10% HCl solution, extracted with ether. The combined organic layers were dried over MgSO<sub>4</sub> and concentrated under vacuum. The crude product was used for the next step without purification. A mixture of the corresponding carboxylic acid (7.00 mmol, 1.0 equiv.), amide (7.70 mmol, 1.1 equiv.), EDCI (7.70 mmol, 1.1 equiv.) and DIPEA (21.00 mmol, 3.0 equiv.) in DCM (500 mM) was stirred for overnight at room temperature. Water was added to the solution and the aqueous layer was extracted 3 times with DCM. The combined organic layers were washed with water, brine, dried with Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. The crude product was recrystallized from DCM/Pentane.

## c. General procedure C for synthesis of amides 5



To a solution of benzaldehyde (8.32 mmol, 1.0 equiv.) in anhydrous THF (500 mM) under an atmosphere of argon at 0 °C was added, vinyl magnesium bromide (9.15 mmol, 1.1 equiv., 1 M sol in THF). The reaction was stirred at 0 °C for 30 min and then allowed to react at room temperature for 3 h. The solution was diluted with Et<sub>2</sub>O, poured into a separating funnel and quenched with a saturated aqueous solution of NH<sub>4</sub>Cl. After phase separation, the aqueous layer was extracted 3 times with Et<sub>2</sub>O. The combined organic layers were washed with brine, dried over MgSO<sub>4</sub> and concentrated under reduced pressure. The crude phenylprop-2-enol was directly used for the next step without purification.



## 4. Biological Activity Assessment

### a. Antibacterial and Antifungal Assays

According to reported procedure,<sup>[3]</sup> antibacterial activity was evaluated using a microdilution method. Briefly, exponentially growing bacteria were plated in 96-well microplates (Costar, Corning Inc.) at a density of  $5 \times 10^3$  gram-negative *E. coli* (ATCC 25922) or  $3.5 \times 10^4$  gram-positive *S. aureus* (ATCC 25923) per well in 100  $\mu$ L nutrient broth (Difco), or  $2 \times 10^3$  *C. albicans* (ATCC 10231) per well in 100  $\mu$ L sabouraud dextrose (Difco). Increasing concentrations of compounds (solubilized in biotech DMSO, then diluted in nutrient broth or sabouraud dextrose) were then added (100  $\mu$ L per well). The final concentration of DMSO in the culture medium was maintained at 0.1% (volume/volume) to avoid solvent toxicity. Absorbance was read after 24h incubation using a Varioskan Ascent plate reader (Thermo Electron) at 600 nm for bacteria and 540 nm for yeasts.

**Table 1:** Antibacterial and antifungal activity of analogs.

Cpds	IC <sub>90</sub> (μM)		
	<i>E. coli</i>	<i>S. aureus</i>	<i>C. albicans</i>
<b>2a</b>	>200	83 ± 12 (IC <sub>50</sub> = 68 ± 10 μM)	>200 (IC <sub>50</sub> = 84 ± 13 μM)
<b>2c</b>	>200	>200	>200
<b>2e</b>	>200	>200	>200
<b>2g</b>	>200	>200	>200
<b>2h</b>	>200	>200	>200
<b>2j</b>	>200	>200	>200
<b>2m</b>	>200	>200	>200
<b>2n</b>	>200	>200	>200
<b>2o</b>	>200	>200	>200
<b>4a</b>	>200	>200	>200
<b>4b</b>	>200	>200	>200
<b>4f</b>	>200	>200	>200
<b>6a</b>	>200	>200	>200
<b>4h</b>	>200	>200 (IC <sub>50</sub> = 131 ± 5 μM)	>200
<b>6d</b>	>200	>200	>200
<b>6f</b>	>200	>200	>200
<b>6g</b>	>200	>200 (IC <sub>50</sub> = 26 ± 6 μM)	>200
<b>6h</b>	>200	>200 (IC <sub>50</sub> = 30 ± 3 μM)	>200
<b>Gentamicin</b>	0.088 ± 0.009 (IC <sub>50</sub> = 0.054 ± 0.006 μg/ml)	0.034 ± 0.004 (IC <sub>50</sub> = 0.013 ± 0.002 μg/ml)	
<b>AmphotericinB</b>			0.18 ± 0.01 (IC <sub>50</sub> = 0.12 ± 0.01 μM)

Note: IC<sub>90</sub>/IC<sub>50</sub>: concentration of compounds inhibiting bacteria growth by 90%/50%. Gentamicin and Amphotericin B are used as standard.

## b. Cytotoxicity assay

According to reported procedure,<sup>[4]</sup> The A-549 human lung carcinoma (CCL-185), DLD-1 human colorectal adenocarcinoma (CCL-221), and WS-1 skin fibroblast (CRL-1502) cell lines were obtained from the American Type Culture Collection (ATCC, Manassas, VA, USA). Exponentially growing cells were plated in 96-well microplates (Costar, Corning Inc.) at a density of 5x10<sup>3</sup> cells per well in 100 μL of culture medium (DMEM supplemented with 10% fetal bovine serum, vitamins 1X, penicillin, and streptomycin) and were allowed to adhere for 16 h before treatment. A concentration gradient of each compound was prepared in biotech DMSO (Sigma-Aldrich) and then diluted in DMEM before it was added to microplates (100 μL per well). Cells were then incubated for 48 h. The final concentration of DMSO in the culture medium was maintained at 0.5% (v/v) to avoid solvent toxicity. Cytotoxicity was assessed using resazurin and Hoechst (bis-

benzimidazole H-33342) on an automated Fluoroskan Ascent F1™ plate reader (Labsystems) using excitation and emission wavelengths of 530 and 590 nm and 358 and 461 nm respectively for each fluorochrome. Survival percentage was defined as the fluorescence in experimental wells compared to that in control wells after the subtraction of blank values. It is expressed as the concentration of compounds inhibiting cell growth by 50% (IC<sub>50</sub>).

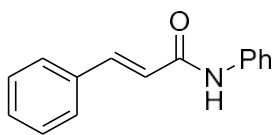
**Table 2:** Cytotoxic activity of analogs.

Cpds	IC <sub>50</sub> (μM)					
	Resazurine	Resazurine	Resazurine	Hoechst	Hoechst	Hoechst
	A-549	DLD-1	WS-1	A-549	DLD-1	WS-1
<b>2a</b>	5.6 ± 0.7	4.2 ± 0.3	6.9 ± 0.1	9 ± 2	6.0 ± 0.7	15 ± 3
<b>2c</b>	>200	>200	>200	>200	>200	>200
<b>2e</b>	31 ± 3	18.5 ± 0.3	52 ± 4	49 ± 10	21 ± 4	80 ± 8
<b>2g</b>	20 ± 2	12.8 ± 0.5	28 ± 1	29 ± 8	14 ± 2	69 ± 10
<b>2h</b>	16.6 ± 0.6	7.1 ± 0.2	18.5 ± 0.9	18 ± 1	9 ± 1	29 ± 5
<b>2j</b>	102 ± 7	39 ± 5	115 ± 8	98 ± 10	60 ± 10	169 ± 11
<b>2m</b>	12.2 ± 0.6	3.5 ± 0.2	8 ± 1	12.4 ± 0.9	4.3 ± 0.9	9 ± 1
<b>2n</b>	6.1 ± 0.5	2.46 ± 0.03	6.7 ± 0.1	9 ± 1	3 ± 1	8.6 ± 0.6
<b>2o</b>	6.5 ± 0.6	2.37 ± 0.02	4.7 ± 0.4	3 ± 1	2.8 ± 0.6	7.0 ± 0.9
<b>4a</b>	>200	>200	>200	>200	>200	>200
<b>4b</b>	>200	>200	>200	>200	>200	>200
<b>4f</b>	>200	>200	>200	>200	>200	>200
<b>6a</b>	>200	>200	>200	>200	>200	>200
<b>4h</b>	>200	>200	>200	>200	>200	>200
<b>6d</b>	>200	>200	>200	171 ± 10	>200	>200
<b>6f</b>	>200	>200	>200	>200	>200	>200
<b>6g</b>	>200	>200	>200	>200	>200	>200
<b>6h</b>	>200	>200	>200	>200	>200	>200
<b>Daunorubicin</b>	0.084 ± 0.005	0.071 ± 0.003	0.116 ± 0.008	0.051 ± 0.006	0.044 ± 0.006	0.31 ± 0.06

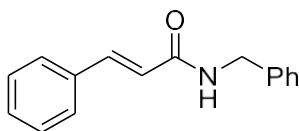
Note: Resazurine and Hoechst are two dyes and represent two different methods of detection. A-549: human lung carcinoma cell line (CCL-185). DLD-1: human colorectal adenocarcinoma cell line (CCL-221). WS-1: skin fibroblast cell line (CRL-1502).



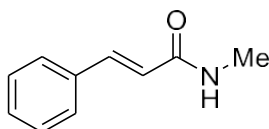
## 5. Characterization of products



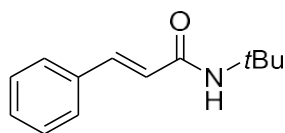
**N-(phenyl)cinnamamide 1a** was synthesized from commercial cinnamic acid and aniline following general procedure A. **1a** was obtained as white powder (879.1 mg, 69% yield). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 7.76 (d, *J* = 15.5 Hz, 1H), 7.63 (d, *J* = 6.9 Hz, 2H), 7.53 (m, 2H), 7.37 (m, 6H), 7.14 (t, *J* = 7.4 Hz, 1H), 6.56 (d, *J* = 15.5 Hz, 1H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 164.4, 142.5, 138.2, 134.7, 130.0, 129.2, 129.0, 128.1, 124.6, 121.1, 120.2. The NMR data correspond to those described in literature.<sup>[5]</sup>



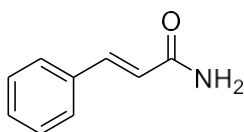
**N-(benzyl)cinnamamide 1b** was synthesized from commercial cinnamic acid and benzylamine following general procedure A. **1b** was obtained as white powder (1.2 g, 72% yield). **<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.67 (d, *J* = 15.6 Hz, 1H), 7.51 – 7.47 (m, 2H), 7.37 – 7.30 (m, 8H), 6.43 (d, *J* = 15.6 Hz, 1H), 6.05 (brs, 1H), 4.57 (d, *J* = 5.8 Hz, 2H). **<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 165.9, 141.5, 138.3, 134.9, 129.8, 128.9, 128.9, 128.1, 127.9, 127.7, 120.6, 44.0. The NMR data correspond to those described in literature.<sup>[6]</sup>



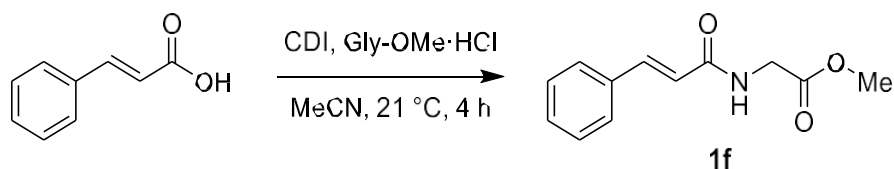
**N-(methyl)cinnamamide 1c** was synthesized from commercial cinnamic acid and methylamine following general procedure A. **1c** was obtained as white powder (454.3 mg, 36% yield). **<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.63 (d, *J* = 15.6 Hz, 1H), 7.50 – 7.47 (m, 2H), 7.36 – 7.33 (m, 3H), 6.41 (d, *J* = 15.6 Hz, 1H), 5.88 (brs, 1H), 2.94 (d, *J* = 4.9 Hz, 3H). **<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 166.8, 140.9, 135.0, 129.7, 128.9, 127.9, 120.7, 26.7. The NMR data correspond to those described in literature.<sup>[7]</sup>



***N*-(*tert*-butyl)cinnamamide **1d**** was synthesized from commercial cinnamic acid and *tert*-butylamine following general procedure A. **1d** was obtained as white powder (1.0 g, 84% yield).  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.57 (d,  $J$  = 15.5 Hz, 1H), 7.49 – 7.46 (m, 2H), 7.39 – 7.32 (m, 3H), 6.32 (d,  $J$  = 15.5 Hz, 1H), 5.46 (s, 1H), 1.43 (s, 9H).  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  165.3, 140.4, 135.1, 129.6, 128.9, 127.8, 122.1, 51.7, 29.0. The NMR data correspond to those described in literature.<sup>[6]</sup>

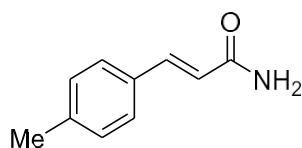


**Cinnamamide **1e**** was synthesized from commercial cinnamic acid and ammonium hydroxide ( $\text{NH}_4\text{OH}$ ) following general procedure A. **1e** was obtained as white powder (10.1 g, 80% yield).  $^1\text{H NMR}$  (400 MHz,  $(\text{CD}_3)_2\text{SO}$ ):  $\delta$  7.55 (d,  $J$  = 7.3 Hz, 3H), 7.44 (d,  $J$  = 16.0 Hz, 1H), 7.38 – 7.34 (m, 3H), 7.16 (brs, 1H), 6.63 (d,  $J$  = 16.0 Hz, 1H).  $^{13}\text{C NMR}$  (101 MHz,  $(\text{CD}_3)_2\text{SO}$ ):  $\delta$  166.8, 139.2, 134.9, 129.5, 128.9, 127.6, 122.3. The NMR data correspond to those described in literature.<sup>[6]</sup>

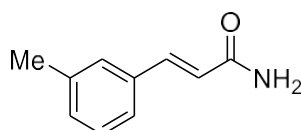


Carbonyldiimidazole (CDI) (411.0 mg, 2.53 mmol, 1.2 equiv.) was added in a suspension of cinnamic acid (313.0 mg, 2.11 mmol, 1.0 equiv.) in acetonitrile (10 mL, 210 mM) and the vial was sealed with a screw cap. The suspension became quickly transparent and was stirred at room temperature for 45 min on the orbital shaker. After this, the vial was unsealed and degassed to slowly add glycine methyl ester hydrochloride (318.0 mg, 2.53 mmol, 1.2 equiv.) and was resealed for another 4 h at room temperature on the orbital shaker. After the reaction completion, the mixture was concentrated at reduced pressure to remove acetonitrile before being resolubilized in ethyl acetate and transferred in a separatory funnel. The organic layer was washed two times with 1 M aqueous NaOH solution and 2 times with 1 M aqueous HCl solution before being dried with  $\text{MgSO}_4$  and concentrated under reduced pressure to give methyl 2-cinnamamidoacetate **1f** as white solid (426.0 mg, 92% yield).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.64 (d,  $J$  = 15.7 Hz, 1H), 7.49 – 7.46 (m, 2H), 7.34 – 7.33 (m, 3H), 6.52 – 6.48 (m, 2H), 4.18 (d,  $J$  = 5.2 Hz, 2H), 3.76 (s, 3H).  $^{13}\text{C NMR}$

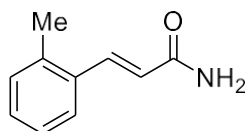
(101 MHz, CDCl<sub>3</sub>):  $\delta$  170.7, 166.2, 141.9, 134.7, 129.9, 128.9, 128.0, 119.9, 52.5, 41.6. The NMR data correspond to those described in literature.<sup>[8]</sup>



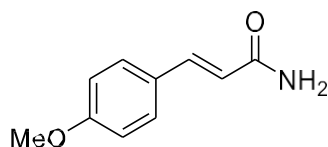
**4-(methyl)cinnamamide 1g** was synthesized from commercial (*E*)-3-(*p*-tolyl)acrylic acid and ammonium hydroxide (NH<sub>4</sub>OH) following general procedure A. **1g** was obtained as white powder (977.1 mg, 99% yield). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.63 (d, *J* = 15.7 Hz, 1H), 7.42 (d, *J* = 8.1 Hz, 2H), 7.19 (d, *J* = 8.1 Hz, 2H), 6.41 (d, *J* = 15.7 Hz, 1H), 5.57 (brs, 2H), 2.37 (s, 3H). **<sup>13</sup>C NMR** (101 MHz, (CD<sub>3</sub>)<sub>2</sub>SO):  $\delta$  167.3, 139.6, 139.5, 132.2, 129.7, 127.7, 121.2, 21.1. **HRMS** (ESI+) *m/z*: calcd for C<sub>10</sub>H<sub>11</sub>NaNO [M+Na]<sup>+</sup>: 184.0733, found 184.0733 ( $\Delta$  = 0.0 ppm). **IR** (neat, cm<sup>-1</sup>):  $\nu$  3302, 3150, 1680, 1600, 1400, 1250.



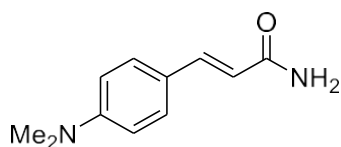
**3-(methyl)cinnamamide 1h** was synthesized from commercial (*E*)-3-(*m*-tolyl)acrylic acid and ammonium hydroxide (NH<sub>4</sub>OH) following general procedure A. **1h** was obtained as white powder (944.3 mg, 95% yield). **<sup>1</sup>H NMR** (400 MHz, (CD<sub>3</sub>)<sub>2</sub>SO):  $\delta$  7.59 (brs, 1H), 7.40 – 7.29 (m, 3H), 7.27 (t, *J* = 7.5 Hz, 1H), 7.17 (d, *J* = 7.5 Hz, 1H), 7.13 (brs, 1H), 6.61 (d, *J* = 15.9 Hz, 1H), 2.30 (s, 3H). **<sup>13</sup>C NMR** (101 MHz, (CD<sub>3</sub>)<sub>2</sub>SO):  $\delta$  167.1, 139.6, 138.3, 134.9, 130.4, 129.0, 128.2, 125.0, 122.1, 21.0. **HRMS** (ESI+) *m/z*: calcd for C<sub>10</sub>H<sub>11</sub>NaNO [M+Na]<sup>+</sup>: 184.0733, found 184.0741 ( $\Delta$  = 4.3 ppm). **IR** (neat, cm<sup>-1</sup>):  $\nu$  3390, 3195, 1640, 1605, 1400, 1260.



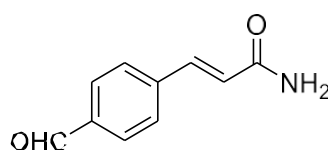
**2-(methyl)cinnamamide 1i** was synthesized from commercial (*E*)-3-(*o*-tolyl)acrylic acid and ammonium hydroxide (NH<sub>4</sub>OH) following general procedure A. **1i** was obtained as white powder (963.1 mg, 97% yield). **<sup>1</sup>H NMR** (400 MHz, (CD<sub>3</sub>)<sub>2</sub>SO):  $\delta$  7.66 (d, *J* = 15.5 Hz, 2H), 7.53 (m, 1H), 7.27 – 7.19 (m, 3H), 7.16 (brs, 1H), 6.52 (d, *J* = 15.5 Hz, 1H), 2.35 (s, 3H). **<sup>13</sup>C NMR** (101 MHz, (CD<sub>3</sub>)<sub>2</sub>SO):  $\delta$  167.2, 137.0, 136.9, 133.8, 130.8, 129.4, 126.5, 126.1, 123.4, 19.5. **HRMS** (ESI+) *m/z*: calcd for C<sub>10</sub>H<sub>11</sub>NaNO [M+Na]<sup>+</sup>: 184.0733, found 184.0735 ( $\Delta$  = 1.1 ppm). **IR** (neat, cm<sup>-1</sup>):  $\nu$  3390, 3197, 1680, 1600, 1390, 1240.



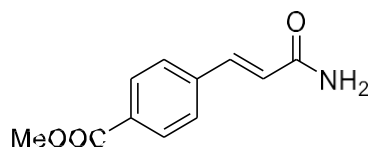
**4-(methoxycinnamamide 1j** was synthesized from commercial (*E*)-3-(*p*-methoxyphenyl)acrylic acid and ammonium hydroxide (NH<sub>4</sub>OH) following general procedure A. **1j** was obtained as white powder (937.6 mg, 95% yield). <sup>1</sup>H NMR (400 MHz, (CD<sub>3</sub>)<sub>2</sub>SO): δ 7.57 (brs, 1H), 7.50 (d, *J* = 8.5 Hz, 2H), 7.37 (dd, *J* = 15.8, 4.9 Hz, 1H), 7.06 (brs, 1H), 6.96 (dd, *J* = 8.5, 2.9 Hz, 2H), 6.49 (dd, *J* = 15.8, 6.8 Hz, 1H), 3.75 (s, 3H). <sup>13</sup>C NMR (101 MHz, (CD<sub>3</sub>)<sub>2</sub>SO): δ 167.5, 160.5, 139.3, 129.4, 127.5, 119.8, 114.5, 55.4. HRMS (ESI+) *m/z*: calcd for C<sub>10</sub>H<sub>11</sub>NaNO<sub>2</sub> [M+Na]<sup>+</sup>: 200.0682, found 200.0682 (Δ = 0.0 ppm). IR (neat, cm<sup>-1</sup>): ν 3450, 3360, 3150, 2910, 1660, 1595, 1500, 1400, 1270.



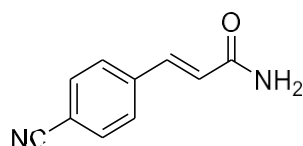
**4-(dimethylaminocinnamamide 1k** was synthesized from commercial (*E*)-3-(*p*-(dimethylamino)phenyl)acrylic acid and ammonium hydroxide (NH<sub>4</sub>OH) following general procedure A. **1k** was obtained as beige powder (648.9 mg, 58% yield). <sup>1</sup>H NMR (300 MHz, (CD<sub>3</sub>)<sub>2</sub>SO): δ 7.47 – 7.43 (m, 4H), 6.67 (d, *J* = 8.9 Hz, 2H), 6.21 (d, *J* = 15.8 Hz, 1H), 2.94 (s, 6H). <sup>13</sup>C NMR (75 MHz, (CD<sub>3</sub>)<sub>2</sub>SO): δ 168.2, 151.6, 144.7, 129.8, 121.6, 113.0, 111.8. The NMR data correspond to those described in literature.<sup>[9]</sup>



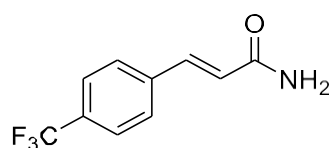
**4-(formylcinnamamide 1l** was synthesized from commercial (*E*)-3-(*p*-formylphenyl)acrylic acid and ammonium hydroxide (NH<sub>4</sub>OH) following general procedure A. **1l** was obtained as orange powder (706.3 mg, 72% yield). <sup>1</sup>H NMR (400 MHz, (CD<sub>3</sub>)<sub>2</sub>SO): δ 10.01 (s, 1H), 7.93 (d, *J* = 8.1 Hz, 2H), 7.77 (d, *J* = 8.1 Hz, 2H), 7.64 (brs, 1H), 7.49 (d, *J* = 15.9 Hz, 1H), 7.25 (brs, 1H), 6.77 (d, *J* = 15.9 Hz, 1H). <sup>13</sup>C NMR (101 MHz, (CD<sub>3</sub>)<sub>2</sub>SO): δ 192.6, 166.2, 140.7, 137.9, 136.4, 130.0, 128.2, 125.5. The NMR data correspond to those described in literature.<sup>[10]</sup>



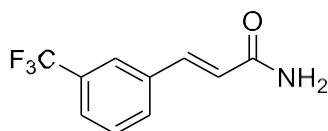
**4-(methoxycarbonyl)cinnamamide 1m** was synthesized from commercial (*E*)-3-(*p*-(methoxycarbonyl)phenyl)acrylic acid and ammonium hydroxide (NH<sub>4</sub>OH) following general procedure A. **1m** was obtained as white powder (690.4 mg, 95% yield). **<sup>1</sup>H NMR** (400 MHz, (CD<sub>3</sub>)<sub>2</sub>SO): δ 7.95 (m, 2H), 7.68 (m, 3H), 7.46 (d, *J* = 15.9 Hz, 1H), 7.23 (brs, 1H), 6.73 (d, *J* = 15.9 Hz, 1H), 3.83 (s, 3H). **<sup>13</sup>C NMR** (101 MHz, (CD<sub>3</sub>)<sub>2</sub>SO): δ 166.6, 166.0, 139.6, 138.2, 130.1, 129.9, 128.0, 125.0, 52.4. **HRMS** (ESI+) *m/z*: calcd for C<sub>11</sub>H<sub>11</sub>NaNO<sub>3</sub> [M+Na]<sup>+</sup>: 228.0631, found 228.0632 (Δ = 0.4 ppm). **IR** (neat, cm<sup>-1</sup>): ν 3400, 3170, 1700, 1680, 1601, 1390, 1295.



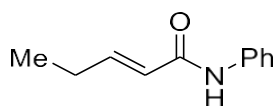
**4-(cyano)cinnamamide 1n** was synthesized from commercial (*E*)-3-(*p*-cyanophenyl)acrylic acid and ammonium hydroxide (NH<sub>4</sub>OH) following general procedure A. **1n** was obtained as beige powder (825.1 mg, 83% yield). **<sup>1</sup>H NMR** (400 MHz, (CD<sub>3</sub>)<sub>2</sub>SO): δ 7.87 (d, *J* = 8.3 Hz, 2H), 7.75 (d, *J* = 8.3 Hz, 2H), 7.64 (brs, 1H), 7.47 (d, *J* = 15.9 Hz, 1H), 7.25 (brs, 1H), 6.75 (d, *J* = 15.9 Hz, 1H). **<sup>13</sup>C NMR** (101 MHz, (CD<sub>3</sub>)<sub>2</sub>SO): δ 166.0, 139.6, 137.3, 132.8, 128.2, 125.9, 118.7, 111.4. **HRMS** (ESI+) *m/z*: calcd for C<sub>10</sub>H<sub>8</sub>NaN<sub>2</sub>O [M+Na]<sup>+</sup>: 195.0529, found 195.0531 (Δ = 1.0 ppm). **IR** (neat, cm<sup>-1</sup>): ν 3490, 3170, 2220, 1660, 1600, 1395.



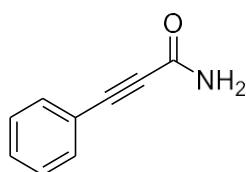
**4-(trifluoromethyl)cinnamamide 1o** was synthesized from commercial (*E*)-3-(*p*-(trifluoromethyl)phenyl)acrylic acid and ammonium hydroxide (NH<sub>4</sub>OH) following general procedure A. **1o** was obtained as white powder (894.6 mg, 89% yield). **<sup>1</sup>H NMR** (400 MHz, (CD<sub>3</sub>)<sub>2</sub>SO): δ 7.78 – 7.69 (m, 5H), 7.48 (d, *J* = 15.9 Hz, 1H), 7.25 (brs, 1H), 6.75 (d, *J* = 15.9 Hz, 1H). **<sup>13</sup>C NMR** (101 MHz, (CD<sub>3</sub>)<sub>2</sub>SO): δ 166.6, 139.0, 137.9, 129.4 (q, *J* = 32.0 Hz), 128.4, 125.9 (q, *J* = 3.3 Hz), 125.2, 124.2 (q, *J* = 272.1 Hz). **<sup>19</sup>F NMR** (377 MHz, (CD<sub>3</sub>)<sub>2</sub>SO): δ -66.36. **HRMS** (ESI+) *m/z*: calcd for C<sub>10</sub>H<sub>8</sub>F<sub>3</sub>NaNO [M+Na]<sup>+</sup>: 238.0450, found 238.0452 (Δ = 0.8 ppm). **IR** (neat, cm<sup>-1</sup>): ν 3330, 3155, 1660, 1600, 1390, 1305, 1100.



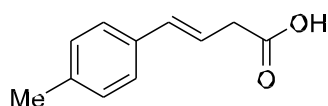
**3-(trifluoromethyl)cinnamamide 1p** was synthesized from commercial (*E*)-3-(*m*-(trifluoromethyl)phenyl)acrylic acid and ammonium hydroxide (NH<sub>4</sub>OH) following general procedure A. **1p** was obtained as white powder (814.6 mg, 84% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.73 (s, 1H), 7.71 – 7.55 (m, 3H), 7.48 – 7.44 (m, 1H), 6.57 (d, *J* = 15.7 Hz, 1H), 6.45 (brs, 1H), 6.09 (brs, 1H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 167.2, 140.8, 135.3, 131.4 (q, *J* = 32.6 Hz), 131.3, 129.4, 126.4 (q, *J* = 7.0 Hz), 124.1 (q, *J* = 3.8 Hz), 123.8 (q, *J* = 272.5 Hz), 121.4. <sup>19</sup>F NMR (282 MHz, CDCl<sub>3</sub>): δ -63.38. HRMS (ESI+) *m/z*: calcd for C<sub>10</sub>H<sub>8</sub>F<sub>3</sub>NaNO [M+Na]<sup>+</sup>: 238.0450, found 238.0453 (Δ = 1.2 ppm). IR (neat, cm<sup>-1</sup>): ν 3320, 3160, 1660, 1600, 1400, 1320, 1110.



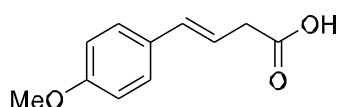
**(E)-hex-2-enamide 1q** was synthesized from commercial (*E*)-pent-2-enoic acid and aniline following general procedure A. **1q** was obtained as white powder (942.5 mg, 88% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.57 (d, *J* = 7.1 Hz, 3H), 7.31 (t, *J* = 7.9 Hz, 2H), 7.10 (t, *J* = 7.3 Hz, 1H), 7.03 (dt, *J* = 15.2, 6.4 Hz, 1H), 5.94 (m, 1H), 2.30 – 2.18 (m, 2H), 1.07 (t, *J* = 7.3 Hz, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>): δ 164.4, 148.0, 138.2, 129.1, 124.3, 123.2, 120.1, 25.3, 12.5. The NMR data correspond to those described in literature.<sup>[11]</sup>



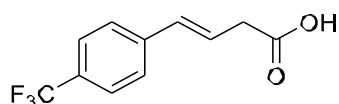
**3-phenylpropiolamide 1t** was synthesized from commercial 3-phenylpropionic acid and ammonium hydroxide (NH<sub>4</sub>OH) following general procedure A. **1t** was obtained as white powder (796.8 mg, 79% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.56 (d, *J* = 1.2 Hz, 1H), 7.54 (d, *J* = 1.5 Hz, 1H), 7.51 – 7.33 (m, 3H), 5.88 (brs, 2H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>): δ 155.0, 132.8, 130.5, 128.7, 120.1, 86.2, 82.4. HRMS (ESI+) *m/z*: calcd for C<sub>9</sub>H<sub>7</sub>NaNO [M+Na]<sup>+</sup>: 168.0420, found 168.0420 (Δ = 0.0 ppm). IR (neat, cm<sup>-1</sup>): ν 3360, 3190, 2205, 1600, 1490, 1390.



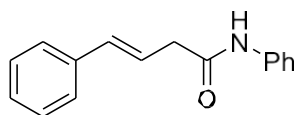
**(E)-4-(*p*-tolyl)but-3-enoic acid S3f** was synthesized from commercial (*p*-tolyl)acetaldehyde following general procedure B. **S3f** was obtained as beige powder (990.0 mg, 75% yield). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 7.27 (d, *J* = 8.0 Hz, 2H), 7.12 (d, *J* = 8.0 Hz, 2H), 6.49 (d, *J* = 15.9 Hz, 1H), 6.23 (dt, *J* = 15.9, 7.1 Hz, 1H), 3.29 (dd, *J* = 7.1, 1.2 Hz, 2H), 2.33 (s, 3H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 177.8, 137.7, 134.0, 129.4, 126.4, 119.9, 38.1, 21.3. **HRMS** (ESI+) *m/z*: calcd for C<sub>11</sub>H<sub>12</sub>NaO<sub>2</sub> [M+Na]<sup>+</sup>: 199.0730, found 199.0726 (Δ = 2.0 ppm). **IR** (neat, cm<sup>-1</sup>): ν 2910, 1710, 1510, 1400, 1300, 1200.



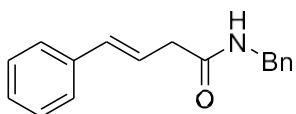
**(E)-4-(*p*-methoxyphenyl)but-3-enoic acid S3g** was synthesized from commercial (*p*-methoxyphenyl)acetaldehyde following general procedure B. **S3g** was obtained as beige powder (770.4 mg, 61% yield). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 7.31 (dt, *J* = 8.7, 2.1 Hz, 2H), 6.85 (dt, *J* = 8.7, 2.1 Hz, 2H), 6.46 (d, *J* = 15.9 Hz, 1H), 6.14 (dt, *J* = 15.9, 7.1 Hz, 1H), 3.81 (s, 3H), 3.28 (dd, *J* = 7.1, 1.4 Hz, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 177.7, 159.4, 133.6, 129.6, 127.6, 118.7, 114.1, 55.4, 38.1. **HRMS** (ESI+) *m/z*: calcd for C<sub>11</sub>H<sub>12</sub>NaO<sub>3</sub> [M+Na]<sup>+</sup>: 215.0679, found 215.0677 (Δ = 0.9 ppm). **IR** (neat, cm<sup>-1</sup>): ν 2910, 1700, 1600, 1500, 1250, 1150.



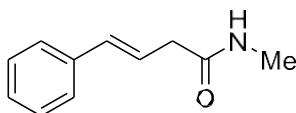
**(E)-4-(*p*-(trifluoromethyl)phenyl)but-3-enoic acid S3h** was synthesized from commercial (*p*-(trifluoromethyl)phenyl)acetaldehyde following general procedure B. **S3h** was obtained as beige powder (220.4 mg, 18% yield). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 7.57 (d, *J* = 8.2 Hz, 2H), 7.47 (d, *J* = 8.2 Hz, 2H), 6.56 (d, *J* = 16.0 Hz, 1H), 6.39 (dt, *J* = 16.0, 7.0 Hz, 1H), 3.34 (dd, *J* = 7.0, 1.2 Hz, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 177.7, 140.2 (d, *J* = 1.2 Hz), 132.9, 129.7 (q, *J* = 32.5 Hz), 127.8 (q, *J* = 271.8 Hz), 126.6, 125.7 (q, *J* = 3.8 Hz), 123.7, 38.0. **<sup>19</sup>F NMR** (377 MHz, CDCl<sub>3</sub>): δ -63.04. **HRMS** (ESI-) *m/z*: calcd for C<sub>11</sub>H<sub>9</sub>F<sub>3</sub>O<sub>2</sub> [M-H]<sup>-</sup>: 229.0482, found 229.0474 (Δ = 3.5 ppm). **IR** (neat, cm<sup>-1</sup>): ν 2920, 1700, 1410, 1310, 1160, 1100, 1050.



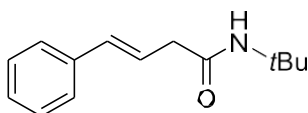
**N-phenyl-4-phenylbut-3-enamide 3a** was synthesized from commercial *trans*-styrylacetic acid and aniline following general procedure B. **3a** was obtained as beige powder (1.5 g, 88% yield).  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.52 – 7.28 (m, 10H), 7.11 (t,  $J = 7.4$  Hz, 1H), 6.64 (d,  $J = 15.9$  Hz, 1H), 6.39 (dt,  $J = 15.9, 7.3$  Hz, 1H), 3.34 (dd,  $J = 7.3, 1.1$  Hz, 2H).  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  168.9, 137.8, 136.5, 135.6, 129.1, 128.8, 128.2, 126.5, 124.6, 122.0, 120.0, 42.1. The NMR data correspond to those described in literature.<sup>[12]</sup>



**N-benzyl-4-phenylbut-3-enamide 3b** was synthesized from commercial *trans*-styrylacetic acid and benzylamine following general procedure B. **3b** was obtained as beige powder (558.1 mg, 36% yield).  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.39 – 7.25 (m, 10H), 6.54 (d,  $J = 15.9$  Hz, 1H), 6.31 (dt,  $J = 15.9, 7.2$  Hz, 1H), 5.94 (brs, 1H), 4.46 (d,  $J = 5.8$  Hz, 2H), 3.22 (dd,  $J = 7.2, 1.0$  Hz, 2H).  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  170.6, 138.3, 136.6, 135.0, 128.9, 128.8, 128.0, 127.9, 127.7, 126.5, 122.3, 43.9, 41.0, 34.1. The NMR data correspond to those described in literature.<sup>[12]</sup>



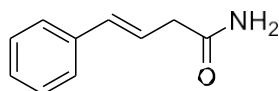
**N-méthyl-4-phenylbut-3-enamide 3c** was synthesized from commercial *trans*-styrylacetic acid and methylamine following general procedure B. **3c** was obtained as beige powder (444.3 mg, 20% yield).  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.40 – 7.25 (m, 5H), 6.53 (d,  $J = 15.9$  Hz, 1H), 6.29 (dt,  $J = 15.9, 7.3$  Hz, 1H), 5.70 (brs, 1H), 3.16 (d,  $J = 7.3$  Hz, 2H), 2.82 (d,  $J = 4.9$  Hz, 3H).  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  171.4, 136.6, 135.0, 128.8, 128.0, 126.4, 122.5, 40.9, 26.6. The NMR data correspond to those described in literature.<sup>[13]</sup>



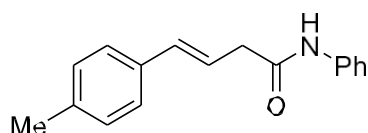
**N-(tert-butyl)-4-phenylbut-3-enamide 3d** was synthesized from commercial *trans*-styrylacetic acid and *tert*-butylamine following general procedure B. **3d** was obtained as beige powder (1.1 g, 90% yield).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.39 (m, 2H), 7.37 – 7.30 (m, 2H), 7.24 (m, 1H), 6.51 (d,  $J$



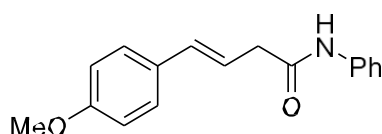
= 15.8 Hz, 1H), 6.29 (dt,  $J = 15.8, 7.3$  Hz, 1H), 5.38 (brs, 1H), 3.08 (dd,  $J = 7.3, 1.3$  Hz, 2H), 1.35 (s, 9H).  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  170.1, 136.9, 134.4, 128.7, 127.8, 126.4, 123.1, 51.5, 42.1, 28.9. The NMR data correspond to those described in literature.<sup>[14]</sup>



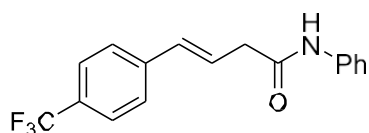
**4-phenylbut-3-enamide 3e** was synthesized from commercial *trans*-styrylacetic acid and ammonium hydroxide ( $\text{NH}_4\text{OH}$ ) following general procedure B. **3e** was obtained as white powder (1.5 g, 75% yield).  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.42 – 7.25 (m, 5H), 6.57 (d,  $J = 15.9$  Hz, 1H), 6.33 (dt,  $J = 15.9, 7.3$  Hz, 1H), 5.81 (brs, 1H), 5.72 (brs, 1H), 3.20 (dd,  $J = 7.3, 1.0$  Hz, 2H).  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  173.3, 136.5, 134.7, 128.6, 127.9, 126.3, 122.2, 40.2. The NMR data correspond to those described in literature.<sup>[15]</sup>



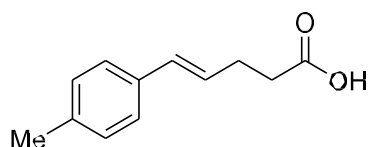
**N-phenyl-4-(*p*-tolyl)but-3-enamide 3f** was synthesized from (*E*)-4-(*p*-tolyl)but-3-enoic acid **S3f** and aniline following general procedure B. **3f** was obtained as beige powder (42.2 mg, 30% yield).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.50 (d,  $J = 7.8$  Hz, 2H), 7.36 – 7.2 (m, 5H), 7.16 (d,  $J = 7.8$  Hz, 2H), 7.11 (t,  $J = 7.4$  Hz, 1H), 6.61 (d,  $J = 15.9$  Hz, 1H), 6.33 (dt,  $J = 15.9, 7.3$  Hz, 1H), 3.32 (dd,  $J = 7.3, 0.9$  Hz, 2H), 2.35 (s, 3H).  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  169.1, 138.1, 137.8, 135.7, 133.7, 129.5, 129.2, 126.5, 124.6, 120.8, 120.0, 42.1, 21.4. **HRMS** (ESI+)  $m/z$ : calcd for  $\text{C}_{17}\text{H}_{17}\text{NaNO}$  [ $\text{M}+\text{Na}$ ] $^+$ : 274.1202, found 274.1209 ( $\Delta = 2.6$  ppm). **IR** (neat,  $\text{cm}^{-1}$ ):  $\nu$  3280, 2902, 1647, 1610, 1440.



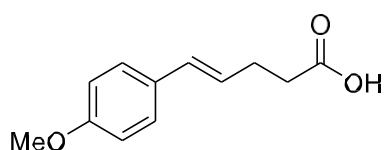
**4-(4-methoxyphenyl)-*N*-phenylbut-3-enamide 3g** was synthesized from (*E*)-4-(*p*-methoxyphenyl)but-3-enoic acid **S3g** and aniline following general procedure B. **3g** was obtained as beige powder (45.0 mg, 18% yield).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.50 (d,  $J = 8.0$  Hz, 2H), 7.36 – 7.29 (m, 5H), 7.11 (t,  $J = 7.4$  Hz, 1H), 6.88 (d,  $J = 8.7$  Hz, 2H), 6.58 (d,  $J = 15.8$  Hz, 1H), 6.23 (dt,  $J = 15.8, 7.2$  Hz, 1H), 3.82 (s, 3H), 3.31 (d,  $J = 7.2$  Hz, 2H).  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  168.8, 159.4, 137.5, 134.9, 129.0, 128.8, 127.4, 124.3, 119.7, 119.2, 113.9, 55.2, 41.8. **HRMS** (ESI+)  $m/z$ : calcd for  $\text{C}_{17}\text{H}_{17}\text{NaNO}_2$  [ $\text{M}+\text{Na}$ ] $^+$ : 290.1151, found 290.1157 ( $\Delta = 2.1$  ppm). **IR** (neat,  $\text{cm}^{-1}$ ):  $\nu$  3285, 2910, 1660, 1600, 1510, 1250, 1180.



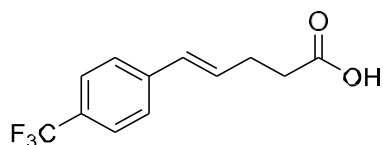
**N-phenyl-4-(4-(trifluoromethyl)phenyl)but-3-enamide 3f** was synthesized from (*E*)-4-(*p*-(trifluoromethyl)phenyl)but-3-enoic acid **S3h** and aniline following general procedure B. **3f** was obtained as beige powder (20.0 mg, 18% yield). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 7.59 (d, *J* = 8.2 Hz, 2H), 7.52 – 7.49 (m, 4H), 7.33 (t, *J* = 7.4 Hz, 3H), 7.12 (t, *J* = 7.4 Hz, 1H), 6.65 (d, *J* = 16.0 Hz, 1H), 6.51 (dt, *J* = 16.0, 7.1 Hz, 1H), 3.36 (d, *J* = 7.1 Hz, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 168.4, 140.0, 137.6, 133.8, 129.6 (q, *J* = 30.3 Hz), 129.2, 126.7, 125.8 (q, *J* = 4.0 Hz), 124.9, 124.8, 124.2 (q, *J* = 274.9 Hz), 120.0, 41.9. **<sup>19</sup>F NMR** (377 MHz, CDCl<sub>3</sub>): δ -63.07. **HRMS** (ESI+) *m/z*: calcd for C<sub>17</sub>H<sub>14</sub>F<sub>3</sub>NaNO [M+Na]<sup>+</sup>: 328.0920, found 328.0932 (Δ = 3.7 ppm). **IR** (neat, cm<sup>-1</sup>): ν 3300, 2920, 1690, 1510, 1320, 1160, 1110, 1070.



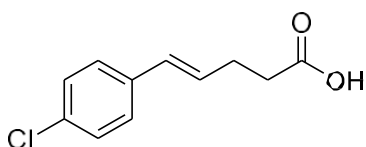
**(E)-5-(*p*-tolyl)pent-4-enoic acid S5e** was synthesized from commercial 4-methylbenzaldehyde following general procedure C. **S5e** was obtained as beige powder (128.4 mg, 48% yield). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 7.24 (d, *J* = 8.1 Hz, 2H), 7.10 (d, *J* = 8.1 Hz, 2H), 6.42 (d, *J* = 15.8 Hz, 1H), 6.21 – 6.12 (m, 1H), 2.54 (m, 4H), 2.33 (s, 3H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 179.0, 137.1, 134.6, 131.2, 130.4, 129.3, 127.1, 126.1, 33.9, 28.1, 21.3. **HRMS** (ESI+) *m/z*: calcd for C<sub>12</sub>H<sub>14</sub>NaO<sub>2</sub> [M+Na]<sup>+</sup>: 213.0886, found 213.0885 (Δ = 0.4 ppm). **IR** (neat, cm<sup>-1</sup>): ν 2950, 2850, 1700, 1610, 1512, 1435.



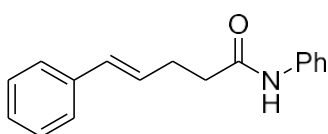
**(E)-5-(4-methoxyphenyl)pent-4-enoic acid S5f** was synthesized from commercial 4-methoxybenzaldehyde following general procedure C. **S5f** was obtained as beige powder (461.3 mg, 37% yield). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 7.27 (d, *J* = 8.7 Hz, 2H), 6.84 (d, *J* = 8.7 Hz, 2H), 6.39 (d, *J* = 15.8 Hz, 1H), 6.15 – 6.01 (m, 1H), 3.80 (s, 3H), 2.53 (s, 4H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>): δ 178.9, 159.1, 130.7, 130.2, 127.3, 125.9, 114.1, 55.4, 34.0, 28.1. **HRMS** (ESI+) *m/z*: calcd for C<sub>12</sub>H<sub>14</sub>NaO<sub>3</sub> [M+Na]<sup>+</sup>: 229.0835, found 229.0842 (Δ = 3.1 ppm). **IR** (neat, cm<sup>-1</sup>): ν 2940, 1698, 1600, 1510, 1250, 1180, 1040.



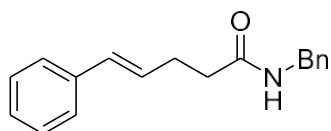
**(E)-5-(4-(trifluoromethyl)phenyl)pent-4-enoic acid S5g** was synthesized from commercial 4-(trifluoromethyl)benzaldehyde following general procedure C. **S5g** was obtained as beige powder (682.9 mg, 75% yield).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.54 (d,  $J = 8.2$  Hz, 2H), 7.43 (d,  $J = 8.2$  Hz, 2H), 6.48 (d,  $J = 15.8$  Hz, 1H), 6.36 – 6.28 (m, 1H), 2.57 (d,  $J = 3.0$  Hz, 4H).  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  178.8, 141.1, 131.2, 130.5, 129.5 (q,  $J = 32.4$  Hz), 126.7, 125.9 (q,  $J = 3.8$  Hz), 124.7 (q,  $J = 271.9$  Hz), 33.8, 28.3.  $^{19}\text{F NMR}$  (377 MHz,  $\text{CDCl}_3$ ):  $\delta$  -62.98. **HRMS** (ESI+)  $m/z$ : calcd for  $\text{C}_{12}\text{H}_{11}\text{F}_3\text{NaO}_2$   $[\text{M}+\text{Na}]^+$ : 267.0603, found 267.0614 ( $\Delta = 4.1$  ppm). **IR** (neat,  $\text{cm}^{-1}$ ):  $\nu$  2920, 1700, 1310, 1180, 1105, 1070.



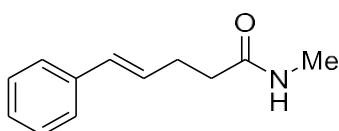
**(E)-5-(4-chlorophenyl)pent-4-enoic acid S5h** was synthesized from commercial 4-chlorobenzaldehyde following general procedure C. **S5h** was obtained as beige powder (724.0 mg, 69% yield).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.30 (m, 5H), 6.44 (d,  $J = 15.8$  Hz, 1H), 6.30 – 6.17 (m, 1H), 2.59 (s, 2H), 2.58 (s, 2H).  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  178.3, 135.9, 133.0, 130.2, 128.8, 128.8, 127.4, 33.6, 28.0. **HRMS** (ESI+)  $m/z$ : calcd for  $\text{C}_{11}\text{H}_{11}^{35}\text{ClNaO}_2$   $[\text{M}+\text{Na}]^+$ : 233.0340, found 233.0334 ( $\Delta = 2.6$  ppm). **IR** (neat,  $\text{cm}^{-1}$ ):  $\nu$  2905, 1700, 1500, 1090, 800.



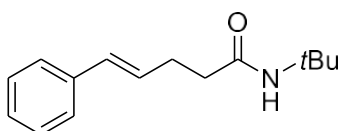
**N-5-diphenylpent-4-enamide 5a** was synthesized from commercial (*E*)-5-phenylpent-4-enoic acid and aniline following general procedure C. **5a** was obtained as beige powder (714.0 mg, 66% yield).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.52 (m, 3H), 7.35 – 7.27 (m, 6H), 7.21 (tt,  $J = 6.7, 1.7$  Hz, 1H), 7.11 (t,  $J = 7.4$  Hz, 1H), 6.47 (d,  $J = 15.8$  Hz, 1H), 6.25 (dt,  $J = 15.8, 6.7$  Hz, 1H), 2.64 (q,  $J = 7.2$  Hz, 2H), 2.52 (m, 2H).  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  170.7, 138.0, 137.3, 131.4, 129.1, 128.6, 128.6, 127.3, 126.2, 124.4, 120.1, 37.3, 28.9. The NMR data correspond to those described in literature.<sup>[16]</sup>



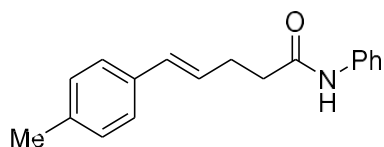
***N*-(benzyl)-5-phenylpent-4-enamide 5b** was synthesized from commercial (*E*)-5-phenylpent-4-enoic acid and benzylamine following general procedure C. **5b** was obtained as beige powder (484.8 mg, 89% yield).  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.31 – 7.16 (m, 10H), 6.45 (d,  $J = 15.8$  Hz, 1H), 6.30 – 6.11 (dt,  $J = 15.8, 6.9$  Hz, 1H), 5.74 (brs, 1H), 4.46 (d,  $J = 5.7$  Hz, 2H), 2.60 (q,  $J = 7.0$  Hz, 2H), 2.39 (t,  $J = 7.3$  Hz, 2H).  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  172.1, 138.4, 137.4, 131.3, 128.8, 128.7, 128.6, 127.9, 127.6, 127.3, 126.2, 43.7, 36.5, 29.1. The NMR data correspond to those described in literature.<sup>[17]</sup>



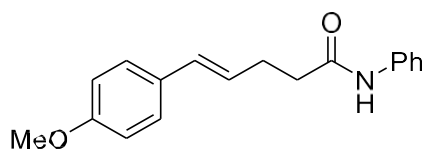
***N*-(methyl)-5-phenylpent-4-enamide 5c** was synthesized from commercial (*E*)-5-phenylpent-4-enoic acid and methylamine following general procedure C. **5c** was obtained as beige powder (647.4 mg, 80% yield).  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.35 – 7.29 (m, 4H), 7.23 – 7.18 (m, 1H), 6.44 (d,  $J = 15.9$  Hz, 1H), 6.21 (dt,  $J = 15.9, 6.8$  Hz, 1H), 5.45 (brs, 1H), 2.82 (d,  $J = 4.9$  Hz, 3H), 2.56 (q,  $J = 7.4$  Hz, 2H), 2.34 (t,  $J = 7.4$  Hz, 2H).  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  173.0, 137.4, 131.0, 128.9, 128.6, 127.2, 126.1, 36.3, 29.1, 26.4. The NMR data correspond to those described in literature.<sup>[18]</sup>



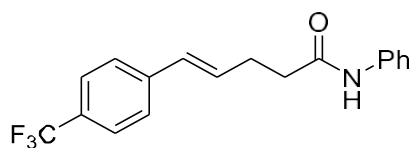
***N*-(*tert*-butyl)-5-phenylpent-4-enamide 5d** was synthesized from commercial (*E*)-5-phenylpent-4-enoic acid and *tert*-butylamine following general procedure C. **5d** was obtained as beige powder (443.5 mg, 93% yield).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.34 – 7.27 (m, 4H), 7.22 – 7.18 (tt,  $J = 6.9, 2.2$  Hz, 1H), 6.43 (d,  $J = 15.8$  Hz, 1H), 6.20 (dt,  $J = 15.8, 6.9$  Hz, 1H), 5.34 (brs, 1H), 2.57 – 2.47 (dq,  $J = 6.9, 1.2$  Hz, 2H), 2.25 (t,  $J = 7.4$  Hz, 2H), 1.34 (s, 9H).  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  171.6, 137.5, 131.0, 129.1, 128.6, 127.2, 126.1, 51.3, 37.3, 29.2, 28.9. The NMR data correspond to those described in literature.<sup>[19]</sup>



**N-phenyl-5-(*p*-tolyl)pent-4-enamide 5e** was synthesized from (*E*)-5-(*p*-tolyl)pent-4-enoic acid **S5e** and aniline following general procedure C. **5e** was obtained as beige powder (140.1 mg, 82% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.50 (d, *J* = 8.0 Hz, 2H), 7.31 (t, *J* = 8.0 Hz, 3H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.11 – 7.08 (m, 3H), 6.46 (d, *J* = 15.8 Hz, 1H), 6.20 (dt, *J* = 15.8, 7.0 Hz, 1H), 2.63 (q, *J* = 7.1 Hz, 2H), 2.52 (t, *J* = 7.1 Hz, 2H), 2.33 (s, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>): δ 170.6, 137.9, 137.2, 134.6, 131.4, 129.4, 129.1, 127.6, 126.1, 124.4, 120.0, 37.5, 29.0, 21.3. HRMS (ESI+) *m/z*: calcd for C<sub>18</sub>H<sub>19</sub>NaNO [M+Na]<sup>+</sup>: 288.1359, found 288.1368 (Δ = 3.1 ppm). IR (neat, cm<sup>-1</sup>): ν 3290, 2910, 2850, 1650, 1600, 1500, 1440.

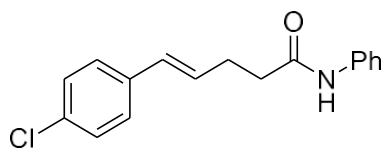


**5-(4-methoxyphenyl)-*N*-phenylpent-4-enamide 5f** was synthesized from (*E*)-5-(*p*-methoxyphenyl)pent-4-enoic acid **S5f** and aniline following general procedure C. **5f** was obtained as beige powder (252.7 mg, 92% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.50 (d, *J* = 8.0 Hz, 2H), 7.33 – 7.26 (m, 5H), 7.11 (t, *J* = 7.4 Hz, 1H), 6.84 (d, *J* = 8.7 Hz, 2H), 6.44 (d, *J* = 15.8 Hz, 1H), 6.12 (dt, *J* = 15.8, 6.8 Hz, 1H), 3.80 (s, 3H), 2.63 (q, *J* = 7.0 Hz, 2H), 2.52 (t, *J* = 7.0 Hz, 2H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>): δ 159.1, 130.9, 130.2, 129.2, 127.3, 126.4, 124.4, 120.0, 119.9, 114.1, 55.4, 48.9, 37.7, 29.0. HRMS (ESI+) *m/z*: calcd for C<sub>18</sub>H<sub>19</sub>NaNO<sub>2</sub> [M+Na]<sup>+</sup>: 304.1308, found 304.1316 (Δ = 2.6 ppm). IR (neat, cm<sup>-1</sup>): ν 3290, 2910, 1660, 1600, 1510, 1440, 1250, 1180.

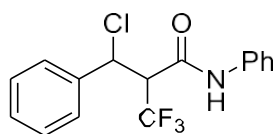


***N*-phenyl-5-(4-(trifluoromethyl)phenyl)pent-4-enamide 5g** was synthesized from (*E*)-5-(*p*-(trifluoromethyl)phenyl)pent-4-enoic acid **S5g** and aniline following general procedure C. **5g** was obtained as beige powder (172.7 mg, 66% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.54 (d, *J* = 8.2 Hz, 2H), 7.50 (d, *J* = 8.0 Hz, 2H), 7.42 (d, *J* = 8.2 Hz, 2H), 7.32 (t, *J* = 8.0 Hz, 2H), 7.16 (brs, 1H), 7.11 (t, *J* = 7.4 Hz, 1H), 6.52 (d, *J* = 16.0 Hz, 1H), 6.37 (dt, *J* = 16.0, 7.0 Hz, 1H), 2.68 (q, *J* = 7.4 Hz, 2H), 2.55 (t, *J* = 7.4 Hz, 2H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>): δ 170.3, 140.9, 137.7, 131.5, 130.2, 129.2, 129.2 (q, *J* = 32.1 Hz), 126.3, 125.6 (q, *J* = 3.8 Hz), 124.5, 124.3 (q, *J* = 271.6 Hz), 120.0, 37.1, 28.8. <sup>19</sup>F NMR

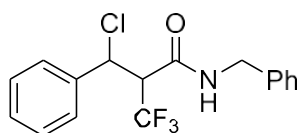
(377 MHz, CDCl<sub>3</sub>):  $\delta$  -62.97. **HRMS** (ESI+) *m/z*: calcd for C<sub>18</sub>H<sub>16</sub>F<sub>3</sub>NaNO [M+Na]<sup>+</sup>: 342.1076, found 342.1085 ( $\Delta$  = 2.6 ppm). **IR** (neat, cm<sup>-1</sup>):  $\nu$  3300, 1650, 1510, 1320, 1160, 1110, 1070.



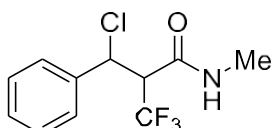
**5-(4-chlorophenyl)-N-phenylpent-4-enamide 5h** was synthesized from (*E*)-5-(*p*-chlorophenyl)pent-4-enoic acid **S5h** and aniline following general procedure C. **5h** was obtained as beige powder (257.1 mg, 95% yield). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.52 (d, *J* = 7.8 Hz, 2H), 7.45 (brs, 1H), 7.36 – 7.28 (m, 6H), 7.12 (t, *J* = 7.4 Hz, 1H), 6.43 (d, *J* = 15.8 Hz, 1H), 6.24 (dt, *J* = 15.8, 6.8 Hz, 1H), 2.64 (q, *J* = 7.1 Hz, 2H), 2.54 (t, *J* = 7.1 Hz, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>):  $\delta$  170.5, 137.9, 135.9, 132.9, 130.2, 129.4, 129.1, 128.8, 127.4, 124.5, 120.0, 37.2, 28.8. **HRMS** (ESI+) *m/z*: calcd for C<sub>17</sub>H<sub>16</sub><sup>35</sup>ClNaNO [M+Na]<sup>+</sup>: 308.0813, found 308.0815 ( $\Delta$  = 0.6 ppm). **IR** (neat, cm<sup>-1</sup>):  $\nu$  3290, 1650, 1600, 1520, 1500, 1440, 1095, 750.



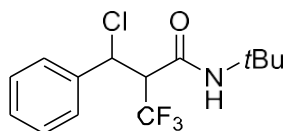
**2-(chloro(phenyl)methyl)-3,3,3-trifluoro-N-phenylpropanamide 2a** was synthesized from *N*-(phenyl)cinnamamide **1a** following general procedure D and purified by silica gel flash chromatography eluting with petroleum ether/ethyl acetate (7/3). **2a** was obtained as white solid (68.8 mg, 70% yield, d.r. = 96:4). *R<sub>f</sub>* (in petroleum ether/ethyl acetate = 7/3): 0.32. **<sup>1</sup>H NMR** (400 MHz, (CD<sub>3</sub>)<sub>2</sub>SO):  $\delta$  10.69 (s, 0.75H, major diastereoisomer), 10.30 (s, 0.20H, minor diastereoisomer), 7.70 (d, *J* = 7.6 Hz, 1.61H, mixture of major and minor diastereoisomers), 7.60 (d, *J* = 7.2 Hz, 1.47H, mixture of major and minor diastereoisomers), 7.58 – 7.54 (m, 0.52H, minor diastereoisomer), 7.49 – 7.18 (m, 6.32H, mixture of major and minor diastereoisomers), 7.14 (m, 0.81H, major diastereoisomer), 7.02 (m, 0.29H, minor diastereoisomer), 5.66 (d, *J* = 11.1 Hz, 0.76H, major diastereoisomer), 5.62 (d, *J* = 11.1 Hz, 1H, minor diastereoisomer), 4.59 – 4.38 (m, 1.06H, mixture of major and minor diastereoisomers). **<sup>13</sup>C NMR** (101 MHz, (CD<sub>3</sub>)<sub>2</sub>SO):  $\delta$  162.5 (q, *J* = 2.2 Hz), 161.6 (q, *J* = 2.5 Hz), 138.0, 137.7, 137.6, 137.3, 129.3, 129.1, 128.8, 128.8, 128.6, 127.9, 124.5, 124.4, 124.4 (q, *J* = 282.3 Hz), 123.4 (q, *J* = 282.6 Hz), 119.7, 119.6, 58.4, 58.4, 57.7 (q, *J* = 24.2 Hz), 57.3 (q, *J* = 24.8 Hz). **<sup>19</sup>F NMR** (377 MHz, (CD<sub>3</sub>)<sub>2</sub>SO):  $\delta$  -62.81 (d, *J* = 7.9 Hz, major diastereoisomer), -62.97 (d, *J* = 7.6 Hz, minor diastereoisomer). **HRMS** (ES+) *m/z*: calcd for C<sub>16</sub>H<sub>14</sub><sup>35</sup>ClF<sub>3</sub>NO [M+H]<sup>+</sup>: 328.0716, found 328.0723 ( $\Delta$  = 2.1 ppm). **IR** (neat, cm<sup>-1</sup>):  $\nu$  3438, 3319, 3196, 1684, 1247, 1168, 1113, 700.



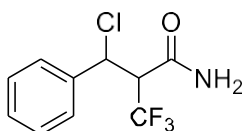
**N-benzyl-2-(chloro(phenyl)methyl)-3,3,3-trifluoropropanamide 2b** was synthesized from *N*-(benzyl)cinnamamide **1b** following general procedure D and purified by silica gel flash chromatography eluting with petroleum ether/ethyl acetate (8/2). **2b** was obtained as white solid (68.7 mg, 67% yield, d.r. = 72:28).  $R_f$  (in petroleum ether/ethyl acetate = 8/2): 0.27.  $^1\text{H NMR}$  (400 MHz,  $(\text{CD}_3)_2\text{SO}$ ):  $\delta$  9.02 (t,  $J = 5.6$  Hz, 0.77H, major diastereoisomer), 8.72 (t,  $J = 5.8$  Hz, 0.24H, minor diastereoisomer), 7.57 – 7.23 (m, 9.37H, mixture of major and minor diastereoisomers), 7.13 (m, 0.79H, major diastereoisomer), 5.52 (d,  $J = 11.1$  Hz, 0.71H, major diastereoisomer), 5.48 (d,  $J = 11.1$  Hz, 0.28H, minor diastereoisomer), 4.44 (qd,  $J = 15.2, 5.8$  Hz, 1.62H, mixture of major and minor diastereoisomers), 4.37 – 4.15 (m, 1.31H, mixture of major and minor diastereoisomers).  $^{13}\text{C NMR}$  (101 MHz,  $(\text{CD}_3)_2\text{SO}$  and  $\text{CDCl}_3$ ):  $\delta$  163.8 (q,  $J = 2.5$  Hz), 162.9 (q,  $J = 2.5$  Hz), 138.3, 137.8, 129.2, 129.1, 128.7, 128.6, 128.4, 128.2, 128.0, 127.8, 127.4, 127.1, 124.3 (q,  $J = 282.2$  Hz), 123.4 (q,  $J = 282.2$  Hz), 58.3 (q,  $J = 2.0$  Hz), 57.5 (q,  $J = 2.0$  Hz), 56.7 (q,  $J = 24.0$  Hz), 56.7 (q,  $J = 24.0$  Hz), 42.6, 41.9.  $^{19}\text{F NMR}$  (377 MHz,  $(\text{CD}_3)_2\text{SO}$ ):  $\delta$  -62.17 (d,  $J = 8.0$  Hz, major diastereoisomer), -62.35 (d,  $J = 8.0$  Hz, minor diastereoisomer). **HRMS** (ESI+)  $m/z$ : calcd for  $\text{C}_{17}\text{H}_{15}^{35}\text{ClF}_3\text{NaNO}$   $[\text{M}+\text{Na}]^+$ : 364.0686, found 364.0693 ( $\Delta = 1.9$  ppm). **IR** (neat,  $\text{cm}^{-1}$ ):  $\nu$  3295, 1656, 1620, 1553, 1454, 1315, 1161, 1120, 694.



**2-(chloro(phenyl)methyl)-3,3,3-trifluoro-N-methylpropanamide 2c** was synthesized from *N*-(methyl)cinnamamide **1c** following general procedure D and purified by silica gel flash chromatography eluting with petroleum ether/ethyl acetate (6/4). **2c** was obtained as white solid (39.8 mg, 50% yield, d.r. = 73:36).  $R_f$  (in petroleum ether/ethyl acetate = 6/3): 0.31.<sup>[20]</sup>  $^1\text{H NMR}$  (400 MHz,  $(\text{CD}_3)_2\text{SO}$ ):  $\delta$  8.47 (d,  $J = 4.4$  Hz, 1H), 7.52 (m, 2H), 7.44 – 7.37 (m, 3H), 5.47 (d,  $J = 11.1$  Hz, 1H), 4.21 (dq,  $J = 11.1, 8.1$  Hz, 1H), 2.72 (d,  $J = 4.7$  Hz, 3H).  $^{13}\text{C NMR}$  (101 MHz,  $(\text{CD}_3)_2\text{SO}$ ):  $\delta$  164.2 (q,  $J = 2.4$  Hz), 137.8, 129.2, 128.7, 127.8, 123.4 (q,  $J = 282.1$  Hz), 58.3 (q,  $J = 2.0$  Hz), 56.6 (q,  $J = 24.1$  Hz), 25.9.  $^{19}\text{F NMR}$  (377 MHz,  $(\text{CD}_3)_2\text{SO}$ ):  $\delta$  -64.08 (d,  $J = 8.1$  Hz), -64.09 (minor diastereoisomer, not isolated). **HRMS** (AP-)  $m/z$ : calcd for  $\text{C}_{11}\text{H}_{11}^{35}\text{ClF}_3\text{NO}$   $[\text{M}]^+$ : 265.0481, found 265.0472 ( $\Delta = -3.4$  ppm). **IR** (neat,  $\text{cm}^{-1}$ ):  $\nu$  3291, 3118, 1657, 1241, 1169, 1126.

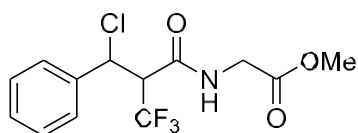


***N*-(*tert*-butyl)-2-(chloro(phenyl)methyl)-3,3,3-trifluoropropanamide **2d**** was synthesized from *N*-(*tert*-butyl)cinnamamide **1d** following general procedure D and purified by silica gel flash chromatography eluting with petroleum ether/ethyl acetate (8/2). **2d** was obtained as white solid (52.6 mg, 57% yield, d.r. = 59:41).  $R_f$  (in petroleum ether/ethyl acetate = 8/2): 0.35.  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.44 – 7.31 (m, 5H, mixture of major and minor diastereoisomers), 5.66 (brs, 0.46H, minor diastereoisomer), 5.39 (d,  $J$  = 10.4 Hz, 0.48H, minor diastereoisomer), 5.30 (d,  $J$  = 10.4 Hz, 0.48H, major diastereoisomer), 5.06 (brs, 0.48H, major diastereoisomer), 3.46 – 3.39 (m, 0.57H, major diastereoisomer), 3.39 – 3.30 (m, 0.51H, minor diastereoisomer), 1.43 (s, 4.56H, major diastereoisomer), 0.99 (s, 4.36H, minor diastereoisomer).  $^{13}\text{C NMR}$  (101 MHz,  $(\text{CD}_3)_2\text{SO}$ ):  $\delta$  162.9 (q,  $J$  = 2.3 Hz), 161.9 (q,  $J$  = 2.5 Hz), 138.0, 137.7, 129.6, 129.1, 128.9, 128.3, 127.8, 127.8, 124.5 (q,  $J$  = 281.1 Hz), 123.6 (q,  $J$  = 282.4 Hz), 58.6 (q,  $J$  = 1.6 Hz), 57.9 (q,  $J$  = 2.3 Hz), 56.6 (q,  $J$  = 24.0 Hz), 56.6 (q,  $J$  = 24.0 Hz), 51.0, 50.4, 28.1, 27.5.  $^{19}\text{F NMR}$  (282 MHz,  $\text{CDCl}_3$ ):  $\delta$  -64.17 (d,  $J$  = 7.0 Hz, major diastereoisomer), -64.09 (d,  $J$  = 7.5 Hz, minor diastereoisomer). **HRMS** (AP-)  $m/z$ : calcd for  $\text{C}_{14}\text{H}_{17}^{35}\text{ClF}_3\text{NO}$   $[\text{M}]^+$ : 307.0951, found 307.0946 ( $\Delta$  = -1.6 ppm). **IR** (neat,  $\text{cm}^{-1}$ ):  $\nu$  3308, 2980, 1657, 1366, 1334, 1241, 1165, 1120.

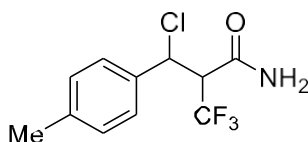


**2-(chloro(phenyl)methyl)-3,3,3-trifluoropropanamide **2e**** was synthesized from cinnamamide **1e** following general procedure D and purified by silica gel flash chromatography eluting with petroleum ether/ethyl acetate (6/4). **2e** was obtained as white solid (203.8 mg, 81% yield, d.r. = 65:35).  $R_f$  (in petroleum ether/ethyl acetate = 6/4): 0.30.<sup>[20]</sup>  $^1\text{H NMR}$  (400 MHz,  $(\text{CD}_3)_2\text{SO}$ ):  $\delta$  8.11 (brs, 1H), 7.79 (brs, 1H), 7.62 (m, 2H), 7.47 – 7.42 (m, 3H), 7.25 (d,  $J$  = 1.6 Hz, 1H).  $^{13}\text{C NMR}$  (101 MHz,  $(\text{CD}_3)_2\text{SO}$ ):  $\delta$  164.4 (q,  $J$  = 1.0 Hz), 133.4 (q,  $J$  = 6.1 Hz), 132.3, 130.1, 129.3, 128.7, 126.4 (q,  $J$  = 29.6 Hz), 122.8 (q,  $J$  = 273.2 Hz).  $^{19}\text{F NMR}$  (377 MHz,  $(\text{CD}_3)_2\text{SO}$ ):  $\delta$  -64.26 (d,  $J$  = 1.7 Hz), -64.29 (minor diastereoisomer, not isolated). **HRMS** (ES+)  $m/z$ : calcd for  $\text{C}_{10}\text{H}_9\text{F}_3\text{NO}$   $[\text{M}+\text{H}-\text{HCl}]^+$ : 216.0636, found 216.0636 ( $\Delta$  = 0.0 ppm). **IR** (neat,  $\text{cm}^{-1}$ ):  $\nu$  3388, 3189, 1613, 1280, 1150, 1116, 1012.

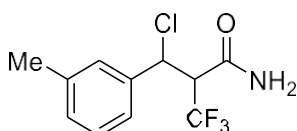




**Methyl (2-(chloro(phenyl)methyl)-3,3,3-trifluoropropanoyl)glycinate 2f** was synthesized from methyl 2-cinnamamidoacetate **1f** following general procedure D and purified by silica gel flash chromatography eluting with petroleum ether/ethyl acetate (7/3). **2f** was obtained as white solid (32.0 mg, 33% yield, d.r. = 26:74).  $R_f$  (in petroleum ether/ethyl acetate = 7/3): 0.30.<sup>[20]</sup> **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.45 – 7.42 (m, 2H), 7.40 – 7.35 (m, 3H), 6.85 (t,  $J$  = 4.9 Hz, 1H), 5.43 (d,  $J$  = 10.5 Hz, 1H), 4.20 (d,  $J$  = 4.9 Hz, 2H), 3.83 – 3.75 (m, 4H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>):  $\delta$  169.9, 164.6 (q,  $J$  = 2.1 Hz), 137.2, 129.5, 128.9, 127.9, 122.9 (q,  $J$  = 282.5 Hz), 59.4 (q,  $J$  = 25.4 Hz), 58.2 (q,  $J$  = 1.4 Hz), 52.8, 41.9. **<sup>19</sup>F NMR** (377 MHz, CDCl<sub>3</sub>):  $\delta$  -63.90 (minor diastereoisomer, not isolated), -63.98 (d,  $J$  = 7.2 Hz). **HRMS** (ES<sup>+</sup>)  $m/z$ : calcd for C<sub>13</sub>H<sub>13</sub><sup>35</sup>ClF<sub>3</sub>NaNO<sub>3</sub> [M+Na]<sup>+</sup>: 346.0434, found 346.0431 ( $\Delta$  = -0.9 ppm). **IR** (neat, cm<sup>-1</sup>):  $\nu$  3284, 1751, 1656, 1562, 1234, 1168, 1125, 698.

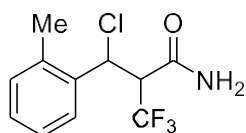


**2-(chloro(*p*-tolyl)methyl)-3,3,3-trifluoropropanamide 2g** was synthesized from 4-(methyl)cinnamamide **1g** following general procedure D and purified by silica gel flash chromatography eluting with petroleum ether/ethyl acetate (7/3). **2g** was obtained as white solid (39.1 mg, 49% yield, d.r. = 23:77).  $R_f$  (in petroleum ether/ethyl acetate = 7/3): 0.33.<sup>[20]</sup> **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.31 (d,  $J$  = 8.1 Hz, 2H), 7.19 (d,  $J$  = 8.1 Hz, 2H), 5.88 (brs, 2H), 5.38 (d,  $J$  = 10.2 Hz, 1H), 3.64 (dq,  $J$  = 10.2, 7.5 Hz, 1H), 2.36 (s, 3H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>):  $\delta$  166.1, 139.6, 134.1, 129.6, 127.7, 122.9 (q,  $J$  = 282.0 Hz), 59.3 (q,  $J$  = 25.3 Hz), 58.1 (q,  $J$  = 1.8 Hz), 21.4. **<sup>19</sup>F NMR** (377 MHz, CDCl<sub>3</sub>):  $\delta$  -63.70 (minor diastereoisomer, not isolated), -63.73 (d,  $J$  = 7.4 Hz). **HRMS** (ESI<sup>+</sup>)  $m/z$ : calcd for C<sub>11</sub>H<sub>11</sub><sup>35</sup>ClF<sub>3</sub>NaNO [M+Na]<sup>+</sup>: 288.0373, found 288.0382 ( $\Delta$  = 3.1 ppm). **IR** (neat, cm<sup>-1</sup>):  $\nu$  3442, 3323, 3194, 1683, 1327, 1243, 1165, 1109.

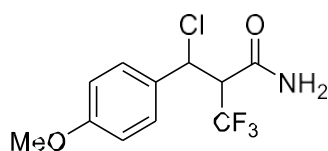


**2-(chloro(*m*-tolyl)methyl)-3,3,3-trifluoropropanamide 2h** was synthesized from 3-(methyl)cinnamamide **1h** following general procedure D and purified by silica gel flash chromatography eluting with petroleum ether/ethyl acetate (7/3). **2h** was obtained as white solid (58.2 mg, 73% yield, d.r. = 26:75).  $R_f$  (in petroleum ether/ethyl acetate = 7/3): 0.33. **<sup>1</sup>H NMR** (400

MHz, (CD<sub>3</sub>)<sub>2</sub>SO):  $\delta$  7.93 (brs, 0.69H, minor diastereoisomer), 7.68 (brs, 0.93H, major diastereoisomer), 7.37 – 7.24 (m, 3.36H, mixture of major and minor diastereoisomers), 7.18 (m, 1.27H, mixture of major and minor diastereoisomers), 5.39 (d,  $J$  = 10.9 Hz, 0.66H, major diastereoisomer), 5.37 (d,  $J$  = 10.9 Hz, 0.32H, minor diastereoisomer), 4.27 – 4.16 (m, 1.06H, mixture of major and minor diastereoisomers), 2.32 (s, 2.40H, major diastereoisomer), 2.30 (s, 0.97H, minor diastereoisomer). <sup>13</sup>C NMR (101 MHz, (CD<sub>3</sub>)<sub>2</sub>SO):  $\delta$  166.7 (q,  $J$  = 2.2 Hz), 165.9 (q,  $J$  = 2.6 Hz), 138.8, 137.8, 138.7, 137.0, 130.4, 130.2, 128.9, 128.8, 128.4, 128.4, 124.9, 124.7, 122.9 (q,  $J$  = 282.5 Hz), 122.9 (q,  $J$  = 282.5 Hz), 59.0 (q,  $J$  = 25.0 Hz), 58.9 (q,  $J$  = 26.0 Hz), 58.2 (q,  $J$  = 1.7 Hz), 57.0 (q,  $J$  = 2.3 Hz), 29.8, 21.5. <sup>19</sup>F NMR (377 MHz, (CD<sub>3</sub>)<sub>2</sub>SO):  $\delta$  -62.29 (d,  $J$  = 8.0 Hz, major diastereoisomer), -62.51 (d,  $J$  = 7.8 Hz, minor diastereoisomer). HRMS (ESI+)  $m/z$ : calcd for C<sub>11</sub>H<sub>11</sub><sup>35</sup>ClF<sub>3</sub>NaNO [M+Na]<sup>+</sup>: 288.0373, found 288.0381 ( $\Delta$  = 2.8 ppm). IR (neat, cm<sup>-1</sup>):  $\nu$  3450, 3319, 3278, 3187, 1683, 1608, 1411, 1325, 1243, 1168, 1116.

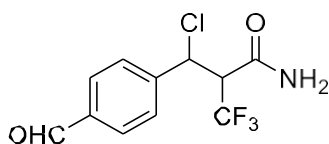


**2-(chloro(*o*-tolyl)methyl)-3,3,3-trifluoropropanamide 2i** was synthesized from 2-(methyl)cinnamamide **1i** following general procedure D and purified by silica gel flash chromatography eluting with petroleum ether/ethyl acetate (7/3). **2i** was obtained as white solid (55.0 mg, 69% yield, d.r. = 38:62).  $R_f$  (in petroleum ether/ethyl acetate = 7/3): 0.33.<sup>[20]</sup> <sup>1</sup>H NMR (400 MHz, (CD<sub>3</sub>)<sub>2</sub>SO):  $\delta$  8.01 (brs, 1H), 7.74 (brs, 1H), 7.48 (d,  $J$  = 7.8 Hz, 1H), 7.31 – 7.22 (m, 3H), 5.60 (d,  $J$  = 11.2 Hz, 1H), 4.37 (dq,  $J$  = 16.7, 8.2 Hz, 1H), 2.39 (s, 3H). <sup>13</sup>C NMR (101 MHz, (CD<sub>3</sub>)<sub>2</sub>SO):  $\delta$  165.6 (q,  $J$  = 2.3 Hz), 135.5, 130.9, 129.1, 127.5, 126.5, 125.0, 123.5 (q,  $J$  = 282.2 Hz), 55.2 (q,  $J$  = 23.8 Hz), 18.6 (q,  $J$  = 4.7 Hz). <sup>19</sup>F NMR (377 MHz, (CD<sub>3</sub>)<sub>2</sub>SO):  $\delta$  -63.91 (minor diastereoisomer, not isolated), -63.93 (d,  $J$  = 9.2 Hz). HRMS (ESI+)  $m/z$ : calcd for C<sub>11</sub>H<sub>11</sub><sup>35</sup>ClF<sub>3</sub>NaNO [M+Na]<sup>+</sup>: 288.0373, found 288.0378 ( $\Delta$  = 1.7 ppm). IR (neat, cm<sup>-1</sup>):  $\nu$  3450, 3320, 3200, 1690, 1240, 1190, 1100, 750.

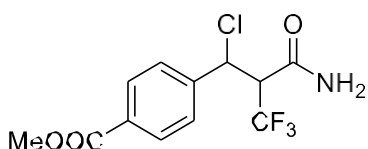


**2-(chloro(4-methoxyphenyl)methyl)-3,3,3-trifluoropropanamide 2j** was synthesized from 4-(methoxy)cinnamamide **1j** following general procedure D and purified by silica gel flash chromatography eluting with petroleum ether/ethyl acetate (7/3). **2j** was obtained as white solid (15.2 mg, 18% yield, d.r. = 88:12).  $R_f$  (in petroleum ether/ethyl acetate = 7/3): 0.29.<sup>[20]</sup> <sup>1</sup>H NMR

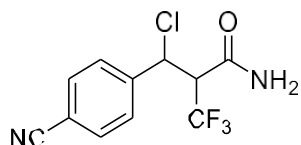
(400 MHz, CDCl<sub>3</sub>): δ 7.48 (d, *J* = 8.8 Hz, 2H), 7.16 (d, *J* = 1.1 Hz, 1H), 6.89 (d, *J* = 8.8 Hz, 2H), 6.16 (brs, 1H), 5.78 (brs, 1H), 3.83 (m, 4H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>): δ 165.7, 161.6, 136.4 (q, *J* = 6.0 Hz), 131.5, 124.2, 123.2 (q, *J* = 30.6 Hz), 122.7 (q, *J* = 272.8 Hz), 114.5, 55.5. <sup>19</sup>F NMR (377 MHz, CDCl<sub>3</sub>): δ -64.31 (d, *J* = 1.6 Hz), -64.40 (minor diastereoisomer, not isolated). HRMS (EI+) *m/z*: calcd for C<sub>11</sub>H<sub>10</sub>F<sub>3</sub>NO<sub>2</sub> [M-HCl]<sup>+</sup>: 245.06636, found 245.06628 (Δ = -0.3 ppm). IR (neat, cm<sup>-1</sup>): ν 3386, 3185, 1605, 1284, 1256, 1182, 1150, 1105.



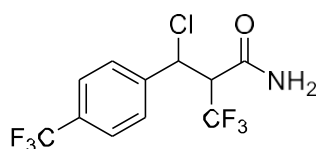
**2-(chloro(4-formylphenyl)methyl)-3,3,3-trifluoropropanamide 2l** was synthesized from 4-(formyl)cinnamamide **1l** following general procedure D and purified by silica gel flash chromatography eluting with petroleum ether/ethyl acetate (7/3). **2l** was obtained as white solid (55.4 mg, 66% yield, d.r. = 56:44). *R<sub>f</sub>* (in petroleum ether/ethyl acetate = 7/3): 0.31.<sup>[20]</sup> <sup>1</sup>H NMR (400 MHz, (CD<sub>3</sub>)<sub>2</sub>SO): δ 10.02 (s, 1H), 7.96 (d, *J* = 8.2 Hz, 3H), 7.76 (d, *J* = 8.2 Hz, 3H), 5.60 (d, *J* = 11.1 Hz, 1H), 4.29 (dq, *J* = 16.5, 8.2 Hz, 1H). <sup>13</sup>C NMR (101 MHz, (CD<sub>3</sub>)<sub>2</sub>SO): δ 192.6, 165.1 (q, *J* = 2.3 Hz), 144.0, 136.5, 129.8, 128.7, 123.4 (q, *J* = 282.3 Hz), 57.2 (q, *J* = 1.7 Hz), 56.2 (q, *J* = 24.0 Hz). <sup>19</sup>F NMR (377 MHz, (CD<sub>3</sub>)<sub>2</sub>SO): δ -64.07 (d, *J* = 8.2 Hz), -64.11 (minor diastereoisomer, not isolated). HRMS (EI+) *m/z*: calcd for C<sub>11</sub>H<sub>8</sub>F<sub>3</sub>NO<sub>2</sub> [M-HCl]<sup>+</sup>: 243.05071, found 243.05101 (Δ = 1.2 ppm). IR (neat, cm<sup>-1</sup>): ν 3290, 3200, 1695, 1250, 1170, 1110.



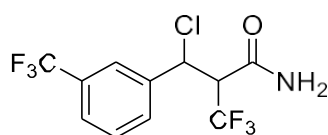
**Methyl 4-(2-carbamoyl-1-chloro-3,3,3-trifluoropropyl)benzoate 2m** was synthesized from 4-(methoxycarbonyl)cinnamamide **1m** following general procedure D and purified by silica gel flash chromatography eluting with petroleum ether/ethyl acetate (7/3). **2m** was obtained as white solid (38.1 mg, 41% yield, d.r. = 73:27). *R<sub>f</sub>* (in petroleum ether/ethyl acetate = 7/3): 0.35.<sup>[20]</sup> <sup>1</sup>H NMR (400 MHz, (CD<sub>3</sub>)<sub>2</sub>SO): δ 8.00 (d, *J* = 7.7 Hz, 2H), 7.97 (brs, 1H), 7.74 (brs, 1H), 7.68 (d, *J* = 7.7 Hz, 2H), 5.57 (d, *J* = 11.1 Hz, 1H), 4.37 – 4.13 (m, 1H), 3.86 (s, 3H). <sup>13</sup>C NMR (101 MHz, (CD<sub>3</sub>)<sub>2</sub>SO): δ 165.7, 165.2 (q, *J* = 2.2 Hz), 142.9, 130.3, 129.6, 128.3, 123.4 (q, *J* = 282.2 Hz), 57.2 (q, *J* = 1.2 Hz), 56.3 (q, *J* = 24.1 Hz), 52.3. <sup>19</sup>F NMR (377 MHz, (CD<sub>3</sub>)<sub>2</sub>SO): δ -63.62 (d, *J* = 8.2 Hz), -63.70 (minor diastereoisomer, not isolated). HRMS (ESI+) *m/z*: calcd for C<sub>12</sub>H<sub>11</sub><sup>35</sup>ClF<sub>3</sub>NaNO<sub>3</sub> [M+Na]<sup>+</sup>: 322.0272, found 322.0283 (Δ = 3.4 ppm). IR (neat, cm<sup>-1</sup>): ν 3431, 3196, 1720, 1684, 1277, 1239, 1178, 1101.



**2-(chloro(4-cyanophenyl)methyl)-3,3,3-trifluoropropanamide 2n** was synthesized from 4-(cyano)cinnamamide **1n** following general procedure D and purified by silica gel flash chromatography eluting with petroleum ether/ethyl acetate (7/3). **2n** was obtained as white solid (21.6 mg, 26% yield, d.r. = 81:19).  $R_f$  (in petroleum ether/ethyl acetate = 7/3): 0.34.<sup>[20]</sup> **<sup>1</sup>H NMR** (400 MHz, (CD<sub>3</sub>)<sub>2</sub>SO): δ 7.95 (brs, 1H), 7.92 (d,  $J$  = 8.4 Hz, 2H), 7.75 (d,  $J$  = 8.4 Hz, 3H), 5.63 (d,  $J$  = 11.1 Hz, 1H), 4.32 – 4.23 (dq,  $J$  = 11.1, 8.2 Hz, 1H). **<sup>13</sup>C NMR** (101 MHz, (CD<sub>3</sub>)<sub>2</sub>SO): δ 165.0 (q,  $J$  = 2.2 Hz), 143.2, 132.8, 128.9, 123.4 (q,  $J$  = 282.1 Hz), 118.3, 111.9, 56.8 (q,  $J$  = 1.4 Hz), 56.0 (q,  $J$  = 24.3 Hz). **<sup>19</sup>F NMR** (377 MHz, (CD<sub>3</sub>)<sub>2</sub>SO): δ -62.28 (d,  $J$  = 8.2 Hz), -68.48 (minor diastereoisomer, not isolated). **HRMS** (ESI+)  $m/z$ : calcd for C<sub>11</sub>H<sub>8</sub><sup>35</sup>ClF<sub>3</sub>NaN<sub>2</sub>O [M+Na]<sup>+</sup>: 299.0169, found 299.0170 ( $\Delta$  = 0.3 ppm). **IR** (neat, cm<sup>-1</sup>): ν 3400, 3200, 2240, 1580, 1230, 1190, 1110.

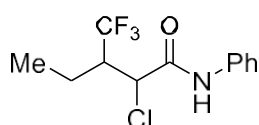


**2-(chloro(4-(trifluoromethyl)phenyl)methyl)-3,3,3-trifluoropropanamide 2o** was synthesized from 4-(trifluoromethyl)cinnamamide **1o** following general procedure D and purified by silica gel flash chromatography eluting with petroleum ether/ethyl acetate (6/4). **2o** was obtained as white solid (29.7 mg, 31% yield, d.r. = 74:26).  $R_f$  (in petroleum ether/ethyl acetate = 6/4): 0.35.<sup>[20]</sup> **<sup>1</sup>H NMR** (400 MHz, (CD<sub>3</sub>)<sub>2</sub>SO): δ 7.97 (brs, 1H), 7.81 (d,  $J$  = 8.5 Hz, 2H), 7.77 (d,  $J$  = 8.5 Hz, 2H), 7.74 (brs, 1H), 5.62 (d,  $J$  = 11.2 Hz, 1H), 4.33 – 4.24 (dq,  $J$  = 11.1, 8.2 Hz, 1H). **<sup>13</sup>C NMR** (101 MHz, (CD<sub>3</sub>)<sub>2</sub>SO): δ 165.1 (q,  $J$  = 2.3 Hz), 142.5 (q,  $J$  = 1.2 Hz), 129.5 (q,  $J$  = 31.9 Hz), 128.8, 125.7 (q,  $J$  = 3.8 Hz), 123.9 (q,  $J$  = 272.3 Hz), 123.4 (q,  $J$  = 282.1 Hz), 56.9 (q,  $J$  = 1.3 Hz), 56.2 (q,  $J$  = 24.3 Hz). **<sup>19</sup>F NMR** (377 MHz, (CD<sub>3</sub>)<sub>2</sub>SO): δ -62.47 (minor diastereoisomer, not isolated), -62.51, -63.55 (d,  $J$  = 8.2 Hz). **HRMS** (ESI+)  $m/z$ : calcd for C<sub>11</sub>H<sub>8</sub><sup>35</sup>ClF<sub>6</sub>NaNO [M+Na]<sup>+</sup>: 342.0091, found 342.0096 ( $\Delta$  = 1.5 ppm). **IR** (neat, cm<sup>-1</sup>): ν 3506, 3360, 1687, 1329, 1241, 1169, 1113, 1074, 1019.

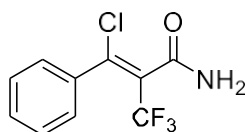


**2-(chloro(3-(trifluoromethyl)phenyl)methyl)-3,3,3-trifluoropropanamide 2p** was synthesized from 3-(trifluoromethyl)cinnamamide **1p** following general procedure D and purified by silica gel flash chromatography eluting with petroleum ether/ethyl acetate (6/4). **2p** was

obtained as white solid (33.6 mg, 35% yield, d.r. = 63:37).  $R_f$  (in petroleum ether/ethyl acetate = 6/4): 0.35.<sup>[20]</sup> **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.71 (s, 1H), 7.64 (d,  $J$  = 8.3 Hz, 1H), 7.61 (d,  $J$  = 9.2 Hz, 1H), 7.52 (t,  $J$  = 7.8 Hz, 1H), 6.28 (brs, 1H), 6.25 (brs, 1H), 5.46 (d,  $J$  = 10.4 Hz, 1H), 3.74 (dq,  $J$  = 10.4, 7.4 Hz, 1H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>):  $\delta$  166.5 (q,  $J$  = 2.2 Hz), 138.5, 131.9 (q,  $J$  = 32.51 Hz), 131.6, 129.9, 126.8 (q,  $J$  = 3.6 Hz), 124.1 (q,  $J$  = 272.0 Hz), 125.1 (q,  $J$  = 3.7 Hz), 123.0 (q,  $J$  = 282.3 Hz), 59.3 (q,  $J$  = 25.5 Hz), 57.5 (q,  $J$  = 1.7 Hz). **<sup>19</sup>F NMR** (377 MHz, CDCl<sub>3</sub>):  $\delta$  -63.28 (minor diastereoisomer, not isolated), -63.35, -64.08 (d,  $J$  = 7.4 Hz), -64.26 (minor diastereoisomer, not isolated). **HRMS** (ES+)  $m/z$ : calcd for C<sub>11</sub>H<sub>8</sub><sup>35</sup>ClF<sub>6</sub>NO [M]<sup>+</sup>: 319.01986, found 319.02101 ( $\Delta$  = 1.1 ppm). **IR** (neat, cm<sup>-1</sup>):  $\nu$  3460, 3195, 1680, 1320, 1250, 1180, 1110, 1070.

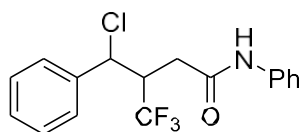


**3-chloro-2-(trifluoromethyl)pentanamide 2q** was synthesized from (*E*)-hex-2-enamide **1q** following general procedure D and purified by silica gel flash chromatography eluting with petroleum ether/ethyl acetate (9.5/0.5). **2q** was obtained as white solid (26.1 mg, 31% yield, d.r. = 98:2).  $R_f$  (in petroleum ether/ethyl acetate = 9.5/0.5): 0.4<sup>[20]</sup>. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.42 (brs, 1H), 7.43 – 7.40 (m, 2H), 7.28 – 7.23 (m, 2H), 7.08 (tt,  $J$  = 7.5, 1.1 Hz, 1H), 4.78 (d,  $J$  = 1.2 Hz, 1H), 3.29 – 3.20 (m, 1H), 1.81 – 1.70 (m, 1H), 1.62 – 1.51 (m, 1H), 0.91 (td,  $J$  = 7.5, 0.8 Hz, 3H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>):  $\delta$  164.4, 136.6, 129.4, 126.9 (q,  $J$  = 280.8 Hz), 125.7, 120.3, 58.5 (q,  $J$  = 3.2 Hz), 46.9 (q,  $J$  = 25.9 Hz), 17.9 (q,  $J$  = 1.5 Hz), 11.8. **<sup>19</sup>F NMR** (377 MHz, CDCl<sub>3</sub>):  $\delta$  -68.58 (d,  $J$  = 8.9 Hz). **HRMS** (EI+)  $m/z$ : calcd for C<sub>12</sub>H<sub>13</sub><sup>35</sup>ClF<sub>3</sub>NO [M+Na]<sup>+</sup>: 279.06378, found 279.06487 ( $\Delta$  = 3.9 ppm). **IR** (neat, cm<sup>-1</sup>):  $\nu$  3320, 3001, 1670, 1601, 1539, 1446, 1243, 1222, 1175, 1131, 1116, 1044, 735.

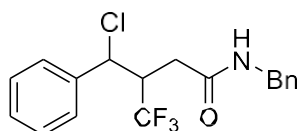


**3-chloro-3-phenyl-2-(trifluoromethyl)acrylamide 2t** was synthesized from 3-phenylpropiolamide **1t** following general procedure D and purified by silica gel flash chromatography eluting with petroleum ether/ethyl acetate (7/3). **2t** was obtained as white solid (29.2 mg, 39% yield).  $R_f$  (in petroleum ether/ethyl acetate = 7/3): 0.32. **<sup>1</sup>H NMR** (400 MHz, (CD<sub>3</sub>)<sub>2</sub>SO):  $\delta$  8.33 (brs, 1H), 7.95 (brs, 1H), 7.51 – 7.49 (m, 3H), 7.42 (m, 2H). **<sup>13</sup>C NMR** (101 MHz, (CD<sub>3</sub>)<sub>2</sub>SO):  $\delta$  162.3 (q,  $J$  = 1.2 Hz), 140.7 (q,  $J$  = 4.6 Hz), 135.4, 130.3, 128.6, 127.5, 127.5 (q,  $J$  = 1.5 Hz), 121.0 (q,  $J$  = 274.4 Hz). **<sup>19</sup>F NMR** (377 MHz, (CD<sub>3</sub>)<sub>2</sub>SO):  $\delta$  -55.06. **HRMS** (ESI+)  $m/z$ : calcd for

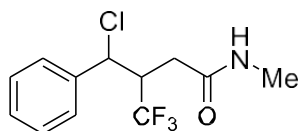
$C_{10}H_7^{35}ClF_3NaNO$   $[M+Na]^+$ : 272.0060, found 272.0068 ( $\Delta = 2.9$  ppm). **IR** (neat,  $cm^{-1}$ ):  $\nu$  3367, 3195, 1668, 1656, 1289, 1173, 1139, 1126, 639.



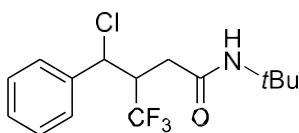
**3-(chloro(phenyl)methyl)-4,4,4-trifluoro-N-phenylbutanamide 4a** was synthesized from *N*-phenyl-4-phenylbut-3-enamide **3a** following general procedure D and purified by silica gel flash chromatography eluting with petroleum ether/ethyl acetate (8/2). **4a** was obtained as white solid (54.3 mg, 53% yield, d.r. = 91:9).  $R_f$  (in petroleum ether/ethyl acetate = 8/2): 0.27.<sup>[20]</sup>  **$^1H$  NMR** (400 MHz,  $(CD_3)_2SO$ ):  $\delta$  10.14 (s, 1H), 7.55 (d,  $J = 7.4$  Hz, 2H), 7.48 (d,  $J = 7.4$  Hz, 2H), 7.34 (m, 3H), 7.27 (t,  $J = 7.9$  Hz, 2H), 7.03 (t,  $J = 7.4$  Hz, 1H), 5.71 (d,  $J = 4.5$  Hz, 1H), 3.74 – 3.64 (m, 1H), 2.88 – 2.77 (m, 2H).  **$^{13}C$  NMR** (101 MHz,  $(CD_3)_2SO$ ):  $\delta$  167.2, 138.8, 138.1, 128.7, 128.6, 128.5, 127.4, 126.6 (q,  $J = 281.3$  Hz), 123.4, 119.2, 59.6 (q,  $J = 2.5$  Hz), 46.08 (q,  $J = 25.0$  Hz), 31.60.  **$^{19}F$  NMR** (282 MHz,  $CDCl_3$ ):  $\delta$  -66.69 (d,  $J = 8.6$  Hz), -72.12 (minor diastereoisomer, not isolated). **HRMS** (ESI+)  $m/z$ : calcd for  $C_{17}H_{15}^{35}ClF_3NaNO$   $[M+Na]^+$ : 364.0686, found 364.0683 ( $\Delta = 0.8$  ppm). **IR** (neat,  $cm^{-1}$ ):  $\nu$  3312, 2924, 2853, 1666, 1599, 1545, 1271, 1246, 1150, 1103.



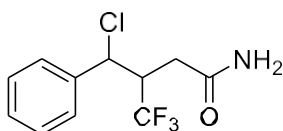
***N*-benzyl-3-(chloro(phenyl)methyl)-4,4,4-trifluorobutanamide 4b** was synthesized from *N*-benzyl-4-phenylbut-3-enamide **3b** following general procedure D and purified by silica gel flash chromatography eluting with petroleum ether/ethyl acetate (8/2). **4b** was obtained as white solid (43.8 mg, 41% yield, d.r. >98:2).  $R_f$  (in petroleum ether/ethyl acetate = 8/2): 0.29.  **$^1H$  NMR** (400 MHz,  $CDCl_3$ ):  $\delta$  7.37 (d,  $J = 7.0$  Hz, 2H), 7.32 – 7.19 (m, 6H), 7.14 (d,  $J = 7.0$  Hz, 2H), 5.90 (brs, 1H), 5.30 (d,  $J = 4.3$  Hz, 1H), 4.33 – 4.18 (m, 2H), 3.68 – 3.58 (m, 1H), 2.62 (dd,  $J = 16.0, 4.2$  Hz, 1H), 2.50 (dd,  $J = 16.0, 7.1$  Hz, 1H).  **$^{13}C$  NMR** (101 MHz,  $CDCl_3$ ):  $\delta$  168.9, 138.2, 137.8, 128.8, 128.8, 127.9, 127.7, 127.2, 126.3 (q,  $J = 281.6$  Hz), 59.7 (q,  $J = 2.7$  Hz), 47.1 (q,  $J = 25.5$  Hz), 44.0, 31.8 (q,  $J = 1.6$  Hz).  **$^{19}F$  NMR** (377 MHz,  $CDCl_3$ ):  $\delta$  -68.82 (d,  $J = 8.6$  Hz). **HRMS** (ES+)  $m/z$ : calcd for  $C_{18}H_{18}^{35}ClF_3NO$   $[M+H]^+$ : 356.1029, found 356.1026 ( $\Delta = -0.3$  ppm). **IR** (neat,  $cm^{-1}$ ):  $\nu$  3278, 2900, 1642, 1545, 1347, 1237, 1150, 1079, 954, 695.



**3-(chloro(phenyl)methyl)-4,4,4-trifluoro-*N*-methylbutanamide 4c** was synthesized from *N*-methyl-4-phenylbut-3-enamide **3c** following general procedure D and purified by silica gel flash chromatography eluting with petroleum ether/ethyl acetate (7/3). **4c** was obtained as white solid (41.1 mg, 49% yield, d.r. = 88:12).  $R_f$  (in petroleum ether/ethyl acetate = 7/3): 0.26.<sup>[20]</sup> **<sup>1</sup>H NMR** (400 MHz, (CD<sub>3</sub>)<sub>2</sub>SO):  $\delta$  7.97 (brs, 1H), 7.48 (d,  $J$  = 7.4 Hz, 2H), 7.40 – 7.29 (m, 3H), 5.61 (d,  $J$  = 4.3 Hz, 1H), 3.62 – 3.51 (m, 1H), 2.47 (m, 5H). **<sup>13</sup>C NMR** (101 MHz, (CD<sub>3</sub>)<sub>2</sub>SO):  $\delta$  168.6, 138.1, 128.5, 128.4, 127.4, 126.5 (q,  $J$  = 282.4 Hz), 59.6 (q,  $J$  = 2.4 Hz), 46.2 (q,  $J$  = 24.6 Hz), 30.4 (q,  $J$  = 1.4 Hz), 25.6. **<sup>19</sup>F NMR** (377 MHz, (CD<sub>3</sub>)<sub>2</sub>SO):  $\delta$  -68.72 (d,  $J$  = 9.1 Hz), -72.23 (minor diastereoisomer, not isolated). **HRMS** (ES+)  $m/z$ : calcd for C<sub>12</sub>H<sub>14</sub><sup>35</sup>ClF<sub>3</sub>NO [M+H]<sup>+</sup>: 280.0716, found 280.0707 ( $\Delta$  = -3.2 ppm). **IR** (neat, cm<sup>-1</sup>):  $\nu$  3290, 3110, 2940, 1640, 1580, 1390, 1245, 1160, 1110, 995, 700.

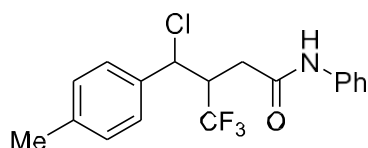


***N*-(tert-butyl)-3-(chloro(phenyl)methyl)-4,4,4-trifluorobutanamide 4d** was synthesized from *N*-tert-butyl-4-phenylbut-3-enamide **3d** following general procedure D and purified by silica gel flash chromatography eluting with petroleum ether/ethyl acetate (8/2). **4d** was obtained as white solid (52.1 mg, 54% yield, d.r. = 96:4).  $R_f$  (in petroleum ether/ethyl acetate = 8/2): 0.33.<sup>[20]</sup> **<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>):  $\delta$  7.34 – 7.15 (m, 5H), 5.25 (d,  $J$  = 4.3 Hz, 2H), 3.57 – 3.45 (m, 1H), 2.45 (dd,  $J$  = 15.7, 4.3 Hz, 1H), 2.33 (dd,  $J$  = 15.7, 7.2 Hz, 1H), 1.16 (s, 9H). **<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>):  $\delta$  168.1, 167.7, 138.3, 128.9, 128.8, 127.2, 126.5 (q,  $J$  = 281.4 Hz), 59.8 (q,  $J$  = 2.7 Hz), 51.6, 47.2 (q,  $J$  = 25.5 Hz), 32.7 (q,  $J$  = 1.5 Hz), 28.7. **<sup>19</sup>F NMR** (282 MHz, CDCl<sub>3</sub>):  $\delta$  -68.80 (d,  $J$  = 8.6 Hz), -72.10 (minor diastereoisomer, not isolated). **HRMS** (ES+)  $m/z$ : calcd for C<sub>15</sub>H<sub>20</sub><sup>35</sup>ClF<sub>3</sub>NO [M+H]<sup>+</sup>: 322.1186, found 322.1178 ( $\Delta$  = -2.5 ppm). **IR** (neat, cm<sup>-1</sup>):  $\nu$  3303, 1670, 1601, 1539, 1446, 1375, 1289, 1276, 1243, 1222, 1175, 1131, 1116, 1091, 1044, 735.

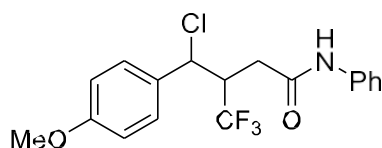


**3-(chloro(phenyl)methyl)-4,4,4-trifluorobutanamide 4e** was synthesized from 4-phenylbut-3-enamide **3e** following general procedure D and purified by silica gel flash chromatography eluting with petroleum ether/ethyl acetate (7/3). **4e** was obtained as white solid (44.6 mg, 56%

yield, d.r. = 79:21).  $R_f$  (in petroleum ether/ethyl acetate = 7/3): 0.36.<sup>[20]</sup>  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.45 – 7.26 (m, 5H), 5.84 (brs, 1H), 5.63 (brs, 1H), 5.34 (d,  $J = 4.6$  Hz, 1H), 3.67 – 3.58 (m, 1H), 2.69 (dd,  $J = 16.5, 4.1$  Hz, 1H), 2.59 (dd,  $J = 16.5, 7.0$  Hz, 1H).  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  171.4, 138.2, 128.9, 128.9, 127.2, 126.3 (q,  $J = 281.5$  Hz), 59.7 (q,  $J = 2.8$  Hz), 47.0 (q,  $J = 25.7$  Hz), 31.1 (q,  $J = 1.7$  Hz).  $^{19}\text{F NMR}$  (282 MHz,  $\text{CDCl}_3$ ):  $\delta$  -68.33 (d,  $J = 8.6$  Hz), -72.14 (minor diastereoisomer, not isolated). **HRMS** (AP-)  $m/z$ : calcd for  $\text{C}_{11}\text{H}_{11}^{35}\text{ClF}_3\text{NO}$   $[\text{M}]^+$ : 265.0481, found 265.0475 ( $\Delta = -2.3$  ppm). **IR** (neat,  $\text{cm}^{-1}$ ):  $\nu$  3290, 2967, 1788, 1272, 1165, 1115, 1000, 698.



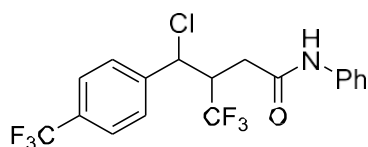
**3-(chloro(*p*-tolyl)methyl)-4,4,4-trifluoro-*N*-phenylbutanamide 4f** was synthesized from *N*-phenyl-4-(*p*-tolyl)but-3-enamide **3f** following general procedure D and purified by silica gel flash chromatography eluting with petroleum ether/ethyl acetate (8/2). **4f** was obtained as white solid (51.2 mg, 48% yield, d.r. = 83:17).  $R_f$  (in petroleum ether/ethyl acetate = 8/2): 0.28.<sup>[20]</sup>  $^1\text{H NMR}$  (400 MHz,  $(\text{CD}_3)_2\text{SO}$ ):  $\delta$  10.11 (s, 1H), 7.47 (d,  $J = 7.8$  Hz, 2H), 7.43 (d,  $J = 7.8$  Hz, 2H), 7.27 (t,  $J = 7.9$  Hz, 2H), 7.18 (s, 1H), 7.16 (s, 1H), 7.03 (t,  $J = 7.4$  Hz, 1H), 5.67 (d,  $J = 4.5$  Hz, 1H), 3.70 – 3.62 (m, 1H), 2.82 – 2.75 (m, 2H), 2.25 (s, 3H).  $^{13}\text{C NMR}$  (101 MHz,  $(\text{CD}_3)_2\text{SO}$ ):  $\delta$  167.2, 138.8, 138.0, 135.1, 129.0, 128.6, 127.2, 126.5 (q,  $J = 281.6$  Hz), 123.3, 119.2, 59.6 (q,  $J = 2.3$  Hz), 46.2 (q,  $J = 24.9$  Hz), 31.6, 20.6.  $^{19}\text{F NMR}$  (377 MHz,  $(\text{CD}_3)_2\text{SO}$ ):  $\delta$  -66.69 (d,  $J = 9.1$  Hz), -72.14 (minor diastereoisomer, not isolated). **HRMS** (ESI+)  $m/z$ : calcd for  $\text{C}_{18}\text{H}_{17}^{35}\text{ClF}_3\text{NaNO}$   $[\text{M}+\text{Na}]^+$ : 378.0843, found 378.0859 ( $\Delta = 4.2$  ppm). **IR** (neat,  $\text{cm}^{-1}$ ):  $\nu$  3300, 1660, 1550, 1250, 1150, 1100.



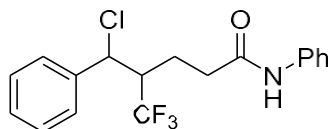
**3-(chloro(*p*-methoxyphenyl)methyl)-4,4,4-trifluoro-*N*-phenylbutanamide 4g** was synthesized from 4-(4-methoxyphenyl)-*N*-phenylbut-3-enamide **3g** following general procedure D and purified by silica gel flash chromatography eluting with petroleum ether/ethyl acetate (7/3). **4g** was obtained as white solid (68.0 mg, 61% yield, d.r. >98:2).  $R_f$  (in petroleum ether/ethyl acetate = 7/3): 0.31.  $^1\text{H NMR}$  (400 MHz,  $(\text{CD}_3)_2\text{SO}$ ):  $\delta$  7.40 (d,  $J = 7.6$  Hz, 2H), 7.30 (d,  $J = 8.7$  Hz, 2H), 7.25 (t,  $J = 7.9$  Hz, 2H), 7.07 (t,  $J = 7.4$  Hz, 1H), 6.85 (d,  $J = 8.7$  Hz, 2H), 5.50 (d,  $J = 5.4$  Hz, 1H), 3.68 (m, 4H), 3.10 (dd,  $J = 17.4, 9.9$  Hz, 1H), 2.69 (dd,  $J = 17.4, 6.6$  Hz, 1H).  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  171.0, 159.8, 137.3, 131.2, 129.1, 127.4, 126.7 (q,  $J = 278.0$  Hz), 126.1, 123.2, 114.9, 63.2 (q,  $J = 2.8$  Hz), 55.4, 45.3 (q,  $J = 28.3$  Hz), 31.1 (q,  $J = 2.1$  Hz).  $^{19}\text{F NMR}$  (377 MHz,  $(\text{CD}_3)_2\text{SO}$ ):  $\delta$  -70.35



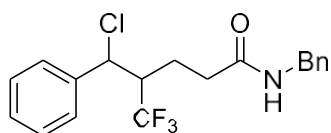
(d,  $J = 9.3$  Hz). **HRMS** (ESI+)  $m/z$ : calcd for  $C_{18}H_{17}^{35}ClF_3NaNO_2$   $[M+Na]^+$ : 394.0792, found 394.0800 ( $\Delta = 2.0$  ppm). **IR** (neat,  $cm^{-1}$ ):  $\nu$  3300, 2960, 1650, 1600, 1500, 1440, 1250, 1150, 1110.



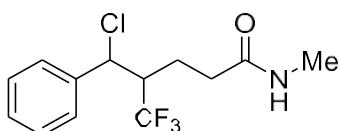
**3-(chloro(*p*-(trifluoromethyl)phenyl)methyl)-4,4,4-trifluoro-*N*-phenylbutanamide 4h** was synthesized from 4-(4-trifluoromethyl)-*N*-phenylbut-3-enamide **3h** following general procedure D and purified by silica gel flash chromatography eluting with petroleum ether/ethyl acetate (8/2). **4h** was obtained as white solid (32.0 mg, 26% yield, d.r. >98:2).  $R_f$  (in petroleum ether/ethyl acetate = 8/2): 0.27.<sup>[20]</sup>  **$^1H$  NMR** (400 MHz,  $(CD_3)_2SO$ ):  $\delta$  10.09 (s, 1H), 7.80 (d,  $J = 8.3$  Hz, 2H), 7.71 (d,  $J = 8.3$  Hz, 2H), 7.41 (dd,  $J = 8.6, 1.0$  Hz, 2H), 7.25 (t,  $J = 8.4$  Hz, 2H), 7.02 (m, 1H), 5.87 (d,  $J = 4.3$  Hz, 1H), 3.82 – 3.71 (m, 1H), 2.88 – 2.75 (m, 2H).  **$^{13}C$  NMR** (101 MHz,  $(CD_3)_2SO$ ):  $\delta$  166.9, 142.3, 138.6, 129.0 (q,  $J = 31.9$  Hz), 128.6, 128.4, 126.4 (q,  $J = 281.9$  Hz), 125.3 (q,  $J = 3.6$  Hz), 123.9 (q,  $J = 273.0$  Hz), 123.4, 119.2, 58.7 (q,  $J = 2.2$  Hz), 45.9 (q,  $J = 25.2$  Hz), 31.3.  **$^{19}F$  NMR** (377 MHz,  $(CD_3)_2SO$ ):  $\delta$  -61.32, -66.74 (d,  $J = 9.2$  Hz). **HRMS** (ESI+)  $m/z$ : calcd for  $C_{18}H_{14}^{35}ClF_6NaNO$   $[M+Na]^+$ : 432.0560, found 432.0576 ( $\Delta = 3.7$  ppm). **IR** (neat,  $cm^{-1}$ ):  $\nu$  3302, 1660, 1550, 1317, 1110, 1069.



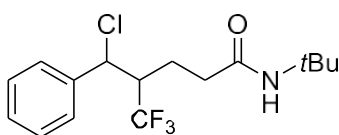
**4-(chloro(phenyl)methyl)-5,5,5-trifluoro-*N*-phenylpentanamide 6a** was synthesized from *N*-5-diphenylpent-4-enamide **5a** following general procedure D and purified by silica gel flash chromatography eluting with petroleum ether/ethyl acetate (8/2). **6a** was obtained as white solid (59.8 mg, 56% yield, d.r. = 91:9).  $R_f$  (in petroleum ether/ethyl acetate = 8/2): 0.28.<sup>[20]</sup>  **$^1H$  NMR** (400 MHz,  $(CD_3)_2SO$ ):  $\delta$  9.93 (s, 1H), 7.55 – 7.53 (m, 4H), 7.37 (m, 3H), 7.27 (t,  $J = 7.9$  Hz, 2H), 7.01 (t,  $J = 7.4$  Hz, 1H), 5.62 (d,  $J = 4.7$  Hz, 1H), 3.33 – 3.26 (m, 1H), 2.46 (d,  $J = 8.5$  Hz, 1H), 2.34 (m, 1H), 2.03 (q,  $J = 7.1$  Hz, 2H).  **$^{13}C$  NMR** (101 MHz,  $(CD_3)_2SO$ ):  $\delta$  169.9, 139.1, 138.3, 128.6, 128.4, 127.4, 126.8 (q,  $J = 282.6$  Hz), 123.1, 119.1, 60.1 (q,  $J = 3.0$  Hz), 48.1 (q,  $J = 23.7$  Hz), 33.0, 20.0.  **$^{19}F$  NMR** (377 MHz,  $(CD_3)_2SO$ ):  $\delta$  -65.15 (minor diastereoisomer, not isolated), -66.95 (d,  $J = 9.1$  Hz). **HRMS** (ES+)  $m/z$ : calcd for  $C_{18}H_{18}^{35}ClF_3NO$   $[M+H]^+$ : 356.1031, found 356.1029 ( $\Delta = 0.6$  ppm). **IR** (neat,  $cm^{-1}$ ):  $\nu$  3245, 3077, 1655, 1599, 1552, 1500, 1446, 1204, 1144, 1109, 752.



**N-benzyl-4-(chloro(phenyl)methyl)-5,5,5-trifluoropentanamide 6b** was synthesized from *N*-(benzyl)-5-phenylpent-4-enamide **5b** following general procedure D and purified by silica gel flash chromatography eluting with petroleum ether/ethyl acetate (8/2). **6b** was obtained as white solid (56.0 mg, 54% yield, d.r. = 95:5).  $R_f$  (in petroleum ether/ethyl acetate = 8/2): 0.30.<sup>[20]</sup> **<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>):  $\delta$  7.40 – 7.15 (m, 10H), 5.77 (brs, 1H), 5.30 (d,  $J$  = 4.0 Hz, 1H), 4.34 – 4.20 (m, 2H), 2.82 – 2.77 (m, 1H), 2.24 – 2.06 (m, 4H). **<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>):  $\delta$  171.2, 138.5, 138.2, 128.8, 128.7, 128.6, 127.9, 127.6, 127.2, 126.6 (q,  $J$  = 282.0 Hz), 59.8 (q,  $J$  = 3.3 Hz), 49.6 (q,  $J$  = 24.5 Hz), 43.6, 33.2, 20.2 (q,  $J$  = 1.3 Hz). **<sup>19</sup>F NMR** (282 MHz, CDCl<sub>3</sub>):  $\delta$  -65.17 (minor diastereoisomer, not isolated), -66.86 (d,  $J$  = 8.7 Hz). **HRMS** (EI+)  $m/z$ : calcd for C<sub>19</sub>H<sub>19</sub><sup>35</sup>ClF<sub>3</sub>NO [M]<sup>+</sup>: 369.11073, found 369.11166 ( $\Delta$  = 2.5 ppm). **IR** (neat, cm<sup>-1</sup>):  $\nu$  3286, 1646, 1544, 1257, 1240, 1147, 1108, 1094, 695.

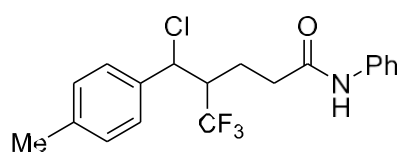


**4-(chloro(phenyl)methyl)-5,5,5-trifluoro-N-methylpentanamide 6c** was synthesized from *N*-(methyl)-5-phenylpent-4-enamide **5c** following general procedure D and purified by silica gel flash chromatography eluting with petroleum ether/ethyl acetate (7/3). **6c** was obtained as white solid (49.3 mg, 56% yield, d.r. >98:2).  $R_f$  (in petroleum ether/ethyl acetate = 7/3): 0.28. **<sup>1</sup>H NMR** (400 MHz, (CD<sub>3</sub>)<sub>2</sub>SO):  $\delta$  7.75 (brs, 1H), 7.52 (d,  $J$  = 7.2 Hz, 2H), 7.38 (m, 3H), 5.58 (d,  $J$  = 4.7 Hz, 1H), 3.27 – 3.16 (m, 1H), 2.51 (d,  $J$  = 4.5 Hz, 3H), 2.24 – 2.16 (m, 1H), 2.09 – 2.01 (m, 1H), 1.92 (q,  $J$  = 8.0 Hz, 2H). **<sup>13</sup>C NMR** (101 MHz, (CD<sub>3</sub>)<sub>2</sub>SO):  $\delta$  171.2, 138.3, 128.4, 127.4, 126.8 (q,  $J$  = 282.6 Hz), 60.1 (q,  $J$  = 3.2 Hz), 48.1 (q,  $J$  = 23.7 Hz), 32.1, 25.4, 20.4 (q,  $J$  = 0.9 Hz). **<sup>19</sup>F NMR** (377 MHz, (CD<sub>3</sub>)<sub>2</sub>SO):  $\delta$  -66.56 (d,  $J$  = 9.1 Hz). **HRMS** (AP-)  $m/z$ : calcd for C<sub>13</sub>H<sub>15</sub><sup>35</sup>ClF<sub>3</sub>NO [M]<sup>+</sup>: 293.0794, found 293.0792 ( $\Delta$  = -0.7 ppm). **IR** (neat, cm<sup>-1</sup>):  $\nu$  3401, 1637, 1564, 1264, 1248, 1196, 1144, 1114, 1095, 1077, 1010, 697.

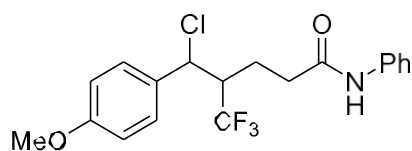


**N-(tert-butyl)-4-(chloro(phenyl)methyl)-5,5,5-trifluoropentanamide 6d** was synthesized from *N*-(tert-butyl)-5-phenylpent-4-enamide **5d** following general procedure D and purified by

silica gel flash chromatography eluting with petroleum ether/ethyl acetate (8/2). **6d** was obtained as white solid (58.4 mg, 58% yield, d.r. = 91:9).  $R_f$ (in petroleum ether/ethyl acetate = 8/2): 0.34.<sup>[20]</sup> **<sup>1</sup>H NMR** (400 MHz, (CD<sub>3</sub>)<sub>2</sub>SO):  $\delta$  7.52 – 7.50 (m, 2H), 7.43 – 7.33 (m, 4H), 5.57 (d,  $J$  = 4.6 Hz, 1H), 3.23 – 3.12 (m, 1H), 2.18 – 2.16 (m, 1H), 2.06 – 1.91 (m, 1H), 1.87 (dd,  $J$  = 14.4, 7.4 Hz, 2H), 1.19 (s, 9H). **<sup>13</sup>C NMR** (101 MHz, (CD<sub>3</sub>)<sub>2</sub>SO):  $\delta$  170.3, 138.3, 128.4, 127.4, 126.8 (q,  $J$  = 282.0 Hz), 60.1 (q,  $J$  = 3.2 Hz), 49.8, 48.2 (q,  $J$  = 23.7 Hz), 32.7, 28.5, 20.4. **<sup>19</sup>F NMR** (377 MHz, (CD<sub>3</sub>)<sub>2</sub>SO):  $\delta$  -62.83 (minor diastereoisomer, not isolated), -64.87. **HRMS** (AP-)  $m/z$ : calcd for C<sub>16</sub>H<sub>21</sub><sup>35</sup>ClF<sub>3</sub>NO [M]<sup>+</sup>: 335.1264, found 335.1251 ( $\Delta$  = -3.9 ppm). **IR** (neat, cm<sup>-1</sup>):  $\nu$  3310, 2990, 1640, 1560, 1250, 1200, 1140, 1105, 1085.

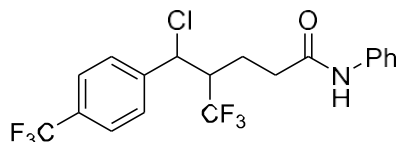


**4-(chloro(p-tolyl)methyl)-5,5,5-trifluoro-N-phenylpentanamide 6e** was synthesized from *N*-phenyl-5-(*p*-tolyl)pent-4-enamide **5e** following general procedure D and purified by silica gel flash chromatography eluting with petroleum ether/ethyl acetate (8/2). **6e** was obtained as orange oil (55.5 mg, 50% yield, d.r. = 95:5).  $R_f$ (in petroleum ether/ethyl acetate = 8/2): 0.29.<sup>[20]</sup> **<sup>1</sup>H NMR** (400 MHz, (CD<sub>3</sub>)<sub>2</sub>SO):  $\delta$  9.88 (s, 1H), 7.50 (d,  $J$  = 8.1 Hz, 2H), 7.38 (d,  $J$  = 8.1 Hz, 2H), 7.23 (t,  $J$  = 8.0 Hz, 2H), 7.16 (d,  $J$  = 8.0 Hz, 2H), 6.97 (t,  $J$  = 7.4 Hz, 1H), 5.54 (d,  $J$  = 4.7 Hz, 1H), 3.21 (m, 1H), 2.46 (m, 2H), 2.25 (s, 3H), 1.98 (q,  $J$  = 7.4 Hz, 2H). **<sup>13</sup>C NMR** (101 MHz, (CD<sub>3</sub>)<sub>2</sub>SO):  $\delta$  169.9, 139.1, 137.8, 135.4, 128.9, 128.6, 127.3, 126.9 (q,  $J$  = 282.5 Hz), 123.0, 119.1, 60.1 (q,  $J$  = 2.8 Hz), 48.2 (q,  $J$  = 23.6 Hz), 33.1, 20.6, 20.0. **<sup>19</sup>F NMR** (377 MHz, (CD<sub>3</sub>)<sub>2</sub>SO):  $\delta$  -64.36 (minor diastereoisomer, not isolated), -64.96 (d,  $J$  = 9.1 Hz). **HRMS** (ESI+)  $m/z$ : calcd for C<sub>19</sub>H<sub>19</sub><sup>35</sup>ClF<sub>3</sub>NaNO [M+Na]<sup>+</sup>: 392.0999, found 392.1011 ( $\Delta$  = 3.1 ppm). **IR** (neat, cm<sup>-1</sup>):  $\nu$  3300, 1660, 1600, 1550, 1440, 1250, 1167, 1108.

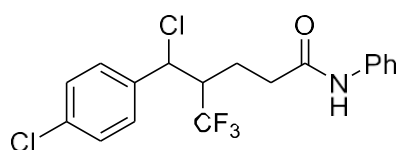


**4-(chloro(4-methoxyphenyl)methyl)-5,5,5-trifluoro-N-phenylpentanamide 6f** was synthesized from 5-(4-methoxyphenyl)-*N*-phenylpent-4-enamide **5f** following general procedure D and purified by silica gel flash chromatography eluting with petroleum ether/ethyl acetate (8/2). **6f** was obtained as orange oil (64.8 mg, 56% yield, d.r. = 61:39).  $R_f$ (in petroleum ether/ethyl acetate = 8/2): 0.26.<sup>[20]</sup> **<sup>1</sup>H NMR** (400 MHz, (CD<sub>3</sub>)<sub>2</sub>SO):  $\delta$  7.27 – 7.21 (m, 4H), 7.15 (tt,  $J$  = 7.4, 1.7 Hz, 1H), 7.03 – 7.01 (m, 2H), 6.89 – 6.86 (m, 2H), 5.09 (d,  $J$  = 5.0 Hz, 1H), 3.71 (s, 3H), 3.17 – 3.13 (m, 1H), 2.75 (dt,  $J$  = 17.6, 7.1 Hz, 1H), 2.55 – 2.47 (m, 2H), 2.06 (m, 2H). **<sup>13</sup>C NMR** (101 MHz,

(CD<sub>3</sub>)<sub>2</sub>SO):  $\delta$  168.5, 158.7, 141.8, 131.4, 128.6, 128.4, 127.5, 127.2 (q,  $J$  = 282.0 Hz), 126.6, 113.9, 62.2 (d,  $J$  = 1.8 Hz), 55.0, 43.7 (q,  $J$  = 25.1 Hz), 29.2, 17.5 (q,  $J$  = 1.8 Hz). **<sup>19</sup>F NMR** (377 MHz, (CD<sub>3</sub>)<sub>2</sub>SO):  $\delta$  -69.00 (minor diastereoisomer, not isolated), -70.00 (d,  $J$  = 9.3 Hz). **HRMS** (ESI+)  $m/z$ : calcd for C<sub>19</sub>H<sub>19</sub><sup>35</sup>ClF<sub>3</sub>NaNO<sub>2</sub> [M+Na]<sup>+</sup>: 408.0949, found 408.0954 ( $\Delta$  = 1.2 ppm). **IR** (neat, cm<sup>-1</sup>):  $\nu$  3304, 2937, 1661, 1601, 1543, 1442, 1247, 1154, 1109, 1031.

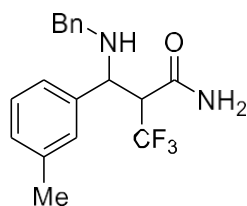


**4-(chloro(4-(trifluoromethyl)phenyl)methyl)-5,5,5-trifluoro-N-phenylpentanamide 6g** was synthesized from 5-(4-trifluoromethyl)-N-phenylpent-4-enamide **5g** following general procedure D and purified by silica gel flash chromatography eluting with petroleum ether/ethyl acetate (8/2). **6g** was obtained as colorless oil (66.1 mg, 52% yield, d.r. >98:2).  $R_f$  (in petroleum ether/ethyl acetate = 8/2): 0.28. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.59 (d,  $J$  = 8.3 Hz, 2H), 7.53 (d,  $J$  = 8.3 Hz, 2H), 7.38 (d,  $J$  = 7.8 Hz, 2H), 7.25 (t,  $J$  = 7.29 Hz, 3H), 7.07 (t,  $J$  = 7.4 Hz, 1H), 5.33 (d,  $J$  = 4.1 Hz, 1H), 2.96 – 2.86 (m, 1H), 2.44 (m, 1H), 2.31 (m, 1H), 2.21 – 2.12 (m, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>):  $\delta$  169.6, 142.4, 137.6, 130.9 (q,  $J$  = 32.7 Hz), 129.1, 127.8, 126.5 (q,  $J$  = 282.1 Hz), 125.8 (q,  $J$  = 3.7 Hz), 124.7, 123.9 (q,  $J$  = 272.4 Hz), 120.1, 59.1 (q,  $J$  = 3.3 Hz), 49.3 (q,  $J$  = 24.7 Hz), 33.9, 20.0. **<sup>19</sup>F NMR** (377 MHz, CDCl<sub>3</sub>):  $\delta$  -63.18, -66.55 (d,  $J$  = 8.6 Hz). **HRMS** (ESI+)  $m/z$ : calcd for C<sub>19</sub>H<sub>16</sub><sup>35</sup>ClF<sub>6</sub>NaNO [M+Na]<sup>+</sup>: 446.0717, found 446.0724 ( $\Delta$  = 1.6 ppm). **IR** (neat, cm<sup>-1</sup>):  $\nu$  3304, 2924, 1664, 1549, 1502, 1325, 1109, 1068, 750.

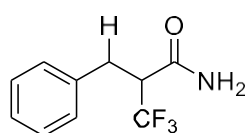


**4-(chloro(4-chlorophenyl)methyl)-5,5,5-trifluoro-N-phenylpentanamide 6h** was synthesized from 5-(4-chloro)-N-phenylpent-4-enamide **5h** following general procedure D and purified by silica gel flash chromatography eluting with petroleum ether/ethyl acetate (8/2). **6h** was obtained as beige oil (49.2 mg, 42% yield, d.r. = 95:5).  $R_f$  (in petroleum ether/ethyl acetate = 8/2): 0.32.<sup>[20]</sup> **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.43 – 7.28 (m, 8H), 7.16 (brs, 1H), 7.11 (t,  $J$  = 7.4 Hz, 1H), 5.31 (d,  $J$  = 4.1 Hz, 1H), 2.92 – 2.84 (m, 1H), 2.49 – 2.15 (m, 4H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>):  $\delta$  169.8, 137.9, 137.4, 134.9, 129.5, 129.3, 129.0, 126.9 (q,  $J$  = 282.2 Hz), 124.9, 120.3, 59.5 (q,  $J$  = 3.2 Hz), 49.7 (q,  $J$  = 24.6 Hz), 34.4, 20.4. **<sup>19</sup>F NMR** (377 MHz, CDCl<sub>3</sub>):  $\delta$  -65.13 (minor diastereoisomer, not isolated), -66.68 (d,  $J$  = 8.6 Hz). **HRMS** (ESI+)  $m/z$ : calcd for

$C_{18}H_{16}^{35}Cl_2F_3NaNO$   $[M+Na]^+$ : 412.0453, found 412.0461 ( $\Delta = 1.9$  ppm). **IR** (neat,  $cm^{-1}$ ):  $\nu$  3315, 2926, 1664, 1601, 1543, 1493, 1442, 1250, 1187, 1150, 1116, 1092, 750.

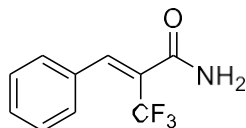


**2-((benzylamino)(*m*-tolyl)methyl)-3,3,3-trifluoropropanamide 7** was synthesized from 2-(chloro(*m*-tolyl)methyl)-3,3,3-trifluoropropanamide **2h**. A solution of **2h** (35.2 mg, 0.13 mmol, 1.0 equiv.) and benzylamine (28.9  $\mu$ L, 0.26 mmol, 2.0 equiv.) in THF (883.0  $\mu$ L, 150 mM) was stirred for 24 h at room temperature. Water and ethyl acetate were added and the solution was extracted 3 times with ethyl acetate. The organic layer was dried over  $MgSO_4$  and concentrated under reduced pressure. The purification was carried out by silica gel flash chromatography eluting with petroleum ether/ethyl acetate (6/4). **7** was obtained as white solid (29.5 mg, 66% yield).  $R_f$  (in petroleum ether/ethyl acetate = 6/4): 0.31.  **$^1H$  NMR** (400 MHz,  $(CD_3)_2SO$ ):  $\delta$  7.68 (brs, 1H), 7.51 – 7.26 (m, 10H), 7.14 (brs, 1H), 4.16 (d,  $J = 10.5$  Hz, 1H), 3.81 – 3.70 (m, 2H), 3.54 (s, 3H), 3.46 (d,  $J = 13.9$  Hz, 1H).  **$^{13}C$  NMR** (101 MHz,  $(CD_3)_2SO$ ):  $\delta$  166.5 (q,  $J = 2.6$  Hz), 140.4, 140.0, 136.8, 128.8, 128.1, 128.0, 127.9, 127.8, 126.6, 125.3 (q,  $J = 281.0$  Hz), 125.2, 59.2, 55.2 (q,  $J = 23.2$  Hz), 49.8, 21.2.  **$^{19}F$  NMR** (377 MHz,  $(CD_3)_2SO$ ):  $\delta$  -62.01 (d,  $J = 8.4$  Hz). **HRMS** (ESI+)  $m/z$ : calcd for  $C_{18}H_{19}F_3N_2O$   $[M+H]^+$ : 337.1522, found 337.1533 ( $\Delta = 3.3$  ppm). **IR** (neat,  $cm^{-1}$ ):  $\nu$  3410, 3320, 3200, 1670, 1250, 1140, 1120, 1100.



**2-benzyl-3,3,3-trifluoropropanamide 8** was synthesized from 2-(chloro(phenyl)methyl)-3,3,3-trifluoropropanamide **2e**. A solution of **2e** (50.0 mg, 0.20 mmol, 1.0 equiv.) and zinc (19.5 mg, 0.30 mmol, 1.5 equiv.) in acetic acid (1.0 mL, 200 mM) was stirred during 3 h at 80  $^{\circ}C$ . After completion of the reaction, the solution was cooled down to room temperature and washed 5 times with water. The combined organic layers were dried over  $MgSO_4$  and concentrated under reduced pressure. The purification was carried out by silica gel flash chromatography eluting with petroleum ether/ethyl acetate (6/4). **8** was obtained as white solid (29.3 mg, 68% yield).  $R_f$  (in petroleum ether/ethyl acetate = 6/4): 0.24.  **$^1H$  NMR** (400 MHz,  $(CD_3)_2SO$ ):  $\delta$  7.64 (brs, 1H), 7.32 – 7.28 (m, 3H), 7.24 – 7.21 (m, 3H), 3.56 – 3.45 (m, 1H), 3.08 (dd,  $J = 13.6, 10.9$  Hz, 1H), 2.93 (dd,  $J = 13.6, 4.2$  Hz, 1H).  **$^{13}C$  NMR** (101 MHz,  $(CD_3)_2SO$ ):  $\delta$  166.6 (q,  $J = 2.6$  Hz), 137.0, 128.8, 128.4, 126.7, 125.5 (q,

$J = 279.9$  Hz),  $50.4$  (q,  $J = 24.6$  Hz),  $31.1$  (q,  $J = 2.5$  Hz).  **$^{19}\text{F}$  NMR** (377 MHz,  $(\text{CD}_3)_2\text{SO}$ ):  $\delta$  -66.97 (d,  $J = 9.0$  Hz). **HRMS** (ESI+)  $m/z$ : calcd for  $\text{C}_{10}\text{H}_{10}\text{F}_3\text{NaNO}$   $[\text{M}+\text{Na}]^+$ : 240.0607, found 240.0606 ( $\Delta = 0.4$  ppm). **IR** (neat,  $\text{cm}^{-1}$ ):  $\nu$  3390, 3210, 1650, 1250, 1150, 1110.



**3-phenyl-2-(trifluoromethyl)acrylamide 9** was synthesized from 2-(chloro(phenyl)methyl)-3,3,3-trifluoropropanamide **2e**. A solution of **2e** (37.7 mg, 0.15 mmol, 1.0 equiv.) and sodium azide (14.6 mg, 0.23 mmol, 1.5 equiv.) in DMF (750  $\mu\text{L}$ , 200 mM) was stirred during 3 h at 75  $^\circ\text{C}$ . After completion of the reaction, the solution was cooled down to room temperature and ethyl acetate and water were added. Organic layer was washed 5 times with water. The organic layer was dried over  $\text{MgSO}_4$  and concentrated under reduced pressure. The purification was carried out by silica gel flash chromatography eluting with petroleum ether/ethyl acetate (7/3). **9** was obtained as white solid (23.4 mg, 73% yield).  $R_f$  (in petroleum ether/ethyl acetate = 7/3): 0.37.  **$^1\text{H}$  NMR** (400 MHz,  $(\text{CD}_3)_2\text{SO}$ ):  $\delta$  8.10 (brs, 1H), 7.79 (brs, 1H), 7.61 (m, 2H), 7.44 (m, 3H), 7.24 (brs, 1H).  **$^{13}\text{C}$  NMR** (101 MHz,  $(\text{CD}_3)_2\text{SO}$ ):  $\delta$  164.4, 133.4 (q,  $J = 6.0$  Hz), 132.3, 130.1, 129.3, 128.7, 126.4 (q,  $J = 29.6$  Hz), 122.8 (q,  $J = 273.2$  Hz).  **$^{19}\text{F}$  NMR** (377 MHz,  $(\text{CD}_3)_2\text{SO}$ ):  $\delta$  -64.74. **HRMS** (ESI+)  $m/z$ : calcd for  $\text{C}_{10}\text{H}_9\text{F}_3\text{NO}$   $[\text{M}+\text{H}]^+$ : 216.0636, found 216.0630 ( $\Delta = -2.8$  ppm). **IR** (neat,  $\text{cm}^{-1}$ ):  $\nu$  3393, 3191, 1637, 1441, 1278, 1116, 1008.

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## 7. NMR spectra

