Exploration toward the synthesis of aliphatic SF_5-containing compounds using the Kolbe reaction

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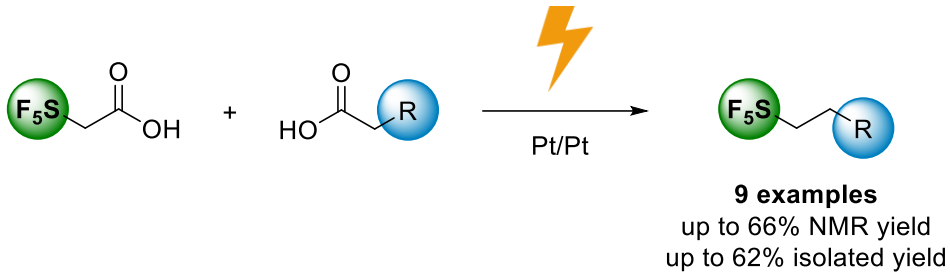
ABSTRACT: The preparation of aliphatic SF_5-compounds (*i.e.*, $RCH_2CH_2SF_5$ where R is functionalized alkyl chain) using a Kolbe-based reaction was explored. In this electrochemical approach, 2-(pentafluoro-λ^6-sulfanyl)acetic acid, used as the "SF_5CH_2" source, is reacted with a aliphatic carboxylic acid. A total of 9 examples of unsymmetrical coupling between 2-(pentafluoro-λ^6-sulfanyl)acetic acid and a range of aliphatic carboxylic acid was achieved with NMR yields ranging from 15% to 66% (up to 62% isolated yield). Even if the method leads to modest yields, it represents one of the very few strategies to rapidly access aliphatic SF_5-containing compounds.

KEYWORDS: Pentafluorosulfanyl substituent, Kolbe reaction, electrochemistry, radical, carboxylic acids.

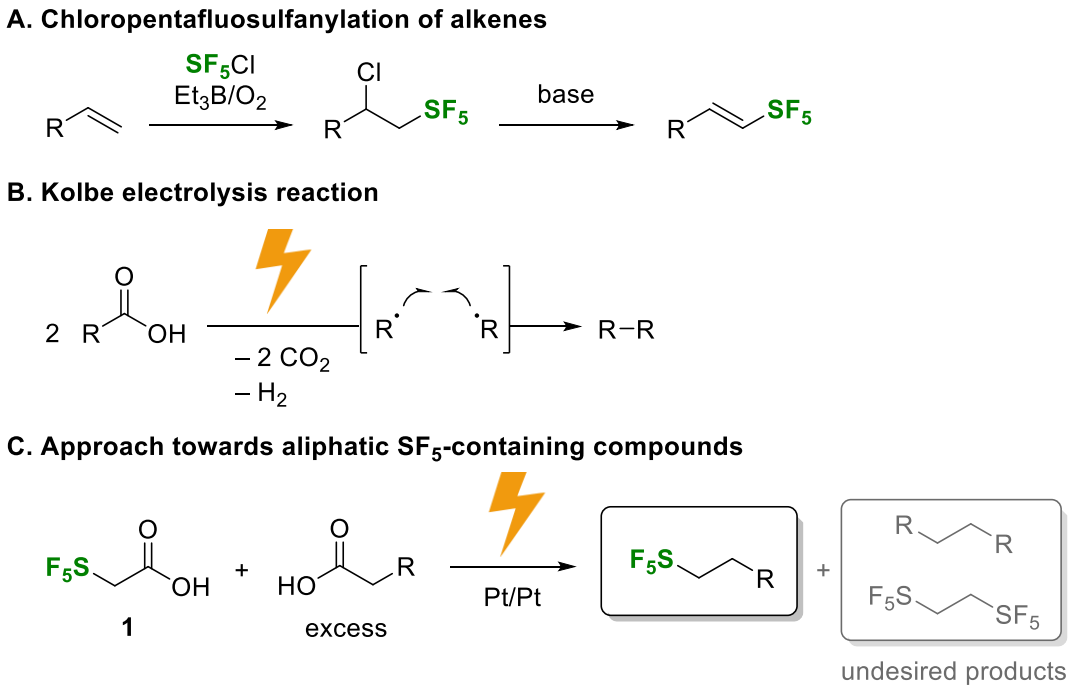
GRAPHICAL ABSTRACT:



1. Introduction

The pentafluorosulfanyl group (−SF_5), also named "super CF_3", is one of the key emerging fluorinated substituents [1]. This group has unique properties (lipophilicity, electron-withdrawing capacity, size, etc.) [2,3] and as such, has been used increasingly in many fields of organic chemistry, including medicinal chemistry, agrochemistry and material sciences [4]. While the interest toward the SF_5 group is growing, synthetic methods to introduce it into organic molecules remain limited [3,4d,5]. In order to incorporate the SF_5 moiety on aliphatic substrates, Dolbier's protocol for the radical addition of SF_5Cl on unsaturated compounds (mainly alkenes and alkynes) [6], using Et_3B as the radical initiator, has emerged as the most versatile one (Scheme 1A) [7,8]. Unfortunately, the C–Cl bond of the chloropentafluorosulfanylated products is difficult to transform [9], and elimination to generate the SF_5-alkene remains the major reaction [3,5]. As such, the preparation of aliphatic SF_5-compounds (*i.e.*, $RCH_2CH_2SF_5$ where R is functionalized alkyl chain) has been scarcely reported with no general method known [10]. Hence, we sought to develop new synthetic protocols for the incorporation of the SF_5-moiety on aliphatic

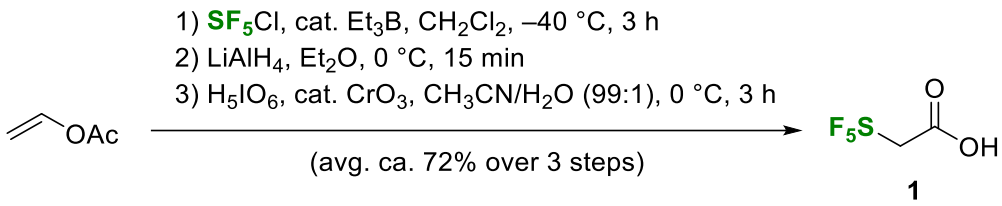
derivatives. In order to do so, we decided to explore the use of the Kolbe electrolysis reaction (Scheme 1B) [11,12]. This reaction was first described as the dimerization of two alkyl-based radicals generated from the anodic decarboxylation of an aliphatic carboxylic acid. While the homodimerization of carboxylic acids remains the major use of this transformation, unsymmetrical coupling of two different carboxylic acids is possible as long as one of them is in excess [12]. In that context, we envision that the synthesis of aliphatic pentafluorosulfanylated derivatives could be achieved by an unsymmetrical coupling between a suitable SF_5-containing carboxylic acid and an excess of a second aliphatic carboxylic acid (Scheme 1C). Herein, we report our investigation towards this goal using 2-(pentafluoro-λ^6-sulfanyl)acetic acid (**1**), as the "SF_5CH_2" source.



Scheme 1. (a) Chloropentafluosulfanylation of alkenes, (b) Kolbe electrolysis reaction and (c) our approach towards aliphatic SF_5-containing compounds.

2. Results and discussion

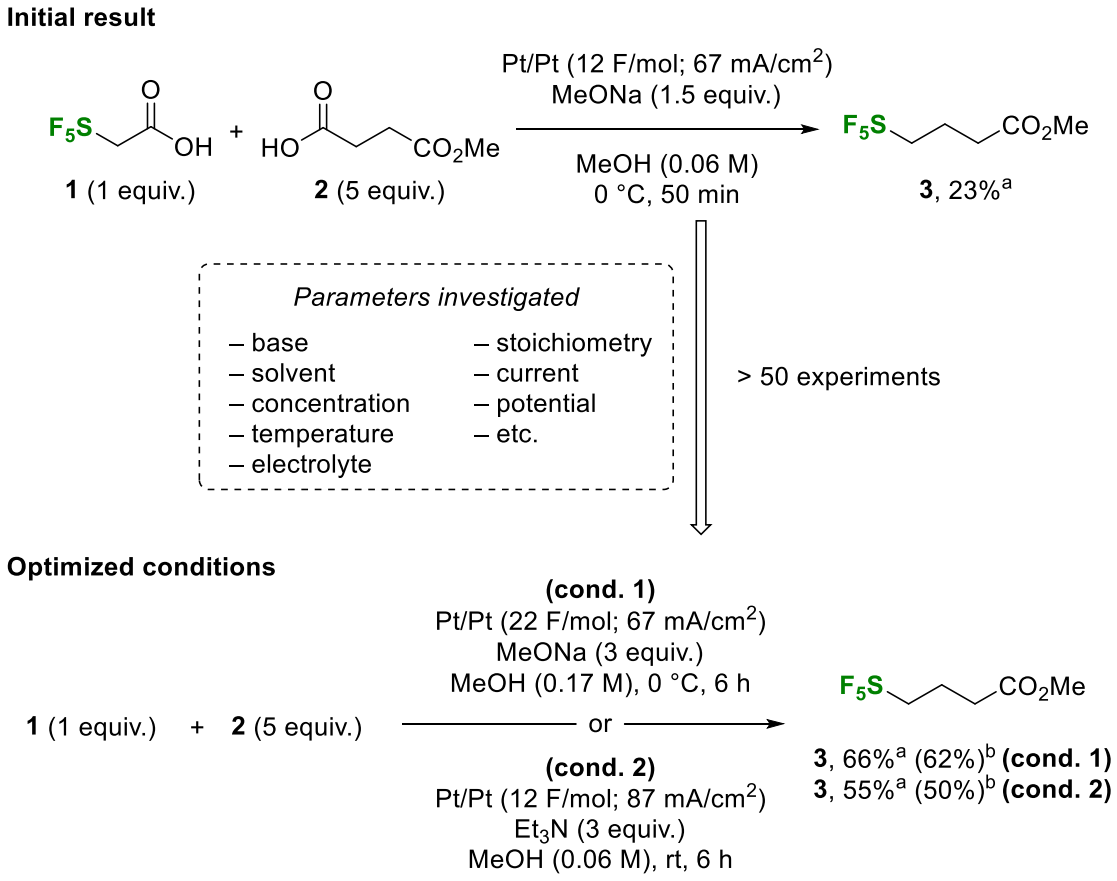
At the outset, the known 2-(pentafluoro-λ^6-sulfanyl)acetic acid (**1**) was identified as a potentially suitable SF_5-containing acid. It was prepared in three steps from vinyl acetate using a sequence inspired by previous work from Carreira (Scheme 2) [13,14]. First, radical addition of SF_5Cl onto vinyl acetate was performed using Dolbier's protocol [7]. The crude chloropentafluorosulfanylation compound was used directly for the next step. Reaction of the latter with $LiAlH_4$ produced the crude alcohol $SF_5CH_2CH_2OH$. Finally, oxidation provided, after purification, the desired acid **1**. The latter is a stable solid that can stored at rt for weeks without any decomposition. The sequence could be easily performed on gram scale and the acid was isolated with an average yield of ca. 72% over three steps (range of 50% to quantitative).



Scheme 2. Synthesis of 2-(pentafluoro-λ^6-sulfanyl)acetic acid (1).

With the acid in hand, we then moved to the investigation of the Kolbe reaction using monomethyl succinate (**2**) as the model co-acid partner. We were delighted to observe the desired product **3** in 23% NMR yield under the initial conditions (Scheme 3), *i.e.*, **1** (1 equiv.), **2** (5 equiv.), MeONa (1.5 equiv.), MeOH (0.06 M), 0 °C for 50 min using Pt/Pt electrodes (12 F/mol @ 87 mA/cm^2). As expected, under those conditions, the dimerization of the monomethyl succinate was a major product while the dimerization of **1** was not observed. To further optimize this result, various parameters were investigated over > 50

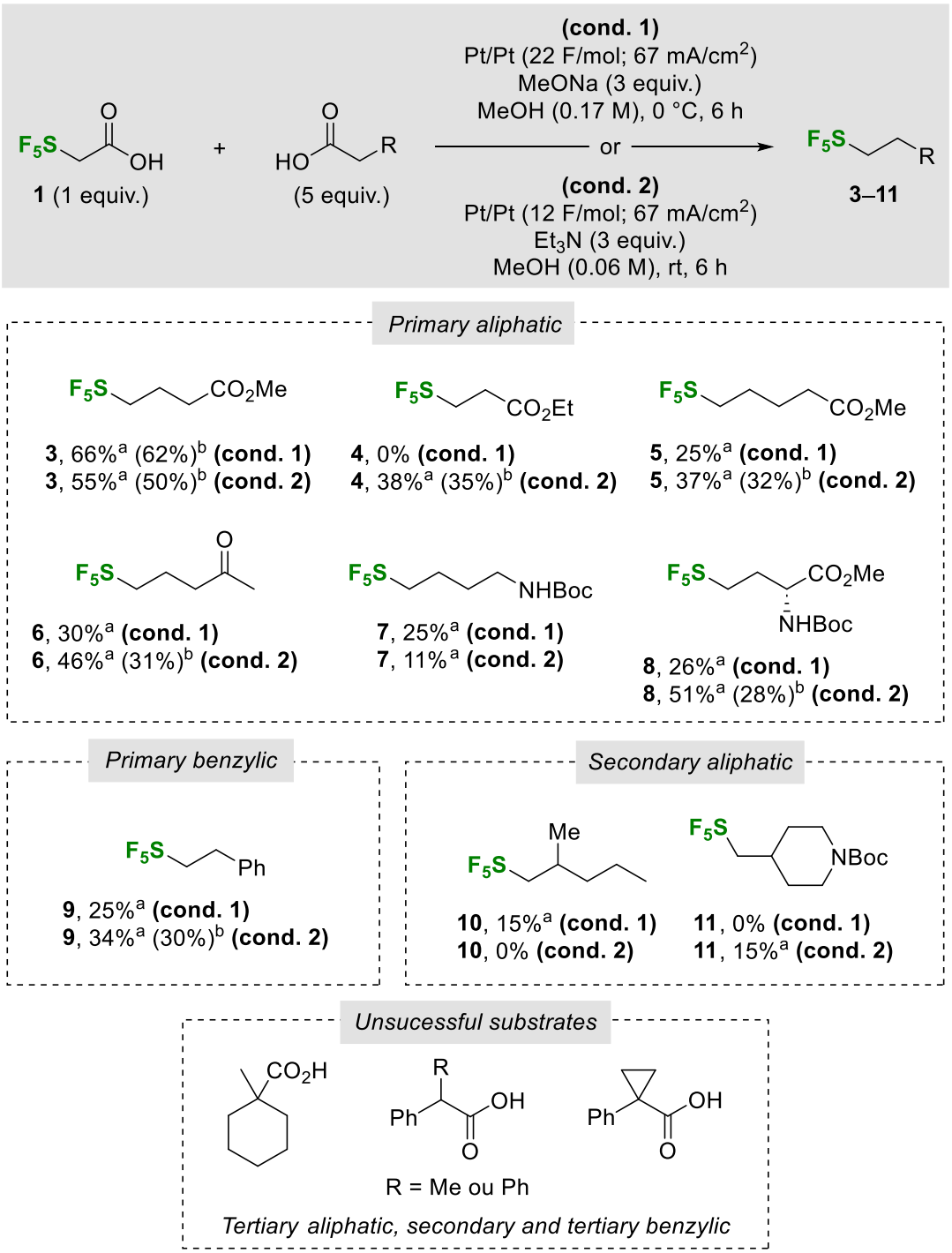
experiments (base, stoichiometry, solvent, intensities, current, concentration, temperature, electrolyte, etc.) [15]. Two sets of conditions with difference bases emerged as optimal ones. In conditions 1, MeONa is used as the base [**1** (1 equiv.), **2** (5 equiv.), MeONa (3 equiv.), MeOH (0.17 M), 0 °C for 6 h using Pt/Pt electrodes (22 F/mol @ 67 mA/cm^2)] whereas conditions 2 used Et_3N [**1** (1 equiv.), **2** (5 equiv.), Et_3N (3 equiv.), MeOH (0.06 M), rt for 6 h using Pt/Pt electrodes (12 F/mol @ 87 mA/cm^2)]. While many teams have tried to study the mechanism of the Kolbe reaction, its exact nature is still unknown. This also explains why a large amount of F is needed since the main side reaction is the anodic oxidation of the solvent, methanol [16].



Scheme 3. Optimization. [a] Estimated by NMR using 2-fluoro-4-nitrotoluene as an internal standard. [b] Isolated yield.

With the optimized conditions in hand, a series of alkyl-based carboxylic acids were submitted to the reaction (Scheme 4). Both the NMR yields and the isolated yields (when possible) are shown. In a few cases, purification proved problematic (mainly because of the presence of the homodimer of the aliphatic carboxylic acid) leading to considerably lower isolated yields than the NMR ones or even the impossibility to isolate the desired product. First, a series of primary aliphatic carboxylic acids aromatic were submitted to the reaction conditions. Using a carboxylic acid one carbon shorter than the model acid (*e.g.*, mono-ethyl malonate) gave no product under conditions 1, yet conditions 2 provided the coupling product **4** in 35% isolated yield. Extending the chain by one carbon (*e.g.*, mono-methyl glutarate) gave the product **5** in moderate NMR yields (25% under conditions 1 and 36% under conditions 2). Unfortunately, the desired product could not be separated from the homodimer. Replacing the methyl ester from monomethyl succinate by a methyl ketone (*i.e.*, levulinic acid) allowed the product **6** to be formed in moderate yields (30-46% by NMR). In this case, conditions 2 allowed product to be formed in a significant amount allowing for its isolation. Interestingly, a Boc-protected amine was tolerated and the corresponding product **7** was formed in low to moderate NMR yields (11-25%). Again, separation from the homodimer proved impossible. Notably, a suitably protected aspartic acid derivative could be used as a substrate for this transformation, providing the first SF_5-containing aliphatic amino acid **8** (26% by NMR under conditions 1 and 51% by NMR under conditions 2) [17]. The higher NMR yield obtained with conditions 2 allowed

product to be isolated in 28% yield. The use of a primary benzylic acid (*i.e.*, phenylacetic acid) was possible and provided compound **9** [10] in moderated yields. Secondary aliphatic carboxylic acid proved more problematic and only low NMR yields for compounds **10** and **11** were observed. Evaluation of tertiary aliphatic carboxylic acids, tertiary or secondary benzylic carboxylic acids showed that these substrates are not compatible with this reaction since no products were observed. Indeed, such substrates are known to easily get overoxidized into their corresponding stabilised carbocations via an Hofer-Moest type reaction.



Scheme 4. Scope of the reaction and limitations encountered. [a]Estimated by NMR using 2-fluoro-4-nitrotoluene as an internal standard. [b]Isolated yield.

3. Conclusion

In conclusion, we have reported a novel approach to the synthesis of aliphatic SF_5-compounds using a Kolbe-based reaction using 2-(pentafluoro-λ^6-sulfanyl)acetic acid, used as the "SF_5CH_2" source. Two sets of reaction conditions were developed on the model substrate, monomethyl succinate. However, upon evaluation of the scope of the reaction, severe limitations were noted. Nonetheless, the reaction proceeded in low to moderate yields (up to 62% isolated yield) for a total of nine examples. The evaluation of alternative reaction conditions for this strategy is underway and results will be reported in due course.

4. Experimental

4.1 General information

All reactions were carried out under an argon atmosphere with dry solvents. All commercially available compounds were used as received. SF_5Cl was purchased at SynQuest Labs inc. and was condensed at a known concentration in hexanes. This solution was then used for the SF_5Cl additions and could be stored for several months in a −35 °C freezer. Thin-layer chromatography (TLC) analysis of reaction mixtures was performed using Silicycle silica gel 60 Å F254 TLC plates, and visualized under UV or by staining with potassium permanganate. Flash column chromatography was carried out on Silicycle silica gel 60 Å, 230–400 mesh. ^1H, ^{13}C and ^{19}F NMR spectra were recorded in $CDCl_3$ at room temperature using an Agilent DD2 500 MHz or a Varian Inova 400 MHz spectrometer. ^1H and ^{13}C NMR chemical shifts are reported in ppm downfield of tetramethylsilane and are respectively referenced to tetramethylsilane (δ = 0.00 ppm) and residual solvent (δ = 77.16 ppm). For ^{19}F NMR, calibration was performed using a unified

scale [18]. Multiplicities are reported using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, sext = sextet, m = multiplet, bs = broad signal. NMR yields were determined using 2-fluoro-4-nitrotoluene as the internal standard. High-resolution mass spectra were obtained on a LC/MS–TOF Agilent 6210 using electrospray ionization (ESI). GC-MS analyses were performed on a Thermo Trace ULTRA GCMS equipped with an Agilent J&W HP-1 capillary column, an ITQ 900 mass selective detector (EI) or (CI) using the following method: 40 °C for 1 min then 10 °C/min until 330 °C. Infrared spectra were recorded using an ABB MB3000 FT-IR spectrometer. The melting points (m.p.) were recorded on a MPA100 apparatus using the following method: 40 °C to 200 °C at 2 °C/min.

4.2 Synthesis of the starting material

4.2.1 1-Chloro-2-(pentafluoro-λ^6-sulfanyle)ethyl acetate (S1)

In a flask was introduced vinyl acetate (2.0 mL, 21.7 mmol, 1 equiv.) and hexane (87 mL), which were then cooled down at –40 °C. SF_5Cl (36 mL, 0.89 M in hexane, 32.5 mmol, 1.5 equiv.) was added. Et_3B (2.0 mL, 1 M in THF, 2.17 mmol, 0.1 equiv.) was added dropwise. The mixture was stirred for 3 h at –40 °C and then warmed at room temperature. Saturated aqueous $NaHCO_3$ solution added, the layers were separated and the aqueous layer was extracted with Et_2O (3×). The combined organic layers were dried with $MgSO_4$ and concentrated under *vacuum* to afford **S1** as a colorless oil, which was used in the next step without any further purification. Analytical data were identical to those previously reported [13].

4.2.2 2-(Pentafluoro-λ^6-sulfanyle)ethan-1-ol (S2)

To a solution of crude **S1** in Et_2O (145 mL) at 0 °C was slowly added $LiAlH_4$ (21.7 mL, 1.0 M in Et_2O, 21.7 mmol, 1 equiv.). After 15 min, a saturated aqueous Rochelle salt solution was added, and the mixture was stirred for 1 h at room temperature. Extraction was made with Et_2O (3×), and the combined organic layers were dried with Na_2SO_4 and concentrated under *vacuum*. The crude alcohol was used in the next step without any further purification. Analytical data were identical to those previously reported [13].

4.2.3 2-(Pentafluoro-λ^6-sulfanyle)acetic acid (1)

To a solution of crude product **S2** in 58 mL of "wet" acetonitrile (containing 1% of H_2O) at 0 °C was added dropwise a solution of H_5IO_6 (9.3 g, 40.7 mmol, 3.5 equiv.) and CrO_3 (23.2 mg, 0.23 mmol, 0.02 equiv.) in "wet" acetonitrile (58 mL). The reaction was stirred at 0 °C for 2 h and then quenched with an aqueous solution of $Na_2HPO_4{\cdot}7H_2O$ (0.22 M). Extraction was made with Et_2O (3x), and the combined organic layers were dried with Na_2SO_4 and concentrated under *vacuo*. The crude SF_5-acetic acid **1** was purified by acid/base purification. The crude **1** was dissolved in Et_2O. A saturated solution of $NaHCO_3$ was added until pH ~ 7. The aqueous layer is then acidified by adding a solution of 3 M HCl until pH ~ 1. Extraction was made with Et_2O (3×), and the combined organic layers were dried with Na_2SO_4 and concentrated under *vacuo* to afford **1** (2.16 g, 11.6 mmol, 100 %) as a white/yellow powder with a distinctly unpleasant odor. M.p.: 64.1 – 65.7 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 10.52 (s, 1H), 4.35 (p, J = 7.5 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 167.2, 70.2 – 69.6 (p, J = 18 Hz); ^{19}F NMR (470 MHz, $CDCl_3$): δ 79.1 – 77.9 (m, 1F), 71.9 (dt, J = 149.3, 5.7 Hz, 4F); HRMS-ESI (–): m/z calcd for $C_2H_3F_5O_2S$ $[M+H]^+$ 186.9774 found 186.9732; IR (ATR, diamond): ν (cm^{-1}) = 3056, 2999, 1733, 1434, 1168, 827, 775.

4.3 General procedures for the Kolbe reaction

Optimized conditions A: In an ElectraSyn vial (5 mL) with a stirring bar was charged the 2-(pentafluoro-λ^6-sulfanyle)acetic acid (**1**) (0.54 mmol, 1 equiv.), the second carboxylic acid (2.69 mmol, 5 equiv), sodium methoxide (1.61 mmol, 3 equiv.) and methanol (3.2 mL, 0.17 M). ElectraSyn vial was equipped with two electrodes (Pt, Platinum foil, 5 mm wide, 4 cm length 1.5 cm of which emerged). After setting up the vial, the mixture was stirred roughly for 30 s. The reaction mixture was electrolyzed at 0 °C (electrolysis parameters: 50 mA, amount of charge 22 F/mol). After reaction completion, the ElectraSyn vial cap was removed and the electrodes were rinsed with methanol, which was combined with the crude mixture. The crude mixture was quenched by adding water. The crude mixture was extracted with dichloromethane (3×). The organic layer was concentrated *in vacuo*. The crude material was purified by column chromatography to afford the desired product.

Optimized conditions B: In an ElectraSyn vial (5 mL) with a stirring bar was charged the 2-(pentafluoro-λ^6-sulfanyle)acetic acid (**1**) (0.27 mmol, 1 equiv.), the second carboxylic acid (1.34 mmol, 5 equiv), triethylamine (0.81 mmol, 3 equiv.) and methanol (4.5 mL, 0.06 M). ElectraSyn vial was equipped with two electrodes (Pt, Platinum foiled, 5 mm wide, 4 cm length, 2.3 cm of which emerged). After setting up the vial, the mixture was stirred roughly for 30 s. The reaction mixture was electrolyzed at room temperature (electrolysis parameters: 100 mA, amount of charge 12 F/mol). After reaction completion, the ElectraSyn vial cap was removed and the electrodes were rinsed with methanol, which was combined with the crude mixture. The crude mixture was quenched by adding water. The crude mixture was extracted by dichloromethane (3×). The organic layer was concentrated

in vacuo. The crude material was purified by column chromatography to afford the desired product.

4.3.1 Methyl 4-(pentafluoro-λ^6-sulfanyle)butanoate (3)

Following Optimized conditions A on a 0.54 mmol scale of **1** and mono-methyl succinate, the crude was purified by flash column chromatography using hexane/EtOAc (90:10) to afford the title compound (76 mg, 62 %) as a colorless oil. Following Optimized conditions B on a 0.27 mmol scale of **1** and mono-methyl succinate, the crude was purified by flash column chromatography using hexane/EtOAc (90:10) to afford of the title compound (31 mg, 50 %) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 3.74 (dp, *J* = 16, 8.1 Hz, 2H), 3.71 (s, 3H), 2.44 (t, *J* = 7.1 Hz, 2H), 2.29 – 2.25 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 172.5, 70.9 (p, *J* = 13.6 Hz), 52.0, 31.8, 21.75 (p, *J* = 4.5 Hz); ^{19}F NMR (470 MHz, $CDCl_3$): δ (ppm) 85.30 – 84.07 (m, 1F), 64.28 (dt, *J* = 144.6, 8.1 Hz, 4F); GC-MS-EI m/z calcd for $C_5H_9F_5O_2S$ $[M+H]^+$ 229.03 found 229.07 (under all conditions tested for high-resolution mass spectra [ESI (+), ESI (–), APPI], no significant ion was detected); IR (ATR, diamond): ν (cm^{-1}) = 2960, 1735, 1439, 1203, 816.

4.3.2 Ethyl 3-(pentafluoro-λ^6-sulfaneyl)propanoate (4)

Following Optimized conditions A on a 0.54 mmol scale of **1** and 3-ethoxy-3-oxopropanoic acid, no desired product was afforded. Following Optimized conditions B on a 0.27 mmol scale of **1** and 3-ethoxy-3-oxopropanoic acid, the crude was purified by flash column chromatography using pentane/CH_2Cl_2 (60:40) to afford the title compound (22 mg, 35 %) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 4.21 (qd, *J* = 7.1, 0.6 Hz, 2H), 4.00 (hept, *J* = 7.8 Hz, 2H), 2.92 (t, *J* = 7.4 Hz, 2H), 1.29 (td, *J* = 7.1, 0.5 Hz, 3H); ^{13}C NMR

(126 MHz, $CDCl_3$): δ (ppm) 169.6, 66.4 (m), 61.4, 31.4 (p, *J* = 4.7 Hz), 14.1; ^{19}F NMR (470 MHz, $CDCl_3$): δ (ppm) 84.4 – 83.2 (m, 1F), 64.4 (dt, *J* = 145.5, 8.0 Hz, 4F); GC-MS-EI m/z calcd for $C_5H_9F_5O_2S$ $[M+H]^+$ 229.03 found 229.02 (under all conditions tested for high-resolution mass spectra [ESI (+), ESI (—), APPI], no significant ion was detected); IR (ATR, diamond): ν (cm^{-1}) = 2924, 2856, 1738, 1215, 839, 733.

4.3.3 Methyl 5-(pentafluoro-λ⁶-sulfanyle)pentanoate (5)

Following Optimized conditions A on a 0.54 mmol scale of **1** and 5-methoxy-5-oxopentanoic acid, the desired product was obtained in 25 % NMR yield. Following Optimized conditions B on a 0.27 mmol scale of **1** and 5-methoxy-5-oxopentanoic acid, the crude was purified by flash column chromatography using hexanes/EtOAc/CH_2Cl_2 (90:5:5) to afford of the title compound (21 mg, 32 %) as a colorless oil. ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 3.72–3.63 (m, 5H), 2.38 (t, *J* = 7.3 Hz, 2H), 2.01–1.94 (m, 2H), 1.69 (dt, *J* = 15.1, 7.4 Hz , 2H); ^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 173.2, 71.5 (p, *J* = 13.3 Hz), 51.8, 33.2, 25.8 (p, *J* = 4.1 Hz), 23.0; ^{19}F NMR (470 MHz, $CDCl_3$): δ (ppm) 85.6–84.4 (m, 1F), 64.0 (dt, *J* = 145.1, 8.0 Hz, 4F); GC-MS-CI m/z calcd for $C_6H_{11}F_5O_2S$ $[M+CH_2CH_3]^+$ 271.27 found 271.08 (under all conditions tested for high-resolution mass spectra [ESI (+), ESI (—), APPI], no significant ion was detected); IR (ATR, diamond): ν (cm^{-1}) = 2959, 2926, 2856, 1736, 818.

4.3.4 5-(Pentafluoro-λ⁶-sulfanyle)pentan-2-one (6)

Following Optimized conditions A on a 0.54 mmol scale of **1** and 4-oxopentanoic acid, the desired product was obtained in 30 % NMR yield. Following Optimized conditions B on a 0.27 mmol scale of **1** and 4-oxopentanoic acid, the crude was purified by flash column chromatography using hexane/EtOAc (70:30) to afford of the title compound (18.0 mg, 31 %) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 3.71 (dp, *J* = 16.3, 8.2 Hz, 2H), 2.58 (t, *J* = 6.9 Hz, 2H), 2.23–2.15 (m, 5H); ^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 206.5, 70.9 (p, *J* = 13.1 Hz), 40.9, 29.98, 20.4 (p, *J* = 4.3 Hz); ^{19}F NMR (470 MHz, $CDCl_3$): δ (ppm) 85.6 – 84.4 (m, 1F), 64.27 (dt, *J* = 144.5, 8.3 Hz, 4F); GC-MS-CI m/z calcd for $C_5H_9F_5O_2S$ $[M+H]^+$ 213.03 found 213.03 (under all conditions tested for high-resolution mass spectra [ESI (+), ESI (─), APPI], no significant ion was detected); IR (ATR, diamond): ν (cm^{-1}) = 2925, 1718, 1164, 912, 835, 733.

4.3.5 tert-Butyl (4-(pentafluoro-λ^6-sulfanyle)butyl)carbamate (7)

Following Optimized conditions A on a 0.54 mmol scale of **1** and 4-((*tert*-butoxycarbonyl)amino)butanoic acid, the desired product was obtained in 25 % NMR yield. Following Optimized conditions B on a 0.27 mmol scale of **1** and 4-((*tert*-butoxycarbonyl)amino)butanoic acid, the desired product was obtained in 11 % NMR yield. ^{19}F NMR (470 MHz, $CDCl_3$): δ (ppm) 84.2 – 83.0 (m, 1F), 63.7 (dt, *J* = 144.7, 7.6 Hz, 4F)

4.3.6 Methyl (S)-2-((tert-butoxycarbonyl)amino)-4-(pentafluoro-λ^6-sulfanyle)butanoate (8)

Following Optimized conditions A on a 0.54 mmol scale of **1** and (3*S*)-3-{[(tert-butoxy)carbonyl]amino}-4-methoxy-4-oxobutanoic acid, the desired product was obtained in 26 % NMR yield. Following Optimized conditions B on a 0.27 mmol scale of **1** and (3*S*)-3-{[(*tert*-butoxy)carbonyl]amino}-4-methoxy-4-oxobutanoic acid, the crude was purified by flash column chromatography using CH_2Cl_2 to afford of the title compound (26.1 mg, 28 %) as a white powder. M.p.: 61.1 – 61.4 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 5.13 – 5.11 (m, 1H), 4.35 – 4.31 (m, 1H), 3.80 (s, 3H), 3.75 – 3.64 (m, 1H), 2.57–2.49 (m, 1H), 2.21 (dddd, *J* = 13.8, 11.6, 8.7, 5.0 Hz, 1H), 1.45 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 171.6, 155.5, 80.7, 68.2, 52.9, 51.8, 29.6 (m), 28.2; ^{19}F NMR (470 MHz, $CDCl_3$): δ (ppm) 84.2 (p, *J* = 145.5 Hz, 1F), 64.8 (dt, *J* = 145.4, 8.0 Hz, 4F); HRMS-ESI m/z calcd for $C_{10}H_{18}F_5NO_4S$ $[M+H]^-$ 342.0842 found 342.0824; IR (ATR, diamond): ν (cm^{-1}) = 3364, 2986, 2935, 1757, 1686, 1512, 1155, 822.

4.3.7 Pentafluoro(phenethyl)-λ^6-sulfane (9)

Following Optimized conditions A on a 0.54 mmol scale of **1** and 2-phenylacetic acid, no desired product was afforded. Following Optimized conditions B on a 0.27 mmol scale of **1** and 2-phenylacetic acid the crude was purified by flash column chromatography using pentane/CH_2Cl_2 (90:10) to afford of the title compound (21 mg, 30 %) as a colorless oil. Analytical data were identical to those previously reported. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.35 – 7.25 (m, 3H), 7.22 – 7.19 (m, 2H), 3.92 – 3.82 (m, 2H), 3.25-3.21 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 136.7, 129.0, 128.6, 127.3, 72.8–72.4 (p, *J* = 12.1

Hz), 32.64 (m); ^{19}F NMR (470 MHz, $CDCl_3$): δ (ppm) 85.3 – 84.1 (m, 1F), 63.7 (dt, *J* = 145.3, 7.9 Hz, 4F); IR (ATR, diamond): ν (cm^{-1}) = 2945, 2829, 1444, 1413, 1012. Analytical data were identical to those previously reported [10].

4.3.8 Pentafluoro(2-methylpentyl)-λ^6-sulfane (10)

Following Optimized conditions A on a 0.54 mmol scale of **1** and 2-methylpentanoic acid, the desired product was obtained in 15 % NMR yield. Following Optimized conditions B on a 0.27 mmol scale of **1** and 2-methylpentanoic acid, no desired product was detected. ^{19}F NMR (470 MHz, $CDCl_3$): δ (ppm) ^{19}F NMR (470 MHz, CDCl3): δ (ppm) 81.8 – 80.7 (m, 1F), 60.0 (d, *J* = 150.5 Hz, 4F).

4.3.9 tert-Butyl 4-((pentafluoro-λ^6-sulfanyle)methyl)piperidine-1-carboxylate (11)

Following Optimized conditions A on a 0.54 mmol scale of **1** and 1-(*tert*-butoxycarbonyl)piperidine-4-carboxylic acid, no desired product was observed. Following Optimized conditions B on a 0.27 mmol scale of **1** and 1-(*tert*-butoxycarbonyl)piperidine-4-carboxylic acid, the desired product was obtained in 15 % NMR yield. ^{19}F NMR (470 MHz, $CDCl_3$): δ (ppm) 81.3 – 80.6 (m, 1F), 66.4 – 66.1 (m, 4F).

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