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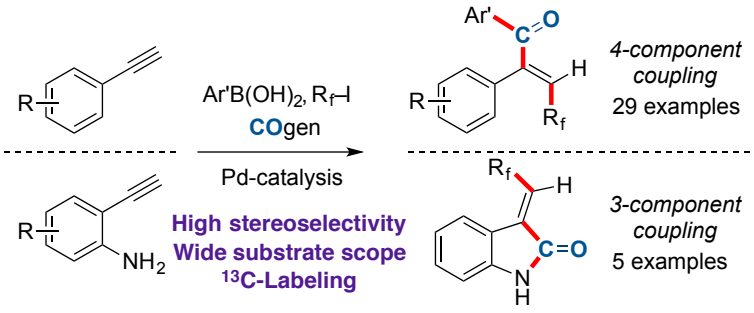
Access to Perfluoroalkyl-Substituted Enones and Indolin-2-ones via Multicomponent Pd-Catalyzed Carbonylative Reactions

Hongfei Yin and Troels Skrydstrup*

Carbon Dioxide Activation Center (CADIAC), Department of Chemistry and the Interdisciplinary Nanoscience Center, Aarhus University, Gustav Wieds Vej 14, 8000 Aarhus, Denmark.

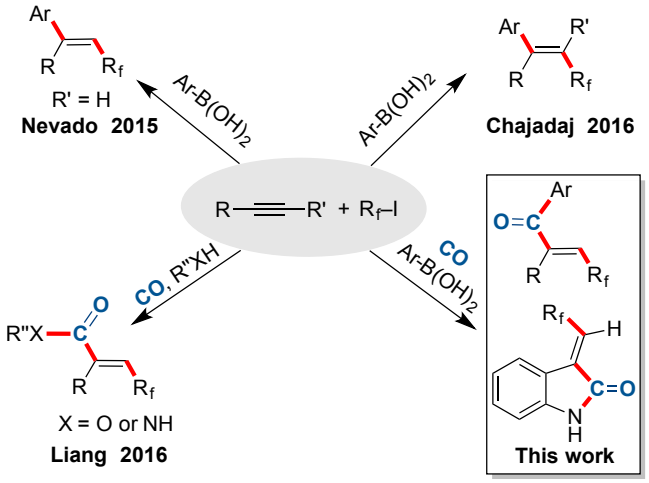
ts@chem.au.dk



ABSTRACT: A simple method for accessing perfluoroalkyl-substituted enones is described applying a four-component palladium-catalyzed carbonylative coupling of aryl boronic acids together with terminal alkynes and perfluoroalkyl iodides in the presence of carbon monoxide. A wide range of highly functionalized enones can thus be prepared in a single operation in good yields. With 2-aminophenylalkynes, an intramolecular aminocarbonylation event overrules providing the indolin-2-one framework. Finally, adaptation of the two-chamber technology expands the method to the synthesis of the aforementioned structures with ^{13}C-isotope-labeling.

The replacement of hydrogen with fluorine in bioactive molecules can produce significant beneficial effects in their biological properties including increased metabolic stability and lipophilicity.[1] Furthermore, the C–F group can operate as an isostere for other functional groups.[1c,2] As such considerable efforts are being made to develop new methodologies for constructing fluorine-containing molecules.[3] Amongst the plethora of such compounds, structures possessing perfluoroalkyl chains also exhibit unique properties such as hormonal effects,[4] and due to their low surface tension, they have also found utility in water-proof materials.[3d,5]

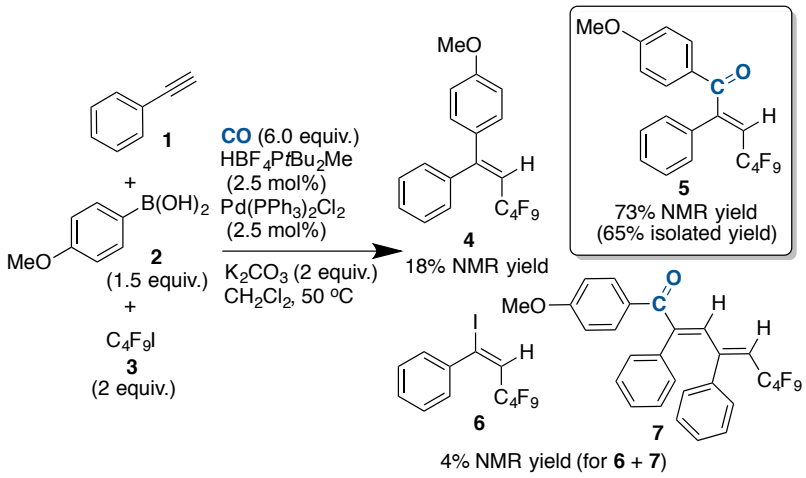
Scheme 1. Recent Examples of Pd-Catalyzed Perfluoroalkylation of Alkynes



The synthetic methods for obtaining perfluoroalkyl displaying compounds have been achieved through metal-mediated reactions with different metal sources by using commercially available perfluoroalkyl iodides or bromides.[6] Alternatively, ultrasound or peroxide can also promote such transformations involving intermediate perfluoroalkyl radicals.[3,7] In 2015, Nevado and coworkers reported the synthesis of perfluoroalkyl substituted alkenes applying a three component Pd-catalyzed transformation with perfluoroalkyl iodides, terminal alkynes and aryl boronic acids.[8] Recently, the scope of this transformation has been expanded to both terminal and internal alkynes by Chaładaj,

applying a palladium(0) pre-catalyst.[9] Moreover, both the aminocarbonylation and alkoxycarbonylation versions of this concept have been studied by Liang (Scheme 1).[10] However, at the time we started this project, a four-component carbonylative Suzuki-type coupling for this chemistry had not yet been investigated. Hence, with our interest in developing new Pd-catalyzed carbonylation reactions,[11] we explored the adaptation of the Nevado approach for the formation of perfluoroalkyl substituted enones *via* a Pd-catalyzed carbonylative Suzuki reaction in the presence of perfluoroalkyl iodides, aryl boronic acids and terminal alkynes.

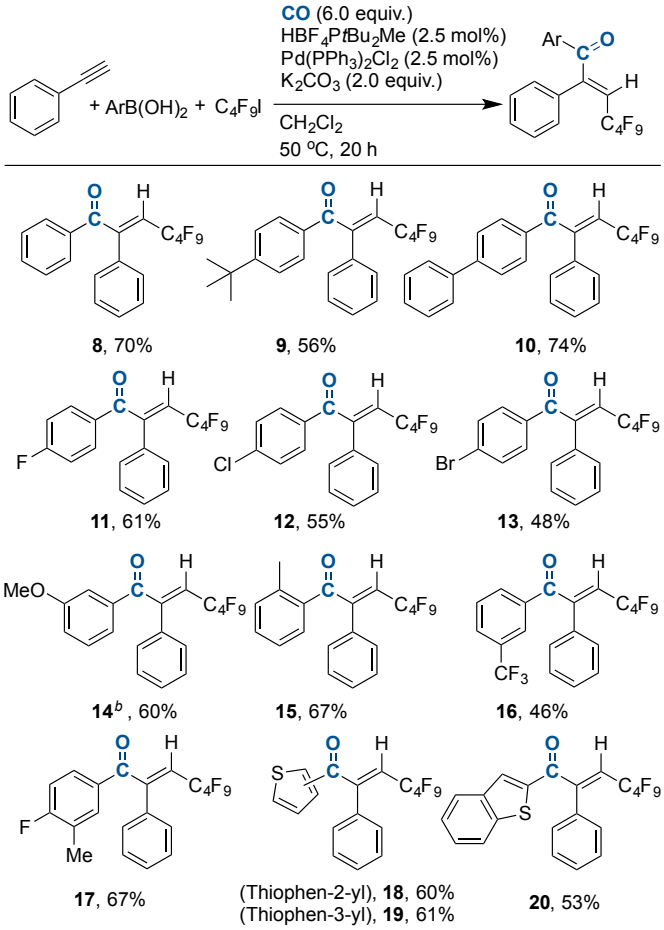
Scheme 2. Optimized Conditions for the Pd-Catalyzed Four-Component Carbonylative Coupling



In order to test this four-component strategy, we initiated a study using phenylacetylene (**1**), 1-(4-methoxyphenyl) boronic acid (**2**) and iodoperfluorobutane (**3**) applying our two-chamber technology as previously described.[11a] After an extensive optimization with respect to the catalyst composition (Pd source and ligand) and base, we finally settled on the reaction conditions illustrated in Scheme 2, with 6 equivalents of carbon monoxide from COgen, 2.0 equivalents of potassium carbonate, 2.5 mol% $Pd(PPh_3)_2Cl_2$ as the Pd source and 2.5 mol% of P*t*Bu_2Me as its HBF_4 salt in dichloromethane at 50 °C (see Supporting Information). This provided a 73% NMR yield of the desired ketone **5** as a colorless

syrup (65% isolated yield after column chromatography), in addition to **5**, the direct coupling product **4** was also obtained in an 18% NMR yield along with a small percentage of the alkenyl iodide **6** and dienone **7** involving the radical addition to two alkynes. The use of other boronic acid derivatives (such as ArBPin, $ArBF_3K$, etc) proved non-rewarding for this coupling transformation.

Scheme 3. Reaction Scope with Different Aryl Boronic Acids[a]



[a]Chamber A: Aryl boronic acid (0.33 mmol), alkyne (0.25 mmol), C_4F_9I (0.50 mmol), $Pd(PPh_3)_2Cl_2$ (2.5 mol%), HBF_4tBu_2MeP (2.5 mol%), K_2CO_3 (0.5 equiv.) in CH_2Cl_2 (1 mL). Chamber B: COgen (1.5 mmol), $Pd(COD)Cl_2$ (0.015 mmol), HBF_4tBu_3P (0.015 mmol), Cy_2NMe (3.0 mmol) in CH_2Cl_2 (3 mL). [b]5 μL of water was added.

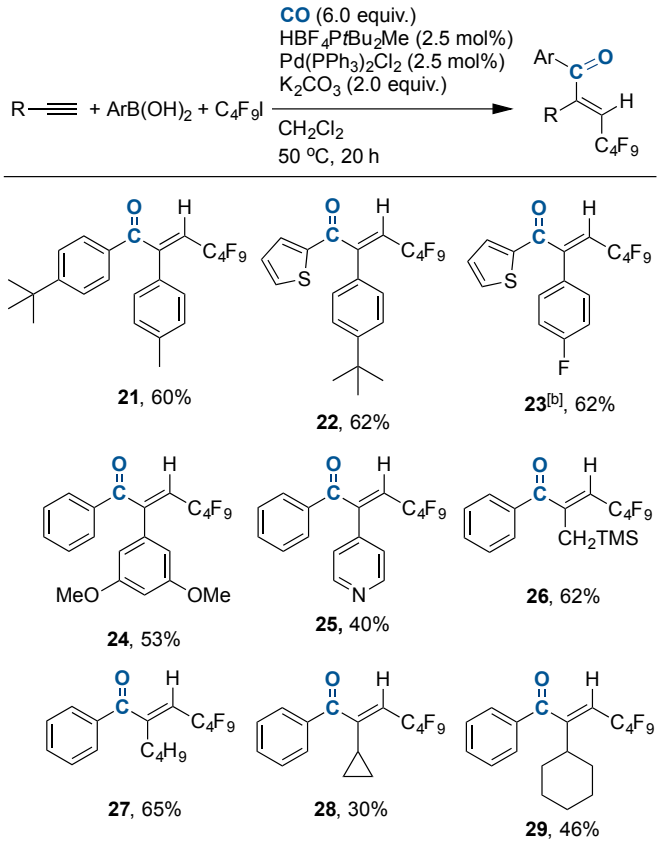
With these reaction conditions in hand favoring the four-component coupling product, we next investigated the scope and limitations of the reaction with different aryl boronic acids (Scheme 3). Generally, the products were obtained in moderate to good yields with the main byproduct represented

by the direct coupling product as illustrated in Scheme 2 with compound **4** in the range of 10–20%. Notably, both compounds could be easily separated from the by column chromatography. Utilizing phenyl boronic acid with phenyl acetylene and perfluorobutyl iodide enabled the formation of the corresponding enone **8** in a 70% yield. Phenyl boronic acids containing a *tert*-butyl or phenyl group on the *p*-position led to **9** and **10** in yields of 56% and 74%, respectively. Enones bearing a fluoride or chloride on the aromatic ring could also be formed in good yields (**11**, 61% and **12**, 55%). However, 4-bromophenyl boronic acid only afforded a 48% yield of **13**. Use of 3-methoxyphenyl boronic acid resulted in a similar yield of enone **14** to that of its 4-methoxy counterpart. Moreover, *o*-methyl substituted phenyl boronic acid proved compatible under these conditions, delivering its corresponding enone **15** in a 67% yield. *m*-Substituted phenyl boronic acids were tolerant as well to these reaction conditions as illustrated with compounds **16** and **17**. Other aryl boronic acids containing electron withdrawing-group such as 4-cyano, 4-CHO and 4-COOMe were tested under the optimal conditions, but all of them gave low conversion. On the other hand, some heteroaromatic boronic acids were converted smoothly to the enones, as shown with the thienyl and benzo[b]thien-2-yl boronic acids, giving yields ranging from 53% to 61% (compounds **18**–**20**).

Next our attention was turned to exploring various alkynes under the reaction conditions. As depicted in Scheme 4, phenylacetylenes bearing different functional groups on the aromatic ring could be incorporated with yields ranging from 53% to 62% (enones **21**–**24**). Employing 4-ethynylpyridine could give rise to enone **25** in a 40% isolated yield. Aliphatic substituted alkynes were also feasible being converted to their corresponding enones **26** and **27**, such as the one bearing $TMSCH_2$- and C_4H_9-substituents, in the yields of 62% and 65%, respectively. The enones carrying cycloaliphatic rings could also be obtained, though in decreased yields (compounds **28** 30% yield, and **29**, 46% yield). The reaction is nevertheless sluggish for internal alkynes. When 1-phenylpropyne was tested under our optimized conditions, only approximately 10% of the desired product could be obtained. The starting material remained.

Instead of employing C_4F_9I, other perfluoroalkyl iodides proved to be compatible with these Pd-catalyzed reaction conditions (Scheme 5). Enones **30**–**32** containing C_6F_{13}-, C_8F_{17}-, and $C_{10}F_{21}$- were synthesized in yields of 68%, 60% and 65%, respectively. Furthermore, ethyl α,α-difluoroiodoacetate revealed itself to also be a suitable coupling partner, providing enone **33** in a 55% yield.

Scheme 4. Reaction Scope with Different Alkynes [a]

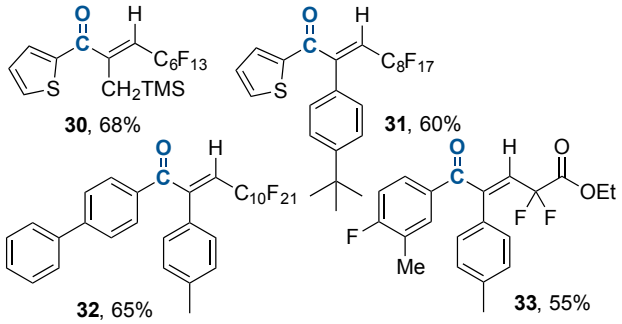


[a] Chamber A: Aryl boronic (0.33 mmol), alkyne (0.25 mmol), iodide (0.50 mmol), $Pd(PPh_3)_2Cl_2$ (2.5 mol%), HBF_4tBu_2MeP (2.5 mol%), K_2CO_3 (0.5 equiv.) in CH_2Cl_2 (1 mL). Chamber B: COgen (1.5 mmol), $Pd(COD)Cl_2$ (0.015 mmol), HBF_4tBu_3P (0.015 mmol), Cy_2NMe (3.0 mmol) in CH_2Cl_2 (3 mL). [b] 36 h.

Interestingly, when 2-ethynylaniline was treated under the coupling conditions, the desired enone product was not formed. Instead an indolin-2-one derivative **34** was obtained in a 48% isolated yield from an intramolecular aminocarbonylation event (Scheme 6). It was surprising to see that the presence of boronic acid was vital for this transformation. When no boronic acid was added to the reaction

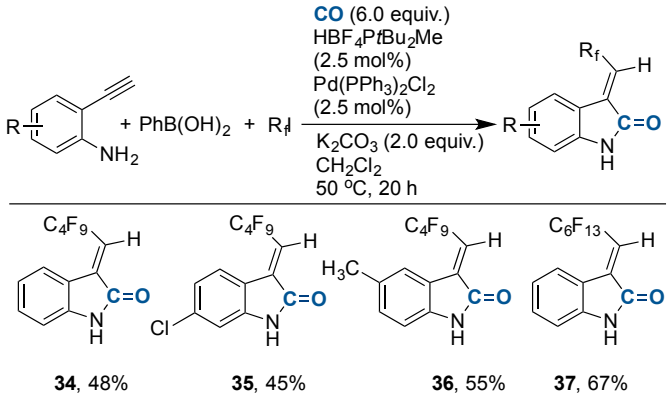
system, only trace amounts of the indolin-2-one could be detected from the ^{19}F-NMR spectrum of the crude reaction mixture. Switching the amount of boronic acid from 1.3 equivalents to 0.1 equivalents resulted in similar yields. Therefore, we assume that the role of the boronic acid might only be essential to facilitate the formation of the Pd(0) species. Next, several indolin-2-ones containing a perfluoroalkyl

Scheme 5. Reaction Scope with Different Perfluoroalkyl Iodides[a]



[a]Standard conditions were used as indicated in the footnote of Scheme 4.

Scheme 6. Synthesis of Indolin-2-one Derivatives[a]



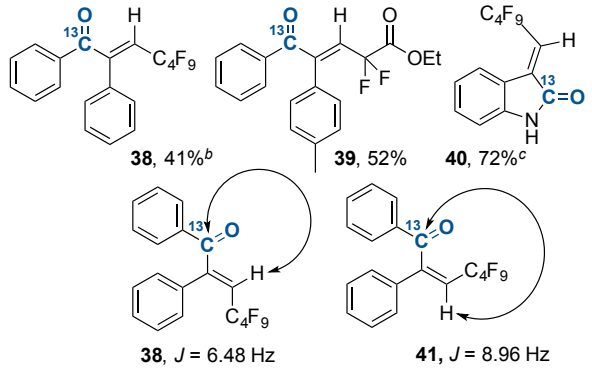
[a]Chamber A: Aryl boronic acid (0.025 mmol), alkyne (0.25 mmol), R_fI (0.75 mmol), $Pd(PPh_3)_2Cl_2$ (2.5 mol%), HBF_4tBu_2MeP (2.5 mol%), K_2CO_3 (0.5 equiv.) in CH_2Cl_2 (1 mL). Chamber B: COgen (2.5 mmol), $Pd(COD)Cl_2$ (0.025 mmol), HBF_4tBu_3P (0.025 mmol), Cy_2NMe (5.0 mmol) in CH_2Cl_2 (3 mL).

chain were synthesized. The corresponding heterocycles were obtained in good yields starting from 2-ethynylaniline derivatives with two examples, **35** and **36**, bearing a substituent on the phenyl ring, as shown in Scheme 6. $C_6F_{13}I$ was also a suitable substrate for this transformation, leading to the

formation of compound **37** in a 67% yield. Confirmation of the *E*-geometry of the double bond was obtained from the single crystal X-ray structure of **34** (see Supporting Information).

As a stable isotope, carbon-13 can be used as metabolic tracers.[12] By using ^{13}CO liberated from ^{13}C-labeled COgen, ^{13}C-isotopically labeled enones **38** and **39** and indolin-2-one **40** were formed under the coupling conditions (Figure 1). It is noteworthy that the double bond in enone **38** isomerized partially

Figure 1. ^{13}C-Labeled Enones Obtained Applying ^{13}C-COgen[a]

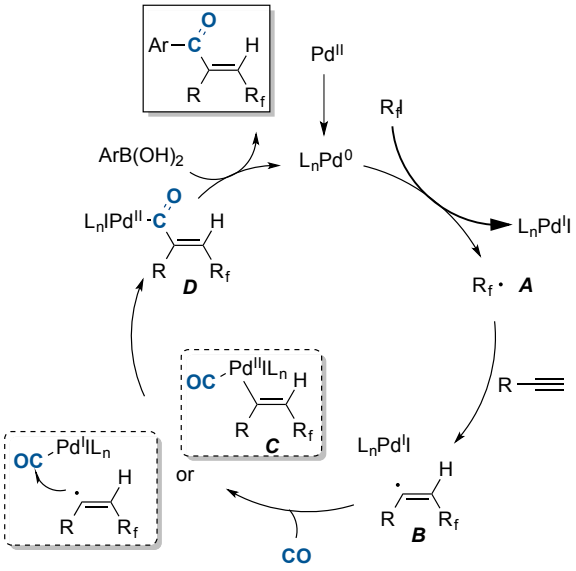


[a]Standard conditions were used as indicated in the footnote of Scheme 4. [b]3.0 equiv. of ^{13}CO was used. [c]Reaction performed on a 0.5 mmol scale with 3.0 equiv. of ^{13}CO.

to the *Z*-configuration in $CDCl_3$ after 3 days. By comparing the ^{1}H-NMR spectra for the ^{13}C-labeled enone **38**, we could clearly observe the protons on the double bond for both stereoisomers, as well as the ^{13}C-enriched carbons from the ^{13}C-NMR spectra. The coupling constant between the ^{13}C-labeled carbon and the alkenyl proton for the *E*-isomer is 6.48 Hz, while that the coupling constant for the newly formed isomer was observed to be 8.96 Hz. According to the literature, a larger coupling constant is generally observed when the proton is situated *trans* to the corresponding carbon atom.[13] This configuration was also confirmed by X-ray crystal structure analysis (see Supporting Information). Therefore, we can tentatively conclude that the main products obtained from the four-component coupling reaction possess the *E*-configuration.

A possible catalytic cycle for this transformation is proposed in Figure 2. Firstly, perfluoroalkyl iodide reacts with Pd(0)-species, generated from the Pd(II) precursor, via single electron transfer generating the perfluoroalkyl radical ***A***, together with a Pd(I) complex. Subsequent addition of ***A*** to the alkyne creates alkenyl radical ***B***. Combination of ***B*** with the Pd(I) complex provides an alkenyl Pd(II) species ***C***, which then follows the common carbonylative mechanism, involving the CO insertion step to acyl Pd complex ***D***, and then transmetallation with the aryl boronic acid and reductive elimination. Alkenyl

Figure 2. Possible Mechanistic Cycle for the Formation of Enones



radical ***B*** could also combine directly to a CO bound Pd(I) species providing directly the acyl Pd complex ***D***.[14]

In conclusion, a Pd-catalyzed four-component carbonylative route for accessing perfluoroalkyl enones has been demonstrated. Various aryl boronic acids, alkynes and perfluoroalkyl iodides revealed to be tolerant under the reaction conditions. Moreover, by using similar conditions, indolin-2-ones derivatives could be obtained from different 2-ethynylanilines through an intramolecular aminocarbonylation reaction. Finally, ^{13}C-labeled enones and indolin-2-ones were prepared by employing ^{13}C-labeled COgen.[15]

Experimental Section

General Methods. All the carbonylative reactions were carried out in a two-chamber system (COware) in a glovebox under argon. All other chemicals were used as received without further purification. Solvents were dried according to standard procedures and flash chromatography was carried out on silica gel 60 (230-400 mesh). The chemical shifts are reported in ppm relative to solvent residual peak. The ^{1}H NMR spectra were recorded at 400 MHz, ^{13}C NMR spectra were recorded at 100 MHz, ^{19}F NMR spectra were recorded at 376 MHz. NMR spectra are reported as follows (s = singlet, d = doublet, t = triplet, q = quartet, quin = quintuplet, sext = sextet, sep = septet, m = multiplet, br = broad, dd = double doublet, dt = double triplet, ddd = double double doublet; coupling constant(s) in Hz; integration). HRMS spectra were recorded on a LC TOF (ES) apparatus.

General Procedure for the Synthesis of Enones. ***Chamber A:*** To chamber A of the two-chamber system was added $Pd(PPh_3)_2Cl_2$ (4.4 mg, 0.0063 mmol, 0.025 equiv.), HBF_4P*t*Bu_2Me (1.6 mg, 0.0063 mmol, 0.025 equiv.), K_2CO_3 (69 mg, 0.5 mmol, 2.0 equiv.), boronic acid (0.33 mmol, 1.3 equiv.) followed by alkyne (0.25 mmol, 1.0 equiv.), perfluoroalkyl iodide (0.5 mmol, 2.0 equiv.), and CH_2Cl_2 (1.0 mL). ***Chamber B:*** To chamber B of the two-chamber system was added $Pd_2(dba)_3$ (13.7 mg, 0.015 mmol, 0.01 equiv.), HBF_4P(*t*Bu)$_3$ (4.4 mg, 0.015 mmol, 0.01 equiv.), COgen (362 mg, 1.5 mmol, 1.0 equiv.), CH_2Cl_2 (3.0 mL) and Cy_2NMe (642 μL, 3.0 mmol, 2.0 equiv.) in that order. Both chambers were sealed using a screw cap and a Teflon® coated silicone seal. The two-chamber system was removed from the glovebox and stirred at 50 °C for 20 h. The two-chamber system was then opened to air carefully and the crude mixture in chamber A was diluted with CH_2Cl_2. The combined organic layers were washed with brine, dried over Na_2SO_4 and filtered. The solvent was removed *in vacuo* and the title compound was obtained through flash column chromatography.

General Procedure for the Synthesis of Indolin-2-ones. ***Chamber A:*** To chamber A of the two-chamber system was added $Pd(PPh_3)_2Cl_2$ (4.4 mg, 0.0063 mmol, 0.025 equiv.), HBF_4P*t*Bu_2Me (1.6 mg, 0.0063 mmol, 0.025 equiv.), K_2CO_3 (69 mg, 0.5 mmol, 2.0 equiv.), phenylboronic acid (0.025 mmol, 0.1 equiv.) followed by alkyne (0.25 mmol, 1.0 equiv.), perfluoroalkyl iodide (0.75 mmol, 3.0 equiv.), and CH_2Cl_2 (1.0 mL). ***Chamber B:*** To chamber B of the two-chamber system was added $Pd_2(dba)_3$ (22.9 mg, 0.025 mmol, 0.01 equiv.), $HBF_4P(tBu)_3$ (6.8 mg, 0.025 mmol, 0.01 equiv.), COgen (602 mg, 2.5 mmol, 1.0 equiv.), CH_2Cl_2 (3.0 mL) and Cy_2NMe (1.07 mL, 5.0 mmol, 2.0 equiv.) in that order. Both chambers were sealed using a screw cap and a Teflon® coated silicone seal. The two-chamber system was removed from the glovebox and stirred at 50 °C for 20 h. The two-chamber system was then opened to air carefully and the crude mixture in chamber A was diluted with CH_2Cl_2. The combined organic layers were washed with brine, dried over Na_2SO_4 and filtered. The solvent was removed *in vacuo* and the title compound was obtained through flash column chromatography.

General Procedure for the Synthesis of Enones and Indolin-2-ones Labeled with ^{13}C-Carbon. ***Chamber A:*** To chamber A of the two-chamber system was added $Pd(PPh_3)_2Cl_2$ (8.8 mg, 0.013 mmol, 0.025 equiv.), HBF_4P*t*Bu_2Me (3.2 mg, 0.013 mmol, 0.025 equiv.), K_2CO_3 (138 mg, 1.0 mmol, 2.0 equiv.), phenylboronic acid (0.05 mmol, 0.1 equiv.) followed by alkyne (0.5 mmol, 1.0 equiv.), perfluoroalkyl iodide (1.5 mmol, 3.0 equiv.), and CH_2Cl_2 (2.0 mL). ***Chamber B:*** To chamber B of the two-chamber system was added $Pd_2(dba)_3$ (13.7 mg, 0.015 mmol, 0.01 equiv.), $HBF_4P(tBu)_3$ (4.4 mg, 0.015 mmol, 0.01 equiv.), ^{13}COgen (363 mg, 1.5 mmol, 1.0 equiv.), CH_2Cl_2 (3.0 mL) and Cy_2NMe (642 μL, 3.0 mmol, 2.0 equiv.) in that order. Both chambers were sealed using a screw cap and a Teflon® coated silicone seal. The two-chamber system was removed from the glovebox and stirred at 50 °C for 20 h. The two-chamber system was then opened to air carefully and the crude mixture in chamber A was diluted with CH_2Cl_2. The combined organic layers were washed with brine, dried over

Na_2SO_4 and filtered. The solvent was removed *in vacuo* and the title compound was obtained through flash column chromatography.

(*E*)-4,4,5,5,6,6,7,7,7-Nonafluoro-1-(4-methoxyphenyl)-2-phenylhept-2-en-1-one (5). Reaction using the general method followed by flash chromatography using pentane/CH_2Cl_2 2:1 as eluent resulted in 70 mg (61% yield) of the title product obtained as a yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 8.8 Hz, 2H), 7.43-7.33 (m, 5H), 6.96 (d, J = 8.8 Hz, 2H), 5.99 (t, J = 14.0 Hz, 1H), 3.86 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.8, 164.6, 152.9 (t, J = 4.5 Hz), 133.3, 132.8, 129.2, 128.3, 128.2 (t, J = 3.0 Hz), 127.7, 117.7 (t, J = 22.0 Hz), 114.3, 55.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ -81.0 (t, J = 11.0 Hz), -105.7 (t, J = 11.0 Hz), -123.7 (m), -125.7 (m). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{20}H_{14}F_9O_2$ 457.0850, found 457.0840.

(*E*)-4,4,5,5,6,6,7,7,7-Nonafluoro-1,2-diphenylhept-2-en-1-one (8).[15] Reaction using the general method followed by flash chromatography using pentane/CH_2Cl_2 2:1 as eluent resulted in 75 mg (70% yield) of the title product obtained as a colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 7.2 Hz, 2H), 7.61 (t, J = 8.0 Hz, 1H), 7.49 (t, J = 8.0 Hz, 2H), 7.42-7.35 (m, 5H), 6.05 (t, J = 14.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.2, 152.5 (t, J = 4.0 Hz), 135.1, 134.2, 133.0, 130.3, 129.2, 129.0, 128.4, 119.0 (t, J = 22.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -81.0 (m), -105.8 (t, J = 11.7 Hz), -123.6 (m), -125.7 (m). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{19}H_{12}F_9O$ $[M+H^+]$427.0744, found 427.0738.

(*E*)-1-(4-(*tert*-Butyl)phenyl)-4,4,5,5,6,6,7,7,7-nonafluoro-2-phenylhept-2-en-1-one (9). Reaction using the general method followed by flash chromatography using pentane/CH_2Cl_2 3:1 as eluent resulted in 67 mg (56% yield) of the title product obtained as a yellow liquid. ^{1}H NMR (400 MHz,

$CDCl_3$) δ 7.90 (d, J = 8.4 Hz, 2H), 7.51 (d, J = 8.4 Hz, 2H), 7.41-7.36 (m, 5H), 6.00 (t, J = 14.2 Hz, 1H), 1.34 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.8, 158.4, 133.1, 132.3, 130.3, 129.3, 128.3, 128.2 (t, J = 3.0 Hz), 126.0, 118.2 (t, J = 2.2 Hz), 35.5, 31.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ -81.0 (m), -105.8 (t, J = 11.0 Hz), -123.6 (m), -125.7 (m). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{23}H_{20}F_9O$ 483.1370, found 483.1367.

(*E*)-1-([1,1'-Biphenyl]-4-yl)-4,4,5,5,6,6,7,7,7-nonafluoro-2-phenylhept-2-en-1-one (10). Reaction using the general method followed by flash chromatography using pentane/CH_2Cl_2 2:1 as eluent resulted in 93 mg (74% yield) of the title product obtained as a colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 8.0 Hz, 2H), 7.71 (d, J = 8.4 Hz, 2H), 7.62 (d, J = 7.6 Hz, 2H), 7.48 (t, J = 7.6 Hz, 2H), 7.44-7.38 (m, 6H), 6.08 (t, J = 14.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.8, 152.6 (t, J = 4.5 Hz), 147.0, 139.6, 133.7, 133.0, 130.9, 129.3, 129.2, 128.7, 128.4, 128.3 (t, J = 3.0 Hz), 127.6, 127.5, 118.7 (t, J = 2.2 Hz). ^{19}F NMR (367 MHz, $CDCl_3$) δ -81.0 (m), -105.8 (t, J = 11.0 Hz), -123.6 (m), -125.7 (m). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{25}H_{16}F_9O$ 503.1057, found 503.1061.

(*E*)-4,4,5,5,6,6,7,7,7-Nonafluoro-1-(4-fluorophenyl)-2-phenylhept-2-en-1-one (11). Reaction using the general method followed by flash chromatography using pentane/CH_2Cl_2 5:1 as eluent resulted in 68 mg (61% yield) of the title product obtained as a yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (dd, J = 8.6, 5.4 Hz, 2H), 7.38 (s, 5H), 7.16 (t, J = 8.6 Hz, 2H), 6.04 (t, J = 14.1 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.6, 166.5 (d, J = 256.0 Hz), 152.4, 133.0, 132.9, 132.8, 131.4 (d, J = 2.9 Hz), 129.4, 128.5, 128.3 (t, J = 2.9 Hz), 118.8 (t, J = 22.1 Hz), 116.4, 116.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ -81.0 (t, J = 9.6 Hz), -102.8 (s), -105.8 (t, J = 12.2 Hz), -123.6 (m), -125.7 (m). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{19}H_{11}F_{10}O$ 445.0650, found 445.0640.

(*E*)-1-(4-Chlorophenyl)-4,4,5,5,6,6,7,7,7-Nonafluoro-2-phenylhept-2-en-1-one (12). Reaction using the general method followed by flash chromatography using pentane/CH_2Cl_2 3:1 as eluent resulted in 63 mg (55% yield) of the title product obtained as a yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 8.6 Hz, 2H), 7.45 (d, J = 8.6 Hz, 2H), 7.38 (s, 5H), 6.05 (t, J = 14.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.0, 152.3 (t, J = 4.5 Hz), 140.9, 133.4, 132.7, 131.5, 129.4, 129.3, 128.5, 128.4 (t, J = 3.0 Hz), 119.2 (t, J = 2.2 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -81.0 (t, J = 9.7 Hz), -105.8 (t, J = 12.1 Hz), -123.6 (m), -125.7 (m). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{19}H_{11}ClF_9O$ 461.0355, found 461.0355.

(*E*)-1-(4-Bromophenyl)-4,4,5,5,6,6,7,7,7-nonafluoro-2-phenylhept-2-en-1-one (13). Reaction using the general method followed by flash chromatography using pentane/CH_2Cl_2 5:1 as eluent resulted in 61 mg (48% yield) of the title product obtained as a yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 8.5 Hz, 2H), 7.62 (d, J = 8.5 Hz, 2H), 7.38 (s, 5H), 6.06 (t, J = 14.1 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.2, 152.2 (t, J = 4.4 Hz), 133.8, 132.7, 132.4, 131.6, 129.7, 129.4, 128.5, 128.4 (t, J = 2.4 Hz), 119.3 (t, J = 22.1 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -81.0 (t, J = 9.9 Hz), -105.8 (t, J = 12.1 Hz), -123.6 (m), -125.7 (m). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{19}H_{11}BrF_9O$ 506.9829, found 506.9826.

(*E*)-4,4,5,5,6,6,7,7,7-Nonafluoro-1-(3-methoxyphenyl)-2-phenylhept-2-en-1-one (14). Reaction using the general method followed by flash chromatography using pentane/CH_2Cl_2 5:1 as eluent resulted in 68 mg (60% yield) of the title product obtained as a yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, J = 7.6 Hz, 1H), 7.46 (s, 1H), 7.41-7.36 (m, 6H), 7.15 (dd, J = 8.2, 2.0, 1H), 6.05 (t, J = 14.2 Hz, 1H), 3.84 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.0, 160.1, 152.6 (t, J = 4.4 Hz), 136.3, 133.0, 129.9, 129.2, 128.4, 123.1, 121.0, 118.9 (t, J = 22.0 Hz), 114.0, 55.6. ^{19}F NMR (376 MHz,

$CDCl_3$) δ -81.0 (t, J = 9.8 Hz), -105.9 (t, J = 12.1 Hz), -123.6 (m), -125.7 (m). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{20}H_{14}F_9O_2$ 457.0850, found 457.0849.

(*E*)-4,4,5,5,6,6,7,7,7-Nonafluoro-2-phenyl-1-(*o*-tolyl)hept-2-en-1-one (15). Reaction using the general method followed by flash chromatography using pentane/CH_2Cl_2 5:1 as eluent resulted in 74 mg (67% yield) of the title product obtained as a yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, J = 7.5 Hz, 1H), 7.44-7.36 (m, 4H), 7.34-7.28 (m, 4H), 6.18 (t, J = 14.1 Hz, 1H), 2.50 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 196.9, 153.1(t, J = 4.0 Hz), 138.9, 135.8, 132.9, 132.0, 131.9, 130.0, 129.0, 128.6 (t, J = 2.4 Hz), 128.2, 125.7, 122.8 (t, J = 22.0 Hz), 20.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ -81.0 (m), -106.4 (t, J = 12.2 Hz), -123.7 (m), -125.8 (m). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{20}H_{14}F_9O$ 441.0901, found 441.0898.

(*E*)-4,4,5,5,6,6,7,7,7-Nonafluoro-2-phenyl-1-(3-(trifluoromethyl)phenyl)hept-2-en-1-one (16). Reaction using the general method followed by flash chromatography using pentane/CH_2Cl_2 7:1 as eluent resulted in 57 mg (46% yield) of the title product obtained as a yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 8.07 (d, J = 7.8 Hz, 1H), 7.84 (d, J = 7.8 Hz, 1H), 7.62 (t, J = 7.8 Hz, 1H), 7.42-7.34 (m, 5H), 6.12 (t, J = 14.0 Hz, 1H).^{13}C NMR (100 MHz, $CDCl_3$) δ 192.8, 151.9 (t, J = 4.0 Hz), 135.8, 133.2, 132.5, 131.7 (q, J = 33.4 Hz), 130.4 (q, J = 3.5 Hz), 129.7, 129.6, 128.6, 128.4 (t, J = 2.6 Hz), 126.9 (q, J = 3.8 Hz), 122.5 (q, J = 273.6 Hz), 120.1 (t, J = 22.3 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.1 (s), -81.0 (t, J = 11.2 Hz), -106.0 (t, J = 12.1 Hz), -123.7 (m), -125.7 (m). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{20}H_{11}F_{12}O$ 495.0618, found 495.0612.

(*E*)-4,4,5,5,6,6,7,7,7-Nonafluoro-1-(4-fluoro-3-methylphenyl)-2-phenylhept-2-en-1-one (17). Reaction using the general method followed by flash chromatography using pentane/CH_2Cl_2 5:1 as

eluent resulted in 77 mg (67% yield) of the title product obtained as a yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J = 7.2 Hz, 1H), 7.79-7.73 (m, 1H), 7.42-7.35 (m, 5H), 7.09 (t, J = 8.8 Hz, 1H), 6.03 (t, J = 14.1 Hz, 1H), 2.32 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 193.0, 165.1(d, J = 254.5 Hz), 152.5 (t, J = 4.2 Hz), 134.0 (d, J = 6.8 Hz), 132.9, 131.1 (d, J = 3.3 Hz), 130.4 (d, J = 9.6 Hz), 129.3, 128.4, 128.3 (t, J = 2.5 Hz), 126.2 (d, J = 18.1 Hz), 118.7 (t, J = 22.2 Hz), 115.7 (d, J = 24.1 Hz), 14.7 (d, J = 3.3 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -81.0 (t, J = 9.8 Hz), -105.8 (t, J = 12.2 Hz), -106.9 (s), -123.7 (m), -125.7 (m). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{20}H_{13}F_{10}O$ 459.0807, found 459.0807.

(*E*)-4,4,5,5,6,6,7,7,7-Nonafluoro-2-phenyl-1-(thiophen-2-yl)hept-2-en-1-one (18). Reaction using the general method followed by flash chromatography using pentane/CH_2Cl_2 5:1 as eluent resulted in 65 mg (60% yield) of the title product obtained as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 4.8 Hz, 1H), 7.58 (d, J = 3.7 Hz, 1H), 7.40 (s, 5H), 7.13 (t, J = 4.8 Hz, 1H), 6.26 (t, J = 14.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.8, 152.0 (t, J = 4.4 Hz), 142.2, 136.5, 135.7, 132.9, 129.4, 128.7, 128.6 (t, J = 2.5 Hz), 128.4, 119.2 (t, J = 21.9 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -81.0 (m), -106.0 (t, J = 12.2 Hz), -123.5 (m), -125.7 (m). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{17}H_{10}F_9OS$ 433.0309, found 433.0305.

(*E*)-4,4,5,5,6,6,7,7,7-Nonafluoro-2-phenyl-1-(thiophen-3-yl)hept-2-en-1-one (19). Reaction using the general method followed by flash chromatography using pentane/CH_2Cl_2 5:1 as eluent resulted in 66 mg (60% yield) of the title product obtained as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02-7.90 (m, 1H), 7.54 (dd, J = 5.1, 0.8 Hz, 1H), 7.39 (s, 5H), 7.34 (dd, J = 5.1, 2.9 Hz, 1H), 6.21 (t, J = 14.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.4, 152.8 (t, J = 4.6 Hz), 140.0, 135.7, 133.1, 129.3, 128.5 (t, J = 2.8 Hz), 128.4, 128.1, 127.2, 119.0 (t, J = 21.8) Hz. ^{19}F NMR (376 MHz, $CDCl_3$) δ -81.0

(t, J = 9.9 Hz), -105.9 (t, J = 12.2 Hz), -123.6 (m), -125.7 (m). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{17}H_{10}F_9OS$ 433.0309, found 433.0305. Mp 60–61 ^oC.

(*E*)-1-(Benzo[b]thiophen-2-yl)-4,4,5,5,6,6,7,7,7-nonafluoro-2-phenylhept-2-en-1-one (20). Reaction using the general method followed by flash chromatography using pentane/CH_2Cl_2 2:1 as eluent resulted in 64 mg (53% yield) of the title product obtained as a colorless liquid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.88 (q, J = 4.0 Hz, 2H), 7.80 (s, 1H), 7.50 (t, J = 8.0 Hz, 1H), 7.46-7.42 (m, 6H), 6.33 (t, J = 14.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.4, 151.7 (t, J = 4.0 Hz), 143.6, 141.7, 138.9, 133.3, 132.8, 129.5, 128.6 (t, J = 3.0 Hz), 128.5, 128.4, 126.7, 125.5, 123.1, 119.5 (t, J = 22.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -81.0 (m), -105.9 (t, J = 11.7 Hz), -123.5 (m), -125.7 (m). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{21}H_{12}F_9OS$ 483.0465, found 483.0459.

(*E*)-1-(4-(*tert*-Butyl)phenyl)-4,4,5,5,6,6,7,7,7-nonafluoro-2-(*p*-tolyl)hept-2-en-1-one (21). Reaction using the general method followed by flash chromatography using pentane/CH_2Cl_2 3:1 as eluent resulted in 74 mg (60% yield) of the title product obtained as a yellow liquid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 8.4 Hz, 2H), 7.50 (d, J = 8.4 Hz, 2H), 7.29 (d, J = 8.0 Hz, 2H), 7.18 (d, J = 8.0 Hz, 2H), 5.97 (t, J = 14.3 Hz, 1H), 2.35 (s, 3H), 1.34 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.0, 158.3, 153.0 (t, J = 4.4 Hz), 139.3, 132.4, 130.3, 130.2, 129.1, 128.3 (t, J = 3.0 Hz), 126.0, 117.6 (t, J = 2.2 Hz), 35.4, 31.1, 21.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ -81.0 (m), -105.6 (t, J = 12.2 Hz), -123.6 (m), -125.9 (m). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{24}H_{22}F_9O$ 497.1527, found 497.1522.

(*E*)-2-(4-(*tert*-Butyl)phenyl)-4,4,5,5,6,6,7,7,7-nonafluoro-1-(thiophen-2-yl)hept-2-en-1-one (22). Reaction using the general method followed by flash chromatography using pentane/CH_2Cl_2 3:1 as eluent resulted in 76 mg (62% yield) of the title product obtained as a yellow liquid. ^1H NMR (400

MHz, $CDCl_3$) δ 7.74 (d, J = 4.0 Hz, 1H), 7.60 (d, J = 4.0 Hz, 1H), 7.40 (d, J = 8.4 Hz, 2H), 7.34 (d, J = 8.4 Hz, 2H), 7.13 (t, J = 4.4 Hz, 1H), 6.19 (t, J = 14.4 Hz, 1H), 1.32(s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.3, 152.7, 152.2 (t, J = 4.5 Hz), 142.4, 136.4, 135.7, 129.8, 128.7, 128.3 (t, J = 2.4 Hz), 125.3, 118.3 (t, J = 21.7 Hz), 34.9, 31.3. ^{19}F NMR (376 MHz, $CDCl_3$) δ -81.0 (m), -105.8 (t, J = 12.2 Hz), -123.6 (m), -125.7 (m). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{21}H_{18}F_9OS$ 489.0935, found 489.0930.

(*E*)-4,4,5,5,6,6,7,7,7-Nonafluoro-2-(4-fluorophenyl)-1-(thiophen-2-yl)hept-2-en-1-one (23). Reaction using the general method for 36h followed by flash chromatography using pentane/CH_2Cl_2 5:1 as eluent resulted in 70 mg (62% yield) of the title product obtained as a yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 4.8 Hz, 1H), 7.61 (d, J = 4.0 Hz, 1H), 7.39 (m, 2H), 7.15 (t, J = 4.4 Hz, 1H), 7.09 (t, J = 8.8 Hz, 2H), 6.27 (t, J = 14.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.7, 163.5 (d, J = 248.0 Hz), 151.0 (t, J = 4.6 Hz), 142.0, 136.7, 135.7, 130.6 (dt, J = 8.4, 2.5 Hz), 128.8, 128.7, 119.8 (t, J = 21.9 Hz), 115.7, 115.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ -81.0 (m), -106.0 (t, J = 12.2 Hz), -111.5 (s), -123.6 (m), -125.7 (m). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{17}H_9F_{10}OS$ 451.0214, found 451.0209.

(*E*)-2-(3,5-Dimethoxyphenyl)-4,4,5,5,6,6,7,7,7-nonafluoro-1-phenylhept-2-en-1-one (24). Reaction using the general method followed by flash chromatography using pentane/CH_2Cl_2 2:1 as eluent resulted in 64 mg (52% yield) of the title product obtained as a yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 7.6 Hz, 2H), 7.61 (t, J = 7.6 Hz, 1H), 7.49 (t, J = 7.6 Hz, 2H), 6.54 (d, J = 1.8 Hz, 2H), 6.46 (d, J = 2.0 Hz, 1H), 6.01 (t, J = 14.0 Hz, 1H), 3.78 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.8, 160.5, 152.4 (t, J = 4.0 Hz), 134.8, 134.4, 134.1, 130.1, 128.8, 118.6 (t, J = 22.1 Hz), 106.5,

101.1, 55.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ -81.0 (m), -106.0 (t, J = 12.2 Hz), -123.6 (m), -125.7 (m). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{21}H_{16}F_9O_3$ 487.0956, found 487.0956.

(*E*)-4,4,5,5,6,6,7,7,7-Nonafluoro-1-phenyl-2-(pyridin-4-yl)hept-2-en-1-one (25). Reaction using the general method followed by flash chromatography using CH_2Cl_2/EtOAc 30:1 as eluent resulted in 43 mg (40% yield) of the title product obtained as a yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68-8.58 (m, 2H), 7.92 (d, J = 7.6 Hz, 2H), 7.75 (d, J = 8.0 Hz, 1H), 7.65 (t, J = 7.4 Hz, 1H), 7.53 (t, J = 7.6 Hz, 2H), 7.34 (dd, J = 7.6, 4.8 Hz, 1H), 6.20 (t, J = 14.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.5, 150.2, 148.6 (m), 135.9, 134.7, 134.5, 130.2, 129.2, 123.1, 121.9 (t, J = 22.1 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -81.0 (m), -106.0 (t, J = 12.2 Hz), -123.5 (m), -125.7 (m). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{18}H_{11}F_9NO$ 428.0697, found 428.0696.

(*Z*)-4,4,5,5,6,6,7,7,7-Nonafluoro-1-phenyl-2-((trimethylsilyl)methyl)hept-2-en-1-one (26). Reaction using the general method followed by flash chromatography using pentane/CH_2Cl_2 5:1 as eluent resulted in 68 mg (62% yield) of the title product obtained as a yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 7.6 Hz, 2H), 7.61 (t, J = 7.4 Hz, 1H), 7.49 (t, J = 7.6 Hz, 2H), 5.75 (t, J = 15.2 Hz, 1H), 2.32 (t, J = 3.2 Hz, 2H), 0.07 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.8, 152.9 (t, J = 4.0 Hz), 135.6, 133.6, 130.0, 128.8, 117.8 (t, J = 22.9 Hz), 21.7, 0.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -81.0 (m), -106.5 (t, J = 12.4 Hz), -124.1 (s), -125.8 (m). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{17}H_{18}F_9OSi$ 437.0983, found 437.0981.

(*E*)-2-Butyl-4,4,5,5,6,6,7,7,7-nonafluoro-1-phenylhept-2-en-1-one (27). Reaction using the general method followed by flash chromatography using pentane/CH_2Cl_2 3:1 as eluent resulted in 66 mg (65% yield) of the title product obtained as a yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 7.6

Hz, 2H), 7.62 (t, *J* = 7.6 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 2H), 5.80 (t, *J* = 14.8 Hz, 1H), 2.72 (t, *J* = 7.2 Hz, 2H), 1.48-1.32 (m, 4H), 0.89 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.7, 154.5 (t, *J* = 4.6 Hz), 135.9, 133.9, 129.9, 128.9, 120.4 (t, *J* = 24.0 Hz), 30.6, 29.2, 22.9, 13.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ -81.1 (m), -107.2 (t, *J* = 12.3 Hz), -124.1 (m), -125.8 (m). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{17}H_{16}F_9O$ 407.1057, found 407.1055.

(*E*)-2-Cyclopropyl-4,4,5,5,6,6,7,7,7-nonafluoro-1-phenylhept-2-en-1-one (28). Reaction using the general method followed by flash chromatography using pentane/CH_2Cl_2 5:1 as eluent resulted in 29 mg (30% yield) of the title product obtained as a yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 7.6 Hz, 2H), 7.63 (t, *J* = 7.6 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 2H), 5.52 (t, *J* = 15.2 Hz, 1H), 2.28-2.14 (m, 1H), 0.96 (q, *J* = 6.8 Hz, 2H), 0.75 (q, *J* = 5.2 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.2, 156.0 (t, *J* = 5.0 Hz), 135.5, 134.5, 130.1, 129.0, 115.6 (t, *J* = 24.3 Hz), 11.3 (t, *J* = 4.0 Hz), 8.1. ^{19}F NMR (376 MHz, $CDCl_3$) δ -81.0 (m), -106.3 (m), -124.0 (m), -125.7 (m). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{16}H_{12}F_9O$ 391.0744, found 391.0741.

(*E*)-2-cyclohexyl-4,4,5,5,6,6,7,7,7-Nonafluoro-1-phenylhept-2-en-1-one (29). Reaction using the general method followed by flash chromatography using pentane/CH_2Cl_2 5:1 as eluent resulted in 50 mg (46% yield, E/Z = 10:1) of the title product obtained as a yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 7.6 Hz, 2H), 7.62 (t, *J* = 7.6 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 2H), 5.47 (t, *J* = 15.2 Hz, 1H), 2.95 (t, *J* = 11.8 Hz, 1H), 1.82-1.63 (m, 5H), 1.46-1.06 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.2, 158.9 (t, *J* = 4.2 Hz), 136.2, 134.2, 130.2, 128.9, 116.0 (t, *J* = 23.9 Hz), 40.8, 31.6, 26.3, 25.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -81.0 (m), -106.2 (m), -124.0 (m), -125.7 (m). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{19}H_{18}F_9O$ 433.1214, found 433.1209.

(*Z*)-4,4,5,5,6,6,7,7,8,8,9,9,9-Tridecafluoro-1-(thiophen-2-yl)-2((trimethylsilyl)methyl)non-2-en-1-one (30). Reaction using the general method followed by flash chromatography using pentane/CH_2Cl_2 5:1 as eluent resulted in 92 mg (68% yield) of the title product obtained as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J = 4.8 Hz, 1H), 7.66 (d, J = 3.6 Hz, 1H), 7.18 (t, J = 4.8 Hz, 1H), 5.94 (t, J = 15.0 Hz, 1H), 2.30 (t, J = 3.2 Hz, 2H), 0.04 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 188.6, 153.0 (t, J = 4.5 Hz), 142.1, 135.9, 134.8, 128.5, 116.3 (t, J = 23.2 Hz), 22.0, -1.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ -80.9 (m), -106.2 (t, J = 12.8 Hz), -121.6 (s), -122.9 (s), -123.1 (m), -126.1 (m). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{17}H_{16}F_{13}OSSi$ 543.0484, found 543.0479.

(*E*)-2-(4-(*tert*-Butyl)phenyl)-4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoro-1-(thiophen-2-yl)undec-2-en-1-one (31). Reaction using the general method followed by flash chromatography using pentane/CH_2Cl_2 3:1 as eluent resulted in 103 mg (60% yield) of the title product obtained as a yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 4.8 Hz, 1H), 7.59 (d, J = 3.6 Hz, 1H), 7.40 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 8.4 Hz, 2H), 7.13 (t, J = 4.4 Hz, 1H), 6.19 (t, J = 14.2 Hz, 1H), 1.32 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 186.3, 152.7, 152.2 (t, J = 4.4 Hz), 142.4, 136.4, 135.7, 129.8, 128.7, 128.3 (t, J = 2.3 Hz), 125.3, 118.5 (t, J = 21.9 Hz), 34.9, 31.3. ^{19}F NMR (376 MHz, $CDCl_3$) δ -80.8 (t, J = 10.1 Hz), -105.6 (t, J = 13.1 Hz), -121.3 (s), -121.9 (s), -122.6 (m), -122.7 (m), -126.1 (m). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{25}H_{18}F_{17}OS$ 689.0807, found 689.0807.

(*E*)-1-([1,1'-Biphenyl]-4-yl)-4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,12,12,13,13,13-henicosafluoro-2-(*p*-tolyl)tridec-2-en-1-one (32). Reaction using the general method followed by flash chromatography using pentane/CH_2Cl_2 3:1 as eluent resulted in 133 mg (65% yield) of the title product obtained as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 8.4 Hz, 2H), 7.71 (d, J = 8.4 Hz, 2H), 7.63 (d, J = 7.2 Hz, 2H), 7.48 (t, J = 7.2 Hz, 2H), 7.42 (t, J = 7.2 Hz, 1H), 7.35 (d, J = 8.0 Hz, 2H), 7.20 (d, J =

8.0 Hz, 2H), 6.07 (t, *J* = 14.2 Hz, 1H), 2.36 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.0, 152.9 (t, *J* = 4.6 Hz), 146.9, 139.7, 139.4, 133.8, 130.9, 130.1, 129.2, 128.7, 128.4, 127.6, 127.5, 118.2 (t, *J* = 22.0 Hz), 118.0, 21.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ -80.9 (t, *J* = 9.9 Hz), -105.4 (t, *J* = 13.0 Hz), -121.4 (s), -121.8 (m), -121.9 (m), -122.6 (s), -122.8 (s), -126.2 (s). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{32}H_{18}F_{21}O$ 817.1022, found 817.1023. Mp 86–87 ^{o}C.

Ethyl (*E*)-2,2-Difluoro-5-(4-fluoro-3-methylphenyl)-5-oxo-4-(*p*-tolyl)pent-3-enoate (33). Reaction using the general method followed by flash chromatography using pentane/EtOAc 20:1 as eluent resulted in 52 mg (55% yield, E/Z = 26 :1) of the title product obtained as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.4 Hz, 1H), 7.75 (s, 1H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 7.06 (t, *J* = 8.8 Hz, 1H), 6.17 (t, *J* = 11.3 Hz, 1H), 3.99 (q, *J* = 7.1 Hz, 2H), 2.34 (s, 3H), 2.31 (s, 3H), 1.18 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.8, 164.8 (d, *J* = 255.3 Hz), 162.9 (t, *J* = 33.3 Hz), 149.0 (t, *J* = 8.4 Hz), 140.0, 134.0 (d, *J* = 6.8 Hz), 131.9 (d, *J* = 3.4 Hz), 130.5 (d, *J* = 9.5 Hz), 130.2, 129.2, 128.9 (t, *J* = 2.0 Hz), 125.8 (d, *J* = 29.1 Hz), 125.7 (d, *J* = 52.4 Hz), 115.5 (d, *J* = 23.1 Hz), 112.1 (t, *J* = 241.7 Hz), 63.3, 21.4, 14.7 (d, *J* = 3.3 Hz), 13.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ -92.9 (s), -107.7 (s). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{21}H_{20}F_3O_3$ 377.1365, found 377.1369.

(*E*)-3-(2,2,3,3,4,4,5,5,5-Nonafluoropentylidene)indolin-2-one (34). Reaction using the general method for the synthesis of indolin-2-ones followed by flash chromatography using pentane/EtOAc 5:1 as eluent resulted in 44 mg (48% yield) of the title product obtained as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.29 (s, 1H), 7.72 (d, *J* = 7.8 Hz, 1H), 7.35 (t, *J* = 7.8 Hz, 1H), 7.05 (t, *J* = 7.8 Hz, 1H), 6.92 (d, *J* = 7.8 Hz, 1H), 6.74 (t, *J* = 16.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.5, 143.9, 137.6 (t, *J* = 4.6 Hz), 133.1, 127.4 (t, *J* = 9.1 Hz), 123.4, 119.0 (t, *J* = 26.0 Hz), 118.6 (t, *J* = 2.1 Hz), 111.1.

^{19}F NMR (376 MHz, $CDCl_3$) δ -81.0 (m), -108.4 (s), -123.9 (s), -125.7 (s). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{13}H_7F_9NO$ 364.0384, found 364.0379. Mp 84–85 ^{o}C.

(*E*)-6-Chloro-3-(2,2,3,3,4,4,5,5,5-nonafluoropentylidene)indolin-2-one (35). Reaction using the general method for the synthesis of indolin-2-ones followed by flash chromatography using pentane/EtOAc 6:1 as eluent resulted in 48 mg (48% yield) of the title product obtained as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (s, 1H), 7.63 (d, J = 8.4 Hz, 1H), 7.04 (dd, J = 8.4, 1.6 Hz, 1H), 6.94 (d, J = 1.6 Hz, 1H), 6.75 (t, J = 16.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.9, 144.6, 139.2, 136.2 (t, J = 5.5 Hz), 128.3 (t, J = 9.4 Hz), 123.6, 119.4 (t, J = 27.7 Hz), 117.0, 111.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ -80.9 (m), -108.4 (m), -123.9 (m), -125.6 (m). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{13}H_6ClF_9NO$ 397.9994, found 397.9990. Mp 158–159 ^{o}C.

(*E*)-5-Methyl-3-(2,2,3,3,4,4,5,5,5-nonafluoropentylidene)indolin-2-one (36). Reaction using the general method for the synthesis of indolin-2-ones followed by flash chromatography using pentane/EtOAc 6:1 as eluent resulted in 52 mg (55% yield) of the title product obtained as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.52 (s, 1H), 7.16 (d, J = 8.0 Hz, 1H), 6.78 (d, J = 8.0 Hz, 1H), 6.71 (t, J = 17.0 Hz, 1H), 2.33 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.1, 141.4, 133.6, 132.8, 127.9 (t, J = 9.0 Hz), 118.8 (m), 118.5 (m), 110.6, 21.3. ^{19}F NMR (376 MHz, $CDCl_3$) δ -80.9 (m), -108.2 (t, J = 11.2 Hz), -123.9 (dt, J = 14.7, 7.3 Hz), -125.6 (m). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{14}H_9F_9NO$ 378.0540, found 378.0543. Mp 108–109 ^{o}C.

(*E*)-3-(2,2,3,3,4,4,5,5,6,6,7,7,7-Tridecafluoroheptylidene)indolin-2-one (37).

Reaction using the general method for the synthesis of indolin-2-ones followed by flash chromatography using pentane/EtOAc 6:1 as eluent resulted in 78 mg (67% yield) of the title product

obtained as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 7.73 (d, J = 7.8 Hz, 1H), 7.35 (t, J = 7.8 Hz, 1H), 7.06 (t, J = 7.8 Hz, 1H), 6.91 (d, J = 7.8 Hz, 1H), 6.75 (t, J = 16.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.0, 164.7, 143.7, 133.1, 127.4 (t, J = 9.4 Hz), 123.4, 119.1 (t, J = 26.3 Hz), 118.6 (t, J = 2.3 Hz), 110.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -80.8 (t, J = 9.7 Hz), -108.1 (m), -121.4 (s), -122.9 (s), -123.0 (m), -126.1 (m). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{15}H_7F_{13}NO$ 464.0320, found 464.0315. Mp 112–113 ^{o}C.

^{13}C-(*E*)-4,4,5,5,6,6,7,7,7-Nonafluoro-1,2-diphenylhept-2-en-1-one (38). Reaction using the general method, while with ^{13}COgen 3.0 equiv. followed by flash chromatography using pentane/CH_2Cl_2 3:1 as eluent resulted in 44 mg (41% yield) of the title product obtained as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (dd, J = 7.4, 4.0 Hz, 2H), 7.61 (t, J = 7.4 Hz, 1H), 7.49 (t, J = 7.6 Hz, 2H), 7.41-7.36 (m, 5H), 6.05 (dt, J = 14.1, 6.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.1, 152.4 (dt, J = 48.7, 5.1 Hz), 134.9 (d, J = 55.9 Hz), 134.1, 132.8, 129.1, 128.9 (d, J = 4.3 Hz), 128.2, 118.9 (dt, J = 21.8, 2.9 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -81.0 (t, J = 9.8 Hz), -105.8 (t, J = 12.1 Hz), -123.6 (m), -125.7 (m). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{18}{}^{13}CH_{12}F_9O$ 428.0778, found 428.0779.

Ethyl 5-^{13}C-(*E*)-2,2-Difluoro-5-oxo-5-phenyl-4-(*p*-tolyl)pent-3-enoate (39). Reaction using the general method, while with ^{13}COgen 6.0 equiv. followed by flash chromatography using pentane/CH_2Cl_2 3:1 as eluent resulted in 45 mg (52% yield, E/Z = 10:1) of the title product obtained as a brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (dd, J = 7.4, 4.0 Hz, 2H), 7.61 (t, J = 7.4 Hz, 1H), 7.49 (t, J = 7.6 Hz, 2H), 7.27 (d, J = 8.0 Hz, 2H), 7.19 (d, J = 80 Hz, 2H), 6.23 (dt, J = 11.3, 6.5 Hz, 1H), 4.01 (q, J = 7.1 Hz, 2H), 2.36 (s, 3H), 1.21 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.1, 171.0, 166.7, 165.9, 162.9 (t, J = 33.4 Hz), 149.0 (d, J = 50.4 Hz), 139.4, 136.1, 135.6, 133.8, 130.3 (d, J = 3.0 Hz), 129.2, 129.0 (d, J = 1.8 Hz), 128.8 (d, J = 4.1 Hz), 126.1 (dt, J = 28.6, 3.0 Hz), 112.1 (d, J

= 6.8 Hz), 63.3, 21.4, 13.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ -93.3 (s). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{19}{}^{13}CH_{19}F_2O_3$ 346.1336, found 346.1341.

2-^{13}C-(*E*)-3-(2,2,3,3,4,4,5,5,5-Nonafluoropentylidene)indolin-2-one (40). Reaction using the general method for 0.5 mmol scale with ^{13}COgen, followed by flash chromatography using pentane/EtOAc 6:1 as eluent resulted in 136 mg (72% yield) of the title product obtained as a yellow powder. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.40 (s, 1H), 7.71 (d, *J* = 7.8 Hz, 1H), 7.34 (t, *J* = 7.7 Hz, 1H), 7.05 (t, *J* = 7.7 Hz, 1H), 6.93 (d, *J* = 7.8 Hz, 1H), 6.74 (dt, *J* = 16.8, 7.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.6, 165.3, 143.9 (d, *J* = 6.6 Hz), 137.6 (dt, *J* = 57.2, 5.6 Hz), 133.1, 127.4 (dt, *J* = 13.0, 6.4 Hz), 123.4, 119.0 (dt, *J* = 25.9, 3.0 Hz), 118.6 (dt, *J* = 7.1, 2.1 Hz), 111.1 (d, *J* = 4.2 Hz).^{19}F NMR (376 MHz, $CDCl_3$) δ -81.0 (m), -108.4 (t, *J* = 11.6 Hz), -123.9 (m), -125.7 (m). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{12}{}^{13}CH_7F_9NO$ 365.0417, found 365.0411. Mp 83–84 ^{o}C.

ASSOCIATED CONTENT

Supporting Information

Description of COware, optimization tables, copies of ^{1}H, ^{13}C and ^{19}F NMR spectrums for all compounds and X-ray structures and data for compounds **19** and **34**. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

* ts@chem.au.dk

Notes

Troels Skrydstrup is co-owner of SyTracks Aps, which commercializes the two-chamber technology and COgen.

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