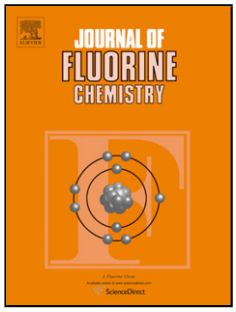

Title: Structure-dependent selective *O*- or *C*-trifluoroethylation of 1,3-dicarbonyls by mesityl(2,2,2-trifluoroethyl)iodonium triflate

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Structure-dependent selective *O*- or *C*-trifluoroethylation of 1,3-dicarbonyls by mesityl(2,2,2-trifluoroethyl)iodonium triflate

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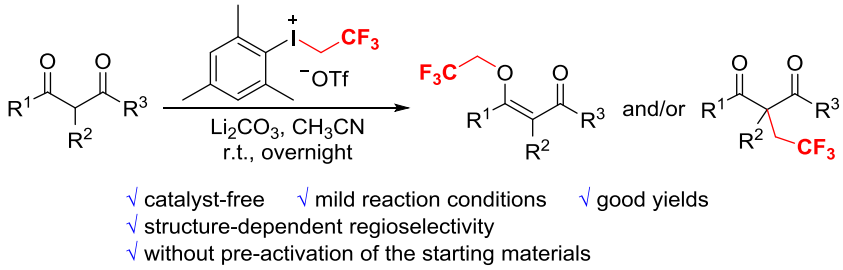
Graphic abstract



Highlights

- A catalyst-free structure-dependent regioselective trifluoroethylation is described.
- Cyclic 1,3-diketones exclusively afforded the *O*-trifluoroethylated products.
- Acyclic 1,3-dicarbonyls selectively formed the *C*-trifluoroethylated products.
- Li_2CO_3 facilitated the *C*-trifluoroethylation of acyclic 1,3-dicarbonyls.
- The reaction avoided pre-activation of 1,3-dicarbonyls and use of strong base.

Abstract

Reaction of [$ArICH_2CF_3$][OTf] with structurally diversified 1,3-dicarbonyls and an appropriate base at room temperature gave *O*-trifluoroethylated products, *C*-trifluoroethylated products, or a mixture of *O*- and *C*-trifluoroethylated products in good yields. The product type was dramatically dependent upon the structure of the starting 1,3-dicarbonyls in this reaction. The cyclic 1,3-diketones exclusively afforded the *O*-trifluoroethylated products, whereas the acyclic 1,3-diketones, *β*-keto esters, and malonates selectively or specifically formed the *C*-trifluoroethylated products. Li_2CO_3 facilitated the *C*-trifluoroethylation of acyclic 1,3-diketones and *β*-keto esters.

The reaction proceeded under mild conditions, without pre-activation of 1,3-dicarbonyls and use of strong base, and demonstrated a catalyst-free structure-dependent regioselective trifluoroethylation of 1,3-dicarbonyls by mesityl(2,2,2-trifluoroethyl)iodonium triflate.

Keywords: (2,2,2-trifluoroethyl)iodonium; trifluoroethylation; 1,3-dicarbonyls; structure-dependent

Introduction

Fluorine-containing functionalities have been widely used to modify the conformation, stability, basicity, and intrinsic properties of organic molecules [1]. Fluorinated analogues of pharmaceutically relevant compounds usually possess properties conducive to drug development, such as improved lipophilicity, metabolic stability, and bioavailability compared to their non-fluorinated counterparts [2a]. The incorporation of fluorine atom(s) into the target molecules has become a general strategy for pharmaceutical research and drug development [2]. Among various fluorine-containing molecules, trifluoroethylated compounds are of great interest for their applications in medicinal chemistry and materials science [2,3]. A growing number of trifluoroethyl-containing compounds with biological activities, such as antimalarial activity, hypolipidemic activity, anesthetic property, anti-inflammatory activity, and enzyme inhibition ability, have been developed [4]. Because the naturally occurring pathway is lacking, chemists have to search for reagents and trifluoroethylation methods to prepare these molecules [5]. The direct carbon- and heteroatom-CH_2CF_3 bond formation has attracted much attention [5]. The transition metal-mediated/catalyzed or transition metal-free trifluoroethylation of organic scaffolds, such as arylboronic acids or esters, aryl iodides, arene, alkynes, alkenes, anilines, and aryl Grignard reagents, have been successfully established [5,6]. Reagents that were efficient for these reactions include CF_3CH_2I or CF_3CH_2OTs, CF_3CHN_2 or $CF_3CH_2NH_2$, CF_3CHCl_2, $(CF_3CH_2SO_2)_2Zn$, $CF_3CH_2SO_2Cl$, CF_3CO_2H, and aryl(2,2,2-trifluoroethyl)iodonium salts ($[ArICH_2CF_3]X$) [5-7].

Aryl(2,2,2-trifluoroethyl)iodoniums, first synthesized by Umemoto and later modified by DesMarteau and Novák, has proved to be highly efficient electrophilic trifluoroethylation reagents for heteroatom and carbon nucleophiles such as amines, peptides, alcohols, phenols, thiols, sulfides, carbohydrates, thioglycosides, fatty acids, phosphines, and electron-rich arenes [8]. These reactions proceeded smoothly under

catalyst-free conditions to form the pivotal *N*-CH_2CF_3, *O*-CH_2CF_3, *S*-CH_2CF_3, *P*-CH_2CF_3, and *C*-CH_2CF_3 bonds for a variety of bioactive molecules, and also demonstrated that [ArICH_2CF_3]X (Ar = C_6H_5, 2,4,6-$(CH_3)_3C_6H_2$; X = OTf, NTf_2) possess much more powerful trifluoroethylation ability than other CF_3CH_2 transfer reagents. Recently, the palladium-catalyzed reactions of aryl(2,2,2-trifluoroethyl)iodonium triflates with anilides, aromatic amides, and indoles via C-H activation or with arylboronic acids via Suzuki-Miyaura cross-coupling have been explored [9], which represent the state-of-the-art transition metal-catalyzed trifluoroethylation methods using [ArICH_2CF_3]X as the CF_3CH_2 source.

The preliminary reaction of carbanions with [PhICH_2CF_3][OTf] was notified by Umemoto and coworkers, wherein [PhICH_2CF_3][OTf] reacted with the sodium salt of diethyl methylmalonate or a silyl enol ether to afford the corresponding *C*-trifluoroethylated product in a very low yield [10a]. Later, reaction of trimethylsilyl enol ethers with [PhICH_2CF_3][OTf] in the presence of KF at room temperature provided *β*-trifluoromethyl carbonyl derivatives in moderate to good yields [10b]. The reaction happened specifically at the *α*-carbon sites of carbonyls. Recently, Shen and coworkers disclosed that 3,3-dimethyl-1-(perfluoroethyl)-1,3-dihydro-1λ^3-benzo[d][1,2]iodaoxole (BIX-C_2F_5) reacted with *β*-keto esters at room temperature in the presence of DBU or K_2CO_3 to give *α*-pentafluoroethylated *β*-keto esters in good yields; pentafluoroethylation occurred at the tertiary active methine group of 1,3-dicarbonyls [11]. Interestingly, we found in this work that the reaction of [ArICH_2CF_3][OTf] with 1,3-dicarbonyls gave specifically *O*-trifluoroethylated or *C*-trifluoroethylated products, which was dramatically dependent upon the structure of 1,3-dicarbonyls.

At the beginning, the reaction of cyclohexane-1,3-dione (**1a**) and mesityl(2,2,2-trifluoroethyl)iodonium triflate (**2a**) was chosen as the model reaction to optimize the reaction conditions. Treatment of **1a** with **2a** (1.5 equiv) in CH_2Cl_2 in the presence of K_2CO_3 (2.0 equiv) at room temperature overnight furnished 3-(2,2,2-trifluoroethoxy)cyclohex-2-en-1-one (**3a**) in 61% yield, as a sole product. This initial result was much different from the previous reports that silyl enol ethers reacted with [PhICH_2CF_3][OTf] providing only *α*-trifluoroethyled carbonyl derivatives [10]. The choice of solvent had a significant influence on the reaction. Acetonitrile appeared to be the best solvent among CH_2Cl_2, CH_3CN, THF, DMF, and

DMSO (entries 1-5, Table 1), as the reaction performed in CH_3CN yielded 75% of **3a**. Other bases such as K_3PO_4, Li_2CO_3, $NaHCO_3$, and Cs_2CO_3 were also suitable agents for the *O*-trifluoroethylation of **1a** (entries 6-9, Table 1). Li_2CO_3 was found to be a better choice, which gave **3a** in 89% yield (entry 10, Table 1). Decreasing the equivalents of Li_2CO_3 from 2.0 to 1.5 equiv lead to **3a** in 99% yield (entry 11, Table 1). Using phenyl(2,2,2-trifluoroethyl)iodonium triflate $[PhICH_2CF_3][OTf]$ (**2b**) instead of **2a** in the same reaction afforded **3a** in a slightly lower isolated yield (entry 12, Table 1).

With the optimized reaction conditions in hand (**1** / **2a** (1.5 equiv) / Li_2CO_3 (1.5 equiv) / CH_3CN / r.t. / N_2 / overnight), various cyclic 1,3-diketones were examined (Table 2). Complex cyclohexane-1,3-diones (**1b-o**) reacted with $[MesICH_2CF_3][OTf]$ in the presence of Li_2CO_3 to afford exclusively the *O*-trifluoroethylated products (**3b-o**) in good yields. The transformation did not require any strong base that is harmful to mesityl(2,2,2-trifluoroethyl)iodonium triflate or process that is usually used for pre-activation of 1,3-dicarbonyls [10,11]. Substituents such as methyl, phenyl, allyl, benzyl, cyclohexylmethyl, and cinnamyl groups at the 2- and/or 5-position of cyclohexane-1,3-diones had a little influence on the reaction. Substrates bearing benzyl groups at the 2-positions, with either electron-withdrawing or -donating functionalities on the phenyl rings, gave comparable yields of the desired products. In the case of **3e** and **3g**, the reaction using K_2CO_3 instead of Li_2CO_3 led to higher yields of the products. Furthermore, reactions of cyclopentane-1,3-dione and its derivatives (**1p-r**) with **2a** under the standard conditions furnished the *O*-trifluoroethylated products (**3p-r**) in good yields. Nevertheless, cycloheptane-1,3-dione (**1s**) reacted with **2a** in the same conditions providing **3s** only in 6% isolated yield, and most of **1s** was recovered. Replacement of Li_2CO_3 with the stronger bases such as KOH and LiOH in the same reaction failed to improve the yield of **3s**.

The acyclic 1,3-dicarbonyl compounds were also tested in this reaction (Table 3). Treatment of methyl 1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**1t**) with **2a** (2.0 equiv) in the presence of Li_2CO_3 (1.5 equiv) and 4Å MS (100 mg) for 24 h provided a mixture of methyl 3-(2,2,2-trifluoroethoxy)-1*H*-indene-2-carboxylate (**3t**, 18%) and

methyl 1-oxo-2-(2,2,2-trifluoroethyl)-2,3-dihydro-1*H*-indene-2-carboxylate (**3t'**, 46%). The *C*-trifluoroethylated compound was obtained as the major product. Addition of 4Å MS to the reaction mixture facilitated the trifluoroethylation (see SI). Taking Cs_2CO_3 instead of Li_2CO_3, the yield of **3t** was promoted and the formation of **3t'** was somewhat inhibited. Similar phenomena were also observed when using 1,3-diphenylpropane-1,3-dione (**1v**) as substrate in the reaction, which formed a mixture of (*Z*)-1,3-diphenyl-3-(2,2,2-trifluoroethoxy)prop-2-en-1-one (**3v**, 19%) [12] and 1,3-diphenyl-2-(2,2,2-trifluoroethyl)propane-1,3-dione (**3v'**, 69%) in the presence of Li_2CO_3, with the *C*-trifluoroethylated product (**3v'**) being predominant. These results indicated that Li_2CO_3 benefited the *C*-trifluoroethylation, which might be attributed to the strong interaction between the Li^+ cation and the oxygen atoms of **1t** or **1v** [13]. This hypothesis was further proved by the observations that reaction of **1v** and **2a** with a mixture of Li_2CO_3/15-crown-5 or [*n*-Bu_4N][OH]•$30H_2O$ gave a higher percentage of *O*-trifluoroethylated product (**3v**) than that using Li_2CO_3 without extra Li^+ cation trap.

In addition, the reaction of methyl 5,6-dimethoxy-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**1u**) or 1-(4-methoxyphenyl)-3-phenylpropane-1,3-dione (**1w**) with **2a** and Li_2CO_3 provided the *C*-trifluoroethylated product (**3u'** or **3w'**) in 43% or 31% isolated yield (Table 3). The corresponding *O*-trifluoroethylated products were likely formed in these reactions according to the ^{19}F NMR analysis of the reaction mixtures; however, they couldn't be isolated due to their formation in trace amounts. Furthermore, the reaction of 1-phenylbutane-1,3-dione (**1x**) or 1-phenylpentane-1,3-dione (**1y**) with [MesICH_2CF_3][OTf] under the standard conditions gave 1-phenyl-2-(2,2,2-trifluoroethyl)butane-1,3-dione (**3x'**) in 68% yield or 1-phenyl-2-(2,2,2-trifluoroethyl)pentane-1,3-dione (**3y'**) in 56% (or 65%) yield. Treatment of excess diethyl malonate (**1z**) or dibenzyl malonate (**1aa**) with **2a** in the presence of KOH and 4Å MS (100 mg) supplied mono *C*-trifluoroethylated product (**3z'** or **3aa'**) in 42% or 51% yield. Since malonates are less acidic than 1,3-diones or *β*-keto esters [14], the stronger base (KOH) was necessary to accomplish the reaction.

In conclusion, we have found that reaction of [ArICH_2CF_3][OTf] with structurally diversified 1,3-dicarbonyls under mild basic conditions gave *O*-trifluoroethylated products, *C*-trifluoroethylated products, or a mixture of *O*- and *C*-trifluoroethylated

products in good yields. The product distribution was dramatically dependent upon the structure of 1,3-dicarbonyls. The cyclic 1,3-diketones exclusively yielded the *O*-trifluoroethylated products, while the acyclic 1,3-diketones, *β*-keto esters, and malonates selectively or specifically constructed the *C*-trifluoroethylated compounds. The use of Li_2CO_3 as base facilitated the *C*-trifluoroethylation of acyclic 1,3-diketones and *β*-keto esters. This mild and simple reaction demonstrated a structure-dependent regioselective *O*- or *C*-trifluoroethylation of 1,3-dicarbonyls by mesityl(2,2,2-trifluoroethyl)iodonium triflate without any pre-activation of the starting materials.

Experimental

1. General considerations

All reactions were carried out under a nitrogen atmosphere. Unless otherwise specified, NMR spectra were recorded in $CDCl_3$ on a 500 or 400 MHz (for ^1H), 471 or 376 MHz (for ^{19}F), or 126 MHz (for ^{13}C) spectrometer. All chemical shifts were reported in ppm relative to TMS (0 ppm) for ^1H NMR and $PhCF_3$ (-63.5 ppm) for ^{19}F NMR as internal or external standard. The HPLC experiments were carried out on a Waters e2695 instrument (column: J&K, RP-C18, 5 μm, 4.6 × 150 mm), and the yields of product were determined by using the corresponding pure compound as the external standard. Melting points of the products were measured and uncorrected. MS experiments were performed on a TOF-Q ESI or CI/EI instrument. Solvents were dried before use according to the literature.[15] Trifluoroethylation reagents **2a** and **2b** were synthesized according to the literature.[8j] 1,3-Dicarbonyls **1b-d**,[16a] **1e-f**,[16b] **1g**,[16a] **1h-j**,[16b] **1l-m**,[16a] **1r**[16a], **1t**,[16c] **1u**,[16c] **1w**,[16d] **1y**,[16d] were synthesized according to the literatures. Other reagents were all purchased from commercial sources and used without further purification.

2. General procedures for the reaction of 1,3-dicarbonyls with [ArICH$_2$CF$_3$][OTf]

Procedure A: In a nitrogen filled glovebox, a sealed tube was charged with 1,3-dione (**1**, 0.4 mmol), [MesICH$_2$CF$_3$][OTf] (**2a**, 0.6 mmol), Li_2CO_3 (0.6 mmol), and CH_3CN (2 mL) with stirring. The mixture was reacted at room temperature overnight and evaporated to dryness under reduced pressure. The residue was purified by column chromatography on silica gel using petroleum ether / ethyl acetate = 2 : 1 (v / v) as

eluents to give the trifluoroethylated product (**3a-s**).

Procedure B: In a nitrogen filled glovebox, a sealed tube was charged with 1,3-dione (**1**, 0.2 mmol), [MesICH$_2$CF$_3$][OTf] (**2a**, 0.4 mmol), Li$_2$CO$_3$ or Cs$_2$CO$_3$ (0.3 mmol), 4 Å MS (100 mg), and CH$_3$CN (2 mL) with stirring. The mixture was reacted at room temperature for 24 h and evaporated to dryness under reduced pressure. The residue was purified by column chromatography on silica gel using petroleum ether / ethyl acetate = 10 : 1 (v / v) as eluents to give the trifluoroethylated product (**3t**, **3v**, and **3t'-3y'**).

Procedure C: In a nitrogen filled glovebox, a sealed tube was charged with malonate (**1**, 1.5 mmol), [MesICH$_2$CF$_3$][OTf] (**2a**, 0.5 mmol), KOH (0.55 mmol), 4 Å MS (100 mg), and CH$_3$CN (2 mL) with stirring. The mixture was reacted at room temperature for 24 h and evaporated to dryness under reduced pressure. The residue was purified by column chromatography on silica gel using a mixture of petroleum ether and ethyl acetate as eluents to give the trifluoroethylated product (**3z'** and **3aa'**).

3-(2,2,2-Trifluoroethoxy)cyclohex-2-en-1-one (**3a**):

White solid, 64.5 mg, 83% yield. M.p.: 61-63 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ 5.31 (s, 1H), 4.17 (q, *J* = 8.0 Hz, 2H), 2.49 (t, *J* = 6.4 Hz, 2H), 2.36 (t, *J* = 6.4 Hz, 2H), 2.01 (m, 2H). ^{19}F NMR (376 MHz, CDCl$_3$) δ -73.6 (t, *J* = 7.9 Hz, 3F). ^{13}C NMR (126 MHz, CDCl$_3$) δ 199.1, 175.8, 122.7 (q, *J* = 277.2 Hz), 103.8, 65.0 (q, *J* = 36.5 Hz), 36.8, 28.5, 21.1. IR (KBr): 3065, 2967, 2925, 2906, 2840, 1679, 1656, 1615, 1455, 1434, 1384, 1355, 1330, 1303, 1283, 1247, 1220, 1187, 1141, 1068, 1039, 968, 912, 868, 853, 834, 762, 692, 635 cm^{-1}. HRMS-EI (m/z) calcd. for $C_8H_9F_3O_2$ ([M]$^+$): 194.0555; Found: 194.0553.

2-Benzyl-3-(2,2,2-trifluoroethoxy)cyclohex-2-en-1-one (**3b**):

Light yellow solid, 76.2 mg, 67% yield. M.p.: 62-64 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.28-7.22 (m, 4H), 7.15 (t, *J* = 7.0 Hz, 1H), 4.35 (q, *J* = 8.0 Hz, 2H), 3.67 (s, 2H), 2.54 (t, *J* = 6.1 Hz, 2H), 2.41 (t, *J* = 6.6 Hz, 2H), 2.04 (m, 2H). ^{19}F NMR (471 MHz, CDCl$_3$) δ -78.1 (t, *J* = 8.0 Hz, 3F). ^{13}C NMR (126 MHz, CDCl$_3$) δ 197.9, 168.5, 141.0, 128.9, 128.2, 125.7, 123.0 (q, *J* = 278.5 Hz), 121.8, 64.4 (q, *J* = 36.5 Hz), 36.4, 28.0, 25.2, 20.7. IR (KBr): 3083, 3059, 3029, 3005, 2952, 2925, 2893, 2868, 2845, 2819, 1648, 1622, 1494, 1454, 1426, 1377, 1362, 1337, 1287, 1232, 1175, 1160, 1108, 1093, 1052, 1030, 983, 967, 921, 877, 853, 759, 714, 702, 691, 671, 608 cm^{-1}. HRMS-EI

(m/z) calcd. for $C_{15}H_{15}F_3O_2$ ($[M]^+$): 284.1024; Found: 284.1012.

2-(4-Chlorobenzyl)-3-(2,2,2-trifluoroethoxy)cyclohex-2-en-1-one (**3c**):
White solid, 86.7 mg, 68% yield. M.p.: 56-58 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16 (s, 4H), 4.34 (q, *J* = 7.8 Hz, 2H), 3.59 (s, 2H), 2.53 (t, *J* = 6.3 Hz, 2H), 2.38 (t, *J* = 6.0 Hz, 2H), 2.02 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -74.1 (t, *J* = 7.8 Hz, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.9, 168.5, 141.0, 128.9, 128.2, 125.7, 123.0 (q, *J* = 278.5 Hz), 121.8, 64.4 (q, *J* = 36.5 Hz), 36.4, 27.9, 25.1, 20.7. IR (KBr): 3042, 3028, 2985, 2964, 2941, 2909, 2876, 2850, 1636, 1621, 1490, 1455, 1423, 1370, 1337, 1302, 1291, 1257, 1226, 1208, 1159, 1111, 1088, 1053, 1016, 974, 925, 877, 857, 841, 814, 801, 735, 703, 689, 663, 641 cm^{-1}. HRMS-EI (m/z) calcd. for $C_{15}H_{14}ClF_3O_2$ ($[M]^+$): 318.0634; Found: 318.0640.

2-(2-Methylbenzyl)-3-(2,2,2-trifluoroethoxy)cyclohex-2-en-1-one (**3d**):
Light yellow solid, 100.2 mg, 84% yield. M.p.: 38-40 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09 (m, 1H), 7.06-7.02 (m, 2H), 6.97 (m, 1H), 4.27 (q, *J* = 8.0 Hz, 2H), 3.61 (s, 2H), 2.56 (t, *J* = 6.2 Hz, 2H), 2.43 (t, *J* = 6.7 Hz, 2H), 2.35 (s, 3H), 2.07 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -74.2 (t, *J* = 8.0 Hz, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.0, 169.1, 138.6, 136.3, 129.9, 127.9, 125.7, 125.7, 122.9 (q, *J* = 278.5 Hz), 121.3, 64.4 (q, *J* = 36.5 Hz), 36.5, 25.4, 25.1, 20.8, 19.8. IR (KBr): 3101, 3060, 3049, 3018, 2953, 2931, 2895, 2873, 1649, 1631, 1619, 1490, 1456, 1422, 1373, 1316, 1286, 1219, 1168, 1117, 1095, 1087, 1050, 986, 960, 919, 858, 831, 783, 744, 670 cm^{-1}. HRMS-EI (m/z) calcd. for $C_{16}H_{17}F_3O_2$ ($[M]^+$): 298.1181; Found: 298.1184.

2-(4-Nitrobenzyl)-3-(2,2,2-trifluoroethoxy)cyclohex-2-en-1-one (**3e**):
Light yellow solid, 90.9 mg, 69% yield (K_2CO_3 as the base). M.p.: 83-85 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.5 Hz, 2H), 7.39 (d, *J* = 8.5 Hz, 2H), 4.40 (q, *J* = 8.0 Hz, 2H), 3.73 (s, 2H), 2.59 (t, *J* = 6.0 Hz, 2H), 2.43 (t, *J* = 6.5 Hz, 2H), 2.07 (m, 2H). ^{19}F NMR (471 MHz, $CDCl_3$) δ -74.2 (t, *J* = 8.0 Hz, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.6, 169.3, 148.9, 146.3, 129.7, 123.5, 122.9 (q, *J* = 278.5 Hz), 120.3, 64.5 (q, *J* = 36.5 Hz), 36.2, 28.1, 25.2, 20.7. IR (KBr): 3108, 2933, 2851, 1658, 1630, 1598, 1515, 1458, 1430, 1370, 1340, 1294, 1231, 1171, 1159, 1107, 1056, 1012, 969, 922, 884, 856, 806, 732, 702, 632 cm^{-1}. HRMS-EI (m/z) calcd. for $C_{15}H_{14}F_3NO_4$ ($[M]^+$): 329.0875; Found: 329.0880.

4-((6-Oxo-2-(2,2,2-trifluoroethoxy)cyclohex-1-en-1-yl)methyl)benzonitrile (**3f**):
White solid, 96.5 mg, 78% yield. M.p.: 130-132 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 4.38 (q, *J* = 8.0 Hz, 2H), 3.68 (s, 2H), 2.57 (t, *J* = 6.0 Hz, 2H), 2.41 (t, *J* = 6.5 Hz, 2H), 2.06 (m, 2H). ^{19}F NMR (471 MHz, $CDCl_3$) δ -74.2 (t, *J* = 8.0 Hz, 3F), ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.6, 169.1, 146.7, 132.0, 129.7, 122.8 (q, *J* = 278.5 Hz), 120.4, 119.4, 109.5, 64.5 (q, *J* = 36.5 Hz), 36.2, 28.3, 25.2, 20.7. IR (KBr): 3071, 3055, 2969, 2934, 2895, 2876, 2837, 2227, 1642, 1616, 1503, 1466, 1431, 1377, 1365, 1295, 1235, 1213, 1172, 1158, 1115, 1086, 1056, 968, 856, 819, 762, 702, 666, 637 cm^{-1}. HRMS-EI (m/z) calcd. for $C_{16}H_{14}F_3NO_2$ ($[M]^+$): 309.0977; Found: 309.0968.

2-(2-Chloro-4-fluorobenzyl)-3-(2,2,2-trifluoroethoxy)cyclohex-2-en-1-one (**3g**):
White solid, 88.9 mg, 66% yield (K_2CO_3 as the base). M.p.: 61-63 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.07 (dd, *J* = 8.6, 2.5 Hz, 1H), 7.02 (dd, *J* = 8.0, 6.8 Hz, 1H), 6.83 (td, *J* = 8.4, 2.4 Hz, 1H), 4.33 (q, *J* = 8.0 Hz, 2H), 3.73 (s, 2H), 2.59 (t, *J* = 6.0 Hz, 2H), 2.45 (t, *J* = 6.5 Hz, 2H), 2.10 (m, 2H). ^{19}F NMR (471 MHz, $CDCl_3$) δ -74.2 (t, *J* = 7.8 Hz, 3F), -116.1 (q, *J* = 8.0 Hz, 1F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.7, 169.6, 160.8 (d, *J* = 246.6 Hz), 134.3 (d, *J* = 10.2 Hz), 133.8 (d, *J* = 3.5 Hz), 130.4 (d, *J* = 8.5 Hz), 122.8 (q, *J* = 278.5 Hz), 119.9, 116.4 (d, *J* = 24.5 Hz), 113.6 (d, *J* = 20.8 Hz), 64.4 (q, *J* = 36.5 Hz), 36.4, 25.3, 25.0, 20.8. IR (KBr): 3284, 3077, 2988, 2967, 2932, 2893, 2877, 2852, 1651, 1622, 1491, 1462, 1422, 1372, 1298, 1265, 1228, 1156, 1107, 1089, 1052, 1039, 988, 965, 925, 906, 879, 853, 808, 782, 741, 702, 687, 642 cm^{-1}. HRMS-EI (m/z) calcd. for $C_{15}H_{13}F_4O_2$ ($[M - Cl]^+$): 301.0852; Found: 301.0853.

2-(4-Methoxybenzyl)-3-(2,2,2-trifluoroethoxy)cyclohex-2-en-1-one (**3h**):
Yellow liquid, 91.8 mg, 73% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.17 (d, *J* = 8.4 Hz, 2H), 6.76 (d, *J* = 8.5 Hz, 2H), 4.33 (q, *J* = 8.0 Hz, 2H), 3.75 (s, 3H), 3.57 (s, 2H), 2.51 (t, *J* = 6.1 Hz, 2H), 2.37 (t, *J* = 6.5 Hz, 2H), 2.01 (m, 2H). ^{19}F NMR (471 MHz, $CDCl_3$) δ -74.1 (t, *J* = 8.0 Hz, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.0, 168.2, 157.7, 133.2, 129.9, 123.0 (q, *J* = 278.5 Hz), 122.3, 113.6, 64.4 (q, *J* = 36.5 Hz), 55.3, 36.4, 27.1, 25.2, 20.8. IR (KBr): 3100, 3061, 3032, 3000, 2954, 2875, 2837, 1660, 1649, 1624, 1584, 1511, 1458, 1428, 1370, 1287, 1245, 1226, 1160, 1110, 1089, 1051, 1034, 968, 921, 877, 853, 833, 816, 769, 726, 698, 668, 644 cm^{-1}. HRMS-EI (m/z) calcd. for

$C_{16}H_{17}F_3O_3$ ([M]$^+$): 314.1130; Found: 314.1137.

2-(Cyclohexylmethyl)-3-(2,2,2-trifluoroethoxy)cyclohex-2-en-1-one (**3i**):
Light yellow solid, 72.0 mg, 62% yield. M.p.: 93-95 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.33 (q, *J* = 8.0 Hz, 2H), 2.54 (t, *J* = 6.0 Hz, 2H), 2.38 (t, *J* = 6.5 Hz, 2H), 2.20 (d, *J* = 7.1 Hz, 2H), 2.04 (m, 2H), 1.66 (m, 2H), 1.60-1.58 (m, 3H), 1.38 (m, 1H), 1.20-1.11 (m, 3H), 0.92 (m, 2H). ^{19}F NMR (471 MHz, $CDCl_3$) δ -74.3 (t, *J* = 8.0 Hz, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.7, 168.1, 123.1 (q, *J* = 278.5 Hz), 121.6, 64.4 (q, *J* = 36.5 Hz), 37.2, 36.6, 33.3, 29.6, 26.7, 26.5, 25.3, 21.0. IR (KBr): 2922, 2848, 1637, 1615, 1448, 1427, 1375, 1351, 1305, 1295, 1255, 1230, 1213, 1190, 1163, 1130, 1087, 1053, 977, 922, 896, 869, 856, 710, 697, 674 cm^{-1}. HRMS-EI (m/z) calcd. for $C_{15}H_{21}F_3O_2$ ([M]$^+$): 290.1494; Found: 290.1500.

2-Cinnamyl-3-(2,2,2-trifluoroethoxy)cyclohex-2-en-1-one (**3j**):
Yellow liquid, 93.7 mg, 72% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (d, *J* = 7.7 Hz, 2H), 7.28 (t, *J* = 7.3 Hz, 2H), 7.18 (t, *J* = 7.2 Hz, 1H), 6.43 (d, *J* = 15.8 Hz, 1H), 6.22-6.16 (m, 1H), 4.38 (q, *J* = 8.0 Hz, 2H), 3.23 (d, *J* = 7.0 Hz, 2H), 2.54 (t, *J* = 6.0 Hz, 2H), 2.41 (t, *J* = 6.5 Hz, 2H), 2.06 (m, 2H). ^{19}F NMR (471 MHz, $CDCl_3$) δ -74.2 (t, *J* = 8.0 Hz, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.8, 168.6, 138.0, 130.5, 128.5, 127.7, 126.9, 126.1, 123.0 (q, *J* = 278.5 Hz), 120.4, 64.5 (q, *J* = 36.5 Hz), 36.4, 25.8, 25.3, 20.8. IR (KBr): 3082, 3060, 3027, 2951, 1719, 1649, 1623, 1495, 1453, 1424, 1372, 1287, 1228, 1163, 1095,1053, 1002, 966, 920, 855, 832, 754, 698, 665 cm^{-1}. HRMS-EI (m/z) calcd. for $C_{17}H_{17}F_3O_2$ ([M]$^+$): 310.1181; Found: 310.1180.

5,5-Dimethyl-3-(2,2,2-trifluoroethoxy)cyclohex-2-en-1-one (**3k**):
White solid, 83.6 mg, 94% yield. M.p.: 66-68 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.31 (s, 1H), 4.17 (q, *J* = 8.0 Hz, 2H), 2.36 (s, 2H), 2.22 (s, 2H), 1.08 (s, 6H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -73.6 (t, *J* = 7.8 Hz, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 199.0, 174.1, 122.7 (q, *J* = 277.2 Hz), 102.6, 65.0 (q, *J* = 36.5 Hz), 50.8, 42.3, 32.6, 28.3. IR (KBr): 3077, 2966, 2947, 2879, 2831, 1741, 1665, 1623, 1471, 1452, 1431, 1418, 1374, 1325, 1285, 1264, 1212, 1183, 1166, 1144, 1123, 1051, 966, 921, 892, 871, 854, 831, 800, 692, 616 cm^{-1}. HRMS-EI (m/z) calcd. for $C_{10}H_{13}F_3O_2$ ([M]$^+$): 222.0868; Found: 222.0871.

2-Benzyl-5,5-dimethyl-3-(2,2,2-trifluoroethoxy)cyclohex-2-en-1-one (**3l**):
Light yellow solid, 87.4 mg, 70% yield. M.p.: 51-53 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 (m, 4H), 7.15 (s, 1H), 4.33 (q, *J* = 7.5 Hz, 2H), 3.67 (s, 2H), 2.39 (s, 2H), 2.30 (s, 2H), 1.10 (s, 6H). ^{19}F NMR (471 MHz, $CDCl_3$) δ -74.2 (t, *J* = 7.5 Hz, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.9, 166.7, 141.0, 128.8, 128.2, 125.7, 123.0 (q, *J* = 279.7 Hz), 120.9, 64.4 (q, *J* = 36.5 Hz), 50.3, 39.2, 32.5, 28.6, 27.9. IR (KBr): 3086, 3061, 3030, 2957, 2930, 2885, 2873, 2818, 1643, 1625, 1603, 1584, 1495, 1465, 1454, 1417, 1370, 1309, 1293, 1226, 1170, 1145, 1103, 1083, 991, 977, 927, 855, 779, 725, 699, 688, 649, 608 cm^{-1}. HRMS-EI (m/z) calcd. for $C_{17}H_{19}F_3O_2$ ($[M]^+$): 312.1337; Found: 312.1335.

2-Allyl-5,5-dimethyl-3-(2,2,2-trifluoroethoxy)cyclohex-2-en-1-one (**3m**):
White solid, 61.3 mg, 58% yield. M.p.: 46-48 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.75 (m, 1H), 4.98 (d, *J* = 17.0 Hz, 1H), 4.90 (d, *J* = 10.0 Hz, 1H), 4.33 (q, *J* = 8.0 Hz, 2H), 3.04 (d, *J* = 6.0 Hz, 2H), 2.37 (s, 2H), 2.25 (s, 2H), 1.09 (s, 6H). ^{19}F NMR (471 MHz, $CDCl_3$) δ -74.4 (t, *J* = 8.0 Hz, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.7, 166.7, 135.7, 123.0 (q, *J* = 279.7 Hz), 119.4, 114.9, 64.5 (q, *J* = 36.5 Hz), 50.4, 39.3, 32.5, 28.6, 26.5. IR (KBr): 3086, 3024, 2962, 2940, 2910, 2896, 2876, 2832, 1639, 1620, 1459, 1430, 1375, 1305, 1294, 1224, 1164, 1131, 1095, 1070, 998, 970, 915, 885, 859, 761, 690, 672 cm^{-1}. HRMS-EI (m/z) calcd. for $C_{13}H_{17}F_3O_2$ ($[M]^+$): 262.1181; Found: 262.1190.

5-Methyl-3-(2,2,2-trifluoroethoxy)cyclohex-2-en-1-one (**3n**):
Light yellow solid, 54.9 mg, 66% yield. M.p.: 44-46 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.29 (s, 1H), 4.16 (m, 2H), 2.52-2.41 (m, 2H), 2.24-2.19 (m, 2H), 2.04 (m, 1H), 1.08 (m, 3H). ^{19}F NMR (471 MHz, $CDCl_3$) δ -73.6 (t, *J* = 7.5 Hz, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 199.0, 175.1, 122.7 (q, *J* = 278.5 Hz), 103.3, 65.0 (q, *J* = 36.5 Hz), 45.0, 36.5, 28.8, 20.8. IR (KBr): 3057, 2981, 2965, 2947, 2937, 2919, 2883, 2851, 2817, 1652, 1611, 1460, 1447, 1432, 1385, 1345, 1297, 1286, 1253, 1221, 1178, 1158, 1142, 1072, 1043, 968, 929, 877, 859, 694, 622 cm^{-1}. HRMS-EI (m/z) calcd. for $C_9H_{11}F_3O_2$ ($[M]^+$): 208.0711; Found: 208.0702.

5-(2,2,2-Trifluoroethoxy)-1,6-dihydro-[1,1'-biphenyl]-3(2H)-one (**3o**):
White solid, 93.0 mg, 86% yield. M.p.: 95-97 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38

(m, 2H), 7.31-7.26 (m, 3H), 5.44 (s, 1H), 4.24 (m, 2H), 3.41 (s, 1H), 2.78-2.58 (m, 4H). ^{19}F NMR (471 MHz, $CDCl_3$) δ -73.5 (t, *J* = 7.2 Hz, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.1, 174.8, 142.2, 129.0, 127.4, 126.8, 122.7 (q, *J* = 277.2 Hz), 103.6, 65.2 (q, *J* = 36.5 Hz), 43.9, 39.3, 36.1. IR (KBr): 3093, 3058, 3029, 2976, 2956, 2889, 2875, 1658, 1615, 1500, 1447, 1429, 1382, 1278, 1258, 1216, 1179, 1154, 1048, 1032, 965, 855, 811, 750, 695, 645 cm^{-1}. HRMS-EI (m/z) calcd. for $C_{14}H_{13}F_3O_2$ ($[M]^+$): 270.0868; Found: 270.0867.

3-(2,2,2-Trifluoroethoxy)cyclopent-2-en-1-one (**3p**):
Yellow oil, 46.1 mg, 64% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.37 (s, 1H), 4.34 (q, *J* = 8.0 Hz, 2H), 2.73 (m, 2H), 2.52 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -73.7 (t, *J* = 7.9 Hz, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 205.0, 188.1, 122.4 (q, *J* = 277.2 Hz), 106.1, 67.7 (q, *J* = 36.5 Hz), 34.5, 28.2. IR (KBr): 3087, 2962, 2940, 2926, 2853, 1712, 1697, 1680, 1609, 1459, 1440, 1411, 1367, 1301, 1274, 1247, 1228, 1190, 1164, 1039, 992, 967, 931, 859, 845, 832, 706 cm^{-1}. HRMS-EI (m/z) calcd. for $C_7H_7F_3O_2$ ($[M]^+$): 180.0398; Found: 180.0394.

2-Methyl-3-(2,2,2-trifluoroethoxy)cyclopent-2-en-1-one (**3q**):
Yellow solid, 62.9 mg, 81% yield. M.p.: 42-44 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.49 (q, *J* = 8.0 Hz, 2H), 2.63 (m, 2H), 2.49 (m, 2H), 1.66 (t, *J* = 1.7 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -74.6 (t, *J* = 8.0 Hz, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 205.2, 180.8, 122.7 (q, *J* = 278.5 Hz), 118.9, 65.6 (q, *J* = 36.5 Hz), 33.7, 24.7, 6.08. IR (KBr): 2963, 2927, 2858, 1733, 1692, 1644, 1445, 1387, 1352, 1284, 1235, 1164, 1123, 1071, 1028, 963, 885, 855, 834, 721, 675, 641 cm^{-1}. HRMS-EI (m/z) calcd. for $C_8H_9F_3O_2$ ($[M]^+$): 194.0555; Found: 194.0549.

2-Benzyl-3-(2,2,2-trifluoroethoxy)cyclopent-2-en-1-one (**3r**):
Light yellow liquid, 98.4 mg, 91% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28-7.24 (m, 4H), 7.18 (m, 1H), 4.49 (q, *J* = 7.9 Hz, 2H), 3.51 (s, 2H), 2.66 (m, 2H), 2.52 (m, 2H). ^{19}F NMR (471 MHz, $CDCl_3$) δ -74.4 (t, *J* = 7.9 Hz, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 203.7, 180.9, 139.3, 128.6, 128.4, 126.1, 122.6, 122.6 (q, *J* = 278.5 Hz), 65.5 (q, *J* = 36.5 Hz), 33.6, 27.3, 24.4. IR (KBr): 3088, 3062, 3033, 3010, 2918, 2850, 1681, 1623, 1495, 1456, 1432, 1289, 1253, 1239, 1171, 1097, 1075, 1047, 990, 965, 857, 840, 772, 720, 699, 682 cm^{-1}. HRMS-EI (m/z) calcd. for $C_{14}H_{13}F_3O_2$ ($[M]^+$): 270.0868; Found:

270.0872.

3-(2,2,2-Trifluoroethoxy)cyclohept-2-en-1-one (**3s**):
Colorless liquid, 4.9 mg, 6% yield, petroleum ether / ethyl acetate = 5 : 1 (v / v) as eluents for column chromatography. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.33 (s, 1H), 4.10 (q, *J* = 7.9 Hz, 2H), 2.66 (t, *J* = 6.3 Hz, 2H), 2.62 (t, *J* = 6.4 Hz, 2H), 1.90 (m, 2H), 1.84 (m, 2H). ^{19}F NMR (471 MHz, $CDCl_3$) δ -73.7 (t, *J* = 8.0 Hz, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.5, 173.7, 122.7 (q, *J* = 278.5 Hz), 107.0, 65.1 (q, *J* = 36.5 Hz), 42.0, 32.5, 23.6, 21.3. IR (KBr): 2944, 2871, 1721, 1699, 1650, 1619, 1455, 1424, 1378, 1286, 1236, 1168, 1047, 976, 881, 817, 689 cm^{-1}. HRMS-EI (m/z) calcd. for $C_9H_{11}F_3O_2$ ([M]$^+$): 208.0711; Found: 208.0716.

Methyl 3-(2,2,2-trifluoroethoxy)-1*H*-indene-2-carboxylate (**3t**):
White solid, 10.0 mg, 18% yield (Li_2CO_3) or 16.5 mg, 30% yield (Cs_2CO_3). M.p.: 80-82 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (d, *J* = 7.3 Hz, 1H), 7.48-7.39 (m, 3H), 4.94 (q, *J* = 8.4 Hz, 2H), 3.85 (s, 3H), 3.71 (s, 2H). ^{19}F NMR (471 MHz, $CDCl_3$) δ -75.1 (t, *J* = 8.6 Hz, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.6, 163.9, 141.7, 139.1, 129.2, 127.1, 124.4, 123.4 (q, *J* = 278.5 Hz), 121.0, 111.0, 70.8 (q, *J* = 35.5 Hz), 51.7, 36.4. IR (KBr): 2965, 2923, 2854, 1697, 1616, 1597, 1578, 1444, 1369, 1329, 1285, 1270, 1249, 1177, 1154, 1099, 1044, 958, 888, 851, 759, 719, 663 cm^{-1}. HRMS-EI (m/z) calcd. for $C_{13}H_{11}F_3O_3$ ([M]$^+$): 272.0660; Found: 272.0655.

Methyl 1-oxo-2-(2,2,2-trifluoroethyl)-2,3-dihydro-1*H*-indene-2-carboxylate (**3t'**):
Yellow liquid, 25.1mg, 46% yield (Li_2CO_3) or 12.9 mg, 24% yield (Cs_2CO_3). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (d, *J* = 7.7 Hz, 1H), 7.69 (t, *J* = 7.5 Hz, 1H), 7.56 (d, *J* = 7.7 Hz, 1H), 7.44 (t, *J* = 7.5 Hz, 1H), 3.90 (d, *J* = 17.5 Hz, 1H), 3.73 (s, 3H), 3.35 (d, *J* = 17.5 Hz 1H), 3.33 (m, 1H), 2.66 (m, 1H). ^{19}F NMR (471 MHz, $CDCl_3$) δ -60.8 (t, *J* = 10.1 Hz, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 199.3, 169.3, 153.2, 136.1, 133.8, 128.2, 126.5, 126.1 (q, *J* = 278.5 Hz), 125.3, 57.3 (q, *J* = 1.7 Hz), 53.6, 37.8 (q, *J* = 29.0 Hz), 35.4 (q, *J* = 1.7 Hz). IR (KBr): 3084, 3039, 3005, 2957, 2848, 1748, 1716, 1609, 1590, 1466, 1435, 1374, 1303, 1258, 1206, 1172, 1141, 1111, 1047, 1015, 970, 957, 926, 864, 842, 813, 785, 752, 697, 652, 600, 577 cm^{-1}. HRMS-EI (m/z) calcd. for $C_{13}H_{11}F_3O_3$ ([M]$^+$): 272.0660; Found: 272.0668.

Methyl 5,6-dimethoxy-1-oxo-2-(2,2,2-trifluoroethyl)-2,3-dihydro-1*H*-indene-2-car-boxylate (**3u'**):

White solid, 43.0 mg, 43% yield, petroleum ether / ethyl acetate = 2 : 1 (v / v) as eluents for column chromatography. M.p.: 160-162 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.17 (s, 1H), 6.94 (s, 1H), 4.00 (s, 3H), 3.91 (s, 3H), 3.78 (d, *J* = 17.1 Hz, 1H), 3.72 (s, 3H), 3.30 (m, 1H), 3.24 (d, *J* = 17.1 Hz, 1H), 2.62 (m, 1H). ^{19}F NMR (471 MHz, $CDCl_3$) δ -60.9 (t, *J* = 10.7 Hz, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.4, 169.5, 156.6, 150.0, 148.8, 126.2, 126.1 (q, *J* = 278.5 Hz), 107.2, 105.2, 57.4 (q, *J* = 1.5 Hz), 56.4, 56.1, 53.3, 37.7 (q, *J* = 29.0 Hz), 35.0 (q, *J* = 1.8 Hz). IR (KBr): 3010, 2960, 2917, 2880, 2839, 1717, 1595, 1504, 1467, 1456, 1444, 1425, 1363, 1320, 1282, 1253, 1221, 1176, 1144, 1117, 1101, 1025, 965, 901, 880, 865, 761, 670, 641 cm^{-1}. HRMS-EI (m/z) calcd. for $C_{15}H_{15}F_3O_5$ ($[M]^+$): 332.0872; Found: 332.0873.

(*Z*)-1,3-diphenyl-3-(2,2,2-trifluoroethoxy)prop-2-en-1-one (**3v**):

White solid, 11.4 mg, 19% yield (Li_2CO_3) or 28.3 mg, 46% yield (Cs_2CO_3). M.p.: 79-81 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, *J* = 7.6 Hz, 2H), 7.80 (d, *J* = 7.6 Hz, 2H), 7.61 (t, *J* = 7.5 Hz, 1H), 7.56-7.47 (m, 5H), 6.78 (s, 1H), 4.59 (q, *J* = 8.4 Hz, 2H). ^{19}F NMR (471 MHz, $CDCl_3$) δ -74.2 (t, *J* = 8.4 Hz, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 189.0, 167.0, 139.0, 134.9, 133.0, 131.6, 128.9, 128.8, 128.5, 127.8, 123.4 (q, *J* = 278.5 Hz), 103.0, 70.8 (q, *J* = 36.5 Hz). IR (KBr): 3088, 3064, 3005, 2960, 2880, 1646, 1599, 1585, 1569, 1489, 1450, 1417, 1370, 1266, 1216, 1165, 1129, 1045, 1026, 984, 966, 906, 850, 832, 796, 765, 705, 696, 689, 603 cm^{-1}. HRMS-EI (m/z) calcd. for $C_{17}H_{13}F_3O_2$ ($[M]^+$): 306.0868; Found: 306.0865.

1,3-Diphenyl-2-(2,2,2-trifluoroethyl)propane-1,3-dione (**3v'**):

White solid, 42.5 mg, 69% yield (Li_2CO_3) or 29.1 mg, 48% (Cs_2CO_3). M.p.: 49-51 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, *J* = 7.9 Hz, 4H), 7.59 (t, *J* = 7.4 Hz, 2H), 7.46 (t, *J* = 7.9 Hz, 4H), 5.59 (t, *J* = 6.1 Hz, 1H), 3.05 (m, 2H). ^{19}F NMR (471 MHz, $CDCl_3$) δ -64.9 (t, *J* = 10.1 Hz, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.3, 135.3, 134.2, 129.2, 128.9, 126.4 (q, *J* = 277.2 Hz), 50.3 (q, *J* = 1.9 Hz), 33.2 (q, *J* = 30.2 Hz). IR (KBr): 3064, 3028, 3010, 2957, 2927, 1701, 1670, 1643, 1630, 1597, 1493, 1449, 1431, 1357, 1332, 1257, 1150, 1113, 1086, 1072, 1020, 963, 944, 927, 839, 775, 747, 688 cm^{-1}. HRMS-EI (m/z) calcd. for $C_{17}H_{13}F_3O_2$ ($[M]^+$): 306.0868; Found:

306.0871.

1-(4-methoxyphenyl)-3-phenyl-2-(2,2,2-trifluoroethyl)propane-1,3-dione (**3w'**):
Colorless liquid, 20.6 mg, 31% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96-7.94 (m, 4H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.45 (t, *J* = 7.8 Hz, 2H), 6.94 (d, *J* = 8.8 Hz, 2H), 5.51 (t, *J* = 6.1 Hz, 1H), 3.84 (s, 3H), 3.03 (dm, *J* = 57.1 Hz, 2H). ^{19}F NMR (471 MHz, $CDCl_3$) δ -64.9 (t, *J* = 10.1 Hz, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.3, 191.6, 164.3, 135.4, 133.9, 131.2, 129.0, 128.7, 128.0, 126.4 (q, *J* = 277.2 Hz), 114.3, 55.6, 50.1 (q, *J* = 1.8 Hz), 33.2 (q, *J* = 30.1 Hz). IR (KBr): 3064, 2962, 2923, 2847, 1731, 1696, 1669, 1600, 1575, 1512, 1449, 1422, 1379, 1337, 1318, 1261, 1226, 1199, 1172, 1145, 1111, 1028, 964, 847, 801, 759, 742, 688 cm^{-1}. HRMS-EI (m/z) calcd. for $C_{18}H_{15}F_3O_3$ ([M]$^+$): 336.0973; Found: 336.0970.

1-Phenyl-2-(2,2,2-trifluoroethyl)butane-1,3-dione (**3x'**):
Colorless liquid, 49.8 mg, 68% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, *J* = 7.5 Hz, 2H), 7.67 (t, *J* = 7.5 Hz, 1H), 7.55 (t, *J* = 7.7 Hz, 2H), 4.85 (t, *J* = 6.4 Hz, 1H), 2.92 (dm, *J* = 52.2 Hz, 2H), 2.18 (s, 3H). ^{19}F NMR (471 MHz, $CDCl_3$) δ -65.0 (t, *J* = 10.7 Hz, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 199.7, 193.9, 135.5, 134.4, 129.2, 128.9, 126.2 (q, *J* = 277.2 Hz), 55.9 (q, *J* = 1.8 Hz), 32.7 (q, *J* = 29.9 Hz), 28.6. IR (KBr): 3066, 3008, 2964, 2929, 2856, 1731, 1682, 1596, 1581, 1449, 1434, 1362, 1336, 1264, 1210, 1146, 1113, 1079, 1069, 1018, 1001, 968, 932, 866, 831, 774, 754, 694, 669, 652, 637, 611 cm^{-1}. HRMS-EI (m/z) calcd. for $C_{12}H_{11}F_3O_2$ ([M]$^+$): 244.0711; Found: 244.0707.

1-Phenyl-2-(2,2,2-trifluoroethyl)pentane-1,3-dione (**3y'**):
Colorless liquid, 43.5 mg, 56% yield (Li_2CO_3) or 50.3 mg, 65% yield (Cs_2CO_3). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (d, *J* = 7.5 Hz, 2H), 7.67 (t, *J* = 7.5 Hz, 1H), 7.56 (t, *J* = 7.8 Hz, 2H), 4.87 (t, *J* = 6.4 Hz, 1H), 2.93 (dm, *J* = 55.1 Hz, 2H), 2.49 (q, *J* = 7.2 Hz, 2H), 1.03 (t, *J* = 7.2 Hz, 3H). ^{19}F NMR (471 MHz, $CDCl_3$) δ -65.0 (t, *J* = 10.0 Hz, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 202.4, 194.1, 135.7, 134.3, 129.2, 128.9, 126.3 (q, *J* = 277.2 Hz), 54.9 (q, *J* = 1.8 Hz), 35.2, 32.8 (q, *J* = 29.8 Hz), 7.6. IR (KBr): 3065, 2982, 2943, 2909, 2880, 1729, 1682, 1628, 1596, 1493, 1449, 1433, 1410, 1380, 1334, 1278, 1260, 1148, 1106, 1059, 1035, 1001, 967, 936, 835, 775, 703, 688 cm^{-1}. HRMS-ESI (m/z) calcd. for $C_{12}H_{11}F_3O_2$ ([M + H]$^+$): 259.0946; Found: 259.0952.

Diethyl 2-(2,2,2-trifluoroethyl)malonate (**3z'**) [17a]:

Colorless liquid, 50.9 mg, 42% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.26 (q, *J* = 7.0 Hz, 4H), 3.65 (t, *J* = 7.0 Hz, 1H), 2.83 (m, 2H), 1.30 (t, *J* = 7.0 Hz, 6H). ^{19}F NMR (471 MHz, $CDCl_3$) δ -65.9 (t, *J* = 10.1 Hz, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.5, 125.9 (q, *J* = 277.2 Hz), 62.4, 46.4 (q, *J* = 2.7 Hz), 33.2 (q, *J* = 30.2 Hz), 14.1.

Dibenzyl 2-(2,2,2-trifluoroethyl)malonate (**3aa'**) [17b]:

Colorless liquid, 94.0 mg, 51% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39-7.37 (m, 6H), 7.32 (m, 4H), 5.22 (m, 4H), 3.81 (t, *J* = 7.0 Hz, 1H), 2.90 (m, 2H). ^{19}F NMR (471 MHz, $CDCl_3$) δ -65.7 (t, *J* = 10.5 Hz, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.1, 134.8, 128.7, 128.6, 128.3, 125.8 (q, *J* = 277.2 Hz), 68.0, 46.3 (q, *J* = 2.5 Hz), 33.0 (q, *J* = 30.3 Hz).

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Figures

Scheme 1. The previous examples of carbon-specific trifluoroethylation and perfluoroethylation of 1,3-dicarbonyls

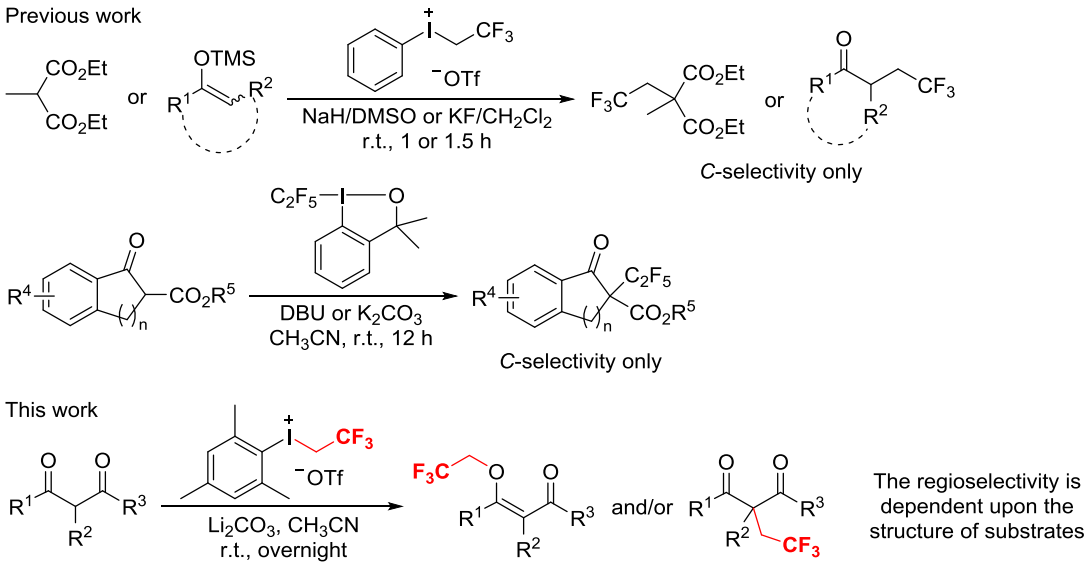
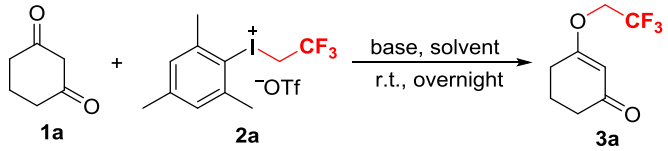


Table 1 Trifluoroethylation of cyclohexane-1,3-dione (**1a**) by mesityl(2,2,2-trifluoroethyl)iodonium triflate (**2a**) in different conditions

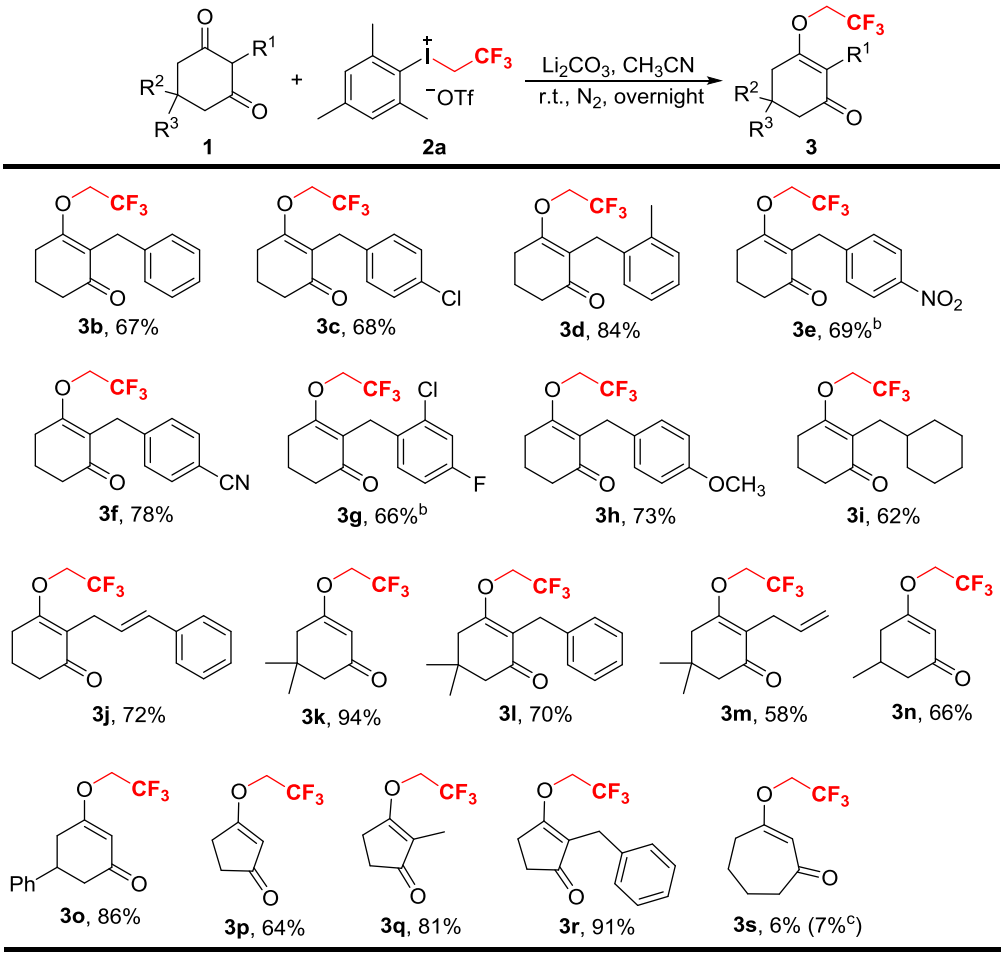


Entry [a]	Base	Solvent	Yield (**3a**, %) [b]
1	K_2CO_3	CH_2Cl_2	61
2	K_2CO_3	CH_3CN	75
3	K_2CO_3	THF	3
4	K_2CO_3	DMF	23
5	K_2CO_3	DMSO	24
6	K_3PO_4	CH_3CN	78
7	Li_2CO_3	CH_3CN	89
8	$NaHCO_3$	CH_3CN	74
9	Cs_2CO_3	CH_3CN	77
10 [c]	Li_2CO_3	CH_3CN	94 (72)
11 [d]	**Li_2CO_3**	**CH_3CN**	**99 (83)**
12 [d,e]	Li_2CO_3	CH_3CN	(80)

[a] Reaction conditions: **1a** (0.1 mmol), **2a** (0.15 mmol), base (0.2 mmol), solvent (2 mL), r.t., N_2, overnight. [b] The yields were determined by HPLC using 3-(2,2,2-trifluoroethoxy)cyclohex-2-en-1-one (**3a**) as an external standard (t_R = 3.0

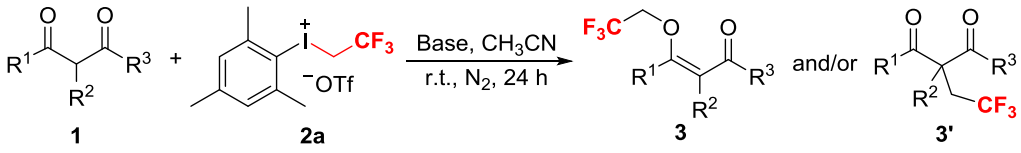
min, λ_{max} = 244.1 nm, water/methanol = 30 : 70 (v / v)). Isolated yield was depicted in the parentheses. [c] **2a** (0.12 mmol), Li_2CO_3 (0.15 mmol). [d] **2a** (0.15 mmol), Li_2CO_3 (0.15 mmol). [e] [$PhICH_2CF_3$][OTf] (**2b**) was used instead of [$MesICH_2CF_3$][OTf] (**2a**).

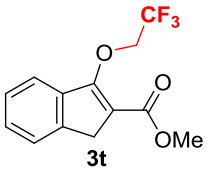
Table 2. *O*-Trifluoroethylation of cyclic 1,3-diketones by **2a** [a]

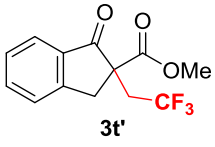


[a] Reaction conditions: **1** (0.4 mmol), **2a** (0.6 mmol), Li_2CO_3 (0.6 mmol), CH_3CN (2 mL), r.t., N_2, overnight. Isolated yields. [b] K_2CO_3 was used instead of Li_2CO_3. [c] Yield was determined by ^{19}F NMR spectroscopy using trifluoromethoxybenzene as an internal standard.

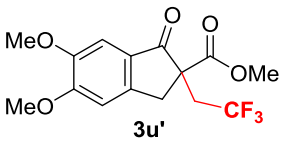
Table 3. *C*- or *C*/*O*-Trifluoroethylation of acyclic 1,3-dicarbonyls by **2a**[a]



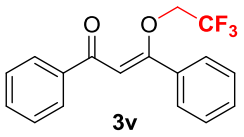


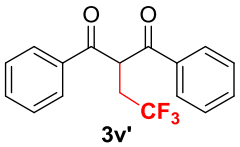


Li_2CO_3: O, 18%; C, 46%
Cs_2CO_3: O, 30%; C, 24%

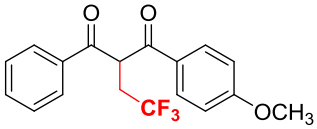


Li_2CO_3: 43%[c] (47%[bc])

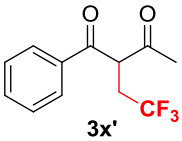




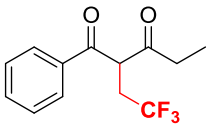
Li_2CO_3: O, 19%; C, 69%
Cs_2CO_3: O, 46%; C, 48%
Li_2CO_3/15-crown-5 (1.5 equiv): O, 42%; C, 54%
[*n*-Bu_4N][OH]•30H_2O: O, 32%; C, 29%



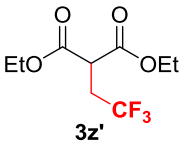
Li_2CO_3: 31% (58%[b])



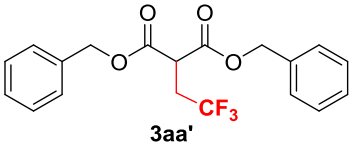
Li_2CO_3: 68%[c]



Li_2CO_3: 56%
Cs_2CO_3: 65%



42%[d] (50%[bd])



51%[d]

[a] Reaction conditions: **1** (0.2 mmol), **2a** (0.4 mmol), base (0.3 mmol), 4Å MS (100 mg), CH_3CN (2 mL), r.t., N_2, 24 h. Isolated yield. [b] Yield was determined by ^{19}F NMR spectroscopy using trifluoromethoxybenzene as an internal standard. [c] **1** (0.3 mmol), **2a** (0.6 mmol), base (0.45 mmol), 4Å MS (100 mg), 24 h. Isolated yield. [d] **1** (1.5 mmol), **2a** (0.5 mmol), KOH (0.55 mmol), 4Å MS (100 mg), 24 h. Isolated yield.