Supporting Information

Visible Light Photoredox Cross-Coupling of Acyl Chlorides with Potassium Alkoxymethyltrifluoroborates: Synthesis of α-Alkoxyketones

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General Considerations: All reactions were carried out under an inert atmosphere of nitrogen or argon unless otherwise noted. THF was dried over activated alumina. IrCl₃·xH₂O, and NiCl₂·dme were purchased from commercial sources. Cs₂CO₃ was used as received. All other reagents were purchased commercially and used as received. Photoredox reactions were irradiated with two or three standard 26 W compact fluorescent light bulbs. Stereoconvergent cross-couplings were irradiated with blue LED light strips (~425 nm). Melting points (°C) are uncorrected. NMR spectra were recorded on a 400 or 500 MHz spectrometer. Data are presented as follows: chemical shift (ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, br = broad), coupling constant *J* (Hz) and integration. Analytical thin-layer chromatography (TLC) was performed on TLC silica gel plates (0.25 mm) precoated with a fluorescent indicator. Visualization of the TLC plates was effected with ultraviolet light. Standard flash chromatography procedures were followed using 100-200 mesh silica gel. HRMS data were obtained by either ESI or CI using a TOF mass spectrometer.

Synthesis of α-alkoxymethyltrifluoroborates:

Most potassium α -alkoxymethyltrifluoroborates were purchased commercially. The unavailable potassium α -alkoxymethyltrifluoroborates were synthesized from the corresponding alcohols according to the literature procedure.¹

Synthesis of Ir[dF(CF₃)ppy]₂(bpy)PF₆ as the photocatalyst I:

Photocatalyst I was synthesized according to the literature procedure.²

High-Throughput Experiments in the design and optimization of the photoredox crosscoupling reaction of hydrocinnamoyl chloride with potassium benzyloxymethyltrifluoroborate as model coupling partners:

High Throughput Experimentation (HTE) was performed at the Penn/Merck Center for High Throughput Experimentation at the University of Pennsylvania. The screens were performed on a 10 μ mol scale. To reaction vials equipped with a Teflon coated magnetic stir bar in a glovebox was added a solution of Ni source and ligand [1:1] dissolved in THF. The solvent was removed *in vacuo* under an inert atmosphere. Then a solution of a desired additive, potassium benzyloxymethyltrifluoroborate, hydrocinnamoyl chloride, and photocatalyst **I** in a desired solvent, was added to each vial. The vials were sealed and stirred over blue LED lights. After 24 h the reactions were opened to air, 1 μ mol of 4,4'-di-*tert*-butylbiphenyl (500 μ L of a 0.002 μ M solution in MeCN) was added to each vial as an internal standard, and the reaction mixtures were diluted with MeCN. The reaction mixtures were then analyzed by UPLC. The product-to-internal standard (P/IS) ratios from the UPLC are shown in Figures S1-S3.



First Screen Variables:



solvents	ligands	bases	Ni sources
THF	L3	no base	Ni(COD) ₂
	L4	pyridine	NiCl ₂ .dme
	L1	lutidine	
	L5		
	L6		
	L7		
	L8		
	L9		



Figure S1. Product to internal standard ratio of the cross coupling reaction of hydrocinnamoyl chloride with potassium benzyloxymethyltrifluoroborate using the first screen variables.

According to this screen the best result was obtained for the reaction in the presence of $NiCl_2 \cdot dme/L1$ and lutidine as a base.

Second Screen Variables:



Figure S2. Product to internal standard ratio of the cross coupling reaction of hydrocinnamoyl chloride with potassium benzyloxymethyltrifluoroborate using the second screen variables.

According to the first and second screens, the highest product to internal standard ratio was obtained for the reaction in the presence of NiCl₂·dme/L1 and lutidine as a base. To improve the yield of the reaction further, screens using a variety of inorganic bases as well as solvents were carried out (Figure S3).

Third Screen Variables:

Solvents	ligands	bases	Ni sources
THF	L1	lutidine	NiCl ₂ ·dme
2-MeTHF		Cs_2CO_3	
CH ₃ CN		CsHCO ₃	
EtOAc		K ₃ PO ₄	
dioxane		K_2HPO_4	
DME		K_2CO_3	
acetone		KHCO ₃	
methyl tert-butyl ether (MTBE)		NH ₄ CO ₃	
		Na ₂ CO ₃	
		NaH ₂ PO ₄	
		KF	
		CsF	



■THF ■MeTHF ■CH3CN ■EtOAc ■dioxane ■DME ■acetone ■MTBE

Figure S3. Product to internal standard ratio of the cross coupling reaction of hydrocinnamoyl chloride with potassium benzyloxymethyltrifluoroborate using the third screen variables.

Accordingly, changing the base of the reaction from lutidine to Cs_2CO_3 has a great impact on the product to internal standard ratio.

Control experiments for the cross-coupling of acyl chlorides with potassium alkoxymethyltrifluoroborates

Ir[dFCE(ppy)](bpy)PF₆I NiCl₂dme L1

	IF[dFC&(ppy)k[0py)kF61 NiClg,dme 0 BF3K <u>11</u> l equivadditive THF,rt,26 W CFL, 24h		
entry	conditions	additive Y Id ^e	ie
1 ^a	6 mol % NiCl ₂ ·dme/L1	lutidine 74	4
2 ^a	6 mol % NiCl ₂ ·dme/L1	Cs_2CO_3 $\frac{82}{6}$	3
3 ^a	no Ir photocatalyst	Cs_2CO_3 0	%
4 ^a	no NiCl ₂ ·dme, no L1	Cs ₂ CO ₃ <	10
5 ^a	no additive	- 5	8
5 ^b	4 mol % NiCl ₂ ·dme/L1	Cs ₂ CO ₃ %	1
6 ^c	4 mol % NiCl₂·dme/L1	Cs_2CO_3 $\frac{8}{\%}$	6
7^{d}	4 mol % NiCl ₂ ·dme/L1	Cs_2CO_3 $\frac{60}{2}$	8

Table S1. Control Experiments.

^a Reactions were carried out using 3 mol % I at 0.1 M. ^b Using 2 mol % I at 0.1 M. ^c Using 2 mol % I at 0.05 M. ^d Using 2 mol % I at 0.2 M.^e Isolated yields.

Screen of various chiral ligands under the optimal conditions for the phtoredox stereoconvergent synthesis of enantioenriched α-alkoxyketones:

Using hydrocinnamoyl chloride and racemic potassium 3-benzyloxy-3trifluoroboratopropylbenzene as a model reaction, a screen of various chiral ligands L1, L2, L11-39 under the optimal conditions was conducted. The screen was performed on a 10 µmol scale. To reaction vials equipped with a Teflon coated magnetic stir bar in a glovebox was added a solution of NiCl₂ dme and a desired ligand [1:1] dissolved in THF. The solvent was removed *in vacuo* under an inert atmosphere. Then Cs₂CO₃ (1.0 equiv) and a solution of potassium 3benzyloxy-3-trifluoroboratopropylbenzene (1.2 equiv), hydrocinnamoyl chloride, and photocatalyst **I** (2 mol %) in THF, was added to each vial. The vials were sealed and stirred over blue LED lights. After 24 h the reactions were opened to air, and diluted with MeCN. The reaction mixtures were then analyzed by SFC. Accordingly, **L2** was the best chiral ligand and afforded the desired ketone with enantiomeric ratio of 81:19 in an excellent yield. Figure S4 shows the SFC chromatograms of the reaction in the presence of ligands **L1** and **L2** [Figure S4, (a) and (b), respectively].





Figure S4. SFC chromatograms of the reaction in the presence of ligands L1 (a) and L2 (b).

General procedure for the photoredox cross-coupling reaction of acyl chlorides with potassium alkoxymethyltrifluoroborates:



To a two dram (8 mL) borosilicate glass vial equipped with a Teflon-coated magnetic stir bar was added 4-*tert*-Butyl-2-(2-pyridyl)oxazoline L1 (4.0 mg, 0.02 mmol) and NiCl₂·dme (4.4 mg, 0.02 mmol). The vial was sealed and evacuated under vacuum and purged with Ar three times.

Anhyd and degassed THF (~1 mL) was added by syringe under Ar, and the resulting mixture was stirred until it appeared as a pale green suspension. Then, the solvent was removed under vacuum. Once dry, alkoxymethyltrifluoroborate (0.6 mmol, 1.2 equiv), $Ir[dFCF_3ppy]_2(bpy)PF_6 I$ (10.1 mg, 0.01 mmol) and Cs₂CO₃ (162.9 mg, 0.5 mmol) were added. Next, the vial was sealed and subsequently purged and evacuated with Ar four times. Anhyd and degassed THF (4 mL) was then added by syringe under Ar followed by the corresponding acyl halide (0.5 mmol). The resulting mixture was stirred for 24 h in the presence of two 26 W fluorescent light bulbs while a fan was blown across the reaction setup to maintain an ambient temperature of 24 °C. After completion, the crude reaction mixture was filtered through a plug of Celite and rinsed with EtOAc (20 mL). The resulting solution was concentrated, and the residue was purified by column chromatography on silica gel, with EtOAc/hexanes mixtures as the eluent, to obtain products in pure form.

Gram scale reaction: To a ~125 mL long, thin-walled vacuum flask equipped with a Tefloncoated magnetic stir bar was added 4-*tert*-Butyl-2-(2-pyridyl)oxazoline L1 (24.5 mg, 0.12 mmol), NiCl₂·dme (26.4 mg, 0.12 mmol). The vial was sealed and evacuated under vacuum and purged with Ar three times. Anhyd and degassed THF (~5 mL) was added by syringe under Ar, and the resulting mixture was stirred until it appeared as a pale green suspension. Then, the solvent was removed under vacuum. Next, potassium benzyloxymethyltrifluoroborate (1.62 g, 7.11 mmol, 1.2 equiv), Ir[dFCF₃ppy]₂(bpy)PF₆ I (59.8 mg, 0.059 mmol, 0.01 equiv), and Cs₂CO₃ (1.93 g, 5.93 mmol, 1.0 equiv) were added. The vial was sealed and subsequently purged and evacuated with Ar four times. Anhyd and degassed THF (59.3 mL) was then added by syringe under Ar followed by hydrocinnamoyl chloride (1.000 g, 5.93 mmol). The resulting mixture was stirred vigorously for 48 h in the presence of three 26 W fluorescent light bulbs while a fan was blown across the reaction setup to maintain an ambient temperature of 24 °C. After completion, the crude reaction mixture was filtered through a plug of Celite and rinsed with EtOAc (50 mL). The resulting solution was concentrated, and the residue was purified by column chromatography on silica gel, with EtOAc/hexanes mixtures as the eluent, to obtain products in pure form.



1-(Benzyloxy)-4-phenylbutan-2-one (1a). The title compound was obtained as a liquid in 81% yield (0.5 mmol scale, 101.7 mg). ¹H NMR (500 MHz, CDCl₃): δ 7.38-7.32 (m, 5H), 7.29 (t, *J* = 7.5 Hz, 2H), 7.22-7.19 (m, 3H), 4.56 (s, 2H), 4.04 (s, 2H), 2.93 (t, *J* = 7.5 Hz, 2H), 2.81 (t, *J* = 7.5 Hz, 2H); ¹³C NMR (125.8 MHz, CDCl₃): δ 208.2, 141.1, 137.4, 128.8, 128.6, 128.3, 128.2, 126.4, 75.4, 73.6, 40.8, 29.5; FT-IR (neat): 3331, 1725, 1139, 1095, 733, 696 cm⁻¹; HRMS (ES+) m/z calcd. for C₁₇H₁₈O₂Na [M+Na]⁺ 277.1204, found 277.1209.



1-(2,6-Dichlorobenzyloxy)-4-phenylbutan-2-one (1b). The title compound was obtained as a solid in 56% yield (0.5 mmol scale, 90.4 mg). mp 62-64 °C; ¹H NMR (500 MHz, CDCl₃): 7.31 (d, *J* = 8 Hz, 2H), 7.25-7.23 (m, 3H), 7.18-7.15 (m, 3H), 4.83 (s, 2H), 4.07 (s, 2H), 2.91-2.87 (m, 2H), 2.83-2.79 (m, 2H); ¹³C NMR (125.8 MHz, CDCl₃): δ 208.4, 141.2, 137.3, 132.9, 130.6, 128.8, 128.7, 126.4, 75.9, 67.9, 40.8, 29.5; FT-IR (neat): 2923, 2853, 1734, 1565, 1436, 1407,

1104, 1090, 1080, 941, 792, 760, 729 cm⁻¹; HRMS (ES+) m/z calcd. for $C_{17}H_{16}O_2NaCl_2$ [M+Na]⁺ 345.0425, found 345.0419.



1-(Hex-5-enyloxy)-4-phenylbutan-2-one (1c). The title compound was obtained as a liquid in 82% yield (0.5 mmol scale, 101.0 mg). ¹H NMR (500 MHz, CDCl₃): 7.29-7.26 (m, 2H), 7.21-7.18 (m, 3H), 5.82-5.77 (m, 1H), 5.02-4.94 (m, 2H), 3.98 (s, 2H), 3.44 (t, J = 6.5 Hz, 2H), 2.92 (t, J = 7.5 Hz, 2H), 2.79 (t, J = 8.0 Hz, 2H), 2.07 (q, J = 7.0, 2H), 1.64-1.58 (m, 2H), 1.48-1.42 (m, 2H); ¹³C NMR (125.8 MHz, CDCl₃): δ 208.9, 141.2, 138.9, 128.8, 128.7, 126.5, 114.9, 76.5, 72.0, 40.8, 33.8, 29.6, 29.3, 25.6; FT-IR (neat): 2934, 1719, 1147, 1113, 1088, 909, 748, 732, 698 cm⁻¹; HRMS (ES+) m/z calcd. for C₁₆H₂₂O₂ [M]⁺ 246.1620, found 246.1622.



4-Phenyl-1-(prop-2-ynyloxy)butan-2-one (1d). The title compound was obtained as a liquid in 60% yield (0.5 mmol scale, 60.6 mg). ¹H NMR (500 MHz, CDCl₃): δ 7.30-7.26 (m, 2H), 7.21-7.18 (m, 3H), 4.24-4.23 (m, 2H), 4.13 (s, 2H), 2.94-2.91 (m, 2H), 2.82-2.79 (m, 2H) 2.45 (t, *J* = 2.4 Hz, 1H); ¹³C NMR (125.8 MHz, CDCl₃): δ 207.5, 141.0, 128.9, 128.7, 126.5, 78.8, 75.9, 74.6, 58.7, 40.9, 29.5; FT-IR (neat): 2936, 1724, 1482, 1452, 1427, 1397, 1332, 1197, 1164, 1105, 1007, 700 cm⁻¹; HRMS (ES+) m/z calcd. for C₁₃H₁₅O₂ [M+H]⁺ 203.1072, found 203.1065.



1-(2-Methoxyethoxy)-4-phenylbutan-2-one (1e). The title compound was obtained as a liquid in 86% yield (0.5 mmol scale, 95.5 mg). ¹H NMR (500 MHz, CDCl₃): 7.28-7.26 (m, 2H), 7.20-7.17 (m, 3H), 4.07 (s, 2H), 3.63-3.62 (m, 2H), 3.56-3.55 (m, 2H), 3.36 (s, 3H), 2.91 (t, J = 7.5Hz, 2H), 2.78 (t, J = 7.5 Hz, 2H); ¹³C NMR (125.8 MHz, CDCl₃): δ 208.4, 141.2, 128.8, 128.7, 126.5, 76.9, 72.2, 71.2, 59.3, 40.7, 29.6; FT-IR (neat): 2924, 1720, 1496, 1453, 1199, 1107, 1088, 749, 699 cm⁻¹; HRMS (ES+) m/z calcd. for C₁₃H₁₈O₃Na [M+Na]⁺ 245.1154, found 245.1122.



4-Phenyl-1-(2-(trimethylsilyl)ethoxy)butan-2-one (1f). The title compound was obtained as a liquid in 82% yield (0.5 mmol scale, 108.4 mg). ¹H NMR (500 MHz, CDCl₃): δ 7.29-7.26 (m, 2H), 7.20-7.18 (m, 3H), 3.97 (m, 2H), 3.53 (t, *J* = 8.3 Hz, 2H), 2.92 (t, *J* = 7.5, 2H), 2.79 (t, *J* = 7.5, 2H), 0.99-0.95 (m, 2H), 0.02 (s, 9H); ¹³C NMR (125.8 MHz, CDCl₃): δ 208.8, 141.2, 128.7, 128.6, 126.4, 75.9, 69.3, 40.7, 29.6, 18.4, -1.12; FT-IR (neat): 2952, 1720, 1454, 1248, 1098, 858, 835, 848, 697 cm⁻¹; HRMS (ES+) m/z calcd. for C₁₅H₂₄O₂SiNa [M+Na]⁺ 287.1443, found 287.1445.



tert-Butyl-4-((2-oxo-4-phenylbutoxy)methyl)piperidine-1-carboxylate (1g). The title compound was obtained as a liquid in 80% yield (0.5 mmol scale, 144.5 mg). ¹H NMR (500 MHz, CDCl₃): δ 7.25 (t, J = 7.5 Hz, 2H), 7.17 (t, J = 7.5 Hz, 3H), 4.09 (m, 2H), 3.95 (s, 2H), 3.25 (d, J = 6.5 Hz, 2H), 2.89 (t, J = 7.5 Hz, 2H), 2.75 (t, J = 7.5 Hz, 2H), 2.66 (m, 2H), 1.78-1.66 (m, 3H), 1.43 (s, 9H), 1.16-1.08 (m, 2H); ¹³C NMR (125.8 MHz, CDCl₃): δ 208.5, 155.0, 141.0, 128.7, 128.6, 126.4, 79.5, 76.7, 76.6, 44.0, 40.7, 36.6, 29.5, 29.1, 28.7; FT-IR (neat): 2924, 1722, 1686, 1452, 1420, 1365, 1274, 1247, 1233, 1170, 1143, 750 cm⁻¹; HRMS (ES+) m/z calcd. for C₂₁H₃₂NO₄ [M+H]⁺ 362.2331, found 362.2325.



1-((2-Chloropyridin-3-yl)methoxy)-4-phenylbutan-2-one (1h). The title compound was obtained as a liquid in 66% yield (0.5 mmol scale, 66.6 mg). ¹H NMR (500 MHz, CDCl₃): δ 8.32-8.30 (m, 1H), 7.85-7.83 (m, 1H), 7.29-7.24 (m, 3H), 7.20-7.17 (m, 3H), 4.60 (s, 2H), 4.15 (s, 2H), 2.94 (t, *J* = 7.5 Hz, 2H), 2.81 (t, *J* = 7.5 Hz, 2H); ¹³C NMR (125.8 MHz, CDCl₃): δ 207.3, 149.6, 148.8, 140.8, 137.5, 132.3, 128.8, 128.6, 126.6, 122.9, 76.2, 69.7, 40.8, 29.6; FT-IR (neat): 3375, 3324, 1687, 1561, 1515, 1434, 1238, 1158, 763 cm⁻¹; HRMS (ES+) m/z calcd. for C₁₆H₁₆NO₂NaCl [M+Na]⁺ 312.0755, found 312.0767.



1-((2,6-Dichlorophenyl)(phenyl)methoxy)-4-phenylbutan-2-one (1i) The title compound was obtained as a liquid in 71% yield (0.5 mmol scale, 141.7 mg). ¹H NMR (500 MHz, CDCl₃): δ 7.37-7.26 (m, 9H), 7.23-7.18 (m, 4H), 6.41 (s, 1H), 4.05 (dd, J = 46.8, 16.4 Hz, 2H), 3.01-2.99 (m, 2H), 2.97-2.94 (m, 2H); ¹³C NMR (125.8 MHz, CDCl₃): δ 208.5, 141.2, 139.4, 136.6, 135.1, 130.3, 129.8, 128.8, 128.7, 128.4, 127.5, 126.4, 126.1, 79.3, 74.6, 41.1, 29.4; FT-IR (neat): 2933, 2855, 1736, 1565, 1436, 1407, 1104, 1090, 1080, 941, 792, 760, 731cm⁻¹; HRMS (ES+) m/z calcd. for C₂₃H₂₀O₂NaCl₂ [M+Na]⁺ 421.0738, found 421.0734.



1-(*tert*-**Butoxy**)-**4**-**phenylbutan-2-one (1j).** The title compound was obtained as a liquid in 75% yield (0.5 mmol scale, 82.6 mg). ¹H NMR (500 MHz, CDCl₃): 7.30-7.27 (m, 2H), 7.21-7.18 (m, 3H), 3.92 (s, 2H), 2.92-2.89 (m, 2H), 2.86-2.82 (m, 2H),1.19 (s, 9H); ¹³C NMR (125.8 MHz, CDCl₃): δ 209.9, 141.4, 128.8, 128.7, 126.4, 74.3, 68.8, 41.0, 29.7, 27.6; FT-IR (neat): 2974, 2359, 2341, 1720, 1564, 1490, 1392, 1365, 1197, 1082, 877, 727 cm⁻¹; HRMS (ES+) m/z calcd. for $C_{13}H_{17}O_2$ [M-CH₃]⁺ 205.1229, found 205.1222.



4-(Benzyloxy)-1,6-diphenylhexan-3-one (1k). The title compound was obtained as a solid in 88% yield (0.5 mmol scale, 155.9 mg). ¹H NMR (500 MHz, CDCl₃): 7.43-7.32 (m, 9H), 7.25 (t, J = 7.5 Hz, 4H), 7.16 (d, J = 7.5 Hz, 2H), 4.55 (d, J = 11.5 Hz, 1H), 4.40 (d, J = 11.5 Hz, 1H), 3.84 (dd, J = 7.9, 4.5 Hz, 1H), 2.93 (dd, J = 14.7, 5.8 Hz, 4H), 2.81-2.75 (m, 1H), 2.71-2.65 (m, 1H), 2.04-2.00 (m, 1H), 1.98-1.93 (m, 1H); ¹³C NMR (125.8 MHz, CDCl₃): δ 212.3, 141.4, 141.3, 137.7, 128.8, 128.7, 128.7, 128.7, 128.3, 126.4, 126.3, 84.3, 72.7, 39.7, 33.9, 31.6, 29.6.; FT-IR (neat): 3027, 1713, 1496, 1453, 1092, 1028 cm⁻¹; HRMS (ES+) m/z calcd. for C₂₅H₂₆O₂Na [M+Na]⁺ 381.1831, found 381.1819.



2-(Benzyloxy)-1-phenylethanone (2a). The title compound was obtained as a solid in 87% yield (0.5 mmol scale, 99.5 mg). mp 58-60 °C; ¹H NMR (500 MHz, CDCl₃): δ 7.92 (d, *J* = 8.0 Hz, 2H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.45 (t, *J* = 7.5 Hz, 2H), 7.40-7.34 (m, 4H), 7.31 (t, *J* = 7.5 Hz, 1H), 4.75 (s, 2H), 4.69 (s, 2H); ¹³C NMR (125.8 MHz, CDCl₃): δ 196.6, 137.6, 135.3, 133.8, 129.0, 128.8, 128.4, 128.3, 128.2, 73.7, 72.9; FT-IR (neat): 2985, 1692, 1226, 1126, 1078, 975, 905, 742 cm⁻¹; HRMS (ES+) m/z calcd. for C₁₅H₁₄O₂Na [M+Na]⁺ 249.0891, found 249.0890.



2-(Cyclopentyloxy)-1-phenylethanone (2b). The title compound was obtained as a liquid in 90% yield (0.5 mmol scale, 93.9 mg). ¹H NMR (500 MHz, CDCl₃): 7.93 (d, J = 8.5 Hz, 2H), 7.57-7.54 (m, 1H), 7.44 (t, J = 7.5 Hz, 2H), 4.68 (s, 2H), 4.04-4.02 (m, 1H), 1.74-1.71 (m, 6H), 1.53-1.52 (m, 2H); ¹³C NMR (125.8 MHz, CDCl₃): δ 197.1, 135.4, 133.6, 128.9, 128.3, 82.8, 72.4, 32.4, 23.7; FT-IR (neat): 2936, 2851, 1720, 1699, 1499, 1270, 1227, 1206, 1146, 1117, 969, 755, 714, 689 cm⁻¹; HRMS (ES+) m/z calcd. for C₁₃H₁₇O₂ [M+H]⁺ 205.1229, found 205.1236.



2-(2-Isopropyl-5-methylcyclohexyloxy)-1-phenylethanone (**2c**) The title compound was obtained as a liquid in 91% yield (0.5 mmol scale, 127.5 mg). ¹H NMR (500 MHz, CDCl₃): 7.96-7.94 (m, 2H), 7.58-7.54 (m, 1H), 7.47-7.43 (m, 2H), 4.82 (d, J = 16.0 Hz, 1H), 4.67 (d, J = 16.0 Hz, 1H), 3.24-3.19 (m, 1H), 2.30-2.24 (m, 1H), 2.14-2.11 (m, 1H), 1.66-1.61 (m, 2H), 1.37-1.31 (m, 2H), 0.98-0.87 (m, 9H), 0.73 (d, J = 6.5 Hz, 3H); ¹³C NMR (125.8 MHz, CDCl₃): δ 197.1, 135.5, 133.6, 128.9, 128.5, 80.5, 71.8, 48.5, 40.3, 34.7, 31.9, 25.7, 23.5, 22.6, 21.3, 16.4; FT-IR (neat): 2954,2923, 2870, 1721, 1271, 1176, 1151, 1128, 1097, 1146, 1117, 969, 755, 714, 689 cm⁻¹; HRMS (ES+) m/z calcd. for C₁₈H₂₇O₂ [M+H]⁺ 275.2011, found 275.2010.



1-Phenyl-2-((tetrahydro-2*H***-pyran-3-yl)methoxy)ethanol (2d).** The title compound was obtained as a liquid in 78% yield (0.5 mmol scale, 91.3 mg). ¹H NMR (500 MHz, CDCl₃): 7.91-7.89 (m, 2H), 7.57-7.53 (m, 1H), 7.45-7.42 (m, 2H), 4.88-4.84 (m, 1H), 4.78-4.64 (m, 1H), 3.98-3.95 (m, 1H), 3.60-3.51 (m, 3H), 3.44-3.39 (m, 1H), 1.84-1.81 (m, 1H), 1.55-1.46 (m, 4H), 1.35-1.27 (m, 1H); ¹³C NMR (125.8 MHz, CDCl₃): δ 196.8, 135.2, 133.7, 128.9, 128.2, 77.32, 75.5, 74.6, 68.6, 28.2, 26.1, 23.3; FT-IR (neat): 2918, 2847, 1728, 1564, 1442, 1407, 1288, 1237, 1148, 1111, 1091, 728 cm⁻¹; HRMS (ES+) m/z calcd. for C₁₄H₁₈O₃ Na [M+Na]⁺ 257.1154, found 257.1146.



2-((2-Chloropyridin-3-yl)methoxy)-1-phenylethanone (2e). The title compound was obtained as a liquid in 74% yield (0.5 mmol scale, 100.7 mg). mp 41-43 °C; ¹H NMR (500 MHz, CDCl₃): δ 8.32-8.31 (m, 1H), 7.97-7.96 (m, 1H), 7.93 (d, *J* = 8.3 Hz, 2H), 7.61-7.58 (m, 1H), 7.48 (t, *J* = 7.7 Hz, 2H), 7.29-7.26 (m, 1H), 4.92 (d, *J* = 0.4 Hz, 2H), 4.76 (s, 2H); ¹³C NMR (125.8 MHz, CDCl₃): δ 195.9, 149.6, 148.8, 137.8, 134.9, 134.1, 132.6, 129.1, 128.1, 123.0, 73.8, 69.8; FT-IR (neat): 2923, 1702, 1583, 1566, 1450, 1414, 1229, 1144, 975, 797, 750, 684 cm⁻¹; HRMS (ES+) m/z calcd. for C₁₄H₁₃NO₂Cl [M+H]⁺ 262.0635, found 262.0639.



2-(2-Methoxyethoxy)-1-phenylethanone (2f). The title compound was obtained as a liquid in 83% yield (0.5 mmol scale, 80.6 mg). ¹H NMR (500 MHz, CDCl₃): 7.91 (dd, J = 7.5, 1.0 Hz, 2H), 7.58-7.55 (m, 1H), 7.45 (t, J = 7.5, 2H), 4.83 (s, 2H), 3.77-3.75 (m, 2H), 3.62-3.60 (m, 2H), 3.37 (s, 3H); ¹³C NMR (125.8 MHz, CDCl₃): δ 196.6, 135.1, 133.8, 129.0, 128.1, 74.4, 72.4, 71.1, 59.3; FT-IR (neat): 2923, 2876, 1720, 1598, 1449, 1270, 1227, 1199, 1174, 1146, 1117, 969, 755, 689 cm⁻¹; HRMS (ES+) m/z calcd. for C₁₁H₁₄O₃Na [M+Na]⁺ 217.0841, found 217.0842.



2-(Benzyloxy)-1-cyclopropylethanone (3a). The title compound was obtained as a liquid in 93% yield (0.5 mmol scale, 88.4 mg). ¹H NMR (500 MHz, CDCl₃): 7.38-7.34 (m, 4H), 7.32-7.29 (m, 1H), 4.61 (s, 2H), 4.21 (s, 2H), 2.17-2.12 (m, 1H), 1.11-1.08 (m, 2H), 0.94-0.90 (m, 2H); ¹³C NMR (125.8 MHz, CDCl₃): δ 208.7, 137.5, 128.7, 128.2, 128.1, 75.6, 73.6, 17.2, 11.6; FT-IR (neat): 2987, 1697, 1454, 1385, 1155, 1103, 1061, 1020, 897, 745 cm⁻¹; HRMS (ES+) m/z calcd. for C₁₂H₁₅O₂ [M+H]⁺ 191.1072, found 191.1063.



2-(Benzyloxy)-1-cyclobutylethanone (3b). The title compound was obtained as a liquid in 80% yield (0.5 mmol scale, 81.7 mg). ¹H NMR (500 MHz, CDCl₃): 7.35-7.34 (m, 4H), 7.31-7.28 (m,

1H), 4.56 (s, 2H), 4.06 (s, 2H), 3.43-3.36 (m, 1H), 2.29-2.21 (m, 2H), 2.15-2.09 (m, 2H), 2.02-1.94 (m, 1H), 1.87-1.82 (m, 1H); ¹³C NMR (125.8 MHz, CDCl₃): δ 209.4, 137.6, 128.7, 128.1, 128.0, 73.6, 73.5, 42.2, 24.4, 18.3; FT-IR (neat): 2985, 2945, 1721, 1454, 1382, 1160, 1094, 1027, 993 cm⁻¹; HRMS (ES+) m/z calcd. for C₁₃H₁₅O₂ [M-H]⁺ 203.1072, found 203.1070.



1-(Adamantan-1-yl)-2-(benzyloxy)ethanone (3c). The title compound was obtained as a liquid in 85% yield (0.5 mmol scale, 120.8 mg). mp 56-58 °C; ¹H NMR (500 MHz, CDCl₃): 7.37-7.33 (m, 4H), 7.31-7.28 (m, 1H), 4.58 (s, 2H), 4.31 (s, 2H), 2.04-2.02 (m, 3H), 1.82-1.81 (m, 6H), 1.75-1.66 (m, 6H); ¹³C NMR (125.8 MHz, CDCl₃): δ 211.5, 137.8, 128.8, 128.3, 128.2, 73.4, 70.7, 45.6, 38.3, 36.8, 28.1; FT-IR (neat): 2904, 2850, 1703, 1452, 1266, 1118, 1024, 1002, 757, 744, 697 cm⁻¹; HRMS (ES+) m/z calcd. for C₁₉H₂₅O₂ [M+H]⁺ 285.11855, found 285.1850.



1-(Benzyloxy)-3-phenylpropan-2-one (3d). The title compound was obtained as a liquid in 61% yield (0.5 mmol scale, 73.2 mg). ¹H NMR (500 MHz, CDCl₃): δ 7.37-7.31 (m, 7H), 7.28-7.20 (m, 3H), 4.56 (s, 2H), 4.12 (s, 2H), 3.78 (s, 2H); ¹³C NMR (125.8 MHz, CDCl₃): δ 206.3, 137.4, 133.7, 129.8, 129.0, 128.8, 128.4, 128.3, 127.4, 74.7, 73.7, 46.6; FT-IR (neat): 2985, 1720, 1226, 1078, 975, 905, 742 cm⁻¹; HRMS (ES⁺) m/z calcd. for C₁₆H₁₇O₂ [M+H]⁺ 241.1229, found 241.1234.



1-(Benzo[*d*][1,3]dioxol-5-yl)-2-(benzyloxy)ethanone (3e). The title compound was obtained as a liquid in 84% yield (0.5 mmol scale, 113.5 mg). ¹H NMR (500 MHz, CDCl₃): 7.50 (dd, J =8.5, 1.5 Hz, 1H), 7.41 (d, J = 1.5 Hz, 1H), 7.39-7.34 (m, 4H), 7.32-7.28 (m, 1H), 6.82 (d, J = 8.0 Hz, 1H), 6.02 (s, 2H), 4.67-4.66 (m, 4H); ¹³C NMR (125.8 MHz, CDCl₃): δ 194.5, 152.3, 148.5, 137.6, 129.9, 128.8, 128.3, 128.2, 124.5, 108.3, 108.0, 102.1. 73.6, 72.7; FT-IR (neat): 3925, 1680, 1603, 1486, 1444, 1426, 1248, 1128, 1100, 1082, 1029, 990, 785 cm⁻¹; HRMS (ES+) m/z calcd. for C₁₆H₁₄O₄Na [M+Na]⁺ 293.0790, found 293.0791.



2-(Benzyloxy)-1-(4-methoxyphenyl)ethanone (3f). The title compound was obtained as a liquid in 88% yield (0.5 mmol scale, 112.7 mg). mp 36-38 °C; ¹H NMR (500 MHz, CDCl₃): δ 7.92 (dd, J = 7.0, 1.7 Hz, 2H), 7.40-7.34 (m, 4H), 7.32-7.29 (m, 1H), 6.93-6.91 (m, 2H), 4.70 (s, 2H), 4.68 (s, 2H), 3.86 (s, 3H); ¹³C NMR (125.8 MHz, CDCl₃): δ 195.1, 164.1, 147.9, 137.7, 130.6, 128.8, 128.4, 128.3, 114.2, 73.7, 72.8, 55.8; FT-IR (neat): 2850, 1685, 1597, 1573, 1509, 1455, 1260, 1235, 1168, 1113, 1021, 832, 749 cm⁻¹; HRMS (ES+) m/z calcd. for C₁₆H₁₇O₃ [M+H]⁺ 257.1178, found 257.1176.



4-(Benzyloxy)-2-methyl-3-oxobutan-2-yl acetate (3g). The title compound was obtained as a liquid in 50% yield (0.5 mmol scale, 62.5 mg). ¹H NMR (500 MHz, CDCl₃): 7.37-7.33 (m, 4H), 7.31-7.29 (m, 1H), 4.59 (s, 2H), 4.31 (s, 2H), 2.02 (s, 3H), 1.50 (s, 6H); ¹³C NMR (125.8 MHz, CDCl₃): δ 205.6, 170.7, 137.7, 128.7, 128.3, 128.2, 82.9, 73.5, 70.9, 24.0, 21.4; FT-IR (neat): 2989, 1730, 1368, 1253, 1146, 1047, 1019, 740, 697 cm⁻¹; HRMS (ES+) m/z calcd. for C₁₄H₁₈O₄Na [M+Na]⁺ 273.1103, found 273.1106.



2-(Benzyloxy)-1-(furan-2-yl)ethanone (3h). The title compound was obtained as a liquid in 36% yield (0.5 mmol scale, 38.9 mg). ¹H NMR (500 MHz, CDCl₃): 7.58-7.57 (m, 1H), 7.40-7.35 (m, 4H), 7.32-7.31 (m, 2H), 6.54-6.53 (m, 1H), 4.68 (s, 2H), 4.59 (s, 2H); ¹³C NMR (125.8 MHz, CDCl₃): δ 185.9, 151.3, 146.9, 137.5, 128.8, 128.4, 128.3, 118.5, 112.6, 73.8, 72.5; FT-IR (neat): 2923, 2856, 1689, 1467, 1132, 1018, 764, 738, 698 cm⁻¹; HRMS (ES+) m/z calcd. for C₁₃H₁₃O₃ [M+H]⁺ 217.0865, found 217.0861.



2-(Benzyloxy)-1-(3-methylthiophen-2-yl)ethanone (3i). The title compound was obtained as a liquid in 46% yield (0.5 mmol scale, 56.6 mg). ¹H NMR (500 MHz, CDCl₃): 7.43-7.40 (m, 3H), 7.38-7.35 (m, 2H), 7.32-7.29 (m, 1H), 6.95 (d, *J* = 4.9 Hz, 1H), 4.69 (s, 2H), 4.52 (s, 2H), 2.58 (s, 3H); ¹³C NMR (125.8 MHz, CDCl₃): δ 190.6, 146.9, 137.6, 137.5, 132.5, 130.9, 128.8, 128.4,

128.3, 74.4, 73.8, 17.3; FT-IR (neat): 2924, 2850, 1656, 1401, 1371, 1210, 1122, 1028, 972, 733, 696 cm⁻¹; HRMS (ES+) m/z calcd. for C₁₄H₁₄O₂NaS [M+Na]⁺ 269.0612, found 269.0609.



2-(Benzyloxy)-1-morpholinoethanone (3j). The title compound was obtained as a liquid in 77% yield (0.5 mmol scale, 42.3 mg). ¹H NMR (500 MHz, CDCl₃): 7.37-7.33 (m, 4H), 7.32-7.29 (m, 1H), 4.59 (s, 2H), 4.17 (s, 2H), 3.68-3.66 (m, 2H), 3.64-3.59 (m, 4H), 3.50-3.48 (m, 2H); ¹³C NMR (125.8 MHz, CDCl₃): δ 168.1, 137.4, 128.8, 128.4, 128.3, 73.6, 69.7, 67.2, 67.0, 45.9, 42.4; FT-IR (neat): 2900, 2857, 1689, 1644, 1453, 1438, 1272, 1111, 1026, 844, 737 cm⁻¹; HRMS (ES+) m/z calcd. for C₁₃H₁₇NO₃Na [M+Na]⁺ 258.1106, found 258.1115.

References:

- 1) Molander, G. A.; Canturk, B. J. Org. Lett. 2008, 10, 2135.
- 2) Tellis, J. C.; Primer, D. N.; Molander, G. A. Science 2014, 345, 433



¹H NMR (500 MHz, CDCl₃) Spectrum of 1-(Benzyloxy)-4-phenylbutan-2-one (1a)



¹³C NMR (125.8 MHz, CDCl₃) Spectrum of 1-(Benzyloxy)-4-phenylbutan-2-one (1a)



¹H NMR (500 MHz, CDCl₃) Spectrum of 1-(2,6-Dichlorobenzyloxy)-4-phenylbutan-2-one (1b)



¹³C NMR (125.8 MHz, CDCl₃) Spectrum of 1-(2,6-Dichlorobenzyloxy)-4-phenylbutan-2-one (1b)



¹H NMR (500 MHz, CDCl₃) Spectrum of 1-(Hex-5-enyloxy)-4-phenylbutan-2-one (1c)



¹³C NMR (125.8 MHz, CDCl₃) Spectrum of 1-(Hex-5-enyloxy)-4-phenylbutan-2-one (1c)



¹H NMR (500 MHz, CDCl₃) Spectrum of 4-Phenyl-1-(prop-2-ynyloxy)butan-2-one (1d)



¹³C NMR (125.8 MHz, CDCl₃) Spectrum of 4-Phenyl-1-(prop-2-ynyloxy)butan-2-one (1d)



¹H NMR (500 MHz, CDCl₃) Spectrum of 1-(2-Methoxyethoxy)-4-phenylbutan-2-one (1e)



¹³C NMR (125.8 MHz, CDCl₃) Spectrum of 1-(2-Methoxyethoxy)-4-phenylbutan-2-one (1e)



¹H NMR (500 MHz, CDCl₃) Spectrum of 4-Phenyl-1-(2-(trimethylsilyl)ethoxy)butan-2-one (1f)



¹³C NMR (125.8 MHz, CDCl₃) Spectrum of 4-Phenyl-1-(2-(trimethylsilyl)ethoxy)butan-2-one (1f)



¹H NMR (500 MHz, CDCl₃) Spectrum of *tert*-Butyl 4-((2-oxo-4-phenylbutoxy)methyl)piperidine-1-carboxylate (1g)


¹³C NMR (125.8 MHz, CDCl₃) Spectrum of *tert*-Butyl 4-((2-oxo-4-phenylbutoxy)methyl)piperidine-1-carboxylate (1g)



¹H NMR (500 MHz, CDCl₃) Spectrum of 1-((2-Chloropyridin-3-yl)methoxy)-4-phenylbutan-2-one (1h)



¹³C NMR (125.8 MHz, CDCl₃) Spectrum of 1-((2-Chloropyridin-3-yl)methoxy)-4-phenylbutan-2-one (1h)



¹H NMR (500 MHz, CDCl₃) Spectrum of 1-((2,6-Dichlorophenyl)(phenyl)methoxy)-4-phenylbutan-2-one (1i)



¹³C NMR (125.8 MHz, CDCl₃) Spectrum of 1-((2,6-Dichlorophenyl)(phenyl)methoxy)-4-phenylbutan-2-one (1i)



¹H NMR (500 MHz, CDCl₃) Spectrum of 1-(*tert*-Butoxy)-4-phenylbutan-2-one (1j)



¹³C NMR (125.8 MHz, CDCl₃) Spectrum of 1-(*tert*-Butoxy)-4-phenylbutan-2-one (1j)



¹H NMR (500 MHz, CDCl₃) Spectrum of 4-(Benzyloxy)-1,6-diphenylhexan-3-one (1k)



¹³C NMR (125.8 MHz, CDCl₃) Spectrum of 4-(Benzyloxy)-1,6-diphenylhexan-3-one (1k)



¹H NMR (500 MHz, CDCl₃) Spectrum of 2-(Benzyloxy)-1-phenylethanone (2a)



¹³C NMR (125.8 MHz, CDCl₃) Spectrum of 2-(Benzyloxy)-1-phenylethanone (2a)



¹H NMR (500 MHz, CDCl₃) Spectrum of 2-(Cyclopentyloxy)-1-phenylethanone (2b)



¹³C NMR (125.8 MHz, CDCl₃) Spectrum of 2-(Cyclopentyloxy)-1-phenylethanone (2b)



¹H NMR (500 MHz, CDCl₃) Spectrum of 2-(2-Isopropyl-5-methylcyclohexyloxy)-1-phenylethanone (2c)



¹³C NMR (125.8 MHz, CDCl₃) Spectrum of 2-(2-Isopropyl-5-methylcyclohexyloxy)-1-phenylethanone (2c)



¹H NMR (500 MHz, CDCl₃) Spectrum of 1-Phenyl-2-((tetrahydro-2*H*-pyran-3-yl)methoxy)ethanol (2d)



¹³C NMR (125.8 MHz, CDCl₃) Spectrum of 1-Phenyl-2-((tetrahydro-2*H*-pyran-3-yl)methoxy)ethanol (2d)



¹H NMR (500 MHz, CDCl₃) Spectrum of 2-((2-Chloropyridin-3-yl)methoxy)-1-phenylethanone (2e)



¹³C NMR (125.8 MHz, CDCl₃) Spectrum of 2-((2-Chloropyridin-3-yl)methoxy)-1-phenylethanone (2e)



¹H NMR (500 MHz, CDCl₃) Spectrum of 2-(2-Methoxyethoxy)-1-phenylethanone (2f)



¹³C NMR (125.8 MHz, CDCl₃) Spectrum of 2-(2-Methoxyethoxy)-1-phenylethanone (2f)



¹H NMR (500 MHz, CDCl₃) Spectrum of 2-(Benzyloxy)-1-cyclopropylethanone (3a)



¹³C NMR (125.8 MHz, CDCl₃) Spectrum of 2-(Benzyloxy)-1-cyclopropylethanone (3a)



¹H NMR (500 MHz, CDCl₃) Spectrum of 2-(Benzyloxy)-1-cyclobutylethanone (3b)



¹³C NMR (125.8 MHz, CDCl₃) Spectrum of 2-(Benzyloxy)-1-cyclobutylethanone (3b)



¹H NMR (500 MHz, CDCl₃) Spectrum of 1-(Adamantan-1-yl)-2-(benzyloxy)ethanone (3c)



¹³C NMR (125.8 MHz, CDCl₃) Spectrum of 1-(Adamantan-1-yl)-2-(benzyloxy)ethanone (3c)



¹H NMR (500 MHz, CDCl₃) Spectrum of 1-(Benzyloxy)-3-phenylpropan-2-one (3d)



¹³C NMR (125.8 MHz, CDCl₃) Spectrum of 1-(Benzyloxy)-3-phenylpropan-2-one (3d)



¹H NMR (500 MHz, CDCl₃) Spectrum of 1-(Benzo[*d*][1,3]dioxol-5-yl)-2-(benzyloxy)ethanone (3e)



¹³C NMR (125.8 MHz, CDCl₃) Spectrum of 1-(Benzo[*d*][1,3]dioxol-5-yl)-2-(benzyloxy)ethanone (3e)



¹H NMR (500 MHz, CDCl₃) Spectrum of 2-(Benzyloxy)-1-(4-methoxyphenyl)ethanone (3f)



¹³C NMR (125.8 MHz, CDCl₃) Spectrum of 2-(Benzyloxy)-1-(4-methoxyphenyl)ethanone (3f)



¹H NMR (500 MHz, CDCl₃) Spectrum of 4-(Benzyloxy)-2-methyl-3-oxobutan-2-yl acetate (3g)



¹³C NMR (125.8 MHz, CDCl₃) Spectrum of 4-(Benzyloxy)-2-methyl-3-oxobutan-2-yl acetate (3g)



¹H NMR (500 MHz, CDCl₃) Spectrum of 2-(Benzyloxy)-1-(furan-2-yl)ethanone (3h)


¹³C NMR (125.8 MHz, CDCl₃) Spectrum of 2-(Benzyloxy)-1-(furan-2-yl)ethanone (3h)



¹H NMR (500 MHz, CDCl₃) Spectrum of 2-(Benzyloxy)-1-(3-methylthiophen-2-yl)ethanone (3i)



¹³C NMR (125.8 MHz, CDCl₃) Spectrum of 2-(Benzyloxy)-1-(3-methylthiophen-2-yl)ethanone (3i)



¹H NMR (500 MHz, CDCl₃) Spectrum of 2-(Benzyloxy)-1-morpholinoethanone (3j)



¹³C NMR (125.8 MHz, CDCl₃) Spectrum of 2-(Benzyloxy)-1-morpholinoethanone (3j)