Cu-Catalyzed Stereoselective γ-Alkylation of Enones

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Supporting Information

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I. General Information

Unless otherwise stated, reactions were performed in oven-dried glassware under a N_2 atmosphere using dry, deoxygenated solvents. Anhydrous dichloromethane, pentane, toluene and THF (BHT-free) were purchased from Aldrich, degassed with argon, and dried by passage through activated drying columns[1] on a Pure Process Technology system. Molecular sieves (MS) were purchased from Aldrich and stored in a 120 °C drying oven until immediately prior to use unless otherwise noted. 1,2-Dichloroethene was purchased from Chem-Impex International, Inc., distilled over CaH_2 prior to use, and stored over 4 Å MS under N_2 atmosphere. Sodium hydride (NaH) was purchased as 60% dispersion in mineral oil from Acros and used as received. Sodium bicarbonate ($NaHCO_3$) was purchase from Fischer Chemical and used as received. Starting materials, including 2-cyclohexen-1-one, were purchased from Aldrich, Alfa Aesar, or Oakwood Chemical and used as received. *N*,*N*,*N'*,*N''*,*N''*-Pentamethyldiethylenetriamine (PMDTA) was purchased from Aldrich and used as received. Copper (II) trifluoromethanesulfonate was purchased from Aldrich and stored in a glovebox. Starting materials were made according to the literature procedures.[3-9] Deuterated chloroform ($CDCl_3$, 99.9%, extra dry) was purchased from Cambridge Isotope Laboratories, Inc. and was used without further purification. Reaction temperatures were controlled by an IKAmag immersion temperature modulator. Thin-layer chromatography (TLC) was performed using Silicycle silica gel 60 F254 precoated plates (0.25 mm) and visualized by UV fluorescence quenching or staining with *p*-anisaldehyde or $KMnO_4$ solutions. Flash chromatography[2] was performed using Silicycle SiliaFlash® P60 silica gel (40–63 μm particle size). Melting points were determined using a Mel-Temp electrothermal capillary melting point apparatus and the values reported are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance DRX-500 (at 500 and 126 MHz, respectively) or DPX-400 instrument (at 400 and 101 MHz, respectively) and are reported relative to Me_4Si (δ 0.0). Data for ^{1}H NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicities are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, sept = septet, m = multiplet, comp. m = complex multiplet, app. = apparent, br s = broad singlet. Data for ^{13}C NMR spectra are reported in terms of chemical shift relative to Me_4Si (δ 0.0). ^{19}F NMR spectra were recorded on a Bruker Avance DRX-400 at 376 MHz and are reported relative to the external standard F_3CCO_2H (δ –76.53 ppm). Infrared (IR) spectra were recorded on a Nicolet iS5 FTIR spectrometer and are reported in frequency of absorption (cm^{-1}). GC/MS analyses were performed on a Hewlett Packard Model 6890 gas chromatograph interfaced to a Hewlett Packard Model 5973 mass selective detector (15 m x 0.25 mm capillary column, HP-5MS). LC/MS analyses were performed on Agilent 1200 liquid chromatography system interfaced with an Agilent 6300 ion trap mass selective detector. 2-bromo-2-methylpropanal,[3] *tert*-butyl benzyl(2-bromopropanoyl) carbamate,[4] ethyl 2-bromo-2-phenylacetate,[5] methyl 2-bromo-3,3-dimethylbutanoate,[6] methyl 2-chloro-2-methylpropanoate,[7] allyl 2-bromopropanoate,[8] and prop-2-yn-1-yl 2-bromopropanoate[8] were prepared according to the literature procedures. TBS-dienol ethers were synthesized by enolization with LiHMDS or by soft enolization according to our previous publication.[9]

II. Optimization of Reaction Conditions

General Procedure for optimization reactions (Table 1 and Table SI1):
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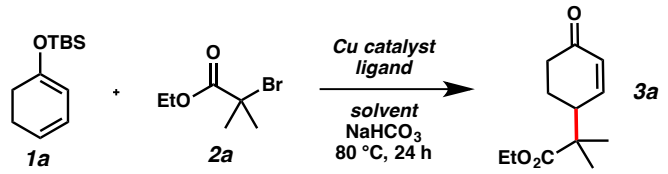
The Cu salt and base were added to an oven-dried 20 mL vial equipped with a magnetic stirring bar. Then the vial was sealed with a septum cap and then evacuated and backfilled with dry N_2 (three cycles). A solution of ligand in anhydrous solvent (1 mL) was injected into the vial via syringe and the mixture was stirred at 22 °C for 10 min. Ethyl 2-bromo-2-methylpropanoate (**2a**, 55.4 μL, 0.375 mmol, 1.5 equiv) and *tert*-butyl(cyclohexa-1,3-dien-1-yloxy)dimethylsilane (**1a**, 52.6 mg, 0.25 mmol, 1.0 equiv) were injected into the vial sequentially via syringe. The mixture was warmed to 80 °C and stirred. After 24 h the reaction was cooled to room temperature, and the solvent was removed in vacuo. The crude compound was purified by flash column chromatography on silica gel.

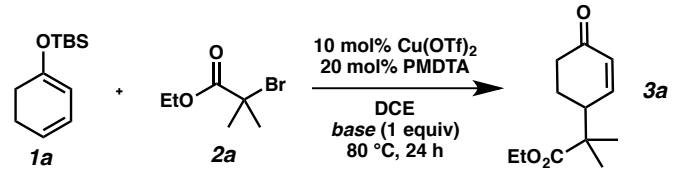
Table 1. Optimization of catalyst, ligand, and solvent.[a]



entry	Cu catalyst (mol %)	ligand (mol %)	solvent	yield (%)
1	$Cu(OTf)_2$ (10)	none	toluene	0
2	$Cu(OTf)_2$ (10)	bipy (20)	toluene	0
3	$Cu(OTf)_2$ (10)	TMEDA (20)	toluene	16
4	$Cu(OTf)_2$ (10)	PMDTA (20)	toluene	58
5	CuI (10)	PMDTA (20)	toluene	16
6	$CuCl_2$ (10)	PMDTA (20)	toluene	12
7	$CuBr{\cdot}SMe_2$ (10)	PMDTA (20)	toluene	49
8	$CuCO_3$ (10)	PMDTA (20)	toluene	42
9	$Cu(OTf)_2$ (10)	PMDTA (20)	CH_3CN	73
10	$Cu(OTf)_2$ (10)	PMDTA (20)	THF	77
11	$Cu(OTf)_2$ (10)	PMDTA (20)	1,4-dioxane	86
12	$Cu(OTf)_2$ (10)	PMDTA (20)	DCE	92
13	***$Cu(OTf)_2$ (7.5)***	***PMDTA (15)***	***DCE***	***94***

[a] Isolated yield from reaction of of dienol ether 1a (0.25 mmol), α-haloester 2a (1.5 equiv), $NaHCO_3$ (1.0 equiv), Cu catalyst, and ligand in 1 mL of solvent at 80 °C for 24 h.

Table SI 1. Optimization of base.[a]



entry	base	yield (%)	entry	base	yield (%)
1	none	16	5	Li_2CO_3	56
2	KO*t*-Bu	8	6	Na_2CO_3	86
3	K_3PO_4	16	7	K_2CO_3	77
4	$NaHCO_3$	92	8	Cs_2CO_3	41

[a] Isolated yield from reaction of of dienol ether 1a (0.25 mmol), α-haloester 2a (1.5 equiv), base (1.0 equiv), $Cu(OTf)_2$ (10 mol%), PMDTA (20 mol%) in 1 mL of DCE at 80 °C for 24 h.

III. General Procedures

The TBS dienol ethers were synthesized by enolization with LiHMDS or by soft enolization according to our previous publication.[9]

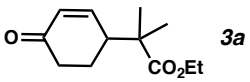
Halo carbonyl compounds were purchased or prepared according to literature procedures.[3–8]

General Procedure for Cu-Catalyzed γ-Alkylation

Anhydrous $Cu(OTf)_2$ (6.8 mg, 0.01875 mmol, 7.5 mol%) and $NaHCO_3$ (21 mg, 0.25 mmol, 1.0 equiv) were added to an oven-dried 20 mL vial equipped with a magnetic stirring bar. Then the vial was sealed with a septum cap and then evacuated and backfilled with dry N_2 (three cycles). Anhydrous 1,2-dichloroethane (1 mL) and *N*,*N*,*N'*,*N''*,*N''*-pentamethyldiethylenetriamine (7.8 μL, 0.0375 mmol, 15 mol%) were injected into the vial via syringe and the mixture was stirred at 22 °C for 10 min. The α-halo compound (0.375 mmol, 1.5 equiv) and TBS dienol ether (0.25 mmol, 1.0 equiv) were injected to the vial sequentially via syringe. The mixture was warmed to 80 °C and stirred. After the reaction was complete (monitored by TLC, typically after 22 h), the mixture was cooled to room temperature, and the solvent was removed in vacuo. The crude residue was purified by flash column chromatography on silica gel.

Specific quantities of reagents, procedural variations, and purification conditions may be found below in the entry containing the characterization data.

IV. Experimental Data for γ-Alkylation Products

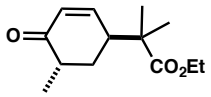


Ethyl 2-methyl-2-(4-oxocyclohex-2-en-1-yl)propanoate (Table 2, entry 1)
The title compound was prepared according to the general procedure using *tert*-butyl(cyclohexa-1,3-dien-1-yloxy)dimethylsilane (52.6 mg, 0.25 mmol, 1.0 equiv) and ethyl 2-bromo-2-

methylpropanoate (55.4 μL, 0.375 mmol, 1.5 equiv) at 80 °C for 22 h. After purification by flash chromatography (SiO_2, hexanes/EtOAc = 4:1), the title compound was isolated as a colorless oil.

1st run: 49 mg (93% yield)
2nd run: 50 mg (95% yield)

TLC (SiO_2) R_f = 0.45 in 4:1 hexanes/EtOAc, *p*-anisaldehyde stain
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.76 (d, *J* = 10.4 Hz, 1H), 5.95 (dd, *J* = 10.4, 2.3 Hz, 1H), 4.09 (q, *J* = 7.1 Hz, 2H), 2.74 (m, 1H), 2.45 (m, 1H), 2.30 (m, 1H), 1.94 (m, 1H), 1.69 (m, 1H), 1.19 (t, *J* = 7.1 Hz, 3H), 1.15 (s, 3H), 1.13 (s, 3H)
^{13}C NMR (126 MHz, $CDCl_3$) δ 199.1, 176.5, 151.2, 130.1, 60.7, 44.8, 43.7, 37.5, 24.3, 22.4, 22.0, 14.1
IR (neat) 2977, 1722, 1683, 1468, 1386, 1368, 1304, 1257, 1141, 1068, 1022, 961, 857, 831, 774, 736, 657 cm^{-1}
GC/MS (*m/z*): 210.1 (2%), 137.1 (100%), 116.1(85%), 107.1 (25%), 95.1 (66%), 81.1 (18%), 67.1 (27%), 59.1 (19%)

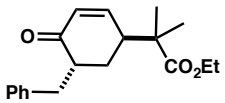


3b

Ethyl 2-methyl-2-(5-methyl-4-oxocyclohex-2-en-1-yl)propanoate (Table 2, entry 2)
The title compound was prepared according to the general procedure using *tert*-butyldimethyl((6-methylcyclohexa-1,3-dien-1-yl)oxy)silane (56.1 mg, 0.25 mmol, 1.0 equiv) and ethyl 2-bromo-2-methylpropanoate (55.4 μL, 0.375 mmol, 1.5 equiv) at 80 °C for 22 h. Crude ^{1}H NMR prior to purification indicated a single diastereomer. After purification by flash chromatography (SiO_2, hexanes/EtOAc = 8:1), the title compound was isolated as a colorless oil, comprising a single diastereomer (based on ^{1}H NMR of purified material).

1st run: 45.4 mg (81% yield)
2nd run: 47.4 mg (84% yield)

TLC (SiO_2) R_f = 0.25 in 8:1 hexanes/EtOAc, *p*-anisaldehyde stain
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.75 (d, *J* = 10.4 Hz, 1H), 5.94 (d, *J* = 10.4 Hz, 1H), 4.14 (m, 2H), 2.85 (m, 1H), 2.53 (m, 1H), 1.91 (m, 1H), 1.75 (m, 1H), 1.19 (m, 12H)
^{13}C NMR (126 MHz, $CDCl_3$) δ 202.5, 176.6, 149.8, 128.9, 60.8, 44.9, 39.8, 39.4, 30.5, 22.5, 22.4, 15.8, 14.2
IR (neat) 2975, 2934, 2874, 1722, 1677, 1463, 1387, 1247, 1170, 1130, 1025, 883, 831, 811, 773, 614 cm^{-1}
GC/MS (*m/z*): 224.1 (2%), 209.1 (1%), 196.1 (1%), 167.1 (3%), 151.1 (66%), 135.1 (8%), 116.1 (100%), 107.1 (1%), 95.0 (27%), 81.1 (43%), 67.1 (8%), 53.1 (16%)



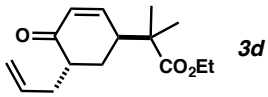
3c

Ethyl 2-(5-benzyl-4-oxocyclohex-2-en-1-yl)-2-methylpropanoate (Table 2, entry 3)
The title compound was prepared according to the general procedure using ((6-benzylcyclohexa-1,3-dien-1-yl)oxy)(*tert*-butyl)dimethylsilane (75.1 mg, 0.25 mmol, 1.0 equiv) and ethyl 2-bromo-2-methylpropanoate (55.4 μL, 0.375 mmol, 1.5 equiv) at 80 °C for 22 h. Crude ^{1}H NMR prior to

purification indicated a single diastereomer. After purification by flash chromatography (SiO_2, hexanes/EtOAc = 8:1), the title compound was isolated as a colorless oil, comprising a single diastereomer (based on ^{1}H NMR of purified material).

1st run: 67.8 mg (90% yield)
2nd run: 64.3 mg (86% yield)

TLC (SiO_2) R_f = 0.22 in 8:1 hexanes/EtOAc, *p*-anisaldehyde stain
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (app. t, *J* = 7.5 Hz, 2H), 7.20 (app. t, *J* = 8.0 Hz, 3H), 6.82 (d, *J* = 10.4 Hz, 1H), 6.04 (dd, *J* = 10.4, 2.7 Hz, 1H), 4.08 (m, 2H), 2.93 (app. t, *J* = 9.8 Hz, 2H), 2.69 (app. t, *J* = 9.4 Hz, 2H), 1.73 (m, 2H), 1.17 (m, 9H)
^{13}C NMR (126 MHz, $CDCl_3$) δ 201.2, 176.5, 150.1, 138.8, 129.3, 128.9, 128.5, 126.5, 60.9, 47.2, 44.9, 39.5, 35.8, 26.3, 22.5, 22.2, 14.1
IR (neat) 3027, 2977, 2934, 1722, 1672, 1496, 1454, 1386, 1365, 1298, 1244, 1179, 1125, 1094, 1026, 886, 854, 786, 733, 699, 614 cm^{-1}
GC/MS (*m/z*): 300.1 (1%), 227.1 (4%), 208.1 (1%), 184.1 (18%), 167.1 (4%), 135.1 (20%), 116.1 (98%), 91.1 (100%), 77.0 (9%), 65.0 (10%), 53.1 (6%)

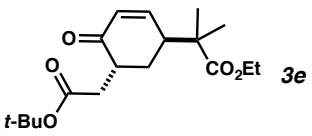


3d

Ethyl 2-(5-allyl-4-oxocyclohex-2-en-1-yl)-2-methylpropanoate (Table 2, entry 4)
The title compound was prepared according to the general procedure using ((6-allylcyclohexa-1,3-dien-1-yl)oxy)(*tert*-butyl)dimethylsilane (62.6 mg, 0.25 mmol, 1.0 equiv) and ethyl 2-bromo-2-methylpropanoate (55.4 μL, 0.375 mmol, 1.5 equiv) at 80 °C for 24 h. Crude ^{1}H NMR prior to purification indicated a single diastereomer. After purification by flash chromatography (SiO_2, hexanes/EtOAc = 8:1), the title compound was isolated as a colorless oil, comprising a single diastereomer (based on ^{1}H NMR of purified material).

1st run: 39.4 mg (62% yield)
2nd run: 41.4 mg (66% yield)

TLC (SiO_2) R_f = 0.25 in 8:1 hexanes/EtOAc, *p*-anisaldehyde stain
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.78 (t, *J* = 10.4 Hz, 1H), 5.97 (dd, *J* = 10.4, 2.8 Hz, 1H), 5.74 (m, 1H), 5.08 (m, 2H), 4.14 (m, 2H), 2.84 (m, 1H), 2.47 (m, 1H), 2.35 (m, 1H), 2.21 (m, 1H), 1.89 (m, 2H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.22 (s, 3H), 1.17 (s, 3H)
^{13}C NMR (126 MHz, $CDCl_3$) δ 201.3, 176.5, 150.0, 135.5, 129.1, 117.3, 60.9, 44.9, 39.4, 34.2, 27.2, 22.5, 22.3, 14.2
IR (neat) 2977, 2931, 1723, 1676, 1446, 1365, 1298, 1248, 1200, 1129, 1025, 914, 877, 862, 773, 632 cm^{-1}
GC/MS (*m/z*): 250.1 (1%), 222.1 (2%), 205.1 (2%), 177.1 (17%), 149.1 (6%), 135.1 (38%), 116.1 (100%), 88.1(40%), 77.1 (14%), 67.1 (10%), 55.1 (14%)



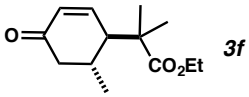
3e

Ethyl 2-(5-(2-(tert-butoxy)-2-oxoethyl)-4-oxocyclohex-2-en-1-yl)-2-methylpropanoate (Table 2, entry 5)

The title compound was prepared according to the general procedure using *tert*-butyl 2-(2-((*tert*-butyldimethylsilyl)oxy)cyclohexa-2,4-dien-1-yl)acetate (81.1 mg, 0.25 mmol, 1.0 equiv) and ethyl 2-bromo-2-methylpropanoate (55.4 μL, 0.375 mmol, 1.5 equiv) at 80 °C for 24 h. Crude ^{1}H NMR prior to purification indicated a single diastereomer. After purification by flash chromatography (SiO_2, hexanes/EtOAc = 8:1), the title compound was isolated as a colorless oil, comprising a single diastereomer (based on ^{1}H NMR of purified material).

1st run: 60.0 mg (74% yield)
2nd run: 56.8 mg (70% yield)

TLC (SiO_2) R_f = 0.24 in 8:1 hexanes/EtOAc, *p*-anisaldehyde stain
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.78 (dd, *J* = 10.4, 2.9 Hz, 1H), 6.01 (dd, *J* = 10.4, 2.5 Hz, 1H), 4.13 (q, *J* = 7.1 Hz, 2H), 2.87 (m, 2H), 2.55 (m, 1H), 2.25 (m, 1H), 1.93 (app. t, *J* = 6.3 Hz, 2H), 1.42 (s, 9H), 1.23 (m, 9H)
^{13}C NMR (126 MHz, $CDCl_3$) δ 199.6, 176.5, 170.8, 149.8, 129.6, 80.8, 60.9, 45.5, 41.4, 40.1, 35.9, 28.0, 22.8, 14.2
IR (neat) 2977, 1723, 1680, 1366, 1249, 1145, 1024, 956, 832, 755, 603 cm^{-1}
GC/MS (*m/z*): 251.1 (10%), 223.0 (4%), 209.1 (18%), 195.0 (11%), 177.0 (36%), 153.0 (28%), 135.0 (79%), 116.1 (100%), 107.0 (63%), 88.0 (30%), 77.0 (10%), 56.1 (98%)



3f

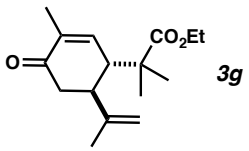
Ethyl 2-methyl-2-(6-methyl-4-oxocyclohex-2-en-1-yl)propanoate (Table 2, entry 6)

The title compound was prepared according to the general procedure using *tert*-butyldimethyl((5-methylcyclohexa-1,3-dien-1-yl)oxy)silane (56.1 mg, 0.25 mmol, 1.0 equiv) and ethyl 2-bromo-2-methylpropanoate (55.4 μL, 0.375 mmol, 1.5 equiv) at 80 °C for 26 h. Crude ^{1}H NMR prior to purification indicated a single diastereomer. After purification by flash chromatography (SiO_2, hexanes/EtOAc = 8:1), the title compound was isolated as a colorless oil, comprising a single diastereomer (based on ^{1}H NMR of purified material).

1st run: 36.6 mg (65% yield)
2nd run: 40.0 mg (71% yield)

TLC (SiO_2) R_f = 0.25 in 8:1 hexanes/EtOAc, *p*-anisaldehyde stain
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.77 (dd, *J* = 10.4, 4.3 Hz, 1H), 6.09 (dd, *J* = 10.4, 2.0 Hz, 1H), 4.16 (m, 2H), 2.64 (m, 1H), 2.57 (m, 1H), 2.17 (m, 2H), 1.25 (m, 9H), 1.04 (d, *J* = 6.8 Hz, 3H)
^{13}C NMR (126 MHz, $CDCl_3$) δ 198.8, 176.9, 147.9, 130.5, 60.9, 48.8, 46.3, 43.4, 30.3, 24.9, 22.3, 21.6, 14.1
IR (neat) 2961, 1722, 1678, 1465, 1417, 1366, 1245, 1172, 1132, 1024, 873, 812, 741, 593, 564 cm^{-1}

GC/MS (*m/z*): 224.1 (1%), 209.1 (1%), 179.1(2%), 151.1 (27%), 135.1 (5%), 116.1 (100%), 88.1 (45%), 79.1 (20%), 65.1 (5%), 53.1 (13%)



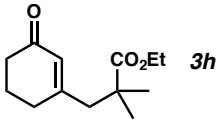
3g

Ethyl 2-methyl-2-((*1S*,6*S*)-3-methyl-4-oxo-6-(prop-1-en-2-yl)cyclohex-2-en-1-yl)propanoate (Table 2, entry 7)

The title compound was prepared according to the general procedure using (*S*)-*tert*-butyldimethyl((2-methyl-5-(prop-1-en-2-yl)cyclohexa-1,3-dien-1-yl)oxy)silane (66.1 mg, 0.25 mmol, 1.0 equiv) and ethyl 2-bromo-2-methylpropanoate (55.4 μL, 0.375 mmol, 1.5 equiv) at 80 °C for 22 h. Crude ^{1}H NMR prior to purification indicated a single diastereomer. After purification by flash chromatography (SiO_2, hexanes/EtOAc = 8:1), the title compound was isolated as a colorless oil, comprising a single diastereomer (based on ^{1}H NMR of purified material).

1st run: 51.0 mg (77% yield)
2nd run: 49.8 mg (75% yield)

TLC (SiO_2) R_f = 0.30 in 8:1 hexanes/EtOAc, *p*-anisaldehyde stain
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.48 (d, *J* = 3.3 Hz, 1H), 4.74 (s, 1H), 4.72 (s, 1H), 4.11 (m, 2H), 2.95 (m, 1H), 2.74 (m, 1H), 2.47 (dd, *J* = 6.9, 2.8 Hz, 2H), 1.81 (s, 3H), 1.71 (s, 3H), 1.25 (m, 9H)
^{13}C NMR (126 MHz, $CDCl_3$) δ 198.9, 176.9, 146.9, 144.1, 136.5, 112.8, 60.7, 46.4, 45.5, 43.8, 42.0, 24.2, 21.9, 19.9, 16.1, 14.0
IR (neat) 2976, 1774, 1723, 1676, 1448, 1385, 1297, 1251, 1174, 1138, 1026, 893, 839, 770, 556 cm^{-1}
GC/MS (*m/z*): 264.0 (1%), 219.0 (2%), 191.0 (2%), 175.0 (4%), 149.1 (100%), 135.0 (10%), 116.1 (56%), 107.0 (31%), 88.0 (22%), 79.1 (17%), 67.1 (8%), 55.0 (10%)



3h

Ethyl 2,2-dimethyl-3-(3-oxocyclohex-1-en-1-yl)propanoate (Table 2, entry 8)

The title compound was prepared according to the general procedure using crude *tert*-butyldimethyl((3-methylenecyclohex-1-en-1-yl)oxy)silane (prepared according to ref 9) (56.1 mg, 0.25 mmol, 1.0 equiv) and ethyl 2-bromo-2-methylpropanoate (55.4 μL, 0.375 mmol, 1.5 equiv) at 80 °C for 24 h. After purification by flash chromatography (SiO_2, hexanes/EtOAc = 4:1), the title compound was isolated as a colorless oil.

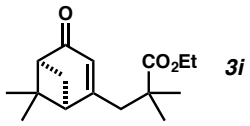
1st run: 41.7 mg (74% yield)
2nd run: 42.5 mg (76% yield)

TLC (SiO_2) R_f = 0.32 in 4:1 hexanes/EtOAc, *p*-anisaldehyde stain
^{1}H NMR (500 MHz, $CDCl_3$) δ 5.81 (s, 1H), 4.13 (q, *J* = 7.1 Hz, 2H), 2.49 (s, 2H), 2.33 (m, 2H), 2.21 (t, *J* = 5.9 Hz, 2H), 1.94 (m, 2H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.20 (s, 6H)

^{13}C NMR (126 MHz, $CDCl_3$) δ 199.5, 177.0, 162.5, 128.9, 60.8, 48.6, 42.3, 37.2, 30.7, 25.8, 22.8, 14.1

IR (neat) 2932, 1722, 1667, 1472, 1429, 1369, 1347, 1293, 1251, 1187, 1131, 1115, 1026, 965, 888, 862, 770, 590 cm^{-1}

GC/MS (*m/z*): 224.1 (15%), 209.1 (1%), 181.1 (2%), 151.1 (100%), 135.1 (7%), 125.0 (7%), 110.1 (58%), 95.1 (15%), 79.1 (17%), 67.1 (12%), 55.1 (18%)



3i

Ethyl 3-((1*R*,5*S*)-6,6-dimethyl-4-oxobicyclo[3.1.1]hept-2-en-2-yl)-2,2-dimethylpropanoate (Table 2, entry 9)

The title compound was prepared according to the general procedure using crude *tert*-butyl(((1*S*,5*R*)-6,6-dimethyl-4-methylenebicyclo[3.1.1]hept-2-en-2-yl)oxy)dimethylsilane (prepared according to ref 9) (66.1 mg, 0.25 mmol, 1.0 equiv) and ethyl 2-bromo-2-methylpropanoate (55.4 μL, 0.375 mmol, 1.5 equiv) at 80 °C for 24 h. After purification by flash chromatography (SiO_2, hexanes/EtOAc = 8:1), the title compound was isolated as a colorless oil.

1st run: 39.6 mg (60% yield)
2nd run: 42.5 mg (64% yield)

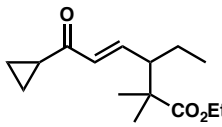
TLC (SiO_2) R*f* = 0.22 in 8:1 hexanes/EtOAc, *p*-anisaldehyde stain

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.68 (s, 1H), 4.12 (m, 2H), 2.78 (m, 1H), 2.64 (m, 1H), 2.55 (d, *J* = 13.6 Hz, 1H), 2.50 (d, *J* = 13.6 Hz, 1H), 2.42 (app. t, *J* = 5.2 Hz, 1H), 2.07 (d, *J* = 9.2 Hz, 1H), 1.47 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.23 (s, 3H), 1.22 (s, 3H), 1.00 (s, 3H)

^{13}C NMR (126 MHz, $CDCl_3$) δ 203.7, 176.7, 169.3, 123.7, 60.7, 57.6, 54.0, 49.7, 47.5, 42.6, 41.4, 26.7, 25.8, 25.7, 22.3, 14.2

IR (neat) 2977, 1725, 1678, 1471, 1386, 1368, 1282, 1241, 1185, 1132, 1030, 945, 863, 762, 677, 592 cm^{-1}

GC/MS (*m/z*): 264.1 (3%), 249.1(6%), 219.1 (2%), 194.1 (7%), 175.1 (14%), 149.1 (38%), 135.1(16%), 121.1 (100%), 107.1 (29%), 91.1 (29%), 79.1 (30%), 69.1 (12%), 55.1(27%)



3j

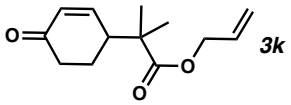
Ethyl (*E*)-6-cyclopropyl-3-ethyl-2,2-dimethyl-6-oxohex-4-enoate (Table 2, entry 10)

The title compound was prepared according to the general procedure using crude *tert*-butyl(((1*E*,3*E*)-1-cyclopropylhepta-1,3-dien-1-yl)oxy)dimethylsilane (prepared according to ref 9) (66.6 mg, 0.25 mmol, 1.0 equiv) and ethyl 2-bromo-2-methylpropanoate (55.4 μL, 0.375 mmol, 1.5 equiv) at 80 °C for 22 h. After purification by flash chromatography (SiO_2, hexanes/EtOAc = 15:1), the title compound was isolated as a colorless oil.

1st run: 39.5 mg (63% yield)
2nd run: 41.2 mg (65% yield)

TLC (SiO_2) R_f = 0.26 in 15:1 hexanes/EtOAc, $KMnO_4$ stain

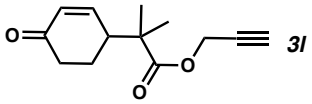
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.63 (dd, *J* = 15.7, 10.2 Hz, 1H), 6.20 (d, *J* = 15.7 Hz, 1H), 4.10 (m, 2H), 2.30 (m, 1H), 2.11 (m, 1H), 1.46 (m, 1H), 1.29 (m, 1H), 1.23 (t, *J* = 7.1 Hz, 3H), 1.13 (s, 3H), 1.12 (s, 3H), 1.07 (m, 2H), 0.91 (m, 4H), 0.81 (t, *J* = 7.4 Hz, 1H)
^{13}C NMR (126 MHz, $CDCl_3$) δ 199.8, 176.9, 145.9, 133.2, 60.5, 52.5, 45.6, 25.6, 24.1, 22.5, 21.3, 18.8, 14.2, 12.6, 11.2
IR (neat) 2965, 2933, 2875, 1724, 1684, 1665, 1624, 1462, 1387, 1174, 1126, 1090, 1024, 987, 908, 862, 770, 709, 615 cm^{-1}
GC/MS (*m/z*): 252.2 (2%), 237.1 (3%), 207.1 (1%), 179.1 (60%), 163.1 (12%), 137.1 (69%), 123.1 (14%), 109.1 (30%), 95.1 (27%), 81.1 (16%), 69.0 (100%), 55.1 (19%)



allyl 2-methyl-2-(4-oxocyclohex-2-en-1-yl)propanoate (Table 3, entry 1)
The title compound was prepared according to the general procedure with *tert*-butyl(cyclohexa-1,3-dien-1-yloxy)dimethylsilane (52.6 mg, 0.25 mmol, 1.0 equiv) and allyl 2-bromo-2-methylpropanoate (77.3, 0.375 mmol, 1.5 equiv) at 80 °C for 24 h. After purification by flash chromatography (SiO_2, hexanes/EtOAc = 16:1), the title compound was isolated as a colorless oil.

1st run: 43.8 mg (79% yield)
2nd run: 45.0 mg (81% yield)

TLC (SiO_2) R_f = 0.30 in 8:1 hexanes/EtOAc, *p*-anisaldehyde stain
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.82 (d, *J* = 10.4 Hz, 1H), 6.04 (dd, *J* = 10.4, 2.8 Hz, 1H), 5.91 (ddd, *J* = 16.2, 10.9, 5.7 Hz, 1H), 5.33 (dd, *J* = 16.2, 1.4 Hz, 1H), 5.25 (dd, *J* = 10.4, 1.4 Hz, 1H), 4.61 (d, *J* = 5.7 Hz, 2H), 2.83 (m, 1H), 2.53 (dt, *J* = 16.7, 3.6 Hz, 1H), 2.37 (ddd, *J* = 16.2, 14.4, 5.0 Hz, 1H), 2.01 (m, 1H), 1.77 (m, 1H), 1.24 (s, 3H), 1.22 (s, 3H)
^{13}C NMR (126 MHz, $CDCl_3$) δ 199.2, 176.3, 151.1, 131.9, 130.4, 118.5, 65.5, 45.1, 43.9, 37.6, 24.4, 22.5, 22.2
IR (neat) 2976, 1725, 1682, 1417, 1256, 1141, 828 cm^{-1}
GC/MS (*m/z*): 222.1 (2%), 177.1 (5%), 135.0 (43%), 95.1 (100%), 83.1 (50%), 67.0 (41%), 55.1 (32%)

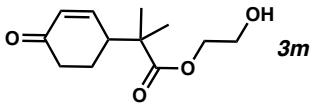


prop-2-yn-1-yl 2-methyl-2-(4-oxocyclohex-2-en-1-yl)propanoate (Table 3, entry 2)
The title compound was prepared according to the general procedure with *tert*-butyl(cyclohexa-1,3-dien-1-yloxy)dimethylsilane (52.6 mg, 0.25 mmol, 1.0 equiv) and prop-2-yn-1-yl 2-bromo-2-methylpropanoate (76.5 mg, 0.375 mmol, 1.5 equiv) at 80 °C for 24 h. After purification by flash chromatography (SiO_2, hexanes/EtOAc = 8:1), the title compound was isolated as a colorless oil.

1st run: 45.1 mg (82% yield)
2nd run: 47.3 mg (86% yield)

TLC (SiO_2) R_f = 0.35 in 4:1 hexanes/EtOAc, *p*-anisaldehyde stain

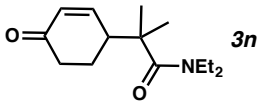
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.81 (d, *J* = 10.4 Hz, 1H), 6.04 (dd, *J* = 10.4, 2.6 Hz, 1H), 4.70 (d, *J* = 2.4 Hz, 2H), 2.84 (d, *J* = 11.2 Hz, 1H), 2.52 (dt, *J* = 16.7, 3.4 Hz, 1H), 2.47 (s, 1H), 2.37 (ddd, *J* = 16.6, 14.4, 5.0 Hz, 1H), 2.02 (m, 1H), 1.78 (m, 1H), 1.25 (s, 3H), 1.22 (s, 3H)
^{13}C NMR (126 MHz, $CDCl_3$) δ 199.1, 175.8, 150.7, 130.5, 77.4, 75.0, 52.3, 45.0, 43.8, 37.5, 24.4, 22.3, 22.1
IR (neat) 3264, 2976, 2101, 1731, 1679, 1305, 1114, 827 cm^{-1}
GC/MS (*m/z*): 220.1 (3%), 137.1 (89%), 126.0 (24%), 111.0 (71%), 95.1 (100%), 81.1 (31%), 67.1 (51%), 55.1 (30%)



2-hydroxyethyl 2-methyl-2-(4-oxocyclohex-2-en-1-yl)propanoate (Table 3, entry 3)
The title compound was prepared according to the general procedure with *tert*-butyl(cyclohexa-1,3-dien-1-yloxy)dimethylsilane (52.6 mg, 0.25 mmol, 1.0 equiv) and 2-hydroxyethyl 2-bromo-2-methylpropanoate (78.75 mg, 0.375 mmol, 1.5 equiv) at 80 °C for 24 h. After purification by flash chromatography (SiO_2, hexanes/EtOAc = 4:1), the title compound was isolated as a colorless oil.

1st run: 53.1 mg (94% yield)
2nd run: 52.0 mg (92% yield)

TLC (SiO_2) R_f = 0.20 in 2:1 hexanes/EtOAc, *p*-anisaldehyde stain
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.83 (d, *J* = 10.4 Hz, 1H), 6.02 (dd, *J* = 10.4, 2.6 Hz, 1H), 4.23 (t, *J* = 4.8 Hz, 2H), 3.81 (t, *J* = 4.8 Hz, 2H), 2.82 (m, 1H), 2.51 (m, 1H), 2.35 (ddd, *J* = 16.7, 14.4, 5.0 Hz, 1H), 2.26 (br. s, 1H), 2.01 (m, 1H), 1.75 (m, 1H), 1.23 (s, 3H), 1.21 (s, 3H)
^{13}C NMR (126 MHz, $CDCl_3$) δ 199.4, 177.0, 151.3, 130.3, 66.4, 61.1, 45.2, 43.8, 37.5, 24.4, 22.6, 22.1
IR (neat) 3431, 2953, 1722, 1664, 1187, 1125, 924 cm^{-1}
GC/MS (*m/z*): $-OCH_2CH_2OH$, 165.0 (5%), 137.1 (100%), 132.0 (42%), 121.0 (20%), 109.0 (21%), 95.0 (70%), 81.1 (21%), 70.1 (80%), 55.0 (26%)

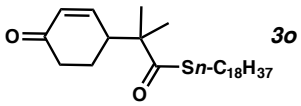


N,N-diethyl-2-methyl-2-(4-oxocyclohex-2-en-1-yl)propanamide (Table 3, entry 4)
The title compound was prepared according to the general procedure with *tert*-butyl(cyclohexa-1,3-dien-1-yloxy)dimethylsilane (52.6 mg, 0.25 mmol, 1.0 equiv) and 2-bromo-N,N-diethyl-2-methylpropanamide (82.9 mg, 0.375 mmol, 1.5 equiv) at 80 °C for 24 h. After purification by flash chromatography (SiO_2, hexanes/EtOAc = 4:1), the title compound was isolated as a colorless oil.

1st run: 45.0 mg (76% yield)
2nd run: 46.2 mg (78% yield)

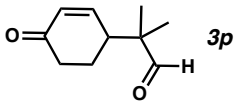
TLC (SiO_2) R_f = 0.25 in 2:1 hexanes/EtOAc, *p*-anisaldehyde stain
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.85 (d, *J* = 10.4 Hz, 1H), 6.03 (dd, *J* = 10.4, 2.7 Hz, 1h), 3.43 (m, 4H), 2.95 (m, 1H), 2.54 (m, 1H), 2.35 (m, 1H), 2.01 (m, 1H),1.85 (m, 1H), 1.29 (s, 3H), 1.26 (s, 3H), 1.15 (comp. m, 6H)

^{13}C NMR (126 MHz, $CDCl_3$) δ 199.4, 174.4, 152.4, 129.9, 109.6, 44.9, 44.2, 37.8, 24.6, 23.6, 23.4, 19.6
IR (neat) 2973, 1682, 1619, 1417, 1267, 1110 cm^{-1}
GC/MS (*m/z*): 237.1 (10%), 222.0 (11%), 206.9 (7%), 137.0 (44%), 126.0 (14%), 114.0 (14%), 100.0 (100%), 72.0 (80%), 58.0 (42%)



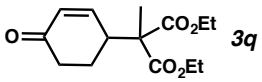
S-octadecyl 2-methyl-2-(4-oxocyclohex-2-en-1-yl)propanethioate (Table 3, entry 5)
The title compound was prepared according to the general procedure with *tert*-butyl(cyclohexa-1,3-dien-1-yloxy)dimethylsilane (52.6 mg, 0.25 mmol, 1.0 equiv) and S-octadecyl 2-bromo-2-methylpropanethioate (162.8 mg, 0.375 mmol, 1.5 equiv) in ethanol at 80 °C for 24 h. After purification by flash chromatography (SiO_2, hexanes/EtOAc = 16:1), the title compound was isolated as a white solid.
1st run: 108.0 mg (96% yield)
2nd run: 110.3 mg (98% yield)

TLC (SiO_2) R_f = 0.30 in 8:1 hexanes/EtOAc, *p*-anisaldehyde stain
mp 45–46 °C
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.81 (d, *J* = 10.4 Hz, 1H), 6.03 (dd, *J* = 10.4, 2.3 Hz, 1H), 2.90 (m, 1H), 2.87 (t, *J* = 7.4 Hz, 2H), 2.52 (d, *J* = 16.6 Hz, 1H), 2.37 (m, 1H), 2.02 (m, 1H), 1.76 (m, 1H), 1.55 (m, 2H), 1.29 (m, 36H), 0.87 (t, *J* = 6.8 Hz, 3H)
^{13}C NMR (126 MHz, $CDCl_3$) δ 205.9, 199.2, 151.0, 130.5, 52.0, 44.3, 37.6, 31.9, 29.7, 29.6, 29.4, 29.1, 28.9, 24.3, 22.7, 22.6, 22.2, 14.1
IR (neat) 2952, 2913, 1687, 1663, 1472, 1390, 1171, 939 cm^{-1}
GC/MS (*m/z*): Fragments, 281.0 (8%), 253.0 (4%, $-C_{18}H_{37}$), 207.0 (55%), 190.9 (8%), 127.0 (100%), 99.0 (12%), 78.0 (20%)



2-Methyl-2-(4-oxocyclohex-2-en-1-yl)propanal (Table 3, entry 6)
The title compound was prepared according to the general procedure using *tert*-butyl(cyclohexa-1,3-dien-1-yloxy)dimethylsilane (52.6 mg, 0.25 mmol, 1.0 equiv) and 2-bromo-2-methylpropanal (56.6 μL, 0.375 mmol, 1.5 equiv) at 80 °C for 24 h. After purification by flash chromatography (SiO_2, hexanes/EtOAc = 4:1), the title compound was isolated as a colorless oil.
1st run: 36 mg (87% yield)
2nd run: 34.5 mg (83% yield)

TLC (SiO_2) R_f = 0.30 in 4:1 hexanes/EtOAc, *p*-anisaldehyde stain
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.52 (s, 1H), 6.75 (d, *J* = 10.4 Hz, 1H), 6.04 (dd, *J* = 10.4, 2.7 Hz, 1H), 2.74 (d, *J* = 13.1 Hz, 1H), 2.52 (m,1H), 2.37 (m, 1H), 2.03 (m, 1H), 1.74 (m, 1H), 1.10 (s, 3H), 1.09 (s, 3H)
^{13}C NMR (101 MHz, $CDCl_3$) δ 204.6, 198.8, 150.2, 130.8, 48.2, 40.8, 37.5, 24.1, 19.3, 18.8
IR (neat) 2960, 2927, 2710, 1724, 1464, 1393, 1379, 1368, 1252, 1197, 1154, 1070, 990, 960, 904, 882, 851, 829, 805, 761, 730, 651, 624, 597 cm^{-1}



3q

Diethyl 2-methyl-2-(4-oxocyclohex-2-en-1-yl)malonate (Table 3, entry 7)

The title compound was prepared according to the general procedure using *tert*-butyl(cyclohexa-1,3-dien-1-yloxy)dimethylsilane (52.6 mg, 0.25 mmol, 1.0 equiv) and diethyl 2-bromo-2-methylmalonate (71.6 μL, 0.375 mmol, 1.5 equiv) at 80 °C for 20 h. After purification by flash chromatography (SiO_2, hexanes/EtOAc = 4:1), the title compound was isolated as a colorless oil.

1st run: 63.8 mg (95% yield)
2nd run: 61.2 mg (91% yield)

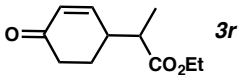
TLC (SiO_2) R_f = 0.34 in 4:1 hexanes/EtOAc, *p*-anisaldehyde stain

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.90 (d, *J* = 10.4 Hz, 1H), 6.02 (dd, *J* = 10.4, 2.7 Hz, 1H), 4.21 (m, 4H), 3.25 (m, 1H), 2.52 (m, 1H), 2.39 (m, 1H), 1.99 (m, 1H), 1.76 (m, 1H), 1.41 (s, 3H), 1.25 (m, 6H)

^{13}C NMR (126 MHz, $CDCl_3$) δ 198.7, 170.8, 170.7, 151.2, 129.9, 61.7, 61.7, 56.3, 41.1, 37.4, 29.6, 24.6, 17.4, 14.0

IR (neat) 2923, 2853, 1759, 1687, 1418, 1391, 1374, 1285, 1148, 1098, 1076, 1019, 976, 851, 745, 636 cm^{-1}

GC/MS (*m/z*): 268.1 (1%), 223.1 (11%), 194.1 (18%), 174.1 (100%), 149.0 (12%), 139.0 (16%), 120.0 (78%), 100.0 (30%), 68.0 (22%), 55.0 (21%)



3r

Ethyl 2-(4-oxocyclohex-2-en-1-yl)propanoate (Table 3, entry 8)

The title compound was prepared according to the general procedure using *tert*-butyl(cyclohexa-1,3-dien-1-yloxy)dimethylsilane (52.6 mg, 0.25 mmol, 1.0 equiv) and ethyl 2-bromopropanoate (48.7 μL, 0.375 mmol, 1.5 equiv) at 80 °C for 20 h. Crude ^{1}H NMR prior to purification indicated a 1:1 mixture of diastereomers. After purification by flash chromatography (SiO_2, hexanes/EtOAc = 4:1), the title compound was isolated as a colorless oil, comprising a 1:1 mixture of diastereomers (based on ^{1}H NMR of purified material).

1st run: 42.7 mg (87% yield)
2nd run: 45.6 mg (93% yield)

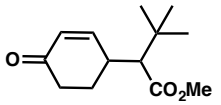
TLC (SiO_2) R_f = 0.35 in 4:1 hexanes/EtOAc, *p*-anisaldehyde stain

^{1}H NMR (500 MHz, $CDCl_3$) for both diastereomers δ 6.91 (d, *J* = 10.3 Hz, 1H), 6.80 (d, *J* = 10.3 Hz, 1H), 6.01 (m, 2H), 4.14 (m, 4H), 2.78 (m, 2H), 2.57 (m, 2H), 2.50 (m, 2H), 2.36 (m, 2H), 2.03 (m, 2H), 1.78 (m, 2H), 1.26 (m, 3H), 1.24 (m, 3H), 1.20 (d, *J* = 2.6 Hz, 3H), 1.19 (d, *J* = 2.7 Hz, 3H)

^{13}C NMR (126 MHz, $CDCl_3$) δ 199.1, 174.6, 152.2, 151.7, 130.1, 129.9, 60.7, 43.1, 42.8, 38.9, 37.0, 26.7, 25.6, 14.2, 14.0, 13.8

IR (neat) 2979, 1726, 1678, 1452, 1418, 1344, 1257, 1173, 1145, 1022, 951, 845, 784, 741 cm^{-1}

GC/MS (*m/z*): 196.1 (2%), 181.0 (1%), 168.1(1%), 151.1 (19%), 139.1(4%), 123.1(98%), 111.0 (7%), 102.1 (100%), 95.1 (98%), 81.1 (25%), 74.1 (46%), 67.1 (46%), 55.1 (28%)



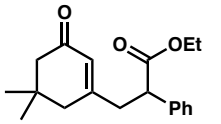
3s

Methyl 3,3-dimethyl-2-(4-oxocyclohex-2-en-1-yl)butanoate (Table 3, entry 9)

The title compound was prepared according to the general procedure using *tert*-butyl(cyclohexa-1,3-dien-1-yloxy)dimethylsilane (52.6 mg, 0.25 mmol, 1.0 equiv) and methyl 2-bromo-3,3-dimethylbutanoate (64.0 μL, 0.375 mmol, 1.5 equiv) at 80 °C for 27 h. Crude ^{1}H NMR prior to purification indicated a 1.43:1 mixture of diastereomers. After purification by flash chromatography (SiO_2, hexanes/EtOAc = 6:1), the title compound was isolated as a colorless oil, comprising a 1.43:1 mixture of diastereomers (based on ^{1}H NMR of purified material).

1st run: 45.4 mg (83% yield)
2nd run: 46.5 mg (81% yield)

TLC (SiO_2) R_f = 0.40 in 6:1 hexanes/EtOAc, *p*-anisaldehyde stain
^{1}H NMR (500 MHz, $CDCl_3$) for the major diastereomers δ 7.19 (d, *J* = 10.4 Hz, 1H), 5.96 (app. t, *J* = 10.4 Hz, 1H), 3.64 (s, 3H), 2.82 (m, 2H), 2.51 (m, 2H), 2.15 (m, 1H), 2.04 (m, 1H), 1.06 (s, 9H)
^{13}C NMR (126 MHz, $CDCl_3$) δ 199.0, 173.6, 173.4, 154.3, 152.8, 129.4, 128.9, 59.4, 59.1, 51.1, 37.6, 36.3, 35.4, 35.2, 33.7, 33.4, 30.9, 28.7, 28.1, 27.5
IR (neat) 2952, 2872, 1728, 1681, 1434, 1392, 1368, 1246, 1215, 1144, 1043, 969, 913, 845, 813, 744, 618 cm^{-1}
GC/MS (*m/z*): 224.1 (10%), 209.0 (1%), 193.1 (4%), 177.0 (4%), 167.0 (94%), 153.0 (20%), 136.0 (28%), 115.1(64%), 107.0 (28%), 95.0 (36%), 79.0 (27%), 67.1 (28%), 57.1 (100%)



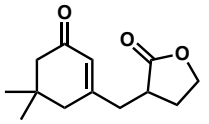
3t

ethyl 3-(5,5-dimethyl-3-oxocyclohex-1-en-1-yl)-2-phenylpropanoate (Table 3, entry 10)

The title compound was prepared according to the general procedure with tert-butyldimethyl((3-methylenecyclohex-1-en-1-yl)oxy)silane (56.0 mg, 0.25 mmol, 1.0 equiv) and ethyl 2-bromo-2-phenylacetate (90.75 mg, 0.375 mmol, 1.5 equiv) at 80 °C for 24 h. After purification by flash chromatography (SiO_2, hexanes/EtOAc = 8:1), the title compound was isolated as a white solid.

1st run: 56.3 mg (75% yield)
2nd run: 54.6 mg (73% yield)

TLC (SiO_2) R_f = 0.44 in 4:1 hexanes/EtOAc, *p*-anisaldehyde stain
mp 50–51 °C
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (m, 5H), 5.85 (s, 1H), 4.14 (dq, *J* = 10.9, 7.1 Hz, 1H), 4.07 (dq, *J* = 10.9, 7.1 Hz, 1H), 3.82 (dd, *J* = 8.8, 6.7 Hz, 1H), 2.98 (dd, *J* = 15.0, 8.8 Hz, 1H), 2.61 (dd, *J* = 15.0, 6.7 Hz, 1H), 2.15 (comp. m, 4H), 1.18 (t, *J* = 7.1 Hz, 3H), 0.97 (s, 6H)
^{13}C NMR (126 MHz, $CDCl_3$) δ 199.6, 172.7, 160.1, 137.9, 128.8, 127.8, 127.7, 126.0, 61.1, 50.9, 49.3, 44.1, 41.1, 33.5, 28.3, 28.1, 14.1
IR (neat) 2928, 1728, 1659, 1490, 1251, 920, 895, 734 cm^{-1}
GC/MS (*m/z*): 300.1 (22%), 239.1 (7%), 227.1 (75%), 211.1 (100%), 171.0 (15%), 143.0 (35%), 128.0 (41%), 107.0 (25%), 91.0 (56%), 79.1 (27%), 67.0 (16%)



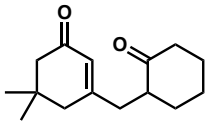
3u

3-((5,5-dimethyl-3-oxocyclohex-1-en-1-yl)methyl)dihydrofuran-2(3H)-one (Table 3, entry 11)

The title compound was prepared according to the general procedure with tert-butyldimethyl((3-methylenecyclohex-1-en-1-yl)oxy)silane (56.0 mg, 0.25 mmol, 1.0 equiv) and 3-bromodihydrofuran-2(3H)-one (61.5 mg, 0.375 mmol, 1.5 equiv) at 80 °C for 24 h. After purification by flash chromatography (SiO_2, hexanes/EtOAc = 2:1), the title compound was isolated as a white solid.

1st run: 35.5 mg (64% yield)
2nd run: 36.6 mg (66% yield)

TLC (SiO_2) R_f = 0.35 in 1:1 hexanes/EtOAc, *p*-anisaldehyde stain
mp 137–138 °C
^{1}H NMR (500 MHz, $CDCl_3$) δ 5.89 (s, 1H), 4.38 (dt, *J* = 8.9, 2.4 Hz, 1H), 4.22 (m, 1H), 2.80 (m, 1H), 2.40 (m, 1H), 2.27 (dd, *J* = 15.2, 10.5 Hz, 1H), 2.24 (d, *J* = 3.0 Hz, 2H), 2.20 (s, 2H), 1.93 (m, 1H), 1.06 (s, 3H), 1.03 (s, 3H)
^{13}C NMR (126 MHz, $CDCl_3$) δ 199.5, 178.1, 159.5, 126.0, 66.5, 51.0, 43.7, 38.7, 37.2, 33.7, 28.6, 28.5, 28.0
IR (neat) 2957, 2925, 1759, 1712, 1663, 1557, 1371, 1018, 931 cm^{-1}
GC/MS (*m/z*): 222.1 (22%), 207.1 (56%), 189.0 (80%), 161.1 (100%), 138.0 (42%), 121.0 (82%), 107.0 (20%), 91.0 (34%), 82.0 (94%), 67.0 (26%), 55.1 (44%)



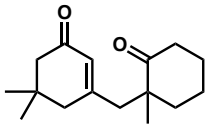
3v

5,5-dimethyl-3-((2-oxocyclohexyl)methyl)cyclohex-2-en-1-one (Table 3, entry 12)

The title compound was prepared according to the general procedure with tert-butyldimethyl((3-methylenecyclohex-1-en-1-yl)oxy)silane (56.0 mg, 0.25 mmol, 1.0 equiv) and 2-bromocyclohexan-1-one (66.0 mg, 0.375 mmol, 1.5 equiv) at 80 °C for 24 h. After purification by flash chromatography (SiO_2, hexanes/EtOAc = 8:1), the title compound was isolated as a white solid.

1st run: 49.1 mg (84% yield)
2nd run: 48.0 mg (82% yield)

TLC (SiO_2) R_f = 0.35 in 4:1 hexanes/EtOAc, *p*-anisaldehyde stain
mp 50–51 °C
^{1}H NMR (500 MHz, $CDCl_3$) δ 5.81 (s, 1H), 2.72 (dd, *J* = 15.1, 5.4 Hz, 1H), 2.55 (m, 1H), 2.43 (m, 1H), 2.33 (m, 1H), 2.19 (m, 3H), 2.06 (m, 4H), 1.88 (br. s, 1H), 1.68 (m, 2H), 1.33 (m, 1H), 1.02 (s, 6H)
^{13}C NMR (126 MHz, $CDCl_3$) δ 211.3, 199.7, 161.9, 125.6, 51.0, 48.2, 44.2, 42.0, 37.6, 33.9, 33.6, 28.3, 28.2, 27.9, 25.1
IR (neat) 2934, 2864, 1708, 1662, 1626, 1448, 1298, 1127, 901 cm^{-1}
GC/MS (*m/z*): 234.1 (20%), 201.1 (42%), 177.1 (17%), 138.1 (30%), 121.0 (100%), 91.1 (24%), 79.1 (30%), 67.1 (19%), 55.1 (30%)

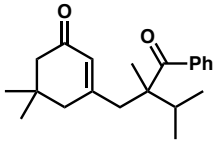


3w

5,5-dimethyl-3-((1-methyl-2-oxocyclohexyl)methyl)cyclohex-2-en-1-one (Table 3, entry 13)
The title compound was prepared according to the general procedure with tert-butyldimethyl((3-methylenecyclohex-1-en-1-yl)oxy)silane (56.0 mg, 0.25 mmol, 1.0 equiv) and 2-bromo-2-methylcyclohexan-1-one (71.3 mg, 0.375 mmol, 1.5 equiv) at 80 °C for 24 h. After purification by flash chromatography (SiO_2, hexanes/EtOAc = 8:1), the title compound was isolated as a white solid.

1st run: 34.7 mg (56% yield)
2nd run: 36.0 mg (58% yield)

TLC (SiO_2) R_f = 0.30 in 4:1 hexanes/EtOAc, *p*-anisaldehyde stain
mp 62–63 °C
^{1}H NMR (500 MHz, $CDCl_3$) δ 5.83 (s, 1H), 2.55 (d, *J* = 13.4 Hz, 1H), 2.46 (m, 3H), 2.17 (s, 2H), 2.11 (m, 1H), 1.89−1.63 (comp. m, 6H), 1.12 (s, 3H), 1.01 (s, 6H)
^{13}C NMR (126 MHz, $CDCl_3$) δ 214.4, 199.6, 160.4, 128.6, 50.9, 49.0, 45.8, 45.6, 39.7, 38.8, 33.9, 28.3, 27.3, 23.6, 21.1
IR (neat) 2933, 2864, 1678, 1450, 1392, 1217, 1122, 832 cm^{-1}
LC/MS (*m/z*): 249.1 (100%), 231.1 (9%), 189.1 (20%)

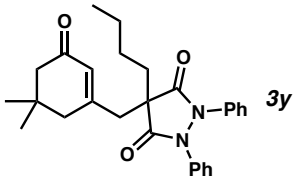


3x

3-(2-benzoyl-2,3-dimethylbutyl)-5,5-dimethylcyclohex-2-en-1-one (Table 3, entry 14)
The title compound was prepared according to the general procedure with tert-butyldimethyl((3-methylenecyclohex-1-en-1-yl)oxy)silane (56.0 mg, 0.25 mmol, 1.0 equiv) and 2-bromo-2,3-dimethyl-1-phenylbutan-1-one (95.3 mg, 0.375 mmol, 1.5 equiv) at 80 °C for 24 h. After purification by flash chromatography (SiO_2, hexanes/EtOAc = 8:1), the title compound was isolated as a colorless oil.

1st run: 55.4 mg (71% yield)
2nd run: 56.9 mg (73% yield)

TLC (SiO_2) R_f = 0.44 in 4:1 hexanes/EtOAc, *p*-anisaldehyde stain
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (app. d, *J* = 7.3 Hz, 2H), 7.48 (app. t, *J* = 7.4 Hz, 1H), 7.40 (app. t, *J* = 7.6 Hz, 2H), 5.81 (s, 1H), 3.05 (d, *J* = 13.8 Hz, 1H), 2.38 (m, 2H), 2.12 (s, 2H), 2.03 (m, 2H), 1.21 (s, 3H), 0.97 (d, *J* = 6.8 Hz, 3H), 0.94 (s, 3H), 0.92 (s, 3H), 0.90 (d, *J* = 6.8 Hz, 3H)
^{13}C NMR (126 MHz, $CDCl_3$) δ 207.6, 199.7, 160.7, 139.3, 131.3, 128.3, 128.2, 128.0, 54.9, 50.8, 45.4, 44.5, 35.8, 33.7, 28.5, 28.0, 18.7, 17.8, 17.5
IR (neat) 2961, 1667, 1621, 1299, 1248, 967 cm^{-1}
GC/MS (*m/z*): −*i*Pr, 269.1 (4%), 207.0 (6%), 105.0 (100%), 77.0 (20%), 51.1 (4%)



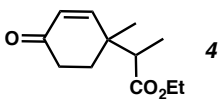
3y

4-butyl-4-((5,5-dimethyl-3-oxocyclohex-1-en-1-yl)methyl)-1,2-diphenylpyrazolidine-3,5-dione (Table 3, entry 15)

The title compound was prepared according to the general procedure with tert-butyldimethyl((3-methylenecyclohex-1-en-1-yl)oxy)silane (56.0 mg, 0.25 mmol, 1.0 equiv) and 4-bromo-4-butyl-1,2-diphenylpyrazolidine-3,5-dione (144.8 mg, 0.375 mmol, 1.5 equiv) at 80 °C for 24 h. After purification by flash chromatography (SiO_2, hexanes/EtOAc = 8:1), the title compound was isolated as a white solid.

1st run: 93.2 mg (84% yield)
2nd run: 95.5 mg (86% yield)

TLC (SiO_2) R_f = 0.35 in 4:1 hexanes/EtOAc, *p*-anisaldehyde stain
mp 105–106 °C
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 (comp. m, 8H), 7.16 (m, 2H), 5.98 (s, 1H), 2.76 (s, 2H), 2.12 (s, 2H), 2.03 (s, 2H), 1.93 (m, 2H), 1.30 (br. s, 4H), 0.85 (m, 11H)
^{13}C NMR (126 MHz, $CDCl_3$) δ 199.2, 172.0, 156.7, 135.1, 129.0, 127.8, 126.9, 122.3, 54.2, 50.7, 45.5, 42.4, 37.6, 33.5, 28.1, 26.5, 22.6, 13.6
IR (neat) 2955, 2873, 1752, 1718, 1666, 1404, 1188, 1072, 1058 cm^{-1}
GC/MS (*m/z*): 444.2 (50%), 425.0 (34%), 373.2 (11%), 309.1 (20%), 183.1 (41%), 121.0 (56%), 77.0 (100%), 57.1 (20%)



4

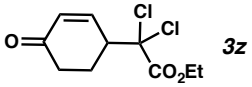
Ethyl 2-(1-methyl-4-oxocyclohex-2-en-1-yl)propanoate (4, equation 1)

The title compound was prepared according to the general procedure with *tert*-butyldimethyl((4-methylcyclohexa-1,3-dien-1-yl)oxy)silane (56.1 mg, 0.25 mmol, 1.0 equiv) and ethyl 2-bromopropanoate (48.7 μL, 0.375 mmol, 1.5 equiv) at 80 °C for 36 h. Crude ^{1}H NMR prior to purification indicated a 1.25:1 mixture of diastereomers. After purification by flash chromatography (SiO_2, hexanes/EtOAc = 4:1), the title compound was isolated as a colorless oil, comprising a 1.25:1 mixture of diastereomers (based on ^{1}H NMR of purified material).

1st run: 27.4 mg (52% yield)
2nd run: 29.6 mg (56% yield)

TLC (SiO_2) R_f = 0.35 in 4:1 hexanes/EtOAc, *p*-anisaldehyde stain
^{1}H NMR (500 MHz, $CDCl_3$) for both diastereomers δ 6.96 (dd, *J* = 10.3, 1.4 Hz, 1H), 6.73 (dd, *J* = 10.3, 1.4 Hz, 1H), 5.92 (dd, *J* = 10.3, 4.5 Hz, 2H), 4.14 (m, 4H), 2.49 (m, 6H), 2.13 (m, 2H), 1.77 (m, 4H), 1.22 (m, 24H)
^{13}C NMR (126 MHz, $CDCl_3$) δ 198.9, 174.4, 174.2, 156.6, 156.4, 128.1, 128.0, 60.5, 48.1, 47.7, 37.7, 33.9, 33.8, 31.4, 31.1, 22.3, 22.1, 14.2, 12.8, 12.3
IR (neat) 2975, 2938, 2876, 1725, 1678, 1456, 1371, 1298, 1227, 1172, 1055, 953, 922, 860, 803, 781, 757, 719, 568 cm^{-1}

GC/MS (*m/z*): 210.1 (2%), 195.1 (1%), 165.1 (16%), 137.1 (17%), 121.0 (6%), 110.1 (12%), 102.1 (100%), 91.1 (7%), 81.1 (50%), 67.1 (9%), 53.1 (16%)



3z

Ethyl 2,2-dichloro-2-(4-oxocyclohex-2-en-1-yl)acetate (Table 4, entry 1)

The title compound was prepared according to the general procedure using *tert*-butyl(cyclohexa-1,3-dien-1-yloxy)dimethylsilane (52.6 mg, 0.25 mmol, 1.0 equiv) and ethyl 2,2,2-trichloroacetate (52.3 μL, 0.375 mmol, 1.5 equiv) at 80 °C for 18 h. After purification by flash chromatography (SiO_2, hexanes/EtOAc = 4:1), the title compound was isolated as a colorless oil.

1st run: 55.9 mg (89% yield)
2nd run: 54.6 mg (87% yield)

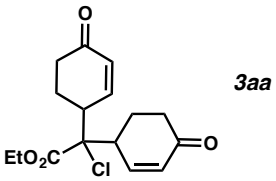
TLC (SiO_2) R_f = 0.35 in 4:1 hexanes/EtOAc, *p*-anisaldehyde stain

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.98 (d, *J* = 10.4 Hz, 1H), 6.16 (d, *J* = 10.4 Hz, 1H), 4.39 (q, *J* = 7.1 Hz, 2H), 3.59 (m, 1H), 2.62 (m, 1H), 2.45 (m, 1H), 2.29 (m, 1H), 2.08 (m, 1H), 1.39 (t, *J* = 7.1 Hz, 3H)

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.7, 164.9, 131.3, 64.4, 48.7, 36.3, 25.1, 13.9

IR (neat) 2982, 2939, 1757, 1740, 1684, 1619, 1448, 1368, 1296, 1237, 1183, 1095, 1017, 932, 833, 785, 749, 691, 640 cm^{-1}

GC/MS (*m/z*): 215.0 (3%), 187.0 (20%), 179.0 (28%), 156.0 (37%), 141.0 (17%), 133.0 (44%), 115.0 (26%), 95.0 (100%), 85.0 (26%), 77.0 (62%), 68.0 (42%), 51.1 (51%)



3aa

Ethyl 2-chloro-2,2-bis(4-oxocyclohex-2-en-1-yl)acetate (Table 4, entry 2)

The title compound was prepared according to the general procedure using *tert*-butyl(cyclohexa-1,3-dien-1-yloxy)dimethylsilane (157.8 mg, 0.75 mmol, 3.0 equiv) and ethyl 2,2,2-trichloroacetate (35 μL, 0.25 mmol, 1.0 equiv) at 80 °C for 24 h. Crude ^{1}H NMR prior to purification indicated a 3.86:1 mixture of diastereomers. After purification by flash chromatography (SiO_2, hexanes/EtOAc = 1:1), the title compound was isolated as a colorless oil, comprising a 3.86:1 mixture of diastereomers (based on ^{1}H NMR of purified material).

1st run: 46.5 mg (60% yield)
2nd run: 44.0 mg (57% yield)

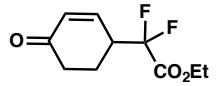
TLC (SiO_2) R_f = 0.25 in 1:1 hexanes/EtOAc, *p*-anisaldehyde stain

^{1}H NMR (400 MHz, $CDCl_3$) for major diastereomer δ 7.02 (m, 1H), 6.81 (m, 1H), 6.10 (m, 2H), 4.26 (m, 2H), 3.37 (m, 2H), 2.59 (m, 2H), 2.38 (m, 2H), 2.21 (m, 2H), 1.99 (m, 2H), 1.28 (m, 3H)

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.8, 197.7, 168.6, 167.7, 148.9, 148.0, 147.6, 146.8, 131.4, 130.6, 63.4, 63.2, 44.1, 43.7, 43.4, 42.3, 36.9, 36.8, 25.3, 25.1, 24.8, 14.2

IR (neat) 2924, 1744, 1720, 1678, 1450, 1392, 1294, 1211, 1182, 1152, 1093, 1039, 915, 859, 786, 729, 647 cm^{-1}

GC/MS (*m/z*): 310.0 (1%), 275.0 (15%), 246.0 (6%), 229.1 (7%), 201.0 (40%), 187.0 (81%), 173.0 (16%), 115.0 (46%), 95.0 (100%), 67.0 (74%), 55.0 (58%)



3ab

Ethyl 2,2-difluoro-2-(4-oxocyclohex-2-en-1-yl)acetate (Table 4, entry 3)

The title compound was prepared according to the general procedure using *tert*-butyl(cyclohexa-1,3-dien-1-yloxy)dimethylsilane (52.6 mg, 0.25 mmol, 1.0 equiv) and ethyl 2-bromo-2,2-difluoroacetate (48.1 μL, 0.375 mmol, 1.5 equiv) at 80 °C for 26 h. After purification by flash chromatography (SiO_2, hexanes/EtOAc = 4:1), the title compound was isolated as a colorless oil.

1st run: 50.2 mg (92% yield)
2nd run: 47.5 mg (87% yield)

TLC (SiO_2) R_f = 0.35 in 4:1 hexanes/EtOAc, *p*-anisaldehyde stain

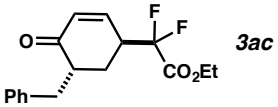
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.91 (d, *J* = 10.4 Hz, 1H), 6.16 (dd, *J* = 10.4, 2.4 Hz, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 3.24 (m, 1H), 2.60 (m, 1H), 2.40 (m, 1H), 2.18 (m, 1H), 1.99 (m, 1H), 1.36 (t, *J* = 7.1 Hz, 3H)

^{13}C NMR (126 MHz, $CDCl_3$) δ 197.5, 162.9 (t, *J* = 37.8 Hz), 143.0, 132.0, 115.4 (t, *J* = 252 Hz), 63.3, 41.4, 41.2, 41.0, 35.9, 22.2, 13.9

^{19}F NMR (376 MHz, $CDCl_3$) δ –109.87 (dd, *J* = 261.3, 12.5 Hz, 1F), –112.05 (dd, *J* = 261.2, 15.7 Hz, 1F)

IR (neat) 2923, 1759, 1687, 1419, 1391, 1374, 1285, 1148, 1098, 1076, 1019, 891, 851, 783, 744, 636 cm^{-1}

GC/MS (*m/z*): 218.0 (1%), 198.0 (3%), 145.0 (14%), 117.0 (100%), 95.0 (46%), 68.0 (42%), 51.0 (6%)



3ac

Ethyl 2-(5-benzyl-4-oxocyclohex-2-en-1-yl)-2,2-difluoroacetate (Table 4, entry 4)

The title compound was prepared according to the general procedure with ((6-benzylcyclohexa-1,3-dien-1-yl)oxy)(tert-butyl)dimethylsilane (75.1 mg, 0.25 mmol, 1.0 equiv) and ethyl 2-bromo-2,2-difluoroacetate (48.1 μL, 0.375 mmol, 1.5 equiv) at 80 °C for 24 h. Crude ^{1}H NMR prior to purification indicated a single diastereomer. After purification by flash chromatography (SiO_2, hexanes/EtOAc = 8:1), the title compound was isolated as a colorless oil, comprising a single diastereomer (based on ^{1}H NMR of purified material).

1st run: 53.2 mg (69% yield)
2nd run: 56.4 mg (73% yield)

TLC (SiO_2) R_f = 0.30 in 8:1 hexanes/EtOAc, *p*-anisaldehyde stain

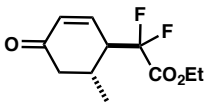
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 (m, 5H), 6.90 (dd, *J* = 10.3, 2.2 Hz, 1H), 6.20 (dd, *J* = 10.3, 2.4 Hz, 1H), 4.25 (m, 2H), 3.31 (m, 1H), 3.11 (dd, *J* = 13.8, 4.8 Hz, 1H), 2.81 (m, 1H), 2.61 (dd, *J* = 13.8, 10.7 Hz, 1H), 1.96 (m, 1H), 1.83 (m, 1H), 1.26 (t, *J* = 7.2 Hz, 3H)

^{13}C NMR (126 MHz, $CDCl_3$) δ 199.3, 162.9, 141.7, 138.3, 131.7, 128.9, 128.6, 126.6, 116.2 (d, *J* = 252 Hz), 63.3, 45.4, 38.2 (t, *J* = 22.3 Hz), 35.6, 24.9, 13.8

^{19}F NMR (376 MHz, $CDCl_3$) δ –107.84 (dd, *J* = 258.9, 11.1 Hz, 1F), –112.24 (dd, *J* = 258.9, 18.6 Hz, 1F)

IR (neat) 2929, 1759, 1736, 1679, 1603, 1496, 1453, 1390, 1373, 1242, 1177, 1143, 1043, 1011, 851, 786, 766, 732, 699, 593 cm^{-1}

GC/MS (*m/z*): 308.1 (3%), 279.1 (1%), 259.1 (2%), 197.0 (6%), 185.1 (10%), 169.0 (6%), 157.0 (2%), 143.0 (4%), 107.0 (23%), 91.1 (100%), 77.0 (5%), 65.0 (8%), 51.0 (4%)



3ad

Ethyl 2,2-difluoro-2-(6-methyl-4-oxocyclohex-2-en-1-yl)acetate (Table 4, entry 5)

The title compound was prepared according to the general procedure with *tert*-butyldimethyl((5-methylcyclohexa-1,3-dien-1-yl)oxy)silane (56.1 mg, 0.25 mmol, 1.0 equiv) and ethyl 2-bromo-2,2-difluoroacetate (48.1 μL, 0.375 mmol, 1.5 equiv) at 80 °C for 24 h. Crude ^{1}H NMR prior to purification indicated a single diastereomer. After purification by flash chromatography (SiO_2, hexanes/EtOAc = 8:1), the title compound was isolated as a colorless oil, comprising a single diastereomer (based on ^{1}H NMR of purified material).

1st run: 37.9 mg (65% yield)
2nd run: 35.5 mg (61% yield)

TLC (SiO_2) R_f = 0.25 in 8:1 hexanes/EtOAc, *p*-anisaldehyde stain

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.80 (dd, *J* = 10.3, 3.5 Hz, 1H), 6.17 (d, *J* = 10.3 Hz, 1H), 4.36 (app. q, *J* = 7.1 Hz, 2H), 2.98 (m, 1H), 2.63 (dd, *J* = 16.6, 4.6 Hz, 1H), 2.39 (m, 1H), 2.22 (dd, *J* = 16.7, 8.3 Hz, 1H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.16 (d, *J* = 6.7 Hz, 3H)

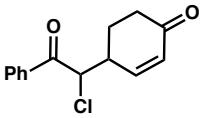
^{13}C NMR (126 MHz, $CDCl_3$) δ 197.7, 163.2, 141.7, 131.9, 115.8 (t, *J* = 264.6), 63.4, 47.1 (t, *J* = 21.5 Hz), 43.8, 29.3, 20.5, 13.9

^{19}F NMR (376 MHz, $CDCl_3$) δ –105.81 (dd, *J* = 261.6, 13.1 Hz, 1F), –107.66 (dd, *J* = 261.6, 14.5 Hz, 1F)

IR (neat) 2963, 2924, 2854, 1760, 1737, 1682, 1461, 1393, 1198, 1164, 1127, 1093, 1075, 1048, 1010, 856, 749, 637, 568 cm^{-1}

GC/MS (*m/z*): 232.0 (1%), 212.1 (2%), 169.0 (2%), 159.0 (8%), 138.0 (4%), 124.0 (6%), 109.1 (100%), 89.0 (23%), 79.1 (6%), 68.0 (38%), 51.1 (4%)

V. Procedures and Experimental Data for Synthetic Applications



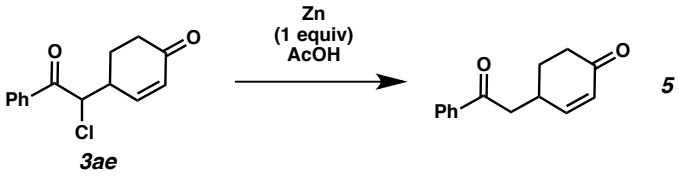
3ae

4-(1-chloro-2-oxo-2-phenylethyl)cyclohex-2-en-1-one (Scheme 2a)

The title compound was prepared according to the general procedure using *tert*-butyl(cyclohexa-1,3-dien-1-yloxy)dimethylsilane (52.6 mg, 0.25 mmol, 1.0 equiv) and 2,2-dichloro-1-phenylethan-1-one (53.0 μL, 0.375 mmol, 1.5 equiv) at 80 °C for 20 h. Crude ^{1}H NMR prior to purification indicated a 1:1 mixture of diastereomers. After purification by flash chromatography (SiO_2, hexanes/EtOAc = 4:1), the title compound was isolated as a colorless oil, comprising a 1:1 mixture of diastereomers (based on ^{1}H NMR of purified material).

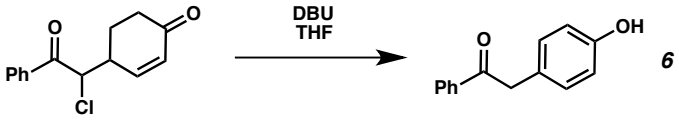
1st run: 51.6 mg (83% yield)
2nd run: 47.9 mg (77% yield)

TLC (SiO_2) R_f = 0.34 in 4:1 hexanes/EtOAc, *p*-anisaldehyde stain
^{1}H NMR (500 MHz, $CDCl_3$) for both diastereomers δ 8.00 (app. d, *J* = 8.0 Hz, 4H), 7.64 (app. t, *J* = 7.4 Hz, 2H), 7.52 (app. t, *J* = 7.7 Hz, 4H), 7.21 (d, *J* = 10.4 Hz, 1H), 6.81 (d, *J* = 10.3 Hz, 1H), 6.13 (dd, *J* = 2.4, 10.4 Hz, 1H), 6.05 (dd, *J* = 10.3, 2.3 Hz, 1H), 5.19 (d, *J* = 7.8 Hz, 1H), 5.07 (d, *J* = 7.0 Hz, 1H), 3.33 (m, 2H), 2.50 (m, 4H), 2.32 (m, 1H), 2.09 (m, 2H), 1.92 (m, 1H)
^{13}C NMR (126 MHz, $CDCl_3$) for both diastereomers δ 198.5, 198.4, 192.3, 192.2, 149.4, 148.8, 134.3, 130.9, 130.8, 129.0, 128.9, 58.9, 58.7, 39.0, 38.8, 36.6, 36.4, 27.1, 25.5
IR (neat) 2954, 1675, 1595, 1579, 1448, 1389, 1272, 1251, 1211, 1181, 1141, 1001, 934, 825, 793, 770, 687, 652, 603 cm^{-1}
GC/MS (*m/z*): 248.0 (1%), 213.1 (2%), 195.0 (1%), 184.0 (2%), 154.0 (12%), 129.1 (2%), 120.0 (6%), 105.0 (100%), 77.1 (39%), 51.1 (18%)



4-(2-oxo-2-phenylethyl)cyclohex-2-en-1-one (Scheme 2a)
The title compound was prepared according to following procedure: To a solution of 4-(1-chloro-2-oxo-2-phenylethyl)cyclohex-2-en-1-one (**3ae**, 49.7 mg, 0.2 mmol, 1.0 equiv) in glacial acetic acid (0.5 mL) was added Zn powder (13.1 mg, 0.2 mmol, 1.0 equiv). The mixture was stirred at room temperature for 16 h after which time TLC showed total consumption of the starting material. Deionized water (5.0 mL) was added to mixture followed by slowly addition of solid K_2CO_3 until bubbling ceased. The mixture was poured into separatory funnel and the aq phase was extracted with EtOAc (3 x 5.0 mL). The organic layers were combined, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. After purification by flash chromatography (SiO_2, hexanes/EtOAc = 4:1), the title compound was isolated as a white solid (35.6 mg, 84% yield).

TLC (SiO_2) R_f = 0.25 in 4:1 hexanes/EtOAc, *p*-anisaldehyde stain
mp 75–76 °C
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.3 Hz, 2H), 7.60 (app. t, *J* = 7.4 Hz, 1H), 7.49 (app. t, *J* = 7.7 Hz, 2H), 6.90 (d, *J* = 10.1 Hz, 1H), 6.02 (dd, *J* = 10.2, 2.2 Hz, 1H), 3.21 (m, 1H), 3.14 (m, 2H), 2.48 (m, 2H), 2.22 (m, 1H), 1.79 (m, 1H)
^{13}C NMR (126 MHz, $CDCl_3$) δ 199.3, 197.7, 153.8, 136.6, 133.5, 129.5, 128.7, 128.0, 42.8, 36.9, 32.0, 29.0
IR (neat) 2953, 2929, 2903, 2880, 1686, 1595, 1580, 1446, 1409, 1389, 1351, 1311, 1250, 1207, 1171, 1140, 1000, 993, 897, 792, 686, 657, 620, 569 cm^{-1}
GC/MS (*m/z*): 214.1 (2%), 171.0 (2%), 157.0 (3%), 120.0 (43%), 105.0 (100%), 94.0 (6%), 77.0 (43%), 66.0 (2%), 51.0 (13%)

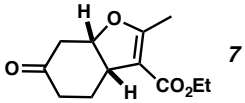


3ae

2-(4-hydroxyphenyl)-1-phenylethan-1-one (Scheme 2a)

The title compound was prepared according to following procedure: To a solution of 4-(1-chloro-2-oxo-2-phenylethyl)cyclohex-2-en-1-one (**3ae**, 49.7 mg, 0.2 mmol, 1.0 equiv) in THF (4 mL) was added DBU (45.6 mg, 0.3 mmol, 1.5 equiv). The mixture was stirred for 1 h at room temperature at which time TLC showed total consumption of the starting material. Deionized water (5.0 mL) was added and the mixture was poured into a separatory funnel. The aq phase was extracted with EtOAc (3 x 5.0 mL). The organic layers were combined, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. After purification by flash chromatography (SiO_2, hexanes/EtOAc = 8:1), the title compound was isolated as a white solid (42.4 mg, 95% yield).

TLC (SiO_2) R_f = 0.35 in 4:1 hexanes/EtOAc, *p*-anisaldehyde stain
mp 122–123 °C
^{1}H NMR (500 MHz, CD_3OD) δ 8.01 (app. d, *J* = 7.4 Hz, 2H), 7.55 (app. t, *J* = 7.4 Hz, 1H), 7.45 (app. t, *J* = 7.7 Hz, 2H), 4.86 (s, 1H), 4.20 (s, 2H)
^{13}C NMR (126 MHz, CD_3OD) δ 199.3, 156.0, 136.5, 132.9, 130.2, 128.3, 125.4, 115.0, 44.0
IR (neat) 3277, 3058, 2907, 1707, 1686, 1613, 1598, 1411, 1200, 688 cm^{-1}
GC/MS (*m/z*): 212.0 (8%), 105.0 (100%), 77.0 (43%), 51.0 (8%)

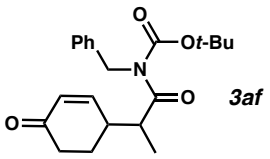


Ethyl 2-methyl-6-oxo-3a,4,5,6,7,7a-hexahydrobenzofuran-3-carboxylate (Scheme 2b)

The title compound was prepared according to the general procedure using *tert*-butyl(cyclohexa-1,3-dien-1-yloxy)dimethylsilane (52.6 mg, 0.25 mmol, 1.0 equiv) and ethyl 2-chloro-3-oxobutanoate (51.9 μL, 0.375 mmol, 1.5 equiv) at 80 °C for 20 h. After purification by flash chromatography (SiO_2, hexanes/EtOAc = 2:1), the title compound was isolated as a colorless oil.

1st run: 50.5 mg (90% yield)
2nd run: 52.3 mg (93% yield)

TLC (SiO_2) R_f = 0.35 in 2:1 hexanes/EtOAc, *p*-anisaldehyde stain
^{1}H NMR (500 MHz, $CDCl_3$) δ 5.04 (m, 1H), 4.17 (m, 2H), 3.50 (m, 1H), 2.72 (m, 2H), 2.29 (m, 1H), 2.20 (m, 1H), 2.17 (s, 3H), 2.07 (m, 1H), 1.95 (m, 1H), 1.27 (t, *J* = 7.1 Hz, 3H)
^{13}C NMR (126 MHz, $CDCl_3$) δ 209.5, 169.1, 165.6, 104.8, 80.2, 59.6, 41.5, 39.4, 35.8, 23.5, 14.4, 14.1
IR (neat) 2928, 1717, 1688, 1640, 1381, 1332, 1256, 1235, 1170, 1081, 980, 952, 902, 844, 781, 753, 622 cm^{-1}
GC/MS (*m/z*): 224.1 (58%), 195.0 (2%), 179.1 (30%), 167.1 (100%), 154.1 (15%), 139.0 (54%), 123.0 (38%), 108.0 (25%), 95.0 (30%), 81.0 (20%), 57.1 (25%)



3af

***tert*-Butyl benzyl(2-(4-oxocyclohex-2-en-1-yl)propanoyl)carbamate (Scheme 2c)**

The title compound was prepared according to the general procedure using *tert*-butyl(cyclohexa-1,3-dien-1-yloxy)dimethylsilane (52.6 mg, 0.25 mmol, 1.0 equiv) and *tert*-butyl benzyl(2-bromopropanoyl)carbamate (128.3 mg, 0.375 mmol, 1.5 equiv) at 80 °C for 26 h. Crude ^{1}H NMR prior to purification indicated a 1.4:1 mixture of diastereomers. After purification by flash chromatography (SiO_2, 100% CH_2Cl_2), the title compound was isolated as a colorless oil, comprising a 1.4:1 mixture of diastereomers (based on ^{1}H NMR of purified material).

1st run: 77.7 mg (87% yield)
2nd run: 76.0 mg (85% yield)

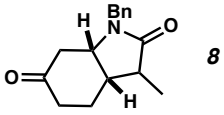
TLC (SiO_2) R_f= 0.32 in 4:1 hexanes/EtOAc, $KMnO_4$ stain

^{1}H NMR (400 MHz, $CDCl_3$) for both diastereomers δ 7.27 (m, 10H), 7.02 (ddd, *J* = 10.3, 2.6, 1.4 Hz, 1H), 6.74 (ddd, *J* = 10.3, 2.3, 1.7 Hz, 1H), 6.03 (dd, *J* = 10.3, 2.2 Hz, 1H), 5.96 (dd, *J* = 10.3, 1.9 Hz, 1H), 4.89 (m, 4H), 3.78 (m, 2H), 2.85 (m, 2H), 2.49 (m, 2H), 2.35 (m, 2H), 2.02 (m, 2H), 1.76 (m, 2H), 1.41 (s, 9H), 1.40 (s, 9H), 1.25 (d, *J* = 4.1 Hz, 3H), 1.23 (d, *J* = 4.1 Hz, 3H)

^{13}C NMR (101 MHz, $CDCl_3$) δ 199.4, 178.6, 178.3, 153.2, 151.8, 138.0, 130.2, 129.5, 128.4, 127.5, 127.4, 127.3, 83.7, 47.8, 43.5, 42.8, 39.5, 39.2, 37.1, 37.0, 27.8, 27.5, 25.7, 15.4, 14.7

IR (neat) 2976, 1728, 1682, 1454, 1366, 1312, 1246, 1210, 1193, 997, 850, 741, 699, 642 cm^{-1}

GC/MS (*m/z*): 257.1 (14%), 200.0 (16%), 163.0 (15%), 132.0 (7%), 106.0 (22%), 91.0 (100%), 77.0 (7%), 65.0 (14%), 55.0 (10%)



8

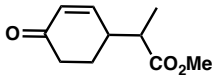
1-Benzyl-3-methylhexahydro-*1H*-indole-2,6-dione (Scheme 2c)

The title compound was prepared according to following procedure: To a stirred solution of *tert*-butyl benzyl(2-(4-oxocyclohex-2-en-1-yl)propanoyl)carbamate (**3af**, 72.5 mg, 0.2 mmol, 1.0 equiv) and dry CH_2Cl_2 (2 mL) at room temperature was added trifluoroacetic acid (0.2 mL), causing vigorous bubbling. After stirring at room temperature for 1 h, the reaction mixture was concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 (10 mL) and washed with saturated aq $NaHCO_3$ (2 x 15.0 mL). The aqueous layer was back-extracted with CH_2Cl_2 (2 x 5.0 mL). The organic layers were combined, dried over $MgSO_4$, filtered, and concentrated under reduced pressure to yield *N*-benzyl-2-(4-oxocyclohex-2-en-1-yl)propanamide as a yellow oil which was used as such without any further purification.

A solution of crude *N*-benzyl-2-(4-oxocyclohex-2-en-1-yl)propanamide and *p*-TsOH•H_2O (66.6 mg, 0.35 mmol, 1.75 equiv) in benzene (10 mL) was heated at reflux for 6 h and then concentrated to dryness. The residue was dissolved in CH_2Cl_2 (4 mL) and washed with saturated aq $NaHCO_3$ (4 mL). The aqueous phase was washes with CH_2Cl_2 (4 mL x 2). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Crude ^{1}H NMR prior to purification indicated a 1.2:1 mixture of diastereomers. After purification by flash chromatography (SiO_2, hexanes/EtOAc = 1:2), the title compound was isolated as a

colorless oil (43.0 mg, 83% yield over two steps), comprising a 1.2:1 mixture of diastereomers (based on ^{1}H NMR of purified material).

TLC (SiO_2) R_f = 0.32 in 1:2 hexanes/EtOAc, *p*-anisaldehyde stain
^{1}H NMR (500 MHz, $CDCl_3$) for both diastereomers δ 7.29 (m, 6H), 7.19 (app. t, *J* = 7.1 Hz, 4H), 5.06 (d, *J* = 15.1 Hz, 1H), 4.97 (d, *J* = 15.0 Hz, 1H), 3.89 (t, *J* = 14.8 Hz, 2H), 3.82 (dd, *J* = 11.8, 5.6 Hz, 1H), 3.74 (m, 1H), 2.73 (m, 1H), 2.57 (m, 4H), 2.38 (m, 4H), 2.19 (m, 4H), 1.85 (m, 3H), 1.30 (d, *J* = 7.2 Hz, 3H), 1.23 (d, *J* = 7.4 Hz, 3H)
^{13}C NMR (126 MHz, $CDCl_3$) for both diastereomers δ 209.5, 209.3, 176.7, 176.5, 136.1, 135.9, 128.8, 128.7, 127.9, 127.8, 127.7, 54.7, 53.8, 44.4, 43.9, 41.7, 41.4, 39.9, 38.2, 36.8, 34.7, 29.7, 25.1, 21.6, 16.0, 10.6
IR (neat) 2928, 1714, 1679, 1495, 1421, 1362, 1295, 1248, 1123, 1029, 944, 816, 701, 635, 615 cm^{-1}
GC/MS (*m/z*): 257.1(23%), 229.1 (2%), 200.1(25%), 186.1 (2%), 166.1 (6%), 146.0 (3%), 132.1 (10%), 118.0 (20%), 91.1 (100%), 77.0 (3%), 65.0 (13%), 55.1 (10%)

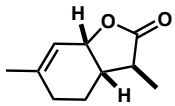


3ag

Methyl 2-(4-oxocyclohex-2-en-1-yl)propanoate (Scheme 2d)
The title compound was prepared according to the general procedure using *tert*-butyl(cyclohexa-1,3-dien-1-yloxy)dimethylsilane (52.6 mg, 0.25 mmol, 1.0 equiv) and methyl 2-chloropropanoate (42.8 μL, 0.375 mmol, 1.5 equiv) at 80 °C for 22 h. Crude ^{1}H NMR prior to purification indicated a 1:1 mixture of diastereomers. After purification by flash chromatography (SiO_2, hexanes/EtOAc = 4:1), the title compound was isolated as a colorless oil, comprising a 1:1 mixture of diastereomers (based on ^{1}H NMR of purified material).

1st run: 40 mg (88% yield, dr = 1:1)
2nd run: 41 mg (90% yield, dr = 1:1)

TLC (SiO_2) R_f = 0.25 in 4:1 hexanes/EtOAc, *p*-anisaldehyde stain
^{1}H NMR (500 MHz, $CDCl_3$) for both diastereomers δ 6.83 (d, *J* = 10.3 Hz, 1H), 6.72 (d, *J* = 10.3 Hz, 1H), 5.92 (m, 2H), 3.61 (s, 3H), 3.60 (s, 3H), 2.71 (m, 2H), 2.54 (m, 2H), 2.41 (m, 2H), 2.28 (m, 2H), 1.96 (m, 2H), 1.71 (m, 2H), 1.13 (d, *J* = 4.2 Hz, 3H), 1.12 (d, *J* = 4.2 Hz, 3H)
^{13}C NMR (126 MHz, $CDCl_3$) δ 198.9, 175.0, 174.9, 152.0, 151.5, 130.0, 129.9, 51.8, 51.7, 42.9, 42.6, 38.9, 36.9, 26.7, 25.6
IR (neat) 2951, 1730, 1679, 1452, 1434, 1350, 1258, 1197, 1165, 1148, 1085, 948, 918, 858, 784, 742, 709, 564 cm^{-1}
GC/MS (*m/z*): 182.1 (3%), 167.0 (1%), 151.1 (14%), 123.1 (83%), 111.0 (17%), 95.1 (92%), 88.1(100%), 81.1 (18%), 67.1 (49%), 55.1 (27%)

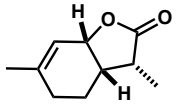


wine lactone (9)

3,6-dimethyl-3a,4,5,7a-tetrahydrobenzofuran-2(3H)-one (Scheme 2d)
The title compound was prepared according to follow procedure: Methyl 2-(4-oxocyclohex-2-en-1-yl)propanoate (**3ag**, 36.4 mg, 0.2 mmol, 1.0 equiv) was weighed into a flame-dried 25 mL

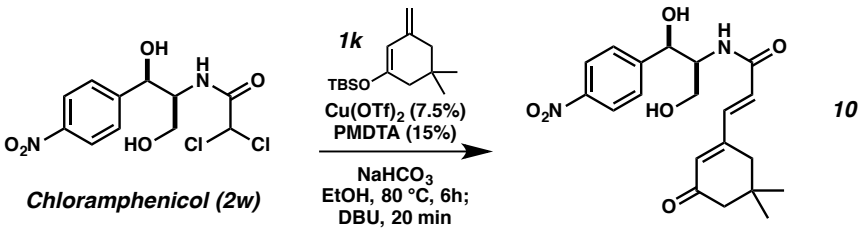
flask equipped with a magnetic stir bar. The flask was sealed with a rubber septum and then it was evacuated and backfilled with nitrogen (three cycles). The flask was charged with dry THF (2.0 mL) and the resulting mixture was cooled to –78 °C. A solution of MeMgBr in Et_2O (80 μL, 3.0 M solution, 0.24 mmol, 1.2 equiv) was added dropwise over 2 min and then the mixture was stirred at –78 °C for 30 min. The mixture was slowly warmed to room temperature and stirred for another 30 min. At this point, 2 M aq HCl solution (3.0 mL) was carefully added to the reaction mixture. After stirring for 2 h, the mixture was diluted with water (3 mL) and then extracted with EtOAc (3x 10 mL). The combined organic layers were washed with brine (1 x 10 mL) and then dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo to obtain a yellow oil. Crude ^{1}H NMR prior to purification indicated a 1:1 mixture of diastereomers. After purification by flash chromatography (SiO_2, hexanes/EtOAc = 4:1), the two diastereomers were isolated as colorless oils (wine lactone, 13.8 mg, 42% yield; epi-wine lactone, 13.8 mg, 42% yield).

TLC (SiO_2) R_f = 0.40 in 4:1 hexanes/EtOAc, *p*-anisaldehyde stain
^{1}H NMR (500 MHz, $CDCl_3$) δ 5.50 (s, 1H), 4.89 (m, 1H), 2.42 (m, 1H), 2.26 (m, 1H), 1.98 (m, 3H), 1.84 (m, 1H), 1.73 (s, 3H), 1.26 (d, *J* = 7.2 Hz, 3H)
^{13}C NMR (126 MHz, $CDCl_3$) δ 179.7, 140.8, 118.8, 75.4, 40.3, 37.6, 25.9, 23.7, 22.3, 14.0
IR (neat) 2925, 1761, 1672, 1448, 1382, 1351, 1322, 1209, 1170, 1148, 1085, 970, 948, 897, 840, 711, 663, 578 cm^{-1}
GC/MS (*m/z*): 166.1 (18%), 151.1 (100%), 138.1 (11%), 123.0 (15%), 107.1(41%), 93.1(89%), 79.0 (57%), 67.1 (17%), 55.1 (41%)



***epi*-wine lactone (*epi*-9)**

TLC (SiO_2) R_f = 0.45 in 4:1 hexanes/EtOAc, *p*-anisaldehyde stain
^{1}H NMR (500 MHz, $CDCl_3$) δ 5.67 (s, 1H), 4.64 (m, 1H), 2.89 (m, 1H), 2.35 (m, 1H), 2.01 (m, 2H), 1.78 (s, 3H), 1.68 (m, 1H), 1.19 (d, *J* = 7.3 Hz, 3H)
^{13}C NMR (126 MHz, $CDCl_3$) δ 178.8, 144.0, 117.0, 74.7, 40.3, 37.9, 28.9, 23.8, 19.7, 9.3
IR (neat) 2917, 2853, 1759, 1672, 1447, 1380, 1350, 1281, 1165, 1123, 1093, 1064, 942, 888, 821, 782, 755, 707, 616 cm^{-1}
GC/MS (*m/z*): 166.0 (25%), 151.0 (94%), 138.0 (8%), 122.0 (21%), 107.1 (46%), 93.1 (100%), 79.0 (54%), 67.1 (14%), 55.1 (35%)



(*E*)-*N*-((1*R*,2*S*)-1,3-dihydroxy-1-(4-nitrophenyl)propan-2-yl)-3-(5,5-dimethyl-3-oxocyclohex-1-en-1-yl)acrylamide (Scheme 2e)
The title compound was prepared according to the general procedure with *tert*-butyldimethyl((3-methylenecyclohex-1-en-1-yl)oxy)silane (56.0 mg, 0.25 mmol, 1.0 equiv) and chloramphenicol (121 mg, 0.375 mmol, 1.5 equiv) in ethanol at 80 °C for 6 h. Then DBU (76.0 mg, 0.5 mmol,

1.5 equiv) was added and the mixture was stirred for another 20 min. After purification by flash chromatography (SiO_2, hexanes/EtOAc = 8:1), the title compound was isolated as a colorless oil.

TLC (SiO_2) R_f = 0.30 in 20:1 EtOAc/MeOH, *p*-anisaldehyde stain
^{1}H NMR (500 MHz, CD_3OD) δ 8.15 (d, *J* = 8.6 Hz, 2H), 7.64 (d, *J* = 8.8 Hz, 2H), 7.12 (d, *J* = 15.7 Hz, 1H), 6.56 (d, *J* = 15.6 Hz, 1H), 6.07 (s, 1H), 5.48 (s, 1H), 5.16 (d, *J* = 2.8 Hz, 1H), 4.28 (dt, *J* = 6.4, 3.0 Hz, 1H), 3.81 (dd, *J* = 10.8, 7.0 Hz, 1H), 3.61 (dd, *J* = 10.8, 5.9 Hz, 1H), 2.41 (s, 2H), 2.29 (s, 2H), 1.05 (s, 6H)
^{13}C NMR (126 MHz, CD_3OD) δ 201.3, 165.9, 153.9, 150.6, 147.1, 140.3, 129.7, 126.9, 122.7, 70.3, 61.2, 56.8, 53.5, 50.7, 38.4, 32.9, 27.1, 27.0
IR (neat) 3337, 2958, 1705, 1657, 1620, 1518, 1345, 1141, 1030 cm^{-1}
LC/MS (*m/z*): 389.2 (100%)

VI. References

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