Copper catalyzed asymmetric conjugate addition of Grignard reagents to trisubstituted enones. Construction of all-carbon quaternary chiral centers.

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Table 2. Optimization of reaction conditions with EtMgBr on methyl cyclohexenone

Entry	ImH ⁺	CuX	Solvent	T (°C)	Conv. ^a (%)	ee ^b (%)
1	2a	Cu(OTf) ₂	Et ₂ O	0	92	68 (-)S
2	2a	Cu(OTf) ₂	THF	0	> 99	0
3	2a	Cu(OTf) ₂	CH ₂ Cl ₂ ^(c)	0	80	40 (-)S
4	2a	Cu(OTf) ₂	TBME	0	77	57 (-)S
5	2a	Cu(OTf) ₂	Dioxane	0	32	41 (-)S
6	2a	Cu(OTf) ₂	Et ₂ O	+20	95	60 (-)S
7	2a	Cu(OTf) ₂	Et ₂ O	-40	85	37 (-)S
8	2a	CuBr	Et ₂ O	0	82	38 (-) S
9	2a	CuTC	Et ₂ O	0	73	8 (-) S
10	2a	Cu(CN) ₄ PF ₆	Et ₂ O	0	98	68 (-) S
11	2a	Cu(CN) ₄ BF ₄	Et ₂ O	0	98	40 (-) S

(a) conversion determined by GC-MS, after 30 min. or 3h. (T < 0 °C). (b) determined by chiral GC (Lipodex E). (c) catalyst is formed in THF; after addition of BuLi, solvent is removed under vacuum and CH₂Cl₂ is added.

Table 3. Identification of the best ligand

Entry	ImH ⁺	Conv. ^a (%)	ee ^b (%)
1	1a	77	55 (+)R
2	1b	86	17 (+)R
3	1c	75	42 (+)R
4	2a	92	68 (-)S
5	2b	82	17 (-)S
6	2c	87	63 (-)S
7	2d	85	10 (-)S
8	3a	87	68 (+)R
9	3b	89	69 (+)R
10	3c	85	81 (+)R
11	3d	85	85 (+)R
12	3e	42	37 (+)R
13	3f	78	62 (+)R
14 ^(c)	2a	89	2 (-) S
15 ^(d)	2a	87	72 (-) S
16 ^(d)	3b	91	73 (+)R
17 ^(d)	3d	98	84 (+)R
18 ^(e)	3d	99	81 (+)R

(a) conversion determined by GC-MS, after 30 min. (b) determined by chiral GC (Lipodex E). (c) The substrate was added first, then the Grignard reagent was added dropwise. (d) The substrate was added dropwise over a period of 1h. (e) deprotonation of ImH⁺ with the Grignard reagent.

General Procedures. ^1H (400 MHz) and ^{13}C (100 MHz) NMR spectra were recorded in CDCl_3 , and chemical shift (δ) are given in ppm relative to residual CHCl_3 . Evolution of reaction was followed by GC-MS Hewlett Packard (EI mode) HP6890-5973. Optical rotations were measured at 20°C in a 10 cm cell in the stated solvent; $[\alpha]_D$ values are given in $10^{-1} \text{ deg cm}^2 \text{ g}^{-1}$ (concentration c given as g/100 mL). Enantiomeric excesses were determined by chiral-GC (capillary column, 10 psi H_2). Temperature programs are described as follows: initial temperature ($^\circ\text{C}$) – initial time (min) – temperature gradient ($^\circ\text{C}/\text{min}$) – final temperature ($^\circ\text{C}$) ; retention time (R_T) are given in min. Flash chromatography were performed using silica gel 32-63 μm , 60 Å and a pentane-diethylether mixture as eluant.

All reactions were conducted under inert atmosphere. All solvent were dried on alumina columns and degassed before used. Substituted cyclohexenones (**4**, **7a-d**) were synthesized by the reaction of corresponding Grignard reagent with 3-ethoxycyclohex-2-en-1-one (commercially available) in THF. Isophorone **6** and 3-methylcyclopentenone **8** are commercially available (Aldrich) and were used without further purification. 3-methyl cyclohept-2-en-1-one is synthesized following a know procedure [8]. All Grignard reagents excepted ethyl and methyl magnesium bromide (Aldrich) were synthesized in Et_2O by addition of the corresponding bromide onto magnesium. The chiral NHC ligands were synthesized following a know procedure.^{1,2,3}

NHC's spectral characterization

1,3-bis((R)-1-(2-methoxyphenyl)ethyl)-1H-imidazol-3-ium (1c):^{1,2}

^1H NMR (400 MHz, CDCl_3) : 9.25 (s, 1H), 7.40-7.33 (m, 4H), 7.04-6.99 (m, 4H), 6.88-6.86 (m, 2H), 6.02-5.97 (q, 2H, $J=7.07\text{Hz}$, 14.15Hz), 3.76 (s, 6H), 1.97-1.96 (d, 6H, $J=7.08\text{Hz}$)
 ^{13}C NMR (125 MHz, CDCl_3) : 157.23, 135.88, 131.07, 127.43, 125.94, 121.36, 120.39, 111.35, 55.67, 55.10, 19.53

(4R,5R)-1,3-di(naphthalen-1-yl)-4,5-diphenylimidazolidine (2a):^{1,2}

^1H NMR (400 MHz, CDCl_3) : 8.57 (s, 1H), 8.09-8.07 (m, 2H), 7.93-7.89 (m, 4H), 7.86-7.84 (m, 2H), 7.76-7.73 (m, 2H), 7.60-7.57 (m, 2H), 7.53-7.46 (m, 6H), 7.35-7.30 (m, 6H), 6.25 (s, 2H)
 ^{13}C NMR (125 MHz, CDCl_3) : 158.64, 134.28, 132.74, 130.69, 130.42, 129.71, 129.29, 128.61, 127.15, 126.15, 125.88, 120.60

(4R,5R)-1,3-di(naphthalen-2-yl)-4,5-diphenylimidazolidine (2b) :^{1,2}

^1H NMR (400 MHz, CDCl_3) : 9.92 (s, 1H), 7.99 (m, 2H), 7.88-7.82 (m, 4H), 7.76-7.74 (m, 2H), 7.56-7.54 (m, 2H), 7.49-7.42 (m, 14H), 5.88 (s, 2H)
 ^{13}C NMR (125 MHz, CDCl_3) : 153.75, 134.81, 133.26, 132.53, 131.75, 130.62, 130.42, 130.35, 128.59, 127.83, 127.64, 127.36, 126.97, 120.09, 118.54, 75.02

(S)-2-(3-mesitylimidazolidin-1-yl)-3,3-dimethylbutan-1-ol (3d):³

¹H NMR (400 MHz, C₃D₆O) : 8.68 (s, 1H), 7.08 (s, 2H), 4.60-4.41 (m, 5H), 4.10-4.06 (m, 1H), 4.02-3.97 (m, 1H), 3.83-3.79 (m, 1H), 2.35 (s, 6H), 2.32 (s, 3H), 1.16 (s, 9H)

¹³C NMR (125 MHz, C₃D₆O): 160.30, 140.74, 130.27, 130.19, 70.27, 57.17, 21.01, 47.86, 33.47, 27.48, 27.27, 21.16, 17.47

Typical procedure for 3-substituted cyclohex-2-en-1-one synthesis. A flame-dried flask was charged with Grignard reagent (2.0 eq.) and cooled to 0°C. The ethoxycyclohex-2-en-1-one (50 mmol) in THF (40mL) was added dropwise. Once the addition was complete the reaction mixture was left at room temperature until complete disappearance of the starting material. The reaction was hydrolyzed by addition of aqueous sulfuric acid (5% w/w). Diethyl ether (50 mL) was added and the aqueous phase was separated and extracted further with diethyl ether (3 x 20mL). The combined organic fractions were washed with NaHCO₃, brine and water, dried over sodium sulfate, filtered and concentrated *in vacuo*. The oily residue was purified by Kugelrohr distillation under reduced pressure.

3-ethylcyclohex-2-en-1-one (7a):⁴

¹H NMR (500 MHz, CDCl₃) : 5.87 (t, 1H, J = 1.4 Hz), 2.36 (t, 2H, J = 3.3 Hz), 2.29 (t, 2H, J = 5.7 Hz), 2.27-2.22 (m, 2H), 1.99 (m, 2H), 1.1 (t, 3H, J = 7.4 Hz).

¹³C NMR (125 MHz, CDCl₃) : 200, 167.8, 124.5, 37.4, 30.8, 29.7, 22.7, 11.2.

3-isobutyl-butylcyclohex-2-en-1-one (7b):⁵

¹H NMR (400 MHz, CDCl₃) : 5.83 (s, 1H), 2.35 (t, 2H, J = 6.7 Hz), 2.26 (t, 2H, J = 5.9 Hz), 2.08 (d, 2H, J = 7.3 Hz), 2.00 (quint., 2H), 1.92 (sept., 1H, J = 6.4 Hz), 0.90 (d, 6H, J = 6.6 Hz).

¹³C NMR (100 MHz, CDCl₃) : 200.0, 165.7, 127.0, 47.8, 37.5, 29.8, 26.5, 22.9, 22.6.

3-phenylcyclohex-2-en-1-one (7c):⁶

¹H NMR (400 MHz, CDCl₃) : 7.55 (m, 2H), 7.42 (m, 3H), 6.42 (s, 1H), 2.79 (m, 2H), 2.51 (t, 2H, J = 6.32 Hz), 2.19 (quint., 2H, J = 6.28)

¹³C NMR (100 MHz, CDCl₃) : 200.16, 160.02, 130.22, 129.01, 126.33, 125.72, 37.53, 28.36, 23.06

3-(3-butenyl)cyclohex-2-en-1-one (7d):⁷

¹H NMR (500 MHz, CDCl₃) : 5.80 (s, 1H), 5.75-5.67 (m, 1H), 4.98 (dd, 1H, J₁ = 17.1 Hz, J₂ = 1.5 Hz), 4.92 (dd, 1H, J₁ = 9.4 Hz, J₂ = 1.6 Hz), 2.29-2.19 (m, 8H), 1.94-1.89 (m, 2H).

¹³C NMR (125 MHz, CDCl₃) : 199.9, 165.6, 137.1, 126.1, 115.7, 37.5, 37.4, 31.1, 29.9, 22.8.

3-(3-butenyl)cyclohex-2-enone (9):⁸

¹H NMR (500 MHz, CDCl₃) : 5.89 (s, 1H), 2.56-2.53 (m, 2H), 2.39-2.37 (m, 2H), 1.93 (s, 3H), 1.81-1.72 (m, 4H).

¹³C NMR (125 MHz, CDCl₃) : 203.56, 158.34, 129.73, 42.07, 34.43, 27.51, 25.04, 21.37.

IR (neat, cm⁻¹) : 2934.3, 2866.3, 1652.4.

MS (EI) : 124 (41), 109 (24), 96 (21), 95 (100), 82 (93), 81 (49), 80 (23), 69 (10), 68 (20), 67 (56), 59 (11), 55 (20), 54 (21), 53 (26),

HRMS (ESI-MS) : [M]⁺ found, 124.08898 calcd. for C₈H₁₂O : 124.08882.

Typical procedure for product (5a-i and 10-13) synthesis: A flame-dried Schlenk tube was charged with copper salt (3.0 mol%) and the chiral carbene ligand (4.0 mol%). The system was again dried in vacuo at RT for 15 minutes. Et₂O (2.5 mL) was added and the mixture was cooled down to the desired reaction temperature in an ethanol cold bath. The Grignard reagent (1.2 eq.) in Et₂O was added dropwise to the solution for 5 minutes. A solution of the substituted cyclohexenone in Et₂O (10 mL) was then added dropwise to the solution at the desired low reaction temperature for 15 minutes, then the solution was stirred for 30 minutes. The reaction was hydrolyzed at reaction temperature by addition of HCl 1M (30 mL) and the aqueous layer was separated and extracted further with diethyl ether (3x10mL). The combined organic layers were dried on MgSO₄, filtrated and concentrated in vacuo to give a oily residue. That crude was purified by flash chromatography on a silica column with pentane:Et₂O 5:1 to give the pure product.

3-ethyl-3-methylcyclohexanone (5a):⁷

¹H NMR (400 MHz, CDCl₃) : 2.26 (t, 2H, J = 6.6 Hz), 2.16 (d of AB sys., 1H, J = 13.6 Hz), 2.08 (d of AB sys., 1H, J = 13.6 Hz), 1.88-1.81 (m, 2H), 1.64-1.48 (2m, 2H), 1.33 (q, 2H, J = 7.3 Hz), 0.88 (s, 3H), 0.83 (t, 3H, J = 7.6 Hz).

¹³C NMR (100 MHz, CDCl₃) : 212.8, 53.7, 41.4, 39.0, 35.7, 34.3, 24.7, 22.5, 8.1.

[α]_D : +4.74 (CHCl₃, c = 1.64, ee = 80% *R*. Absolute configuration was assigned in analogy with ⁷). Enantiomeric excess was measured by chiral GC (lipodex E, 75-23-20-170-5 v=40cm/s), Rt₁ = 15.5 (*R*), Rt₂ = 19.9 (*S*)).

3-butyl-3-methylcyclohexanone (5b):⁹

¹H NMR (400 MHz, CDCl₃) : 2.19 (t, 2H) ; 2.11 (q, 2H) ; 1.78 (qint., 2H) ; 1.55-1.41 (m, 2H) ; 1.18 (m, 6H) ; 0.83 (m, 6H, CH₃)

¹³C NMR (100 MHz, CDCl₃) : 212.19, 53.77, 41.28, 40.99, 38.49, 35.81, 25.53, 25.07, 23.35, 22.13, 14.04

[α]_D : +4.74 (CHCl₃, c = 1.64, ee = 77% *R*. Absolute configuration was assigned in analogy with ⁷). Enantiomeric excess was measured by chiral GC (lipodex E, 80-0-1-170-5 v=40cm/s), Rt₁ = 26.5 (*R*), Rt₂ = 27.2 (*S*)).

3-(3-butenyl)-3-methylcyclohexanone (5c):⁷

¹H NMR (400 MHz, CDCl₃) : 5.82-5.72 (m, 1H), 5.01-4.97 (d, 1H, J=16.92Hz), 4.93-4.91 (d, 1H, J=10.12Hz), 2.28-2.24 (t, 2H, J=6.82Hz), 2.20-2.08 (q, 2H, J=13.64Hz), 2.03-1.97 (m, 2H), 1.88-1.82 (m, 2H), 1.66-1.51 (m, 2H), 1.36-1.32 (t, 2H, J=8.59Hz), 0.92 (s, 3H)

¹³C NMR (125 MHz, CDCl₃) : 212.2, 138.9, 114.5, 53.8, 41.1, 41.0, 38.6, 35.9, 27.9, 25.0, 22.2

$[\alpha]_D$: -2.45 (CHCl₃, c = 1.71, ee = 90% *S*. Absolute configuration was assigned in analogy with ⁷). Enantiomeric excess was measured by chiral GC (Hydrodex B-3P, isotherm 135°C, Rt₁ = 6.5 (*S*), Rt₂ = 6.7 (*R*)).

3-*i*-butyl-3-methylcyclohexanone (5d):⁷

¹H NMR (400 MHz, CDCl₃) : 2.29-2.26 (m, 2H), 2.24-2.10 (q, 2H, J=13.39Hz, 42.45 Hz), 1.92-1.83 (m, 2H), 1.74-1.64 (m, 2H), 1.60-1.56 (m, 1H), 1.26-1.17 (m, 2H), 0.95 (s, 6H), 0.93 (m, 3H).

¹³C NMR (100 MHz, CDCl₃) : 212.7, 54.6, 51.2, 41.3, 39.7, 36.8, 25.8, 25.7, 25.6, 24.2, 22.5.

IR (neat, cm⁻¹) : 2956, 1716, 1467.

MS (EI) : 153(2), 125 (9), 112 (9), 111 (100), 110 (3), 107 (2), 98 (2), 97 (9), 95 (7), 93 (2), 85 (1), 84 (2), 83 (22), 82 (4), 81 (2), 79 (2), 77 (1), 71 (2), 70 (6), 69 (25), 68 (3), 67 (6), 65 (1), 58 (1), 57 (5), 56 (15), 55 (98), 54 (2), 53 (5).

HRMS (ESI-MS) : [M+Na]⁺ found 191.1408390, calcd. for C₁₁H₂₀ONa : 191.1406364.

$[\alpha]_D$: +2.19 (CHCl₃, c = 1.73, ee = 96% *S*. Absolute configuration was assigned in analogy with ⁷). Enantiomeric excess was measured by chiral GC (lipodex E, isotherm 80°C, Rt₁ = 12.9 (*S*), Rt₂ = 15.8 (*R*)).

3-*i*-propyl-3-methylcyclohexanone (5e):¹⁰

¹H NMR (400 MHz, CDCl₃) : 2.32-2.22 (m, 3H), 2.11 (dt, 1H), 1.98-1.77 (m, 2H), 1.64 (m, 2H), 1.51 (sept., 1H), 0.85-0.86 (d, 6H, J=0.017 Hz), 0.80 (s, 3H)

¹³C NMR (100 MHz, CDCl₃) : 212.9, 51.99, 41.21, 36.37, 34.17, 22.12, 19.94, 17.13, 16.94

$[\alpha]_D$: +12.17 (CHCl₃, c = 1.70, ee = 77% *R*. Absolute configuration was assigned in analogy with ⁷). Enantiomeric excess was measured by chiral GC (Hydrodex B-3P, isotherm 130°C, Rt₁ = 24.3 (*R*), Rt₂ = 26.3 (*S*)).

3-*c*-pentyl-3-methylcyclohexanone (5f):

¹H NMR (400 MHz, CDCl₃) : 2.23-2.17 (m, 3H), 2.06-2.02 (d, 1H), 1.85-1.69 (m, 3H), 1.61-1.50 (m, 8H), 1.17-1.13 (m, 2H), 0.79 (s, 3H)

¹³C NMR (100 MHz, CDCl₃) : 212.71, 94.01, 52.44, 49.64, 41.15, 35.14, 26.35, 40.58, 35.14, 26.35, 25.61, 22.07, 20.89

MS (EI) : 180 (2), 122 (14), 112 (10), 111 (77), 110 (18), 97 (18), 83 (14), 82 (13), 69 (25), 67 (17), 55 (100).

HRMS (EI-MS) : [M]⁺ found 180.151440, calcd. for C₁₂H₂₀O : 180.151415.

$[\alpha]_D$: +7.11 (CHCl₃, c = 1.70, ee = 85% *R*. Absolute configuration was assigned in analogy with ⁷). Enantiomeric excess was measured by chiral GC (Lipodex E, isotherm 125°C, Rt₁ = 6.9 (*R*), Rt₂ = 7.4 (*S*)).

3-*c*-hexyl-3-methylcyclohexanone (5g):

¹H NMR (400 MHz, CDCl₃) : 2.31-2.12 (m, 3H), 2.02-1.99 (m, 1H), 1.85-1.78 (m, 1H), 1.77-1.62 (m, 5H), 1.60-1.56 (m, 2H), 1.52-1.46 (m, 1H), 1.17-1.00 (m, 4H), 0.93-0.83 (m, 2H), 0.75 (s, 3H)

¹³C NMR (100 MHz, CDCl₃) : 212.84, 51.87, 46.62, 41.11, 41.02, 34.07, 26.99, 26.95, 26.80, 26.59, 26.55, 21.89, 20.99

MS (EI) : 194 (<1), 112 (12), 111 (90), 110 (17), 97 (39), 83 (20), 82 (17), 69 (17), 67 (14), 55 (100).

HRMS (EI-MS) : [M]⁺ found 194.166980, calcd. for C₁₃H₂₂O : 194.167066.

$[\alpha]_D$: +4.55 (CHCl_3 , $c = 1.70$, $ee = 74\%$ *R*. Absolute configuration was assigned in analogy with ⁷). Enantiomeric excess was measured by chiral GC (Lipodex E, isotherm 125°C, $R_{t1} = 10.9$ (*R*), $R_{t2} = 11.2$ (*S*)).

3-phenyl-3-methylcyclohexanone (5i):¹¹

¹H NMR (400 MHz, CDCl_3) : 7.33-7.32 (m, 4H), 7.22-7.19 (m, 1H), 2.90-2.42 (quart, 2H), 2.33-2.30 (t, 2H), 2.22-2.16 (m, 1H), 1.96-1.84 (m, 2H), 1.71-1.63 (m, 1H), 1.33 (s, 3H)

¹³C NMR (100 MHz, CDCl_3) : 211.54, 147.52, 128.61, 126.27, 125.65, 53.16, 42.90, 40.87, 38.01, 29.88, 22.10

$[\alpha]_D$: -26.26 (CHCl_3 , $c = 1.70$, $ee = 66\%$ *R*. Absolute configuration was assigned in analogy with ⁷). Enantiomeric excess was measured by chiral GC (Hydrodex-B-3P, isotherm 140°C, $R_{t1} = 31.7$ (*R*), $R_{t2} = 32.7$ (*S*)).

5,5-dimethyl-3-ethyl-3-methylisophorone (10):¹²

¹H NMR (400 MHz, CDCl_3) : 2.19-2.06 (m, 4H), 1.61-1.45 (dd, 2H, $J=14.15, 46.23$), 1.43-1.24 (m, 2H), 1.02 (m, 6H), 0.96 (s, 3H), 0.85-0.82 (t, 3H, $J=7.58$)

¹³C NMR (100 MHz, CDCl_3) : 212.90, 54.51, 52.98, 48.84, 39.03, 37.28, 36.28, 32.52, 30.85, 27.01, 8.41

$[\alpha]_D$: +8.519 (CHCl_3 , $c = 1.70$, $ee = 82\%$ *R*. Absolute configuration was assigned in analogy with ⁷). Enantiomeric excess was measured by chiral GC (Chirasil DEX-CB, 60-110-2-170-5, $R_{t1} = 133.8$ (*R*), $R_{t2} = 134.5$ (*S*)).

5,5-dimethyl-3-ethyl-3-methylisophorone (ent-10):¹²

¹H NMR (400 MHz, CDCl_3) : 2.19-2.06 (m, 4H), 1.61-1.45 (dd, 2H, $J=14.15, 46.23$), 1.43-1.24 (m, 2H), 1.02 (m, 6H), 0.96 (s, 3H), 0.85-0.82 (t, 3H, $J=7.58$)

¹³C NMR (100 MHz, CDCl_3) : 212.90, 54.51, 52.98, 48.84, 39.03, 37.28, 36.28, 32.52, 30.85, 27.01, 8.41

$[\alpha]_D$: -1.89 (CHCl_3 , $c = 1.70$, $ee = 71\%$ *S*. Absolute configuration was assigned in analogy with ⁷). Enantiomeric excess was measured by chiral GC (Chirasil DEX-CB, 60-110-2-170-5, $R_{t1} = 133.7$ (*R*), $R_{t2} = 134.0$ (*S*)).

3-ethyl-3-methylcyclohexanone (11a):⁷

¹H NMR (400 MHz, CDCl_3) : 2.28-2.25 (t, 2H, $J=6.82\text{Hz}$), 2.18-2.07 (q, 2H, $J=13.39\text{Hz}, 32.34\text{Hz}$), 1.89-1.82 (m, 2H), 1.65-1.48 (m, 2H), 1.33-1.28 (m, 2H), 0.89 (s, 3H), 0.85-0.81 (t, 3H, $J=7.58\text{Hz}$)

¹³C NMR (100 MHz, CDCl_3) : 212.66, 53.54, 41.22, 38.81, 35.53, 34.08, 24.56, 22.27, 7.89

$[\alpha]_D$: -4.50 (CHCl_3 , $c = 1.70$, $ee = 68\%$ *S*. Absolute configuration was assigned in analogy with ⁷). Enantiomeric excess was measured by chiral GC (lipodex E, isotherm 75°C $v=40\text{cm/s}$), $R_{t1} = 16.3$ (*R*), $R_{t2} = 19.5$ (*S*)).

3-ethyl-3-i-butylcyclohexanone (11b):

¹H NMR (400 MHz, CDCl_3) : 2.28-2.24 (t, 2H, $J=6.83\text{ Hz}$), 2.20-2.12 (dd, 2H, $J=13.65, 18.95\text{ Hz}$), 1.91-1.75 (m, 2H), 1.70-1.63 (m, 1H), 1.61-1.58 (t, 2H, $J=12.38\text{ Hz}$), 1.37-1.36 (d, 1H, $J=7.58\text{ Hz}$), 1.35-1.33 (d, 1H, $J=7.33\text{ Hz}$), 1.19-1.15 (m, 2H), 0.92-0.85 (m, 6H), 0.81-0.77 (t, 3H, $J=7.32\text{ Hz}$)

¹³C NMR (100 MHz, CDCl_3) : 212.90, 52.66, 45.99, 42.00, 41.29, 33.95,

29.76, 25.64, 25.56, 23.66, 21.92, 7.77

MS (EI) : 182 (<1), 153 (32), 125 (66), 97 (69), 95 (11), 83 (22), 70 (10), 69 (28), 67 (11), 55 (100).

HRMS (EI-MS) : $[M]^+$ found 182.167160, calcd. for $C_{12}H_{22}O$: 182.167066.

$[\alpha]_D$: +4.43 ($CHCl_3$, $c = 1.70$, $ee = 81\%$ *S*. Absolute configuration was assigned in analogy with ⁷). Enantiomeric excess was measured by chiral GC (lipodex E, isotherm 87°C $v=40$ cm/s), $Rt_1 = 25.8$ (*R*), $Rt_2 = 27.9$ (*S*)).

3-ethyl-3-phenylcyclohexanone (11c):

^1H NMR (400 MHz, CDCl_3) : 7.33-7.29 (m, 2H), 7.27-7.24 (m, 2H), 7.21-7.17 (m, 1H), 2.94-2.39 (dd, 2H, $J=14.4\text{Hz}$, 201.35 Hz), 2.31-2.27 (m, 2H), 2.20-2.14 (m, 1H), 2.02-1.95 (m, 1H), 1.87-1.53 (m, 4H), 0.62-0.58 (t, 3H, $J=7.33\text{Hz}$)

^{13}C NMR (100 MHz, CDCl_3) : 211.80, 145.95, 128.64, 126.73, 126.28, 50.79, 46.65, 41.25, 36.47, 35.93, 21.76, 8.19

IR (neat, cm^{-1}) : 2993, 2961, 2873, 1710, 1444, 1227.

MS (EI) : 202 (12), 174 (11), 173 (72), 145 (13), 131 (13), 117 (15), 115 (12), 103 (10), 91 (28), 69 (13), 55 (100).

$[\alpha]_{\text{D}}$: +58.28 (CHCl_3 , $c = 1.70$, $ee = 72\%$ *S*. Absolute configuration was assigned in analogy with ⁷). Enantiomeric excess was measured by chiral GC (Chirasil DEX-CB 135-0-1-160 $v=40\text{cm/s}$, $R_{\text{t}1} = 18.5$ (*S*), $R_{\text{t}2} = 19.0$ (*R*)).

3-butenyl-3-ethylcyclohexanone (11d):

^1H NMR (400 MHz, CDCl_3) : 5.82-5.72 (ddt, 1H, $J=6.57\text{Hz}$, 10.11Hz, 13.14Hz), 5.02-4.91 (m, 2H), 2.28-2.25 (m, 2H), 2.15 (s, 2H), 1.97-1.90 (m, 2H), 1.86-1.80 (m, 2H), 1.60-1.57 (m, 2H), 1.34-1.28 (m, 4H), 0.81-0.77 (t, 3H, $J=7.33\text{Hz}$)

^{13}C NMR (100 MHz, CDCl_3) : 212.55, 138.96, 114.61, 51.99, 41.30, 41.05, 36.07, 33.55, 29.51, 27.54, 21.83, 7.54

$[\alpha]_{\text{D}}$: +7.58 (CHCl_3 , $c = 1.70$, $ee = 69\%$ *R*. Absolute configuration was assigned in analogy with ⁷). Enantiomeric excess was measured by chiral GC (Hydrodex-B-3P isotherm 135°C $v=40\text{cm/s}$, $R_{\text{t}1} = 13.1$ (*S*), $R_{\text{t}2} = 13.3$ (*R*)).

3-ethyl-3-methylcyclopentanone (12):¹³

^1H NMR (400 MHz, CDCl_3) : 2.30-2.26 (m, 2H), 2.09-1.97 (dd, 2H, $J=17.93\text{Hz}$, 29.81Hz), 1.83-1.70 (m, 2H), 1.47-1.41 (q, 2H, $J=7.58\text{Hz}$), 1.03 (s, 3H), 0.91-0.87 (t, 3H, $J=7.32$)

^{13}C NMR (100 MHz, CDCl_3) : 220.37, 52.02, 39.91, 36.99, 34.89, 34.13, 24.65, 9.15

$[\alpha]_{\text{D}}$: +22.59 (CHCl_3 , $c = 1.70$, $ee = 46\%$ *R*. Absolute configuration was assigned in analogy with ⁷). Enantiomeric excess was measured by chiral GC (Lipodex E isotherm 60°C $v=40\text{cm/s}$, $R_{\text{t}1} = 15.2$ (*R*), $R_{\text{t}2} = 18.0$ (*S*)).

3-ethyl-3-methylcycloheptanone (13):

^1H NMR (400 MHz, CDCl_3) : 2.58-2.39 (q, 2H, $J=12.16\text{Hz}$, 62.92Hz), 2.46-2.42 (m, 2H), 1.83-1.51 (m, 6H), 1.41-1.23 (m, 2H), 0.91 (s, 3H), 0.90-0.87 (m, 3H)

^{13}C NMR (100 MHz, CDCl_3) : 214.44, 54.42, 44.02, 42.12, 35.30, 34.89, 25.35, 24.68, 24.22, 7.95

IR (neat, cm^{-1}) : 2966, 2932, 1736, 1797, 1457

MS (EI) : 154 (2), 125 (23), 112 (10), 97 (40), 96 (50), 86 (47), 84m (19), 84 (74), 83 (18), 81 (15), 70 (17), 69 (21), 56 (15), 55 (100), 49 (16), 47 (20).

HRMS (ESI-MS) : $[\text{M}+\text{H}]^+$ found, 155.1436 calcd. for $\text{C}_{10}\text{H}_{19}\text{O}$: 155.1439.

$[\alpha]_{\text{D}}$: +10.33 (CHCl_3 , $c = 1.41$, $ee = 82\%$ *R*. Absolute configuration was assigned in analogy with ⁷). Enantiomeric excess was measured by chiral GC (Lipodex E isotherm 60°C $v=50\text{cm/s}$, $R_{\text{t}1} = 24.3$ (*R*), $R_{\text{t}2} = 25.7$ (*S*)).

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1c

¹H 1c (400 MHz, CDCl₃)

¹³C 1c (400 MHz, CDCl₃)

2a¹H 2a (400 MHz, CDCl₃) ¹³C 2a (400 MHz, CDCl₃)

2b

¹H 2b (400MHz, CDCl₃)

¹³C 2b (400MHz, CDCl₃)

Dept135 2b (400MHz, CDCl3)

3d¹H 3d (400 MHz, CDCl₃) ¹³C 3d (400MHz, CDCl₃)

7a**¹H 7a** (400MHz,CDCl₃) **¹³C 7a** (400MHz,CDCl₃)

7b¹H 7b (400 MHz, CDCl₃) ¹³C 7b (400 MHz, CDCl₃)

7c

¹H 7c (400 MHz, CDCl₃)

¹³C 7c (400 MHz, CDCl₃)

7d

¹H 9 (400MHz, CDCl₃)

¹³C 9 (400MHz, CDCl₃)

5a

Sum of corrected areas: 151094103

5b

5c

5d

5e

¹H 5e (400MHz, CDCl₃)

Dept135p 5e (400MHz, CDCl₃)

5f

Dept135 5f (400 MHz, CDCl₃)

5g

11a

¹H 11a (400MHz, CDCl₃)

¹³C 11a (400MHz, CDCl₃)

11b

Signal #2 : FID2B.CH

1	25.242	24.933	26.695	M	360175	124237049	97.89%	49.468%
2	27.537	27.154	29.336	M	294778	126911614	100.00%	50.532%

Sum of corrected areas: 251148663

Dept135 11b (400MHz,CDCl3)

¹H 11c (400 MHz, CDCl₃) ¹³C 11c (400 MHz, CDCl₃)

Dept135 11c (400 MHz,CDCl3)

11d

Signal #2 : FID2B.CH

1	15.460	15.134	16.805	M	90577	27318139	100.00%	50.245%
2	17.614	17.229	19.154	M	78418	27052182	99.03%	49.755%

Sum of corrected areas: 54370321

peak #	R.T. min	Start min	End min	PK TY	peak height	peak area	peak % max.	% of total
1	15.197	14.897	17.327	M	463331	268094146	100.00%	72.864%
2	18.007	17.631	19.805	M	198630	99842111	37.24%	27.136%

Sum of corrected areas: 367936257