Organocatalytic Asymmetric Direct α -Alkynylation of Cyclic β -Ketoesters

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Table S1. Screening of different catalysts, bases and solvents in the reaction of **1g** with **2c**:

<div style="display: flex; align-items: center; justify-content: space-around;"> <div style="text-align: center;"> <p>0.15 M</p> </div> <div>+</div> <div style="text-align: center;"> <p>1.3 equiv</p> </div> <div style="text-align: center;"> <p>cat. 3 mol% base solvent -20°C, 18-24 h</p> </div> </div>					
entry	catalyst	solvent	base	conv (%) ^a	ee (%) ^b
1		<i>o</i> -Xyl./CHCl ₃ 7/1	K ₂ CO ₃ aq. 33%	nd	90
2		<i>o</i> -Xyl./CHCl ₃ 7/1	K ₂ CO ₃ aq. 33%	95	86
3		<i>o</i> -Xyl./CHCl ₃ 7/1	K ₂ CO ₃ aq. 33%	93	90
4		<i>o</i> -Xyl./CHCl ₃ 7/1	K ₂ CO ₃ aq. 33%	nd	90
5		<i>o</i> -Xyl./CHCl ₃ 7/1	K ₂ CO ₃ aq. 33%	nd	89
6		Tol./CHCl ₃ 7/1	K ₂ CO ₃ aq. 33%	95	84
7		<i>o</i> -Xyl./CHCl ₃ 7/1	Cs ₂ CO ₃ (s)	35	46
8		<i>o</i> -Xyl./CHCl ₃ 7/1	Cs ₂ CO ₃ aq. 66%	93 ^c	95

^a Determined by TLC and/or ¹H NMR spectroscopy of the crude mixture. ^b Determined by chiral stationary phase GC. ^c Isolated yield. nd = not determined.

Table S2. Screening of different catalysts, bases and solvents in the reaction of **1d** with **2a**:

<div style="text-align: center;"> <p>0.15 M 1.3 equiv.</p> <p>Solvent Base cat., 3 mol% -20 °C, 14-30 h</p> </div>					
entry	catalyst	solvent	base	conv (%) ^a	ee (%) ^b
1		<i>o</i> -Xyl./CHCl ₃ 7/1	K ₂ CO ₃ aq. 33%	>90	18
2 ^c		<i>o</i> -Xyl./CHCl ₃ 7/1	NaHCO ₃ aq. sat.	>90	68
3		<i>o</i> -Xyl./CHCl ₃ 7/1	Na ₂ CO ₃ (s)	50	27
4		<i>o</i> -Xyl./CHCl ₃ 7/1	KF aq. 33%	40	76
5		<i>o</i> -Xyl./CHCl ₃ 7/1	K ₂ HPO ₄ aq. 44%	90	76
6 ^d		<i>o</i> -Xyl./CHCl ₃ 7/1	K ₂ HPO ₄ aq. 44%	90	77
7 ^e		<i>o</i> -Xyl./CHCl ₃ 7/1	K ₂ HPO ₄ aq. 50%	72 ^f	80
8		<i>o</i> -Xyl.	K ₂ HPO ₄ aq. 50%	90	68
9		<i>o</i> -Xyl./CHCl ₃ 2:1	K ₂ HPO ₄ 50%	90	72
10		<i>o</i> -Xyl./CHCl ₃ 7:1 ^g	K ₂ HPO ₄ aq. 50%	90	77
11		Mesitylene/CHCl ₃ 7:1	K ₂ HPO ₄ aq. 50%	90	72

12		<i>o</i> -Xyl./CH ₂ Cl ₂ 7/1	K ₂ HPO ₄ aq. 50%	90	76
13		<i>o</i> -Xyl./CHCl ₃ 7/1	K ₂ HPO ₄ aq. 50%	90	72
14		<i>o</i> -Xyl./CHCl ₃ 7/1	K ₂ HPO ₄ aq. 50%	80	68
15		<i>o</i> -Xyl./CHCl ₃ 7/1	K ₂ HPO ₄ aq. 50%	60	73

^a Estimated by TLC analysis of the crude mixture. ^b Determined by chiral stationary phase HPLC. ^c Reaction performed at 0 °C. ^d 6 mol% catalyst loading. ^e Chloroalkyne **2b** as the electrophile. ^f Isolated yield. ^g 0.075 M reaction.

Table S3. Screening of different conditions in the reaction of **1h** with **2a,b**:

entry	X (equiv.), conc.	cat. loading	base	T	t	conv (%) ^a	ee (%) ^b
1	Br (1.3), 0.15 M	6 mol%	Cs ₂ CO ₃ 66%	-20 °C	48 h	≈ 40	97
2	Br (2.0), 0.3 M	6 mol%	Cs ₂ CO ₃ 66%	+4 °C	60 h	≈ 50	72
3	Br (1.3), 0.15M	6 mol%	Cs ₂ CO ₃ (s)	-20 °C	48 h	≈ 60	nd
4	Br (2.0), 0.3 M	6 mol%	K ₃ PO ₄ 40%	+4 °C	20 h	≈ 80	nd
5	Br (1.3), 0.15M	3 mol%	K ₃ PO ₄ 50%	-20 °C	48 h	≈ 50	97
6	Br (2.0), 0.3 M	6 mol%	K ₃ PO ₄ 50%	-20 °C	48 h	≈ 60	95
7	Cl (2.0), 0.3 M	6 mol%	Cs ₂ CO ₃ 66%	+4 °C	20 h	≈ 80	nd
8	Cl (2.0), 0.3 M	6 mol%	K ₃ PO ₄ 50%	-20 °C	42 h	>90	96
9	Cl (1.3), 0.15 M	3 mol%	K ₃ PO ₄ 50%	+4 °C	48 h	84 ^c	96

^a Estimated by TLC analysis of the crude mixture. ^b Determined by chiral stationary phase HPLC. ^c Isolated yield. nd = not determined.

Table S4. Screening of different conditions in the reaction of **1j** with **2a,b**:

entry	X (equiv.), conc.	cat. loading	base	T	t	conv (%) ^a	ee (%) ^b
1	Cl (1.3), 0.15 M	3 mol%	K ₃ PO ₄ 50%	+4 °C	48 h	34 ^c	96
2	Cl (2.0), 0.3 M	6 mol%	K ₃ PO ₄ 50%	+4 °C	48 h	25 ^c	nd
3	Cl (1.3), 0.15 M	3 mol%	K ₃ PO ₄ 50%	rt	48 h	36 ^c	90
4	Cl (2.0), 0.3 M	6 mol%	K ₃ PO ₄ 50%	rt	40 h	39 ^c	80
5	Br (2.0), 0.3 M	6 mol%	K ₃ PO ₄ 50%	+4 °C	5 d	≈ 50 (+ byproduct)	nd
6	Cl (4.0), 0.3 M	6 mol%	K ₃ PO ₄ 50%	+4 °C	5 d	≈ 60	nd
7	Cl (2.0), 0.3 M	6 mol%	Cs ₂ CO ₃	+4 °C	48 h	50 ^c	60
8	Cl (2.0), 0.3 M	6 mol%	K ₃ PO ₄	+4 °C	48 h	≈ 40	nd
9	Cl (1.3), 0.15 M	3 mol%	NaOH 10%	+4 °C	20 h	69 ^c	97
10	Br (1.3), 0.15 M	3 mol%	NaOH 10%	+4 °C	20 h	≈ 80 (+ byproduct)	nd
11	Cl (2.0), 0.15 M	3 mol%	NaOH 10%	+4 °C	16 h	78 ^c	97

^a Estimated by TLC analysis of the crude mixture. ^b Determined by chiral stationary phase HPLC. ^c Isolated Yield. nd = not determined

General Methods. NMR spectra were acquired on a Varian AS 400 spectrometer, running at 400 and 100 MHz for ^1H and ^{13}C , respectively. Chemical shifts (δ) are reported in ppm relative to residual solvent signals (CHCl_3 , 7.26 ppm for ^1H NMR, CDCl_3 , 77.0 ppm for ^{13}C NMR; CHD_2OD , 3.30 ppm for ^1H NMR, CD_3OD , 52.0 ppm for ^{13}C NMR). ^{13}C NMR spectra were acquired on a broad band decoupled mode. Mass spectra were recorded on a micromass LCT spectrometer using electrospray (ES^+) ionization techniques. Analytical thin layer chromatography (TLC) was performed using pre-coated aluminium-backed plates (Merck Kieselgel 60 F254) and visualized by ultraviolet irradiation or KMnO_4 dip. Melting points are uncorrected. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. The enantiomeric excess (ee) of the products was determined by chiral stationary phase HPLC (Daicel Chiralpak AS/AD or Daicel Chiralcel OD/OJ columns).

Materials. Analytical grade solvents and commercially available reagents were used as received. For flash chromatography (FC) silica gel was purchased from Iatron Laboratories Inc. (Iatrobeads 6RS-8060) or from Fluka (Silica gel 60, 230-400 mesh). The *tert*-butyl β -ketoesters were either prepared by Claisen-condensation (**1g** and **1h**),¹ or from the corresponding methyl esters² by Bu_2SnO catalyzed transesterification with *tert*-BuOH in refluxing toluene (**1a-d**).³ Additional *tert*-butyl β -ketoesters **1e-f** and **1i-k** were prepared by acylation of the lithium enolate of the corresponding ketone with *tert*-butyl cyanoformate **6**.⁴ The activated β -haloalkynes **2** were synthesized as outlined below. *N*-9-anthracenylmethyl dihydrocinchoninium chloride **5a** and *N*-9-anthracenylmethyl dihydrocinchonidinium chloride **5'a** were prepared following a literature procedure.⁵ Racemic samples were prepared using TBAI as the catalyst.

Representative procedure for the synthesis of chloroalkynes **2**⁶

To a stirred solution of allyl propiolate (550 mg, 5.0 mmol) and *t*-BuOCl (593 μL , 5.0 mmol) in *t*-BuOH (5 mL), *t*-BuOK (56 mg, 0.5 mmol) was added in two equal portions, giving each time a slightly exothermic reaction. The mixture was stirred for the time indicated below, and then filtered through a pad of silica. The pad was washed with Et_2O and the solvent was evaporated. The mixture was purified by column chromatography (eluent is indicated in each case).

Allyl 3-chloropropiolate (**2b**):

Reaction time 3 h. Purified by FC (5% Et₂O in *n*-pentane). After evaporation of the solvents (*p* > 200 mBar, 25-30 °C), were obtained 398 mg (55% yield) of compound **2b** as a colourless liquid. ¹H NMR (CDCl₃) δ 5.97-5.86 (m, 1H), 5.37 (dq, *J*_d = 17.2 Hz, *J*_q = 1.2 Hz, 1H), 5.29 (br d, *J* = 10.4 Hz, 1H), 4.67 (br d, *J* = 5.9 Hz, 2H). ¹³C NMR (CDCl₃) δ 152.0, 130.7, 119.6, 68.6, 66.8, 61.6.

3-Chloro-1-phenylprop-2-yn-1-one (**2g**):

Carried out on a 1.08 mmol-scale using the procedure above, reaction time was 1h. The product was isolated by FC (10% Et₂O in *n*-hexane). After evaporation of the solvent were obtained 168 mg (82% yield) of compound **2g** as yellow liquid that solidified upon standing. ¹H NMR (CDCl₃) δ 8.12 (d, *J* = 7.8 Hz, 2H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.8 Hz, 2H). ¹³C NMR (CDCl₃) δ 176.4, 136.2, 134.5, 129.6, 128.7, 74.6, 67.8.

1-(2-Chloroethynylsulfonyl)-4-methylbenzene (**2i**):

Reaction time 1h. Purified by FC (10% Et₂O in *n*-hexane). After evaporation of the solvents **2i** was obtained as a yellow solid (92% yield, mp = 64-66 °C). ¹H NMR (CDCl₃) δ 7.84 (d, *J* = 8.4 Hz, 2H), 7.36 (d, *J* = 8.4 Hz, 2H), 2.43 (s, 3H). ¹³C NMR (CDCl₃) δ 145.9, 137.8, 130.0, 127.4, 75.9, 67.2, 21.6.

General procedure for the synthesis of bromoalkynes **2**⁷

In a 100 mL, one necked, round-bottomed flask is placed 5 mmol of the corresponding alkyne in 10 mL of acetone. To the solution at room temperature was added 0.5 mmol of silver nitrate. After 5 min, 5.5 mmol of NBS was added. The mixture was stirred for 2 h, and the solids were filtered off on a pad of Celite, which was washed several times with acetone. After rotary evaporation of the acetone (*p* > 200 mBar, 25-30 °C), the residue was purified by column chromatography (eluent is indicated in each case).

Ethyl 3-bromopropiolate (2c):⁸

The title compound was obtained by the general procedure starting from commercially available ethyl propiolate, as a white solid (yield 90%, mp 21-22 °C) after purification by FC (15% Et₂O in *n*-pentane). ¹H NMR (CDCl₃) δ 4.22 (q, *J* = 7.2 Hz, 2H), 1.30 (t, *J* = 7.2 Hz, 3H).

3-Bromo-1-(pyrrolidin-1-yl)prop-2-yn-1-one (2d):

The title compound was obtained starting from 1-(pyrrolidin-1-yl)prop-2-yn-1-one⁹ (415 mg, 1.8 mmol), following the general procedure. The residue was purified by FC (25% AcOEt in *n*-hexane), affording 537 mg (98% yield) of compound **2d** as a white solid (mp = 99-101 °C). ¹H NMR (CDCl₃) δ 3.62-3.58 (m, 2H), 3.56-3.40 (m, 2H), 1.93-1.80 (m, 4H). ¹³C NMR (CDCl₃) δ 151.1, 74.6, 53.9, 47.9, 45.3, 25.2, 24.5. HRMS calc.: C₇H₈BrNaNO 223.9687; found: 223.9678.

4-Bromobut-3-yn-2-one (2e):

Carried out using the general procedure above, reaction time was 1.3h. The product was isolated by FC (10% Et₂O in *n*-pentane). After evaporation of the solvent were obtained 448 mg (61% yield) of compound **2e** as a yellow liquid. ¹H NMR (CDCl₃) δ 2.34 (s, 3H). ¹³C NMR (CDCl₃) δ 182.9, 80.2, 57.1, 32.4.

4-Bromobut-3-yn-2-one (2f):

Carried out using the general procedure above, reaction time was 2.0h. The product was isolated by FC (50% CH₂Cl₂ in *n*-hexane). After evaporation of the solvent were obtained 820 mg (78% yield) of compound **2f** as a yellow solid (mp = 80-82 °C). ¹H NMR (CDCl₃) δ 8.12 (d, *J* = 7.9 Hz, 2H), 7.63 (t, *J* = 7.4 Hz, 1H), 7.49 (t, *J* = 8.0 Hz, 2H). ¹³C NMR (CDCl₃) δ 176.5, 136.1, 134.5, 129.7, 128.7, 78.9, 58.9.

1-(2-Bromoethynylsulfonyl)-4-methylbenzene (2h):

The title compound was obtained starting from trimethyl(*p*-tolylsulfonyl)ethynyl)silane using the same procedure as above. After purification by FC (33% AcOEt in *n*-hexane) compound **2h** was obtained as a yellow solid (99% yield, mp = 94-96 °C). ¹H NMR (CDCl₃) δ 7.81

(d, $J = 8.0$ Hz, 2H), 7.34 (d, $J = 8.0$ Hz, 2H), 2.42 (s, 3H). ^{13}C NMR (CDCl_3) δ 145.9, 137.6, 129.9, 127.3, 77.6, 61.6, 21.5. HRMS calc.: $\text{C}_9\text{H}_7\text{NaBrO}_2\text{S}$ 280.9248; found: 280.9251

Procedure for the synthesis of allyl 3-bromopropiolate (2a).

Allyl 3-bromopropiolate (2a):

To a stirred solution of methyl 3-bromopropiolate¹⁰ (3.8 g, 23 mmol) in 50 mL of dry toluene, allyl alcohol (13.3 g, 230 mmol), and Bu_2SnO (572 mg, 2.3 mmol) were added and the mixture was heated to reflux employing a Dean Stark apparatus to separate the MeOH formed (8 h). When the reaction was complete, the solvents were removed under reduced pressure and the residue was purified by FC (30% CH_2Cl_2 in *n*-hexane), affording the title compound as a colorless liquid (3.0 g, 69% yield). ^1H NMR (CDCl_3) δ 5.86 (ddt, $J_d = 17.4$, 10.4 Hz, $J_t = 5.9$ Hz, 1H), 5.31 (dq, $J_d = 17.4$ Hz, $J_q = 0.8$ Hz, 1H), 5.22 (dq, $J_d = 10.4$ Hz, $J_q = 0.8$ Hz, 1H), 4.68-4.66 (m, 2H). ^{13}C NMR (CDCl_3) δ 151.9, 130.6, 119.5, 72.4, 66.7, 52.9.

General procedure for the preparation of *tert*-butyl β -ketoesters 1e,f and 1i-k by acylation with *tert*-butyl cyanoformate 6.¹¹

A solution of a ketone (1.5 mmol) in dry THF (3 mL) was slowly added to a cooled (-78°C), stirred solution of LDA or LHMDS (1.65 or 3.0 mmol) in dry THF (3 mL). After 30 min stirring at the same temperature, a solution of *tert*-butyl cyanoformate **6** (1.65 mmol) in dry THF (1 mL) was added, and the resulting mixture was stirred for 1 h at -78°C , then allowed to warm to room temperature. The reaction was then quenched by addition of sat. NH_4Cl (aq.), and the product extracted with Et_2O (3 x). The combined organic phases were then dried over Na_2SO_4 , filtered and evaporated under reduced pressure. Purification of the crude mixture by FC (Et_2O in *n*-pentane 5:95), gave the corresponding β -ketoesters **1**.

***tert*-Butyl 1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (1e):**

The title compound was obtained according to the general procedure, using 1.1 equiv. of LDA as the base, as a colorless thick oil (41% yield).

^1H NMR (CDCl_3) [enol form, 70%] δ 12.60 (br s, 1H), 7.79 (br d, $J = 7.0$ Hz, 1H), 7.34-7.20 (m, 2H), 7.14 (br d, $J = 6.9$ Hz, 1H), 2.78 (t, $J = 7.3$ Hz, 2H), 2.52 (t, $J = 7.2$ Hz, 2H), 1.56 (s, 9H); [keto form, 30%] δ 8.08 (br d, $J = 7.8$ Hz, 1H), 7.47 (br t, $J = 7.0$ Hz, 1H), 7.34-7.20 (m, 2H), 3.50 (dd, $J = 10.0, 4.7$ Hz, 1H), 3.10-2.90 (m, 2H), 2.49-2.40 (m, 1H), 2.34 (dq, $J_d = 13.5$ Hz, $J_q = 4.9$ Hz, 1H), 1.48 (s, 9H). ^{13}C NMR (CDCl_3) [enol and keto form] δ 193.7, 172.5, 169.5, 164.4, 143.5, 139.2, 133.6, 131.9, 130.2, 130.1, 128.7, 127.5, 127.2, 126.7, 126.4, 124.0, 98.2, 81.7, 81.1, 55.3, 28.2, 27.9, 27.5, 26.4, 20.9. HRMS calc.: $\text{C}_{15}\text{H}_{18}\text{NaO}_3$ 269.1148; found: 269.1142.

***tert*-Butyl 5-oxo-6,7,8,9-tetrahydro-5H-benzo[7]annulene-6-carboxylate (1f):**

The title compound was obtained according to the general procedure, using

1.1 equiv. of LDA as the base, as a colorless thick oil (36% yield). ^1H

NMR (CDCl_3) [enol form, 76%] δ 12.80 (br s, 1H), 7.64-7.58 (m, 1H),

7.35-7.16 (m, 3H), 2.66-2.60 (m, 2H), 2.16-2.02 (m, 4H), 1.56 (s, 9H);

[keto form, 24%] δ 7.72 (dd, $J = 7.7, 1.4$ Hz, 1H), 7.42 (dt, $J_t = 7.5$ Hz, $J_d = 1.5$ Hz, 1H), 7.35-7.16 (m, 2H), 3.70 (dd, $J = 9.4, 4.5$ Hz, 1H), 2.66-2.60 (m, 2H), 2.22-1.96 (m, 2H), 1.93-1.81 (m, 2H), 1.42 (s, 9H). ^{13}C NMR (CDCl_3) [enol and keto form] δ 201.5, 173.1, 169.8, 141.4, 141.3, 138.6, 136.3, 132.2, 130.0, 129.3, 129.1, 127.2, 126.8, 126.5, 101.9, 81.8, 81.5, 57.9, 33.8, 33.2, 32.0, 28.6, 28.1, 25.6, 24.6, 22.4. HRMS calc.: $\text{C}_{16}\text{H}_{20}\text{NaO}_3$ 283.1305; found: 283.1309.

***tert*-Butyl 2-oxocyclohex-3-enecarboxylate (1i):**

The title compound was obtained according to the general procedure, using 2 equiv. of LHMDs as the base, as a colourless liquid (62% yield). ^1H

NMR (CDCl_3) [keto form, 97%] δ 6.96 (dt, $J_d = 10.1$ Hz, $J_t = 3.8$ Hz, 1H), 6.03 (dt,

$J_d = 10.2$ Hz, $J_t = 2.0$ Hz, 1H), 3.28 (dd, $J = 9.4, 5.5$ Hz, 1H), 2.50-2.25 (m,

3H), 2.20-2.10 (m, 1H), 1.45 (s, 9H). ^{13}C NMR (CDCl_3) [keto form, 97%] δ 194.5, 169.2, 150.2, 129.2, 81.7, 54.2, 27.9, 25.7, 24.2. HRMS calc.: $\text{C}_{11}\text{H}_{16}\text{NaO}_3$ 219.0992; found: 219.1006.

***tert*-Butyl 4-methyl-2-oxocyclohex-3-enecarboxylate (1j):**

The title compound was obtained according to the general procedure, using LDA (2 equiv.) as the base, as a yellow oil (69% yield). ^1H NMR (CDCl_3) δ 5.88 (q, J = 1.3 Hz, 1H), 3.22-3.16 (m, 1H), 2.43-2.23 (m, 3H), 2.19-2.10 (m, 1H), 1.95 (br s, 3H), 1.45 (s, 9H). ^{13}C NMR (CDCl_3) δ 194.3, 169.6, 162.4, 125.9, 81.5, 53.2, 29.3, 27.9, 25.6, 24.3. HRMS calc.: $\text{C}_{12}\text{H}_{18}\text{NaO}_3$ 233.1154; found: 233.1150.

***tert*-Butyl 4-ethoxy-2-oxocyclohex-3-enecarboxylate (1k):**

The title compound was obtained according to the general procedure, using 2 equiv. of LHMDs as the base, as a white solid (70% yield). ^1H NMR (CDCl_3) [keto form > 97%] δ 5.26 (s, 1H), 3.85-3.79 (m, 2H), 3.10 (dd, J = 8.8, 4.8 Hz, 1H), 2.47-2.40 (m, 1H), 2.35-2.27 (m, 1H), 2.23-2.14 (m, 1H), 2.09-2.01 (m, 1H), 1.37 (s, 9H), 1.27 (t, J = 7.2 Hz, 3H). ^{13}C NMR (CDCl_3) [keto form, >97%] δ 194.1, 177.9, 169.4, 101.8, 81.7, 64.2, 52.9, 27.7, 28.0, 24.1, 13.8. HRMS calc.: $\text{C}_{13}\text{H}_{20}\text{NaO}_4$ 263.1259; found: 263.1269.

Procedure for the preparation triisopropyl ether indole (1l).

N-Me-oxindole¹² (100 mg, 0.68 mmol) dissolved in 1 mL THF was added dropwise to a cold (-78 °C) solution of LHMDs (2.3 equiv.) in 3.5 mL THF. The mixture was stirred at -78 °C for 35 min, after which the temperature was increased to 0 °C (ice-water bath) for 25 min. The enolate-solution was then added slowly (using a syringe) to a solution of *tert*-butyl cyanofornate **6** (1.3 equiv., 0.90 mmol, 114.3 mg) in THF (2 mL) at 0 °C. The resulting mixture was stirred at 0 °C for 1 h and was then quenched by addition of 3 mL sat. NH_4Cl (aq.). 1M HCl (aq.) was added until the water layer was acidic, and then the mixture was extracted with Et_2O (3 x). The organic extracts were combined and washed with 1M HCl (aq.), water (2 x), and brine. The solution was dried over anhydrous Na_2SO_4 , filtered, and concentrated under reduced pressure. The crude mixture was then redissolved in dry CH_2Cl_2 (10 mL) and a magnetic stirring bar was added. To the stirred mixture was added triethylamine (1.5 equiv. 1.02 mmol, 141 μL), and TIPSOTf (1.05 equiv., 0.71 mmol, 193 μL). The mixture was stirred for 20 min at ambient temperature and then the reaction was quenched by addition of 3 mL sat. NaHCO_3 (aq.) followed by dilution with water (ca. 5 mL). The phases were separated and the water phase was extracted with CH_2Cl_2 . The solvent was removed under reduced pressure and resulting residue was subjected to FC to afford the product.

***tert*-Butyl 1-methyl-2-(triisopropylsilyloxy)-1H-indole-3-carboxylate (1l):**

The title compound was obtained after FC (SiO₂, CH₂Cl₂ in *n*-hexane 25:75) as a white solid (113 mg, 0.28 mmol, 41% yield, mp = 88-90 °C). ¹H NMR (CDCl₃) δ 7.90 (m, 1H), 7.18-7.13 (m, 3H), 3.57 (s, 3H), 1.62 (s, 9H), 1.54 (sept, *J* = 7.6 Hz, 3H), 1.13 (d, *J* = 7.6 Hz, 18H). ¹³C NMR (CDCl₃) δ 164.1, 153.4, 131.2, 124.9, 121.2, 120.6, 120.5, 108.2, 90.4, 78.9, 28.6, 27.7, 17.9, 14.2.

***O*-1-Adamantoyl-*N*-9-anthracenylmethyl dihydrocinchoninium chloride (5b):**

To a stirred suspension of *N*-9-anthracenylmethyl dihydrocinchoninium chloride **5a** (261 mg, 0.5 mmol) in CH₂Cl₂ (5 mL), were sequentially added 1-adamantanecarbonyl chloride (299 mg, 2.5 mmol) and a 30% w/w NaOH solution (0.7 mL). After 30 min of vigorous stirring, during which time all the solid dissolved, H₂O and CH₂Cl₂ were added. The two layers were separated and the aqueous layer extracted with CH₂Cl₂, the combined organic extracts were dried over MgSO₄, filtered and evaporated under reduced pressure. The crude product was dissolved in CH₂Cl₂ (ca 1.5 mL), poured onto Et₂O (15 mL) with stirring. The resulting precipitate was collected by suction filtration, washed several times with Et₂O, giving **5b** as a yellow solid (285 mg, 83% yield). Mp 133-138 °C. ¹H NMR (CD₃OD) δ 9.02 (d, *J* = 4.7 Hz, 1H), 8.90 (s, 1H), 8.76 (d, *J* = 8.4 Hz, 1H), 8.51 (d, *J* = 8.4 Hz, 1H), 8.25 (t, *J* = 6.6 Hz, 2H), 8.14 (dd, *J* = 8.4, 1.2 Hz, 1H), 8.01 (br s, 1H), 7.98-7.80 (m, 5H), 7.66 (dd, *J* = 8.4, 6.5 Hz, 1H), 7.55 (dd, *J* = 8.3, 6.5 Hz, 1H), 7.38 (ddd, *J* = 8.8, 6.6, 1.0 Hz, 1H), 5.96 (d, *J* = 14.0 Hz, 1H), 5.86 (d, *J* = 14.0 Hz, 1H), 4.51 (br t, *J* = 9.6 Hz, 1H), 4.19 (br t, *J* = 11.6 Hz, 1H), 3.64-3.58 (m, 1H), 3.42-3.36 (m, 1H), 2.80-2.70 (m, 2H), 2.30-2.20 (m, 3H), 2.25 (br s, 6H), 2.10-1.70 (m, 9H), 1.68-1.50 (m, 4H), 0.80 (t, *J* = 6.8 Hz, 3H). ¹³C NMR (CD₃OD) δ 179.8, 152.8, 150.2, 147.4, 137.3, 137.0, 136.9, 135.9, 135.7, 135.0, 134.4, 133.9, 132.5, 132.3, 132.1, 131.6, 129.5, 129.2, 128.6, 128.2, 127.1, 126.6, 123.2, 120.9, 72.2, 71.1, 61.9, 61.7, 59.7, 45.4, 43.1, 40.0, 39.6, 32.0, 28.5, 28.3, 27.9, 26.3, 14.2. HRMS calc.: C₄₅H₄₉N₂O₂ 649.3789; found: 649.3788. [α]_D²⁵ +192 (c 0.49, CH₃OH).

***O*-1-Adamantoyl-*N*-9-anthracenylmethyl dihydrocinchonidinium chloride (5'b):**

Starting from *N*-9-anthracenylmethyl dihydrocinchonidinium chloride and following the procedure used for **5b**, the title compound was obtained as a yellow solid in 73% yield. Mp 118-121 °C. ¹H NMR (CD₃OD) δ 8.98 (d, *J* = 4.8 Hz, 1H), 8.91 (s, 1H), 8.59 (d, *J* = 8.8 Hz, 1H), 8.49 (d, *J* = 8.4 Hz, 1H), 8.28-8.24 (m, 2H), 8.20-8.10 (m, 3H),

7.89 (t, $J = 7.2$ Hz, 1H), 7.86-7.75 (m, 3H), 7.68-7.52 (m, 3H), 6.40 (d, $J = 14.0$ Hz, 1H), 5.77 (d, $J = 14.0$ Hz, 1H), 4.52-4.49 (m, 1H), 3.86 (br t, $J = 12.0$ Hz, 1H), 3.50-3.46 (m, 1H), 3.30-3.22 (m, 1H), 2.92-2.80 (m, 1H), 2.61-2.52 (m, 1H), 2.25-2.12 (m, 10H), 1.96-1.80 (m, 8H), 1.74-1.54 (m, 2H), 1.30-1.20 (m, 2H), 0.65 (t, $J = 6.8$ Hz, 3H). ^{13}C NMR (CD_3OD) δ 179.9, 152.9, 150.3, 147.5, 137.4, 137.1, 137.0, 136.0, 135.7, 135.1, 134.5, 134.0, 132.5, 132.3, 132.2, 131.7, 129.6, 128.7, 128.2, 127.2, 126.6, 123.3, 120.9, 72.2, 71.2, 61.9, 61.7, 59.7, 45.5, 43.2, 40.1, 39.9, 32.0, 28.6, 28.4, 27.9, 26.3, 14.2. $[\alpha]_{\text{D}}^{25}$ -162 (c 0.27, CH_3OH).

General procedure for the acetylenic substitution reaction.

To a sample vial equipped with a magnetic stirring bar was added **1** (0.20 mmol), *o*-xylene/ CHCl_3 (7:1, 1.3 mL), **2** (0.26 mmol), and the catalyst **5b** (3 mol%, 0.006 mmol, 4.1 mg). The mixture was stirred for a short time at ambient temperature and was then placed at -20 °C or $+4$ °C. When the mixture had cooled, a cold solution of the appropriate aqueous base (0.6 mL) was added and the biphasic mixture was vigorously stirred for the time stated below. After the reaction was judged to be complete by TLC analysis, the organic phase was collected, and the aqueous layer was extracted two times with toluene. The combined organic fractions were loaded onto a chromatographic column and the product **3** was obtained by FC (eluent stated below).

(+)-*tert*-Butyl 2-(3-(allyloxy)-3-oxoprop-1-ynyl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**3a**):

The title compound was obtained according to the general procedure, after 18 h reaction at -20 °C using K_2CO_3 33% w/w as the base and bromoalkyne **2a** as the electrophile, as a viscous colorless oil (99% yield) after FC (SiO_2 , Et_2O in *n*-pentane 0:100 to 20:80). ^1H NMR (CDCl_3) δ 7.75 (br d, $J = 7.7$ Hz, 1H), 7.63 (td, $J_t = 7.6$ Hz, $J_d = 1.2$ Hz, 1H), 7.48 (dt, $J_d = 7.7$ Hz, $J_t = 0.8$ Hz, 1H), 7.42 (td, $J_t = 7.9$ Hz, $J_d = 0.8$ Hz, 1H), 5.88 (ddt, $J_d = 17.1$, 10.4 Hz, $J_t = 5.9$ Hz, 1H), 5.33 (dq, $J_d = 17.2$ Hz, $J_q = 1.5$ Hz, 1H), 5.25 (dq, $J_d = 10.4$ Hz, $J_q = 1.2$ Hz, 1H), 4.69-4.57 (m, 2H), 3.88 (d, $J = 17.2$ Hz, 1H), 3.58 (d, $J = 17.2$ Hz, 1H), 1.44 (s, 9H). ^{13}C NMR (CDCl_3) δ 194.6, 165.4, 152.8, 152.0, 136.1, 133.0, 131.0, 128.3, 126.3, 125.8, 119.3, 84.2, 83.8, 75.0, 66.5, 56.2, 39.7, 27.6. HRMS calc.: $\text{C}_{20}\text{H}_{20}\text{NaO}_5$ 363.1203; found: 363.1199. The ee was determined by HPLC using a Chiralcel OJ column [hexane/*i*PrOH (80:20)]; flow rate 1.0 mL/min; $\tau_{\text{major}} = 9.8$ min, $\tau_{\text{minor}} = 16.8$ min (96% ee). $[\alpha]_{\text{D}}^{25} +7$ (c 0.97, CH_2Cl_2).

(-)-tert-Butyl 2-(3-(allyloxy)-3-oxoprop-1-ynyl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (ent-3a):

The title compound was obtained according to the general procedure after 18 h reaction at -20 °C using the catalyst derived from dihydrocinchonidine **5'b**, K₂CO₃ 33% w/w as the base and bromoalkyne **2a** as the electrophile, as a viscous colorless oil (97% yield) after FC (SiO₂, Et₂O in *n*-pentane 0:100 to 20:80). Spectral data were identical to compound **3a**. The ee was determined by HPLC using a Chiralcel OJ column [hexane/*i*PrOH (80:20)]; flow rate 1.0 mL/min; τ_{major} = 16.8 min, τ_{minor} = 9.8 min (88% ee). $[\alpha]_{\text{D}}^{25}$ -6 (c 0.94, CH₂Cl₂).

(+)-tert-Butyl 2-(3-ethoxy-3-oxoprop-1-ynyl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (3b):

The title compound was obtained according to the general procedure, after 18 h reaction at -20 °C using K₂CO₃ 33% w/w as the base and bromoalkyne **2c** as the electrophile, as a viscous colorless oil (99% yield) after FC (SiO₂, Et₂O in *n*-pentane 0:100 to 20:80). ¹H NMR (CDCl₃) δ 7.78 (br d, *J* = 7.8 Hz, 1H), 7.65 (td, *J*_t = 7.7 Hz, *J*_d = 1.2 Hz, 1H), 7.48 (dt, *J*_d = 7.7 Hz, *J*_t = 0.8 Hz, 1H), 7.42 (td, *J*_t = 7.6 Hz, *J*_d = 0.8 Hz, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.85 (d, *J* = 17.1 Hz, 1H), 3.54 (d, *J* = 17.2 Hz, 1H), 1.44 (s, 9H), 1.28 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (CDCl₃) δ 194.7, 165.4, 153.2, 152.0, 136.1, 133.1, 128.3, 126.3, 125.7, 84.2, 83.4, 75.3, 62.1, 56.1, 39.8, 27.6, 13.9. HRMS calc.: C₁₉H₂₀NaO₅ 351.1203; found: 351.1239. The ee was determined by HPLC using a Chiralcel OJ column [hexane/*i*PrOH (80:20)]; flow rate 1.0 mL/min; τ_{major} = 10.0 min, τ_{minor} = 23.2 min (96% ee). $[\alpha]_{\text{D}}^{25}$ +7 (c 0.96, CH₂Cl₂).

(-)-tert-Butyl 1-oxo-2-(3-oxo-3-(pyrrolidin-1-yl)prop-1-ynyl)-2,3-dihydro-1H-indene-2-carboxylate (3c):

The title compound was obtained according to the general procedure, after 20 h reaction at -20 °C using 0.2 mmol (40 mg) of bromoalkyne **2d**, 0.26 mmol (60 mg) of β -ketoester **1a** and Cs₂CO₃ 50% w/w as the base, as a white solid (96% yield based on **2d**) after FC (SiO₂, *n*-pentane then Et₂O in CH₂Cl₂ 0:100 to 2:98). Mp 150-153 °C. ¹H NMR (CDCl₃) δ 7.78 (br d, *J* = 7.7 Hz, 1H), 7.64 (td, *J*_t = 7.7 Hz, *J*_d = 1.0 Hz, 1H), 7.46 (br d, *J* = 7.7 Hz, 1H), 7.42 (br t, *J* = 7.7 Hz, 1H), 3.84 (d, *J* = 17.2 Hz, 1H), 3.71 (br t, *J* = 6.6 Hz, 2H), 3.54 (d, *J* = 17.2 Hz, 1H), 3.42 (br t, *J* = 6.7 Hz, 2H), 1.98-1.84 (m, 4H), 1.44 (s, 9H). ¹³C NMR (CDCl₃) δ 195.3, 165.8, 152.2, 151.9,

136.0, 133.1, 128.1, 126.3, 125.6, 85.8, 83.8, 77.3, 56.3, 48.2, 45.2, 39.8, 27.6, 25.2, 24.6. HRMS calc.: $C_{21}H_{23}NNaO_4$ 376.1519; found: 376.1518. The ee was determined by HPLC using a Chiralcel OJ column [hexane/*i*PrOH (80:20)]; flow rate 1.0 mL/min; $\tau_{\text{major}} = 10.1$ min, $\tau_{\text{minor}} = 15.6$ min (96% ee). $[\alpha]_D^{25} -22$ (c 1.0, CH_2Cl_2).

(+)-(S)-tert-Butyl 1-oxo-2-(3-oxobut-1-ynyl)-2,3-dihydro-1H-indene-2-carboxylate (3d):

The title compound was obtained according to the general procedure, after 18 h reaction at -20 °C using K_2CO_3 33% w/w as the base and bromoalkyne **2e** as the electrophile, as a viscous colorless oil (88% yield) after FC (SiO_2 , Et_2O in *n*-pentane 0:100 to 20:80). 1H NMR ($CDCl_3$) δ 7.80 (br d, $J = 7.8$ Hz, 1H), 7.65 (td, $J_t = 7.5$ Hz, $J_d = 1.2$ Hz, 1H), 7.48 (br d, $J = 7.8$ Hz, 1H), 7.42 (br t, $J = 7.6$ Hz, 1H), 3.86 (d, $J = 17.1$ Hz, 1H), 3.51 (d, $J = 17.1$ Hz, 1H), 2.36 (s, 3H), 1.44 (s, 9H). ^{13}C NMR ($CDCl_3$) δ 194.9, 184.2, 165.5, 152.0, 136.1, 133.1, 128.3, 126.3, 125.7, 87.8, 84.1, 82.5, 56.4, 39.9, 32.7, 27.6. HRMS calc.: $C_{18}H_{18}NaO_4$ 321.1097; found: 321.1107. The ee was determined by HPLC using a Chiralcel OJ column [hexane/*i*PrOH (80:20)]; flow rate 1.0 mL/min; $\tau_{\text{major}} = 14.6$ min, $\tau_{\text{minor}} = 12.6$ min (95% ee). $[\alpha]_D^{25} +15$ (c 0.92, CH_2Cl_2).

After reduction of the C-C triple bond [H_2 (1 atm.), Pd/C, EtOH, rt, 30 min] the optical rotation ($[\alpha]_D^{25} +47$ [c 0.80, benzene], 95% ee) could be compared to a literature value^{3b} for the corresponding (*R*)-enantiomer ($[\alpha]_D^{20} +47$ [c 1.03, benzene], 84% ee). Therefore the configuration of the stereocenter formed could be assigned to be (*R*) for the hydrogenated compound (and thus (*S*) for the parent alkynylated compound **3d** due to a priority change according to the CIP-system).

(-)-tert-Butyl 1-oxo-2-(3-oxo-3-phenylprop-1-ynyl)-2,3-dihydro-1H-indene-2-carboxylate (3e):

The title compound was obtained according to the general procedure, after 18 h reaction at -20 °C using K_2CO_3 33% w/w as the base and chloroalkyne **2g** as the electrophile, as a viscous colorless oil (90% yield) after FC (Iatrobeds, Et_2O in *n*-hexane 0:100 to 20:80). 1H NMR ($CDCl_3$) δ 8.24 (d, $J = 7.2$ Hz, 2H), 7.83 (d, $J = 7.7$ Hz, 1H), 7.68 (t, $J = 7.7$ Hz, 1H), 7.61 (t, $J = 7.3$ Hz, 1H), 7.54-7.43 (m, 4H), 3.95 (d, $J = 17.1$ Hz, 1H), 3.63 (d, $J = 17.1$ Hz, 1H), 1.51 (s, 9H). ^{13}C NMR ($CDCl_3$) δ 194.8, 177.5, 165.5, 152.2, 136.5, 136.1, 134.1, 132.9, 129.7, 128.4, 128.2, 126.3, 125.7, 90.4, 84.2, 81.0, 56.6, 39.7, 27.7. HRMS calc.: $C_{23}H_{20}NaO_4$ 383.1259; found: 383.1261. The ee was determined by HPLC using a Chiralcel OJ column [hexane/*i*PrOH (80:20)]; flow rate 1.0 mL/min; $\tau_{\text{major}} = 9.2$ min, $\tau_{\text{minor}} = 11.8$ min (97% ee). $[\alpha]_D^{25} -43$ (c 0.54, CH_2Cl_2).

(-)-tert-Butyl 1-oxo-2-(*p*-toluensulfonylethynyl)-2,3-dihydro-1H-indene-2-carboxylate (3f):

The title compound was obtained according to the general procedure, after 36 h reaction at 4 °C using Cs₂CO₃ 50% w/w as the base and chloroalkyne **2i** as the electrophile, as a viscous colorless oil (74% yield) after FC (SiO₂, AcOEt in *n*-hexane 25:75). ¹H NMR (CDCl₃) δ 7.89 (d, *J* = 8.4 Hz, 2H), 7.77 (d, *J* = 7.6 Hz, 1H), 7.67 (td, *J*_t = 7.6 Hz, *J*_d = 0.8 Hz, 1H), 7.48 (d, *J* = 7.6 Hz, 1H), 7.43 (td, *J*_t = 8.0 Hz, *J*_d = 0.8 Hz, 1H), 7.35 (d, *J* = 8.4 Hz, 2H), 3.87 (d, *J* = 17.2 Hz, 1H), 3.49 (d, *J* = 17.2 Hz, 1H), 2.45 (s, 3H), 1.37 (s, 9H). ¹³C NMR (CDCl₃) δ 193.7, 164.7, 152.1, 145.6, 138.8, 136.6, 132.9, 130.1, 128.7, 127.7, 126.6, 126.1, 91.1, 84.9, 80.6, 56.5, 39.5, 27.8, 21.9. HRMS calc.: C₂₃H₂₂NaSO₅ 433.1086; found: 433.1080. The ee was determined by HPLC using a Chiralcel OJ column [hexane/*i*PrOH (80:20)]; flow rate 1.0 mL/min; τ_{major} = 18.1 min, τ_{minor} = 22.9 min (80% ee). [α]_D^{rt} -11 (c 1.00, CH₂Cl₂).

(-)-tert-Butyl 2-(3-(allyloxy)-3-oxoprop-1-ynyl)-5,6-dimethoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (3g):

The title compound was obtained according to the general procedure, after 66 h reaction at -20 °C using K₂CO₃ 33% w/w as the base and bromoalkyne **2a** as the electrophile, as a viscous colorless oil (89% yield) after FC (SiO₂, Et₂O/CH₂Cl₂/*n*-hexane 0:75:25 to 0:100:0 to 1:99:0). ¹H NMR (CDCl₃) δ 7.15 (s, 1H), 6.86 (s, 1H), 5.86 (ddt, *J*_d = 17.1, 10.4 Hz, *J*_t = 5.9 Hz, 1H), 5.31 (dq, *J*_d = 17.2 Hz, *J*_q = 1.3 Hz, 1H), 5.22 (dq, *J*_d = 10.4 Hz, *J*_q = 1.1 Hz, 1H), 4.64-4.59 (m, 2H), 3.95 (s, 3H), 3.87 (s, 3H), 3.73 (d, *J* = 16.9 Hz, 1H), 3.41 (d, *J* = 16.9 Hz, 1H), 1.43 (s, 9H). ¹³C NMR (CDCl₃) δ 192.9, 165.6, 156.5, 152.8, 149.9, 147.8, 130.9, 125.5, 119.1, 106.9, 105.4, 84.2, 83.9, 74.7, 66.4, 56.4, 56.3, 56.0, 39.3, 27.5. HRMS calc.: C₂₂H₂₄NaO₇ 423.1420; found: 423.1426. The ee was determined by HPLC using a Chiralpak AD column [hexane/*i*PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 23.0 min, τ_{minor} = 14.0 min (95% ee). [α]_D^{rt} -15 (c 0.52, CH₂Cl₂).

(-)-tert-Butyl 2-(3-(allyloxy)-3-oxoprop-1-ynyl)-5-chloro-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (3h):

The title compound was obtained according to the general procedure, after 18 h reaction at -20 °C using K₂HPO₄ 50% w/w as the base and chloroalkyne **2b** as the electrophile (added at -20 °C), as a viscous colorless oil (96% yield) after FC (Iatrobeads, Et₂O in *n*-pentane 0:100 to 30:70). ¹H NMR (CDCl₃) δ 7.73 (br d, *J* = 8.3 Hz, 1H), 7.49 (br s, 1H), 7.41 (dd, *J* = 8.2, 1.7 Hz, 1H), 5.88 (ddt, *J*_d = 17.2, 10.4 Hz, *J*_t = 5.9 Hz, 1H), 5.33 (dq, *J*_d = 17.2 Hz, *J*_q = 1.4 Hz, 1H), 5.25 (dq, *J*_d = 10.4 Hz, *J*_q = 1.1 Hz, 1H), 4.69-4.57 (m, 2H) 3.84 (d, *J* = 17.4 Hz, 1H), 3.51 (d, *J* = 17.3 Hz, 1H), 1.44 (s, 9H). ¹³C NMR (CDCl₃) δ 193.2, 165.0, 153.4, 152.7, 142.8, 131.5, 130.9, 129.2, 126.8, 126.5, 119.4, 84.5, 83.2, 75.3, 66.6, 56.3, 39.3, 27.6. HRMS calc.: C₂₀H₁₉ClNaO₅ 397.0813; found: 397.0815. The ee was determined by HPLC using a Chiralpak AD column [hexane/*i*PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 7.8 min, τ_{minor} = 7.2 min (96% ee). [α]_D²⁵ -30 (c 0.93, CH₂Cl₂).

(-)-tert-Butyl 1-(3-(allyloxy)-3-oxoprop-1-ynyl)-2-oxo-2,3-dihydro-1H-indene-1-carboxylate (3i):

The title compound was obtained according to the general procedure, after 18 h reaction at -20 °C using K₂HPO₄ 50% w/w as the base and chloroalkyne **2b** as the electrophile (added at -20 °C), as a viscous colorless oil (72% yield) after FC (Iatrobeads, Et₂O in *n*-pentane 0:100 to 30:70). ¹H NMR (CDCl₃) δ 7.52-7.47 (m, 1H), 7.41-7.33 (m, 3H), 5.88 (ddt, *J*_d = 17.2, 10.4 Hz, *J*_t = 5.9 Hz, 1H), 5.33 (dq, *J*_d = 17.2 Hz, *J*_q = 1.4 Hz, 1H), 5.25 (dq, *J*_d = 10.4 Hz, *J*_q = 1.1 Hz, 1H), 4.69-4.57 (m, 2H) 3.87 (d, *J* = 22.4 Hz, 1H), 3.67 (d, *J* = 22.3 Hz, 1H), 1.39 (s, 9H). ¹³C NMR (CDCl₃) δ 203.2, 164.8, 153.0, 138.4, 136.7, 131.3, 130.0, 128.8, 125.4, 125.0, 119.7, 84.6, 81.8, 77.6, 66.9, 62.1, 42.8, 27.8. HRMS calc.: C₂₀H₂₀NaO₅ 363.1203; found: 363.1141. The ee was determined by HPLC using a Chiralpak AD and a Chiralcel OJ column in sequence [hexane/*i*PrOH (90:10)]; flow rate 0.75 mL/min; τ_{major} = 49.4 min, τ_{minor} = 21.6 min (80% ee). [α]_D²⁵ -67 (c 0.90, CH₂Cl₂).

(+)-*tert*-Butyl 2-(3-(allyloxy)-3-oxoprop-1-ynyl)-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (3j):

The title compound was obtained according to the general procedure, after 48 h reaction at -20 °C using Cs₂CO₃ 66% w/w as the base and bromoalkyne **2a** as the electrophile, as a viscous colorless oil (82% yield) after FC (SiO₂, Et₂O in *n*-pentane 0:100 to 10:90). ¹H NMR (CDCl₃) δ 8.04 (br d, *J* = 7.9 Hz, 1H), 7.51 (td, *J*_t = 7.6 Hz, *J*_d = 1.3 Hz, 1H), 7.33 (br t, *J* = 7.5 Hz, 1H), 7.25 (br d, *J* = 7.5 Hz, 1H), 5.88 (ddt, *J*_d = 17.1, 10.5 Hz, *J*_t = 5.9 Hz, 1H), 5.33 (dq, *J*_d = 17.2 Hz, *J*_q = 1.4 Hz, 1H), 5.25 (dq, *J*_d = 10.4 Hz, *J*_q = 1.1 Hz, 1H), 4.72-4.54 (m, 2H), 3.24 (ddd, *J* = 17.1, 9.7, 4.5 Hz, 1H), 3.00 (dt, *J*_d = 17.3 Hz, *J*_t = 5.2 Hz, 1H), 2.77 (ddd, *J* = 13.8, 9.8, 4.4 Hz, 1H), 2.46 (ddd, *J* = 14.5, 5.8, 4.6 Hz, 1H), 1.49 (s, 9H). ¹³C NMR (CDCl₃) δ 188.3, 166.1, 152.7, 142.8, 134.2, 131.0, 130.2, 128.8, 128.7, 127.1, 119.3, 83.9, 82.3, 77.4, 66.6, 56.0, 36.6, 27.7, 25.7. HRMS calc.: C₂₁H₂₂NaO₅ 377.1359; found: 377.1340. The ee was determined by HPLC using a Chiralcel OJ column [hexane/*i*PrOH (80:20)]; flow rate 1.0 mL/min; τ_{major} = 8.9 min, τ_{minor} = 12.7 min (98% ee). [α]_D^{rt} +20 (c 0.93, CH₂Cl₂).

(-)-*tert*-Butyl 2-(3-(allyloxy)-3-oxoprop-1-ynyl)-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (*ent*-3j):

The title compound was obtained according to the general procedure after 44 h reaction at -20 °C using the catalyst derived from dihydrocinchonidine **5'b**, Cs₂CO₃ 66% w/w as the base and bromoalkyne **2a** as the electrophile, as a viscous colorless oil (68% yield) after FC (SiO₂, Et₂O in *n*-pentane 0:100 to 10:90). Spectral data were identical to compound **3j**. The ee was determined by HPLC using a Chiralcel OJ column [hexane/*i*PrOH (80:20)]; flow rate 1.0 mL/min; τ_{major} = 12.7 min, τ_{minor} = 8.9 min (92% ee). [α]_D^{rt} -19 (c 0.94, CH₂Cl₂).

(-)-*tert*-Butyl 6-(3-(allyloxy)-3-oxoprop-1-ynyl)-5-oxo-6,7,8,9-tetrahydro-5H-benzo[7]annulene-6-carboxylate (3k):

The title compound was obtained according to the general procedure, after 48 h reaction at -20 °C using Cs₂CO₃ 66% w/w as the base and chloroalkyne **2b** as the electrophile, as a viscous colorless oil (85% yield) after FC (SiO₂, Et₂O in *n*-pentane 0:100 to

20:80). ^1H NMR (CDCl_3) δ 7.49 (br d, $J = 7.6$ Hz, 1H), 7.42 (br t, $J = 7.5$ Hz, 1H), 7.30 (br t, $J = 7.5$ Hz, 1H), 7.16 (br d, $J = 7.5$ Hz, 1H), 5.89 (ddt, $J_d = 17.1$, 10.5 Hz, $J_t = 5.9$ Hz, 1H), 5.33 (dq, $J_d = 17.2$ Hz, $J_q = 1.4$ Hz, 1H), 5.25 (br d, $J = 10.5$ Hz, 1H), 4.72-4.54 (m, 2H), 2.98 (ddd, $J = 15.2$, 10.9, 5.2 Hz, 1H), 2.86 (dt, $J_d = 15.1$ Hz, $J_t = 5.0$ Hz, 1H), 2.41-2.29 (m, 1H), 2.21-2.06 (m, 2H), 1.99-1.86 (m, 1H), 1.38 (s, 9H). ^{13}C NMR (CDCl_3) δ 199.0, 166.4, 152.8, 138.3, 138.1, 132.2, 131.1, 129.0, 128.9, 126.7, 119.2, 83.8, 82.9, 77.3, 66.5, 59.3, 32.4, 31.8, 27.5, 22.7. HRMS calc.: $\text{C}_{22}\text{H}_{24}\text{NaO}_5$ 391.1516; found: 391.1511. The ee was determined by HPLC using a Chiralcel OJ column [hexane/*i*PrOH (90:10)]; flow rate 1.0 mL/min; $\tau_{\text{major}} = 11.7$ min, $\tau_{\text{minor}} = 8.8$ min (44% ee). $[\alpha]_{\text{D}}^{25} -4.5$ (c 0.87, CH_2Cl_2).

(+)-*tert*-Butyl 1-(3-(allyloxy)-3-oxoprop-1-ynyl)-2-oxocyclopentanecarboxylate (3l):

The title compound was obtained according to the general procedure, after 14 h reaction at -20 °C using Cs_2CO_3 66% w/w as the base and bromoalkyne **2a** as the electrophile as a colorless oil (93% yield) after FC (Iatrobeds, Et_2O in *n*-hexane 10:90 to 30:70). ^1H NMR (CDCl_3) δ 5.88 (ddt, $J_d = 16.3$, 10.5 Hz, $J_t = 5.9$ Hz, 1H), 5.36 (dq, $J_d = 17.2$ Hz, $J_q = 1.3$ Hz, 1H), 5.28 (dq, $J_d = 10.4$ Hz, $J_q = 1.1$ Hz, 1H), 4.68-4.64 (m, 2H), 2.64 (dt, $J_d = 13.5$ Hz, $J_t = 7.2$ Hz, 1H), 2.51-2.38 (m, 3H), 2.15-2.04 (m, 2H), 1.48 (s, 9H). ^{13}C NMR (CDCl_3) δ 206.1, 165.6, 152.6, 130.9, 119.1, 83.8, 82.8, 76.1, 66.4, 56.5, 36.7, 36.0, 27.5, 19.8. HRMS calc.: $\text{C}_{16}\text{H}_{20}\text{NaO}_5$ 315.1208; found: 315.1208. The ee was determined by GC on a Chrompack CP-Chiralsil DEX CB-column. The temperature program: 70 °C to 140 °C at a rate of 10 °C/min, maintain 140 °C for 15 min, 140 °C to 180 °C at a rate of 10 °C/min, maintain 180 °C for 10 min; $\tau_{\text{major}} = 29.35$ min, $\tau_{\text{minor}} = 29.18$ min (95% ee). $[\alpha]_{\text{D}}^{25} +41$ (c 0.55, CH_2Cl_2).

(+)-(*S*)-*tert*-Butyl 2-oxo-1-(3-oxobut-1-ynyl)cyclopentanecarboxylate (3m):

The title compound was obtained according to the general procedure, after 18 h reaction at -20 °C using Cs_2CO_3 66% w/w as the base and bromoalkyne **2e** as the electrophile as a slightly yellow oil (94% yield) after FC (Iatrobeds, Et_2O in *n*-hexane 10:90 to 30:70). ^1H NMR (CDCl_3) δ 2.64 (dt, $J_d = 13.9$, $J_t = 7.4$ Hz, 1H), 2.49-2.36 (m, 3H), 2.37 (s, 3H), 2.10-2.00 (m, 2H), 1.49 (s, 9H). ^{13}C NMR (CDCl_3) δ 206.6, 184.1, 165.9, 86.9, 83.9, 83.8, 56.8, 36.9, 36.3, 32.7, 27.7, 19.9. HRMS calc.: $\text{C}_{14}\text{H}_{18}\text{NaO}_4$ 273.1103; found: 273.1103. The ee was determined by HPLC using a Chiralcel OJ column [hexane/*i*PrOH (97:3)]; flow rate 1.0 mL/min; $\tau_{\text{major}} = 10.8$ min, $\tau_{\text{minor}} = 9.0$ min (84% ee). $[\alpha]_{\text{D}}^{25} +60$ (c 0.50, CH_2Cl_2).

After reduction of the C-C triple bond [H_2 (1 atm.), Pd/C, *i*PrOH, rt, 45 min, 95% yield] the optical rotation ($[\alpha]_{\text{D}}^{25}$ -6.4 [c 0.87, CHCl_3], 84% ee) could be compared to a literature value¹³ for the corresponding (*R*)-enantiomer ($[\alpha]_{\text{D}}^{20}$ +8.7 [c 0.41, CHCl_3], 92% ee). Therefore, the configuration of the stereocenter formed could be assigned to be (*S*).

(+)-*tert*-Butyl 1-(3-(allyloxy)-3-oxoprop-1-ynyl)-2-oxocyclohexanecarboxylate (3n):

The title compound was obtained according to the general procedure, after 48 h reaction at +4 °C using K_3PO_4 50% w/w as the base and chloroalkyne **2b** as the electrophile, as a viscous colorless oil (84% yield) after FC (Iatrobeds, Et_2O in *n*-pentane 0:100 to 10:90). ^1H NMR (CDCl_3) δ 5.97-5.85 (m, 1H), 5.40-5.31 (m, 1H), 5.30-5.24 (m, 1H), 4.80-4.54 (m, 2H), 2.77 (ddd, J = 14.5, 9.2, 5.4 Hz, 1H), 2.50-2.36 (m, 2H), 2.18-2.09 (m, 1H), 2.01-1.73 (m, 4H), 1.49 (s, 9H). ^{13}C NMR (CDCl_3) δ 201.1, 165.5, 152.8, 131.0, 119.4, 83.7, 83.5, 78.4, 66.6, 59.0, 39.1, 36.8, 27.7, 27.2, 21.5. HRMS calc.: $\text{C}_{17}\text{H}_{22}\text{NaO}_5$ 329.1359; found: 329.1373. The ee was determined by HPLC using a Chiralcel OJ column [hexane/*i*PrOH (99:1)]; flow rate 1.0 mL/min; τ_{major} = 13.1 min, τ_{minor} = 11.3 min (96% ee). $[\alpha]_{\text{D}}^{25}$ +103 (c 0.90, CH_2Cl_2).

(+)-*tert*-Butyl 1-(3-(allyloxy)-3-oxoprop-1-ynyl)-2-oxocyclohex-3-enecarboxylate (3o):

The title compound was obtained according to the general procedure, after 8 h reaction at +4 °C using NaOH 10% w/w as the base and chloroalkyne **2b** (2 equiv.) as the electrophile, as a viscous colorless oil (79% yield) after FC (Iatrobeds, CH_2Cl_2 in *n*-pentane 0:100 to 100:0). ^1H NMR (CDCl_3) δ 7.00 (dt, J_{d} = 10.2 Hz, J_{t} = 4.0 Hz, 1H), 6.06 (br d, J = 10.1 Hz, 1H), 5.95-5.84 (m, 1H), 5.34 (br d, J = 1.1 Hz, 1H), 5.26 (br d, J = 10.4 Hz, 1H), 4.68-4.61 (m, 2H), 2.70-2.52 (m, 2H), 2.50-2.40 (m, 1H), 2.36-2.28 (m, 1H), 1.48 (s, 9H). ^{13}C NMR (CDCl_3) δ 188.5, 165.7, 152.7, 150.6, 131.0, 127.4, 119.3, 83.9, 82.2, 77.1, 66.6, 55.2, 32.0, 27.7, 23.2. HRMS calc.: $\text{C}_{17}\text{H}_{20}\text{KO}_5$ 343.0942; found: 343.0989. The ee was determined by HPLC using a Chiralcel OJ column [hexane/*i*PrOH (95:5)]; flow rate 1.0 mL/min; τ_{major} = 16.2 min, τ_{minor} = 13.2 min (97% ee). $[\alpha]_{\text{D}}^{25}$ +26 (c 0.78, CH_2Cl_2).

(+)-*tert*-Butyl 1-(3-(allyloxy)-3-oxoprop-1-ynyl)-4-methyl-2-oxocyclohex-3-enecarboxylate (3p):

The title compound was obtained according to the general procedure, after 16 h reaction at +4 °C using NaOH 10% w/w as the base and chloroalkyne **2b** (2 equiv.) as the electrophile, as a viscous colorless oil (78% yield) after FC (Iatrobeads, CH₂Cl₂ in *n*-pentane 0:100 to 100:0).

¹H NMR (CDCl₃) δ 5.95-5.84 (m, 1H), 5.90 (br s, 1H), 5.33 (dq, *J*_d = 17.2 Hz, *J*_q = 1.4 Hz, 1H), 5.25 (dq, *J*_d = 10.4 Hz, *J*_q = 1.2 Hz, 1H), 4.78-4.50 (m, 2H), 2.65-2.48 (m, 2H), 2.42-2.22 (m, 2H), 1.98 (br s, 3H), 1.48 (s, 9H). ¹³C NMR (CDCl₃) δ 188.3, 166.0, 163.2, 152.8, 131.0, 124.1, 119.3, 83.7, 82.6, 76.8, 66.5, 54.4, 31.8, 28.1, 27.7, 24.4. HRMS calc.: C₁₈H₂₂NaO₅ 341.1359; found: 341.1365. The ee was determined by HPLC using a Chiralpak AS column [hexane/*i*PrOH (98:2)]; flow rate 1.0 mL/min; τ_{major} = 11.2 min, τ_{minor} = 14.5 min (97% ee). [α]_D^{rt} +12 (c 0.96, CH₂Cl₂).

(-)-*tert*-Butyl 1-(3-(allyloxy)-3-oxoprop-1-ynyl)-4-methyl-2-oxocyclohex-3-enecarboxylate (*ent*-3p):

The title compound was obtained according to the general procedure after 16 h reaction at +4 °C using the catalyst derived from dihydrocinchonidine **5'b**, NaOH 10% w/w as the base and chloroalkyne **2b** (2 equiv.) as the electrophile, as a viscous colorless oil (66% yield) after FC (Iatrobeads, CH₂Cl₂ in *n*-pentane 0:100 to 100:0). Spectral data were identical to compound **3p**. The ee was determined by HPLC using a

Chiralpak AS column [hexane/*i*PrOH (98:2)]; flow rate 1.0 mL/min; τ_{major} = 14.5 min, τ_{minor} = 11.2 min (87% ee). [α]_D^{rt} -10 (c 0.82, CH₂Cl₂).

(+)-*tert*-Butyl 1-(3-(allyloxy)-3-oxoprop-1-ynyl)-4-ethoxy-2-oxocyclohex-3-enecarboxylate (3q):

The title compound was obtained according to the general procedure after 6 h reaction at +4 °C using NaOH 10% w/w as the base and chloroalkyne **2b** (2 equiv.) as the electrophile, as a yellow solid (62% yield, mp = 87-89 °C) after FC (Iatrobeads, AcOEt in *n*-hexane 25:75).

¹H NMR (CDCl₃) δ 5.95-5.84 (m, 1H), 5.36 (dq, *J*_d = 18.2 Hz, *J*_q = 1.2 Hz, 1H), 5.34 (s, 1H), 5.26 (dq, *J*_d = 10.4 Hz, *J*_q = 1.2 Hz, 1H), 4.65-4.63 (m, 2H), 3.93 (q, *J* = 7.2 Hz, 2H), 2.74-2.57 (m, 2H), 2.50-2.22 (m, 2H), 1.49 (s, 9H), 1.37 (t,

$J = 7.2$ Hz, 3H). ^{13}C NMR (CDCl_3) δ 188.7, 177.3, 166.3, 152.9, 131.1, 119.3, 100.4, 83.6, 83.0, 76.6, 66.5, 64.8, 54.6, 30.3, 27.7, 26.1, 14.0. HRMS calc.: $\text{C}_{13}\text{H}_{20}\text{NaO}_4$ 371.1471; found: 371.1462. The ee was determined by HPLC using a Chiralpak AS column [hexane/*i*PrOH (98:2)]; flow rate 1.0 mL/min; $\tau_{\text{major}} = 19.7$ min, $\tau_{\text{minor}} = 13.8$ min (93% ee). $[\alpha]_{\text{D}}^{25} +20$ (c 0.90, CH_2Cl_2).

(-)-*tert*-Butyl 3-(3-(allyloxy)-3-oxoprop-1-ynyl)-1-methyl-2-oxoindoline-3-carboxylate (3r):

The title compound was obtained according to the general procedure, after 46 h reaction at -20 °C using KF 33% w/w as the base and chloroalkyne **2b** as the electrophile as a viscous yellow oil (95% yield) after FC (SiO_2 , Et_2O in *n*-hexane 20:80 to 40:60 to 60:40). ^1H NMR (CDCl_3) 7.42-7.35 (m, 2H), 7.12 (td, $J_t = 7.7$ Hz, $J_d = 0.8$ Hz, 1H), 6.86 (d, $J = 7.8$ Hz, 1H), 5.89 (ddt, $J_d = 16.3$, 10.4 Hz, $J_t = 5.9$ Hz, 1H), 5.34 (dq, $J_d = 17.2$ Hz, $J_q = 1.4$ Hz, 1H), 5.26 (dq, $J_d = 10.3$ Hz, $J_q = 1.1$ Hz, 1H), 4.64 (dt, $J_d = 5.9$ Hz, $J_t = 1.3$ Hz, 2H), 3.25 (s, 3H), 1.42 (s, 9H). ^{13}C NMR (CDCl_3) δ 168.5, 163.4, 152.6, 143.5, 130.9, 130.3, 125.7, 123.9, 123.6, 119.4, 108.9, 84.8, 80.4, 75.5, 66.6, 55.3, 27.6, 27.0. HRMS calc.: $\text{C}_{20}\text{H}_{21}\text{NNaO}_5$ 378.1317; found: 378.1318. The ee was determined by HPLC using a Chiralpak AD [hexane/*i*PrOH (95:5)]; flow rate 1.0 mL/min; $\tau_{\text{major}} = 13.8$ min, $\tau_{\text{minor}} = 12.4$ min (85% ee). $[\alpha]_{\text{D}}^{25} -111$ (c 0.57, CH_2Cl_2).

General procedure for the Alloc deprotection

A round-bottom flask (5 mL) containing freshly prepared $\text{Pd}(\text{PPh}_3)_4$ (0.022 mmol, 10.0 mol%), and PhSO_2Na or morpholine (0.26 mmol, 120.0 mol%) was evacuated and purged with argon gas. Allylic alkynoate **3** (0.22 mmol) in dry toluene (2.0 mL) was added to the flask and the reaction mixture was stirred at the temperature and time required for each case, then cooled to room temperature. The filtrate was concentrated and the residue was purified on a column containing Iatrobeads using *n*-hexane-EtOAc (6:1) as eluent to afford the alkyne product.

(+)-*tert*-Butyl 1-(et-1-ynyl)-2-oxo-2,3-dihydro-1H-indene-1-carboxylate (7a):

The title compound was obtained according to the general procedure (from **3a**, 96% ee) using morpholine as additive, after 5 min at 65 °C as a colorless oil (75% yield). ^1H NMR (CDCl_3) δ 7.82 (d, $J = 7.6$ Hz, 1H), 7.65 (td, $J_t = 7.6$ Hz, $J_d = 1.6$ Hz, 1H), 7.49 (dt, $J_d = 8.0$ Hz, $J_d = 1.2$ Hz, 1H), 7.42 (t, $J = 8.0$ Hz, 1H), 3.84 (d, $J = 16.8$ Hz, 1H), 3.50 (d, $J = 16.8$ Hz, 1H), 2.39 (s, 1H), 1.42 (s, 9H). ^{13}C NMR (CDCl_3) δ 196.5, 166.6, 152.2, 135.7, 133.4, 128.1, 126.2, 125.6, 83.5, 80.2, 72.1, 56.2, 40.6, 27.6. HRMS calc.: $\text{C}_{16}\text{H}_{16}\text{NaO}_3$ 279.0991; found: 279.1012. The ee was

determined by GC on a Chrompack CP-Chiralsil DEX CB-column. The temperature program: 70 °C to 140 °C at a rate of 10 °C/min, maintain 140 °C for 15 min, 140 °C to 180 °C at a rate of 10 °C/min, maintain 180 °C for 10 min; $\tau_{\text{major}} = 46.49$ min, $\tau_{\text{minor}} = 46.37$ min (98% ee). $[\alpha]_{\text{D}}^{25} +3.3$ (c 1.40, CH₂Cl₂).

(+)-*tert*-Butyl 1-(*et*-1-ynyl)-2-oxocyclopentanecarboxylate (7b):

The title compound was obtained according to the general procedure (from **3l**, 88% ee) using PhSO₂Na (1.2 equiv.) as additive, after 30 min at 60 °C as a colorless oil (58% yield). ¹H NMR (CDCl₃) δ 2.62-2.55 (m, 2H), 2.46-2.30 (m, 2H), 2.41 (s, 1H), 2.12-2.01 (m, 2H), 1.47 (s, 9H). ¹³C NMR (CDCl₃) δ 208.2, 167.2, 83.3, 73.3, 56.7, 36.7, 36.6, 27.8, 27.7, 19.8. HRMS calc.: C₁₂H₁₆KO₃: 247.0737; found: 247.0738. The ee was determined by GC on a Chrompack CP-Chiralsil DEX CB-column. The temperature program: 70 °C to 140 °C at a rate of 10 °C/min, maintain 140 °C for 15 min, 140 °C to 180 °C at a rate of 10 °C/min, maintain 180 °C for 10 min; $\tau_{\text{major}} = 8.87$ min, $\tau_{\text{minor}} = 8.97$ min (88% ee). $[\alpha]_{\text{D}}^{25} +2.0$ (c 1.00, CH₂Cl₂).

(+)-*tert*-Butyl 1-(*et*-1-ynyl)-3-oxoprop-1-ynyl)-2-oxocyclohex-3-enecarboxylate (7c):

The title compound was obtained according to the general procedure (from **3o**, 97% ee) using morpholine as additive, after 20 min at 65 °C as a colorless oil (72% yield). ¹H NMR (CDCl₃) δ 6.97 (dt, $J_{\text{d}} = 10.4$ Hz, $J_{\text{t}} = 4.0$ Hz, 1H), 6.07 (dt, $J_{\text{d}} = 10.4$ Hz, $J_{\text{t}} = 1.6$ Hz, 1H), 2.67-2.52 (m, 2H), 2.50-2.41 (m, 1H), 2.45 (s, 1H), 2.29-2.23 (m, 1H), 1.48 (s, 9H). ¹³C NMR (CDCl₃) δ 190.3, 166.9, 150.2, 127.5, 83.2, 78.6, 74.0, 55.2, 32.6, 27.7, 23.3. HRMS calc.: C₁₃H₁₆NaO₃ 243.0997; found: 243.1004. The ee was determined by HPLC using a Chiralpak OJ column [hexane/*i*PrOH (80:20)]; flow rate 1.0 mL/min; $\tau_{\text{major}} = 19.2$ min, $\tau_{\text{minor}} = 20.2$ min (97% ee). $[\alpha]_{\text{D}}^{25} +17$ (c 0.92, CH₂Cl₂).

(+)-*tert*-Butyl 1-(*et*-1-ynyl)-3-oxoprop-1-ynyl)-4-methyl-2-oxocyclohex-3-enecarboxylate (7d):

The title compound was obtained according to the general procedure (from **3p**, 97% ee) using morpholine as additive, after 25 min at 65 °C as a white solid (71% yield). ¹H NMR (CDCl₃) δ 5.91 (d, $J = 1.2$, 1H), 2.62-2.51 (m, 2H), 2.42 (s, 1H), 2.39-2.21 (m, 2H), 1.98 (s, 3H), 1.48 (s, 9H). ¹³C NMR (CDCl₃) δ 190.2, 167.3, 162.7, 124.1, 83.5, 78.9, 73.8, 54.3, 32.4, 28.3, 27.7, 24.3. HRMS calc.: C₁₄H₁₈NaO₃ 257.1154; found: 257.1150. The ee was determined by HPLC using a Chiralpak OJ

column [hexane/*i*PrOH (90:10)]; flow rate 1.0 mL/min; $\tau_{\text{major}} = 9.8$ min, $\tau_{\text{minor}} = 8.7$ min (97% ee). $[\alpha]_{\text{D}}^{\text{rt}} +18$ (c 0.47, CH₂Cl₂).

(-)-*tert*-Butyl 1-(*ent*-1-ynyl)-3-oxoprop-1-ynyl)-4-methyl-2-oxocyclohex-3-enecarboxylate (*ent*-7d):

The title compound was obtained according to the general procedure (from *ent*-3p, 87% ee) using morpholine as additive, after 25 min reaction at 65 °C as a white solid (69% yield). Spectral data were identical to compound 7d.

The ee was determined by HPLC using a Chiralpak OJ column [hexane/*i*PrOH (90:10)]; flow rate 1.0 mL/min; $\tau_{\text{major}} = 8.7$ min, $\tau_{\text{minor}} = 9.8$ min (86% ee). $[\alpha]_{\text{D}}^{\text{rt}} -22$ (c 0.85, CH₂Cl₂).

Procedure for the decarboxylative coupling¹⁴

A round-bottom flask (5 mL) containing freshly prepared Pd(PPh₃)₄ (0.022 mmol, 10.0 mol%)¹⁵ was evacuated and purged with argon gas. Allylic alkynoate 3l (0.22 mmol) and dry toluene (2.0 mL) were added to the flask and the reaction mixture was stirred at 100 °C for 10 min. Then the reaction mixture was cooled to room temperature, concentrated and the residue was purified on a column containing Iatrobeds using hexane-ethyl acetate (6:1) as eluent to afford the 1,4-enyne product.

(+)-*tert*-Butyl 1-(pent-4-en-1-ynyl)-2-oxocyclopentanecarboxylate (8):

The title compound was obtained according to the procedure above (from 3l, 88% ee) after 10 min at 100 °C as a colorless oil (74% yield). ¹H NMR (CDCl₃) δ 5.77 (ddt, $J_{\text{d}} = 17.2$, 10.0 Hz, $J_{\text{t}} = 4.8$ Hz, 1H), 5.33 (dq, $J_{\text{d}} = 17.2$

Hz, $J_{\text{q}} = 2.0$ Hz 1H), 5.09 (dq, $J_{\text{d}} = 10.0$ Hz, $J_{\text{q}} = 1.6$ Hz 1H), 3.00-2.97 (m, 2H), 2.60-2.51 (m, 1H), 2.47-2.22 (m, 3H), 2.09-2.00 (m, 2H), 1.45 (s, 9H). ¹³C NMR (CDCl₃) δ 209.1, 167.8, 132.1, 116.1, 82.8, 82.3, 78.0, 56.9, 37.0, 36.7, 27.7, 23.1, 19.8. HRMS calc.: C₁₅H₂₀NaO₃ 271.1310; found: 271.1345. The ee was determined by GC on a Chrompack CP-Chiralsil DEX CB-column. The temperature program: 70 °C to 140 °C at a rate of 10 °C/min, maintain 140 °C for 15 min, 140 °C to 180 °C at a rate of 10 °C/min, maintain 180 °C for 10 min; $\tau_{\text{major}} = 29.35$ min, $\tau_{\text{minor}} = 29.18$ min (88% ee). $[\alpha]_{\text{D}}^{\text{rt}} +35$ (c 0.30, CH₂Cl₂).

Spectra

References

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