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Enantioselective synthesis of (+)-gossonorol and related systems using organozinc reagents

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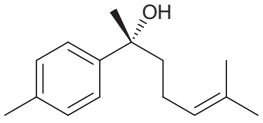
Dedicated to Professor Dr. Lutz F. Tietze on occasion of his 70th birthday

ABSTRACT

The sesquiterpene (+)-gossonorol is prepared in only three synthetic steps in 60% overall yield and 82% ee from commercially available reagents. The key asymmetric step is the catalytic enantioselective addition of dimethylzinc to 5-methyl-1-(2-methylphenyl)hex-4-en-1-one catalyzed by chiral isoborneolsulfonamide ligands in the presence of titanium tetraisopropoxide. The modular approach allows the synthesis not only of the aforementioned natural product but also other products arising from the corresponding processes of ethylation, phenylation, and ethynylation, just by changing the final nucleophilic reagent and using the same isoborneol type ligand.

1. Introduction

The sesquiterpene gossonorol **1a** was first isolated in 1984 from the cotton plant.[1] Since then, it has been found in many other plant species, including *Artemisia sieberi*,[2] *Chamomilla recutita*,[3] *Laurencia tristicha*,[4] *Hypericum linarioides*,[5] *Croton flavens*,[6] *Ferula orientalis*,[7] *Teucrium*,[8] *Pleurospermun austriacum*,[9] and it presents some interesting biological properties, among others antifungal, anticancer and antioxidant activities, biochemical communicator, and floral scent.



(+)-(*R*)-Gossonorol **1a**

Despite the widespread occurrence of alcohol **1a** in the plant kingdom and its use as a starting material for the synthesis of several natural products,[10] there are only two published approaches to its asymmetric synthesis. The first one involved the enantioselective deprotonation of a benzyl ether chromium complex derivative using excess of butyllithium and stoichiometric amounts of a chiral diamine and methylation of the prepared benzyllithium intermediate, as the key step, performing other synthetic steps such as benzylic deprotonation and alkylation, and finally double deprotection processes. This seven-steps synthesis rendered the final product **1a** in a 17% yield and 97% ee.[11] Besides, this is a long reaction sequence, a large amount of waste is generated and the use of chromium species makes this approach non-environmentally friendly. The second approach involved the kinetic resolution of the corresponding racemic acetate derivative by several esterases with enantiomeric excesses lower than 10%,[12] with this low enantioselectivity hampering its practical use.

Recently, we have developed a new class of chiral isoborneol sulfonamides,[13] which have been successfully used in the enantioselective addition of various zinc reagents to simple ketones[14] catalyzed by titanium alkoxides,[15] yielding the expected tertiary alcohols with excellent enantioselectivities.[16] Herein we report the enantioselective synthesis of compound **1a** through a catalytic addition of dimethylzinc to 5-methyl-1-(2-methylphenyl)hex-4-en-1-one as the key asymmetric step. This approach permitted the synthesis of related compounds with similar results and in a routine way.

2. Results and discussion

The synthesis started with the preparation of amide **3** from the commercially available carboxylic acid **2** using the classical standard protocols[17] with an excellent yield (Scheme 1). Then, the lithiation of 5-bromo-2-methylpent-2-ene using lithium powder and a substoichiometric amount of naphthalene[18] under Barbier conditions rendered the expected ketone **4**,[19] with an overall yield of 74%.

Once ketone **4** was prepared, we addressed the problem of the enantioselective addition of dialkylzinc reagents **5** (Table 1).

The study started using the first generation chiral isoborneol ligands **6**.[20] The enantioselective addition of dimethylzinc **5a** to

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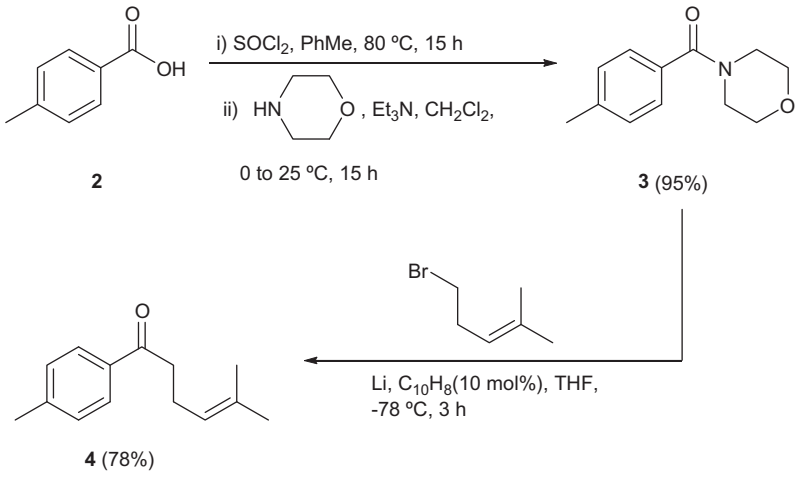
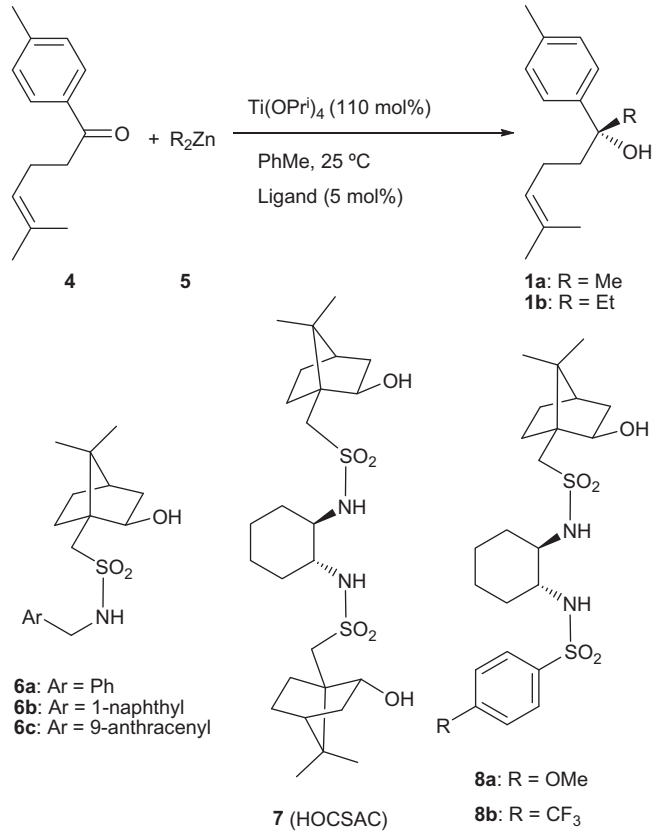


Scheme 1. Synthesis of starting ketone **4**.

Table 1
Catalytic enantioselective addition of dialkyllzincs to ketone **4**

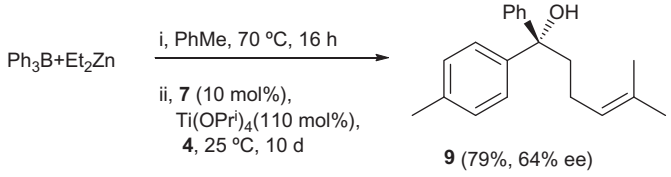


Entry	Ligand	Product	Time (h)	Yield[a] (%)	ee[b] (%)
1	**6a**	**1a**	180	60	26
2	**6b**	**1a**	180	59	72
3	**6c**	**1a**	280	48	70
4	**7**	**1a**	180	81	82
5	**8a**	**1a**	280	0	—
6	**8b**	**1a**	280	0	—
7	**7**	**1b**	180	25 (45)[c]	64

[a] Isolated yield based on the starting ketone **4** after column chromatography (hexane/ethyl acetate).
[b] Enantiomeric excess determined by HPLC using a Chiralcel AD column.
[c] Estimated yield by CG-analysis using Mesitylen as internal standard.

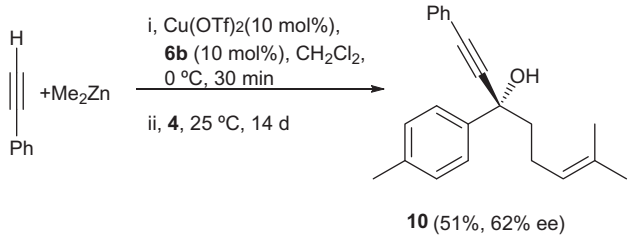
ketone **4** in the presence of substoichiometric amounts of the benzyl ligand **6a** gave the expected (+)-gossonorol **1a** after more than seven days with modest yield and enantioselectivity (Table 1, entry 1). The increase of the hindrance of the ligand from the phenyl derivative to the related 1-naphthyl one **6b** showed an important increase in the enantiomeric excess of the natural product **1a** (entry 2 in Table 1). The above result prompted us to use a more crowded 9-anthracenyl derivative ligand **6c**.[21] However, the result obtained was practically the same as that obtained in the naphthyl case (compare entries 2 and 3 in Table 1). Next, we repeated the reaction but using the second generation[22] chiral ligand HOCSAC **7**, obtaining the expected product **1a** in a good chemical yield and enantioselectivity (Table 1, entry 4). It should be pointed out that the addition failed using the third generation ligands **8**,[23] recovering the starting ketone **4** being recovered unchanged after more than 11 days (entries 5 and 6 in Table 1). When the reaction was performed using diethylzinc **5a** with the HOCSAC ligand **7**, the related gossonorol product **1b** was obtained in a moderate yield, due to difficulty in its purification (Table 1, entry 7).

After proving that this modular approach was effective for the synthesis of gossonorol, we tried to expand the possibilities with other reagents of a different nature. Recently, the preparation of ethyl phenyl zinc reagent has been described by transmetallation of diethylzinc with triphenylboron,[24] and this intermediate showed a higher reactivity and enantioselectivity compared with the related diethyl or diphenylzinc reagents.[25] The corresponding ethyl phenyl zinc intermediate was obtained starting from commercially available triphenyl boron and diethylzinc by heating in toluene at 70 °C. This intermediate was reacted in situ with the ketone **4** in the presence of substoichiometric amounts of ligand **7** and a small excess of titanium tetraisopropoxide, giving the expected diaryl ethanol derivative **9** with good chemical yield and enantioselectivity, with the absolute configuration being proposed according to the outcome of the reaction for the methylation process (Scheme 2).



Scheme 2. Phenylation process.

Finally, we studied the alkynylation process following the Chan's copper protocol[26] since the use of titanium tetraisopropoxide failed for simple ketones.[22e,23a] Thus, the reaction of phenylacetylene, dimethylzinc, and the ketone **4** in the presence of substoichiometric amounts of copper(II) triflate and ligand **6b** gave the expected tertiary alcohol **10** with moderate yield and enantioselectivity (Scheme 3), with the absolute configuration being proposed according to that obtained for simple ketones.[21]



Scheme 3. Alkynylation process.

3. Conclusion

The synthesis of (+)-gossonorol was accomplished in 60% overall yield by a three-step process and 82% ee from commercially available reagents, which permits its easy multigram scale-up, avoiding the economical and environmental problems associated with other reported synthesis. The key asymmetric step was the catalytic enantioselective addition of dimethyzinc to 5-methyl-1-(2-methylphenyl)hex-4-en-1-one catalyzed by substoichiometric amounts of chiral isoborneolsulfonamide ligands in the presence of titanium tetraisopropoxide. The modular approach permitted the synthesis not only of the (+)-gossonorol (methylation process) but other related products arising from processes of ethylation, phenylation, and ethynylation, just by changing the final nucleophilic reagent and using in all processes the same isoborneol type ligand

4. Experimental

The reactions carried out under argon atmosphere were performed with flame dried Schlenk glassware. Me_2Zn (2.0 M in toluene) and Et_2Zn (1.1 M in toluene) were purchased from Aldrich. Dichloromethane was distilled from P_2O_5. Phenylacetylene was purified by bulb-to-bulb distillation. The other chemicals were used without further purifications. Column Chromatography was carried out using Silica Gel 60, 40–63 microns RE, thin layer chromatography TLC with Machery-Nagel Silica Gel 60, 0.20 mm. Compounds were visualized by UV and phosphomolybdic acid staining. NMR spectra were recorded on Bruker AC-300 (300 and 75 MHz, respectively) or a Bruker Avance-400 (400 and 101 MHz, respectively) using $CDCl_3$ and $(CD_3)_2SO$ as solvent. Chemical shift values are reported in ppm with TMS as the internal standard, proton chemical shift (δ) and coupling constants (J) are given in ppm and Hz. Spin multiplicities are given as s (singlet), d (doublet), t (triplet), and m (multiplet) as well as br (broad). Optical rotations were measured on a Perkin Elmer instruments (Model 341) with a 5 cm cell (c given in g/100 mL). Melting points were measured in a Reichtert Thermovar hot plate apparatus. Enantioselectivities were determined by HPLC analysis (Agilent 1100 Series HPLC) equipped with a G1315B diode array detector and a Quat Pump G1311A.

4.1. Synthesis of chiral ligands

The ligands **6a**,[20a] **6b**,[20a] **7**,[22e] **8a**,[22e] and **8b**[20d] were synthesized following the protocol describe by us.

4.1.1. *N*-(Anthracenyl-9-ylmethyl)-1-[(1*S*-,2*R*,4*R*)-2-hydroxy-7,7-dimethylbicyclo[2.2.1]-heptan-1-yl]methanesulfonamide 6c[21]

To a solution of 9-aminomethylanthracene (0.265 g, 1.3 mmol, 1.3 equiv) (previously synthesized as reported in the literature[27]) and triethylamine (0.181 mL, 1.3 mmol, 1.3 equiv) in acetonitrile (10 mL) was added dropwise a solution of (*S*)-(+)-camphorsulfonyl chloride (0.25 g, 1 mmol, 1.0 equiv) in acetonitrile (10 mL) at 0 °C. The reaction mixture was allowed to rise to room temperature and stirred for 8 h. Then, it was hydrolyzed with 2 M NaOH (20 mL) and extracted with ethyl acetate (3 × 15 mL). The resulting organic layers were washed with 2 M HCl (30 mL), dried over anhydrous Mg_2SO_4, filtered, and concentrated under vacuum to give 0.360 g of the corresponding ketone. This ketone (0.360 g, 0.87 mmol, 1.0 equiv) was treated with sodium borohydride (0.132 g, 3.48 mmol, 4.0 equiv) in EtOH (10 mL) at 0 °C and the reaction mixture was allowed to rise to room temperature and stirred for 8 h. Then, it was hydrolyzed with 2 M HCl (10 mL), extracted with ethyl acetate (3 × 10 mL), and washed with saturated NaCl solution (30 mL), dried over anhydrous Mg_2SO_4, filtered, and concentrated under vacuum. The residue was purified by flash column chromatography (using as solvents from hexane until hexane/ethyl acetate: 9.5/0.5) to give 0.080 g (22% yield) of a white solid. R_f = 0.53 (hexane/ethyl acetate: 9.5/0.5); mp 192–196 °C (from ethyl acetate/hexane) (lit:[21] 167–169 °C); $[\alpha]_D^{20} = -35.6$ (c 1, CH_2Cl_2) [lit: [21] −34.5 (c 1, CH_2Cl_2)]; ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ = 8.66 (br s, 1H), 8.53 (d, J = 9.0 Hz, 2H), 8.14 (d, J = 7.70 Hz, 2H), 7.65–7.55 (m, 5H), 5.30–5.15 (m, 2H), 4.41 (br s, 1H), 3.96–3.92 (m, 1H), 3.5 (d, J = 14.0 Hz, 1H), 2.84 (d, J = 14.0 Hz, 1H), 1.71–1.61 (m, 5H), 1.40–1.35 (m, 1H), 1.05–0.95 (m with a s at 0.95, 4H), 0.66 (s, 3H); ^{13}C NMR [75 MHz, $(CD_3)_2SO$], δ = 20.74, 21.12, 27.88, 30.08, 39.60, 41.13, 44.70, 49.05, 50.57, 51.20, 75.61, 125.50 (2C), 126.12 (2C), 127.18 (2C), 128.69, 129.51, 129.77 (2C), 130.89 (2C), 131.97 (2C); Ms (DIP): m/z (%) 423 $[M]^+$ (33), 271 (12), 208 (15), 207 (100), 206 (58), 205 (72), 204 (64), 192(13), 191 (56), 189 (11), 179(34), 178 (33), 176 (10).

4.2. Synthesis of starting ketone 4

To a suspension of 4-methylbenzoic acid **2** (1.94 g, 14.25 mmol, 1.0 equiv) in toluene (15 mL), was added $SOCl_2$ (6.25 mL, 85.5 mmol, 6.0 equiv) and some drops of DMF. The reaction mixture was stirred at 80 °C for 15 h. Then the temperature was allowed to rise to room temperature, and the solvent evaporated under vacuum. The residue was solved in toluene (20 mL) and it was evaporated again to eliminate the excess of $SOCl_2$. The 4-methylbenzoic acid chloride was obtained as yellow oil and was used in the next step without further purification. To a solution of 4-methylbenzoic acid chloride (2.20 g, 14.25 mmol, 1.0 equiv) in dichloromethane (25 mL) were added morpholine (2.5 mL, 28.5 mmol, 2.0 equiv) and triethylamine (2 mL, 14.25 mmol, 1.0 equiv) at 0 °C. The reaction mixture was allowed to rise to room temperature and stirred for 15 h. Then, 2 M NaOH (30 mL) was added to the reaction mixture, and extracted with ethyl acetate (2 × 30 mL). The resulting organic layers were washed with 2 M HCl (30 mL), and saturated NaCl solution (30 mL), dried over anhydrous Mg_2SO_4, filtered, and concentrated under vacuum to yield 2.78 g of (4-methylphenyl)-morpholin-4-ylmethanone **3**[28] (95% yield) as a pale yellow solid. R_f = 0.52 (hexane/ethyl acetate: 7/3); mp 74.1–76.3 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 2.38 (s, 3H), 3.69 (br s, 8H), 7.21 (d, J = 7.8 Hz, 2H), 7.31 (d, J = 7.8 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 21.6, 43.0, 48.5, 67.1 (2C), 127.5 (2C), 129.4 (2C), 132.6, 140.3, 170.90; Ms (EI): m/z (%) 205 $[M]^+$ (15), 204 (33), 119 (100), 91 (27).

To a suspension of lithium powder (0.168 g, 24 mmol, 6.0 equiv) and naphthalene (0.051 g, 0.4 mmol, 0.1 equiv) in dry THF (10 mL) under argon atmosphere at −78 °C were successively added

dropwise 5-bromo-2-methyl-2-pentene (0.588 mL, 4.4 mmol, 1.1 equiv) and (4-methylphenyl)-morpholine-4-ylmethanone **3** (0.821 g, 4 mmol, 1.0 equiv). The reaction mixture was stirred for 3 h at the same temperature, quenched by addition of saturated NH_4Cl (15 mL), and extracted with ethyl acetate (3 × 10 mL). The organic layers were dried over anhydrous Mg_2SO_4, filtered, and concentrated under vacuum. The residue was purified by flash chromatography (using as solvents from hexane until hexane/ethyl acetate: 9/1) to give 0.637 g of 5-methyl-1-(4-methylphenyl)hex-4-en-1-one **4**[19] (78% yield) as a white solid. R_f = 0.43 (hexane/ether: 9/1); mp 46.3–46.8 °C; ^{1}H NMR (300 MHz,$CDCl_3$) δ = 1.63 (s, 3H), 1.69 (d, J = 1.1 Hz, 3H), 2.35–2.45 (m with a s at 2.41, 5H), 2.96 (t, J = 7.26 Hz, 2H), 5.15–5.20 (m, 1H), 7.25, 7.86 (2d, J = 7.32 Hz, 2H each); ^{13}C NMR (75 MHz,$CDCl_3$) δ = 18.0, 22.0, 23.4, 26.0, 39.0, 123.4, 128.5 (2C), 129.5 (2C), 133.0, 134.9, 144.0, 200.0; Ms (EI): m/z (%): 202 $[M]^+$ (15), 134 (60), 119 (100), 91 (37), 65 (12).

4.3. General procedure for the enantioselective addition of commercially available diorganozinc reagents to ketone 4

To a solution of the corresponding chiral ligand **6a**, **6b**, **6c**, **7**, **8a**, **8b**, (0.02 mmol, 0.1 equiv) and the diorganozinc reagent in toluene (**5a** or **5b**, 2.4 mmol, 12.0 equiv) was added Ti(O*i*Pr)$_4$ (65 μL, 0.22 mmol, 1.1 equiv) at 25 °C and under argon atmosphere. The reaction mixture was stirred at 25 °C (in case of diethylzinc at 0 °C) for 15 min and after that the ketone **4** (40 mg, 0.2 mmol, 1.0 equiv) was added. The reaction mixture was stirred for several days (see Table 1) at the same temperature and finally quenched by the successive addition of methanol (1 mL) and a saturated solution of NH_4Cl (15 mL). The mixture was extracted with EtOAc (3 × 5 mL) and the resulting organic layers were washed with a saturated solution of $NaHCO_3$ (5 mL), dried over anhydrous Mg_2SO_4, filtered, and concentrated under vacuum. The residue was purified by flash column chromatography (using as solvents from hexane until hexane/ethyl acetate: 9/1) for **1a**, and purified by bulb-to-bulb distillation for **1b**. Yields and ee are included in Table 1.

4.3.1. (+)-(*R*)-6-Methyl-2-(4-methylphenyl)hept-5-en-2-ol, (+)-Gossonorol, 1a[11]

Colorless oil R_f = 0.53 (hexane/ether: 3/2); $[\alpha]_D^{20} = +15.3$ (c 1, $CHCl_3$); HPLC (AD Chiralpak, UV 210 nm, hexane/2-propanol 98:2, flow 0.5 mL/min): t_r = 20.6 min (major) t_r = 23.9 min (minor), 82% ee; ^{1}H NMR (300 MHz,$CDCl_3$) δ = 1.49, 1.52 (2s, 3H each), 1.65 (s, 3H), 1.80–1.95 (m, 5H), 2.34 (s, 3H), 5.05–5.10 (m, 1H), 7.15, 7.31 (2d, J = 8.2 Hz, 2H each); ^{13}C NMR (75 MHz,$CDCl_3$) δ = 18.0, 21.3, 23.3, 26.0, 30.9, 44.0, 75.2, 124.6, 125.0 (2C), 129.1 (2C), 132.5, 136.3, 145.2; Ms (EI): m/z (%) 218 $[M]^+$ (<1%), 200 $[M-18]^+$ (15), 85 (16), 158 (14), 157 (100), 143 (16), 142 (16), 135 (13), 132 (13), 129 (16), 128 (15), 115 (21), 105 (11), 90(16), 69(25).

4.3.2. (*R*)-7-Methyl-3-(4-methylphenyl)loct-6-en-3-ol 1b

Colorless oil. R_f = 0.42 (hexane/ethyl acetate: 9/1)); $[\alpha]_D^{20} = +6$ (c 0.3, $CHCl_3$); HPLC (AD Chiralpak, UV 210 nm, hexane/2-propanol 98:2, flow 0.5 mL/min): t_r = 19.9 min (major) t_r = 26.5 min (minor), 64% ee; ^{1}H NMR (300 MHz,$CDCl_3$) δ = 0.75 (t, J = 9 Hz, 3H), 1.47, 1.65 (2s, 3H each), 1.85–1.75 (m, 7H), 2.34 (s, 3H), 5.05–5.15 (m, 1H), 7.15, 7.25 (2d, J = 9 Hz, 2H each); ^{13}C NMR (75 MHz,$CDCl_3$) δ = 8.1, 18.0, 21.3, 22.9, 26.0, 36.1, 42.4, 77.5, 124.7, 125.7 (2C), 129.0 (2C), 132.5, 136.0, 143.2; HMRS calcd for $C_{16}H_{24}O$ 232.1827, found 232.1825.

4.4. Enantioselective synthesis of (*S*)-5-methyl-1-(4-methylphenyl)-1-phenylhex-4-en-1-ol 9

A solution of Et_2Zn (1.1 M in toluene, 1.6 mL, 1.8 mmol, 7.2 equiv) was slowly added to a pressure tube charged with triphenylborane (0.097 g, 0.4 mmol, 1.6 equiv) at 0 °C under argon atmosphere. The resulting solution was warmed up to 70 °C, and stirred for 16 h. After that, it was cooled to 0 °C and poured into a Schlenk tube charged with the ligand HOCSAC (**7**) (0.011 g, 0.02 mmol, 0.1 equiv) the reaction mixture was stirred, allowed to warm to room temperature and, then, Ti(O*i*Pr)$_4$ (65 μL, 0.22 mmol, 1.1 equiv) was added. After 15 min, the ketone **4** (40 mg, 0.2 mmol, 1.0 equiv) was added. The resulting mixture was stirred at the same temperature for 10 d and finally quenched by the successive addition of methanol (1 mL) and a saturated solution of NH_4Cl (10 mL). The mixture was extracted with EtOAc (3 × 5 mL). The organic layers were washed with a saturated solution of $NaHCO_3$ (15 mL), dried over anhydrous Mg_2SO_4, filtered, and concentrated under vacuum. The residue was purified by flash chromatography (using as solvents from hexane until hexane/ethyl acetate: 9.5/0.5) to give 0.033 g (79% yield) of **9** as a colorless oil. R_f = 0.42 (hexane/ethyl acetate: 9/1); $[\alpha]_D^{20} = -1.2$ (c 1, $CHCl_3$); HPLC (OJ Chiralcel, UV 210 nm, hexane/2-propanol 99:1, flow 1 mL/min): t_r = 13.2 min (major) t_r = 16.3 min (minor), 64% ee; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.47, 1.66 (2s, 3H each), 1.95–2.05 (m, 2H), 2.25–2.35 (m with a s at 2.30, 6H), 5.15–5.20 (m, 1H), 7.10 (d, J = 8.0 Hz, 2H), 7.20–7.15 (m, 1H), 7.28 (t, J = 7.5 Hz, 4H), 7.41 (dd, J = 8.2, 1.0 Hz,); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 18.0, 21.3, 23.2, 26.1, 42.1, 78.7, 124.5, 126.2 (4C), 127.0, 128.4 (2C), 129.2 (2C), 132.8, 136.6, 144.5, 147.5; HMRS calcd for $C_{10}H_{24}O$ 280.1827, found 280.1486.

4.5. Enantioselective synthesis of (*R*)-7-methyl-3-(4-methylphenyl)-1-phenyl-oct-6-en-1-yn-3-ol 10

A solution of copper(II) triflate (14.47 mg, 0.04 mmol, 0.1 equiv), and the chiral ligand **6b** (14.94 mg, 0.04 mmol, 0.1 equiv) in dry dichloromethane (2 mL) was stirred at 25 °C for 30 min under argon atmosphere. A solution of Me_2Zn (1 mL, 1.2 M, 1.2 mmol, 3.0 equiv) and phenylacetylene (114 μL, 1.04 mmol, 2.6 equiv) was stirred at 0 °C under argon atmosphere for 15 min. Then, the previous formed copper solution was added to the solution of Me_2Zn at 0 °C for 30 min under argon atmosphere. After that, the ketone **4** (0.080 g, 0.4 mmol, 1.0 equiv) was added, and the reaction mixture was stirred for 14 days at the same temperature. The mixture was hydrolyzed with 2 M HCl (5 mL) and was extracted with EtOAc (3 × 5 mL). The resulting organic layers were washed with a saturated solution of $NaHCO_3$ (15 mL), dried over anhydrous Mg_2SO_4, filtered, and concentrated under vacuum. The residue was purified by flash chromatography to give compound **10** 0.061 g (51% yield) as a yellow oil. R_f = 0.56 (hexane/ethyl acetate: 8.5/1.5); $[\alpha]_D^{20} = -3.7$ (c 1, $CHCl_3$); HPLC (OJ Chiralcel, UV 210 nm, hexane/2-propanol 99:1, flow 1 mL/min): t_r = 12.9 min (major) t_r = 16.4 min (minor), 62% ee, ^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.53, 1.59 (2s, 3H each), 2.19–1.84 (m, 3H), 2.4–2.17 (m with a s at 2.4, 4H), 2.57 (s, 1H), 5.13–5.16 (m, 1H), 7.18 (d, J = 7.93 Hz, 2H), 7.30–7.35 (m, 3H) 7.45–7.50 (m, 2H), 7.58 (d, J = 8.19 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 17.7, 21.1, 23.9, 25.7, 45.2, 73.7, 86.1, 91.5, 122.7, 123.6, 125.4 (2C), 128.3, 128.4, 128.9 (2C), 131.7 (2C), 132.5, 137.4, 141.8; HMRS calcd for $C_{22}H_{24}O$ 304.1827, found 304.1828.

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