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Asymmetric synthesis of cyclopentenones with benzylic α-quaternary carbon stereogenic centres from furans

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Abstract—A new procedure for the synthesis of cyclopentenones containing benzylic α-quaternary carbon stereogenic centres is reported. This method makes use of a one-pot alkylation–elimination sequence from readily available starting materials and simple procedures, which makes it useful for the large-scale preparation of densely functionalised cyclopentanoids.

1. Introduction

The cyclopentanoid skeleton is a ubiquitous feature among natural and nonnatural organic molecules. For this reason, simple cyclopentenones have become important intermediates in the synthesis of complex targets. Accordingly, a wide variety of methods for the construction of optically active cyclopentenones have been developed in recent years.[1] One of the forefront aspects of asymmetric synthesis is the construction of quaternary stereogenic centres.[2] In particular, the synthesis of compounds containing chiral benzylic quaternary carbons is specially challenging.[3] Herein we present results in which these aspects have been conveniently addressed.

Optically active 2-alkyl-2-aryl-cyclopentanones are known to be important intermediates for the synthesis of natural bioactive products.[4,5] It was our goal to develop an expeditious route to 4,5,5-substituted cyclopentenones **1** with benzylic α-quaternary carbon stereogenic centres (Fig. 1). This procedure could be useful for preparing new analogues of natural or pharmacologically active products in large quantities to be used as standards during mechanistic or biological studies.

Among the different procedures for the assembly of α-arylcyclopentenones, we are particularly interested in the use of simple furan derivatives as starting materials.[6,7] This method is characterised by the ready availability of the precursors and the simplicity of the synthetic procedures. These issues are of interest from a large-scale synthesis standpoint.

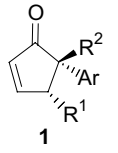

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Figure 1.

2. Results and discussion

Furylphenylcarbinol **2** was easily prepared by the addition of phenylmagnesium bromide to inexpensive furfural (Scheme 1). Compound **2** was rearranged to 2-phenyl-4-hydroxy-2-cyclopentenone **3** by aqueous acid treatment, and the latter isomerised to 5-phenyl-4-hydroxy-2-cyclopentenone **4** by adsorption on alumina following literature procedures.[8]

The synthesis of the enantiomerically pure final compounds required a resolution step. This is most efficiently carried out on a common precursor at an early stage of the synthesis. Therefore, compound (±)-**4** was kinetically resolved by treatment with PLE using vinyl acetate as reagent and solvent to afford (+)-**4** (48%, >98% ee) and the acetate (+)-**5** (52%, >98% ee).[9] In

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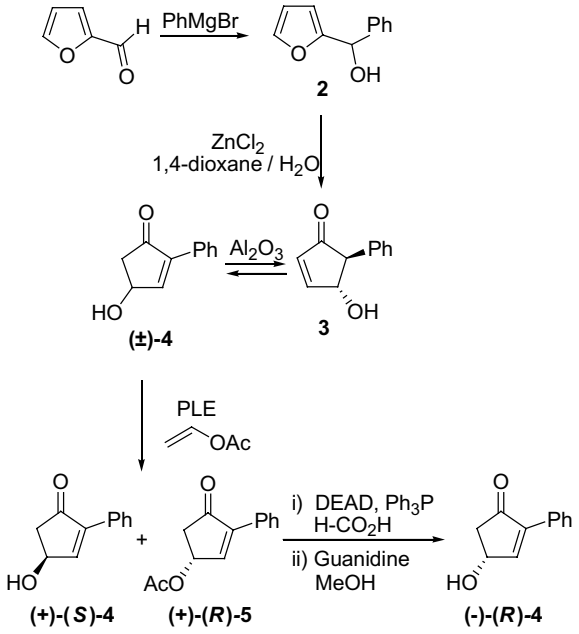
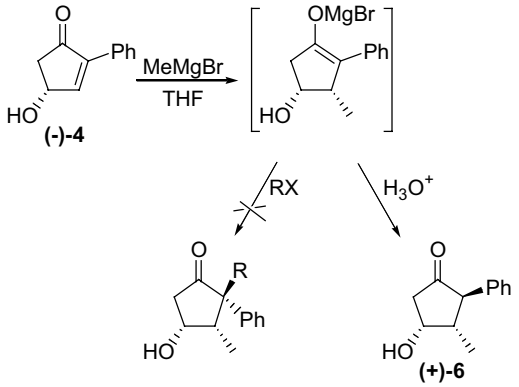


Scheme 1.

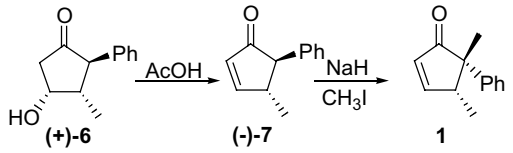
order to ensure the maximum yield in the synthesis of the enantiomerically pure material, the unseparated mixture of (+)-**4** and (+)-**5** was transformed into (−)-**4** by inversion of the free OH group of (+)-**4** by a Mitsunobu reaction with formic acid followed by deprotection of the corresponding formate group as well as the acetate group in (+)-**5** with guanidine in MeOH.

As previously reported,[6] the addition of Grignard reagents to 4-hydroxycyclopent-2-enones takes place in a highly diastereoselective conjugate fashion to afford the corresponding cyclopentanones (Scheme 2). Therefore, treatment of (−)-**4** with MeMgBr in THF followed by aqueous quench afforded compound (+)-**6**. However, it was observed that the intermediate magnesium enolates were not suitable for electrophilic capture with either MeI or activated halides.



Scheme 2.

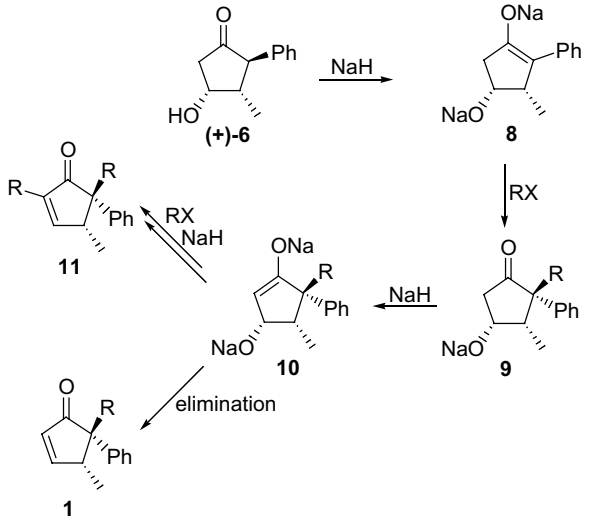
Therefore, we decided to proceed to the final targets **1** by dehydration of compound (+)-**6** followed by alkylation of cyclopentenone (−)-**7** (Scheme 3). After treatment of



Scheme 3.

(+)-**6** with AcOH, cyclopentenone (−)-**7** was submitted to α-alkylation using MeI as electrophile. However, we found a rather disappointing level of 1,2-asymmetric induction of the quaternary centre at C-2 by the contiguous stereocentre at carbon C-3 (75% overall yield, 40% de).

In order to make up for this low diastereoselectivity and improve the synthesis of compounds **1** in enantiomerically pure form, we devised the possibility of carrying out a tandem alkylation–elimination sequence on compounds (+)-**6**. This approach could benefit from the 1,3-asymmetric induction of the alcohol group at carbon C-3 on the new quaternary stereogenic centre at carbon C-5 (Scheme 4).



Scheme 4.

This strategy was performed in a one-pot fashion using NaH as the base in the presence of the alkylating agent RX, with no need for prior protection of the alcohol group in (+)-**6**. The stereochemical assignments of compounds **1** was based on NOE measurements on the corresponding ^{1}H NMR (300 MHz) spectra, and was determined to be 4,5-*syn* in all cases. The results are gathered in Table 1.

The inspection of these data revealed that, when MeI was used as the electrophile (entry 1), the diastereoselectivity improved up to 80%. This result is to be compared with the 40% de previously obtained (Scheme 3). The procedure was then extended to a series of representative primary and activated electrophiles (entries 2–5). In all cases studied the reaction took place with

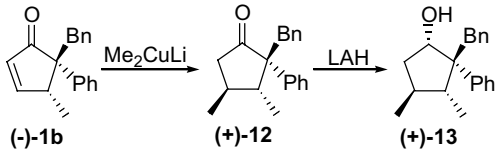
Table 1. Asymmetric synthesis of cyclopentenones **1**

Entry	R	**1** (%)[a]	De[b]	**11** (%)[a]
1	CH_3	**1a** (65)	85	**11a** (10)
2	Bn	**1b** (90)	>98	—
3	Et	**1c** (70)	95	—
4	CH_2=CH–CH_2	**1d** (80)	>98	**11d** (10)
5	EtO_2C–CH_2	**1e** (80)	>98	—

[a] Pure isolated yield.
[b] Determined by integration of the ^1H NMR spectra ($CDCl_3$, 200 MHz).

good diastereoselectivity. It must be pointed out that compounds **11**, which may arise from a second alkylation–dehydration sequence on **10** (Scheme 4), were only detected as minor products, indicating that elimination on the intermediate enolate **10** was faster than its alkylation.

As a further example of the utility of compounds **1** in the synthesis of densely functionalised enantiomerically pure cyclopentanoids, we have transformed compound (−)-**1b** into the cyclopentanol (+)-**13** (Scheme 5). Reaction of (−)-**1b** with Me_2CuLi gave rise to cyclopentanone (+)-**12** with high diastereoselectivity (>98% de). Compound (+)-**12** was reduced with $LiAlH_4$ to cyclopentanol (+)-**13**, which was also obtained with high diastereoselectivity (>98% de). These reactions are useful because they are able to install highly substituted carbons in a stereodefined manner.



Scheme 5.

Mosher's ester formation on (+)-**13** and comparison of the corresponding ^{19}F NMR spectrum with that of a racemic sample obtained starting from (±)-**6** confirmed that all transformations reported herein took place without loss of the enantiomeric purity attained in the kinetic resolution step.

3. Conclusion

In summary, we have developed a procedure, which allows for the asymmetric synthesis of 4,5,5-trisubstituted cyclopent-2-enones bearing a benzylic chiral α-quaternary carbon stereogenic centre via a one-pot alkylation–elimination sequence. This method makes use of readily available starting materials and relatively simple procedures, which makes it useful for the large-scale preparation of these and related types of compounds. The procedure reported herein widens the well-known versatility of 4-hydroxycyclopent-2-enones as useful synthetic intermediates.[10,11]

4. Experimental

4.1. General

All starting materials were commercially available research-grade chemicals and used without further purification. THF was distilled after refluxing over Na-benzophenone under Ar. Silica gel 60 F_{254} was used for TLC, and the spots were detected with UV or vanillin solution. Flash column chromatography was carried out on silica gel 60. IR spectra have been recorded as $CHCl_3$ solutions. ^1H NMR spectra were recorded at 200 or 300 MHz as indicated, in $CDCl_3$ solution. ^{13}C and ^{19}F NMR spectra were recorded at 50.5 and 141.2 MHz, respectively, in $CDCl_3$ solution. MS spectra were carried out by EI at 70 eV.

4.1.1. (*R*)-4-Hydroxy-2-phenylcyclopentenone, (−)-4. PPL (5.00 g) was added to a solution of (±)-4-hydroxy-2-phenylcyclopentenone[8] **4** (3.48 g, 20 mmol) in vinyl acetate (40 mL). The mixture was stirred at rt for 7 days, then filtered trough Celite and concentrated to afford 3.9 g of a mixture of (*S*)-4-hydroxy-2-phenylcyclopentenone (+)-**4** and (*R*)-4-acetoxy-2-phenylcyclopentenone (+)-**5**. The crude mixture was dissolved in anhydrous THF (50 mL) and triphenylphosphine (20 mmol) and formic acid (20 mmol) were added. The solution was cooled at 0 °C and a commercial solution of diethyl azodicarboxylate was added dropwise (0.12 mmol). The reaction mixture was allowed to reach rt and was stirred for 18 h. After concentration, the resulting oil was chromatographed (hexane/EtOAc, 2:1). The mixture of acetate and formate derivatives were dissolved in MeOH (50 mL), cooled at 0 °C and treated with a 0.5 M solution of guanidine in MeOH (20 mL, 10 mmol) for 15 min. The mixture was concentrated and the residue was partitioned between water (25 mL) and AcOEt (25 mL). The organic layer was decanted and the aqueous one was extracted with AcOEt (3×25 mL). The combined organic layers were washed with water (50 mL) and brine (50 mL), and dried over $MgSO_4$. The solvent was removed under reduce pressure and the crude product was purified by chromatography (hexane/EtOAc, 2:1). Enantiomeric excess (ee) was determined by Mosher's ester formation. White solid, yield 4.0 g (80%); mp 58–59 °C; $[\alpha]_D = -14.1$ (*c* 0.82, $CHCl_3$), 98% ee; ^1H NMR (200 MHz) δ 7.72–7.69 (2H, m), 7.64 (1H, d, $^3J = 2.6$ Hz), 7.41–7.27 (3H, m), 5.05–4.97 (1H, m), 2.96 (1H, B part of ABX system, $^3J = 6.2$ Hz, $^2J = 18.5$ Hz), 2.48 (1H, A part of ABX system, $^3J = 2.2$ Hz, $^2J = 18.5$ Hz), 2.21 (1H, br s). Anal. Calcd for $C_{11}H_{10}O_2$: C, 75.84; H, 5.79. Found: C, 75.99; H, 5.53.

4.1.2. (3*R*,4*S*,5*R*)-3-Hydroxy-4-methyl-5-phenyl-cyclopentanone, (+)-6. To a solution of (−)-**4** (5 mmol) in THF (25 mL) at 0 °C was added dropwise a solution of MeMgI (11.0 mmol, 3 M in Et_2O). The mixture was refluxed for 2 h, cooled to rt and hydrolysed with saturated NH_4Cl solution (25 mL). The organic layer was decanted and the aqueous one was extracted with

AcOEt (3×25 mL). The combined extracts were dried on $MgSO_4$ and the solvent was evaporated under reduced pressure. The resulting oil was purified by chromatography (hexane/EtOAc, 2:1) to give (+)-**6** as a colourless oil. Yield 570 mg (60%); $[\alpha]_D = +42.0$ (*c* 1.57, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.30–7.13 (3H, m), 7.02–6.98 (2H, m), 3.20 (1H, d, $^3J = 12.6$ Hz), 2.48–2.46 (2H, m), 2.37–2.13 (1H, m), 1.04 (3H, d, $^3J = 6.7$ Hz). Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.55; H, 7.61.

4.2. General procedure for the synthesis of (4*R*,5*S*)-5-alkyl-4-methyl-5-phenylcyclopentenones

To a solution of (+)-**6** (100 mg, 0.53 mmol) in THF (5 mL) at 0 °C were sequentially added NaH (64 mg, 60% mineral oil, 1.59 mmol), and RX (0.64 mmol). The mixture was allowed to reach rt, was stirred for 5 h, and hydrolysed with saturated NH_4Cl solution (5 mL). The organic layer was decanted and the aqueous one was extracted with Et_2O (3×5 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure to afford an oil that was purified by chromatography (hexane/Et_2O, 10:1).

4.2.1. (4*R*,5*S*)- and (4*R*,5*R*)-4,5-Dimethyl-5-phenyl-cyclopentenone, 1a. (+)-**6** (100 mg, 0.53 mmol), NaH (64 mg, 60% mineral oil, 1.59 mmol) and MeI (40 μL, 0.64 mmol) were reacted as described above. Compound **1a** was obtained as a 90:10 mixture of diastereomers (4*R*,5*S*)-**1a** and (4*R*,5*R*)-**1a**. Yield 65 mg (65%); $[\alpha]_D = -295.7$ (*c* 1.50, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.65–7.61 ($1H_I$+$1H_{II}$, m), 7.32–7.11 ($5H_I$+$5H_{II}$, m), 6.32 ($1H_I$, dd, $^3J = 5.7$ Hz, $^4J = 1.6$ Hz), 6.26 ($1H_{II}$, d, $^3J = 5.7$ Hz), 3.21–3.18 ($1H_{II}$, m), 2.95–2.88 ($1H_I$, m), 1.57 ($3H_I$, s), 1.39 ($1H_{II}$, s), 0.70 ($3H_I$, d, $^3J = 7.5$ Hz), 0.64 ($3H_{II}$, d, $^3J = 6.5$ Hz); ^{13}C NMR (50.5 MHz, $CDCl_3$, majoritary diastereomer) δ 213.6, 168.2, 141.5, 131.8, 128.0, 127.7, 126.5, 54.8, 50.1, 24.2, 16.8; MS (*m*/*z*, %) 186 (M, 85), 171 (100), 143 (86), 142 (19), 141 (16), 129 (25), 128 (70), 127 (15), 115 (30), 91 (17), 77 (30), 70 (17), 51 (21).

4.2.2. (4*R*,5*S*)-5-Benzyl-4-methyl-5-phenylcyclopentenone, (−)-1b. (+)-**6** (100 mg, 0.53 mmol), NaH (64 mg, 60% mineral oil, 1.59 mmol) and benzyl bromide (76 μL, 0.64 mmol) were reacted as described above to afford (−)-**1d** as a single diastereomer. Yield 125 mg (90%); white solid, mp 107–108 °C; $[\alpha]_D = -203.5$ (*c* 1.10, $CHCl_3$); IR ($CHCl_3$) *v* 1697 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.40–7.00 (11H, m), 6.09 (1H, dd, $^3J = 5.8$ Hz, $^4J = 2.0$ Hz), 3.50 (1H, B part of AB system, $^2J = 12.9$ Hz), 3.30 (1H, A part of AB system, $^2J = 12.9$ Hz), 3.22–3.13 (1H, m), 0.72 (3H, d, $^2J = 7.5$ Hz); ^{13}C NMR (50.5 MHz, $CDCl_3$) δ 212.9, 169.2, 141.4, 136.5, 133.3, 130.7, 128.1, 128.0, 128.0, 126.7, 126.6, 59.6, 44.8, 42.4, 16.6; MS (*m*/*z*, %) 262 (M, 34), 171 (38), 143 (22), 128 (32), 115 (10), 92 (13), 91 (100). Anal. Calcd for $C_{19}H_{18}O$: C, 86.99; H, 6.92. Found: C, 87.11; H, 7.17.

4.2.3. (4*R*,5*S*)- and (4*R*,5*R*)-5-Ethyl-4-methyl-5-phenyl-cyclopentenone, 1c. (+)-**6** (100 mg, 0.53 mmol), NaH (64 mg, 60% mineral oil, 1.59 mmol) and EtBr (48 μL, 0.64 mmol) were reacted as described above. Compound **1c** was obtained as a 95:05 mixture of diastereomers (4*R*,5*S*)-**1b** and (4*R*,5*R*)-**1b**. Yield 75 mg (70%); $[\alpha]_D = -232.5$ (*c* 0.65, $CHCl_3$); IR ($CHCl_3$) *v* 1701 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.64 ($1H_I$, dd, $^3J = 5.9$ Hz, $^3J = 2.7$ Hz), 7.52 ($1H_{II}$, dd, $^3J = 5.9$ Hz, $^3J = 2.4$ Hz), 7.38–7.06 ($5H_I$+$5H_{II}$, m), 6.28 ($1H_I$, dd, $^3J = 5.9$ Hz, $^4J = 1.9$ Hz), 6.19 ($1H_{II}$, dd, $^3J = 5.9$ Hz, $^4J = 2.4$ Hz), 3.24–3.15 ($1H_{II}$, m), 3.04–2.87 ($1H_I$, m), 2.18 ($1H_I$, B part of ABX system, $^2J = 13.7$ Hz, $^3J = 7.3$ Hz), 1.97 ($1H_I$, A part of ABX system, $^2J = 13.7$ Hz, $^3J = 7.3$ Hz), 0.84 ($3H_I$+$3H_{II}$, t, $^3J = 7.3$ Hz), 0.66 ($3H_I$+$3H_{II}$, d, $^3J = 7.6$ Hz); ^{13}C NMR (50.5 MHz, $CDCl_3$) δ 213.1, 168.6, 141.1, 132.9, 128.1, 128.0, 126.9, 58.9, 47.6, 30.3, 17.2, 8.6; MS (*m*/*z*, %) 200 (M, 22), 185 (31), 172 (92), 171 (100), 143 (64), 129 (31), 128 (62), 115 (31), 91 (24), 77 (16).

4.2.4. (4*R*,5*S*)-5-Allyl-4-methyl-5-phenylcyclopentenone, (−)-1d. (+)-**6** (100 mg, 0.53 mmol), NaH (64 mg, 60% mineral oil, 1.59 mmol) and allyl bromide (56 μL, 0.64 mmol) were reacted as described above to afford (−)-**1d** as a single diastereomer. Yield 90 mg (80%); white solid, mp 59–60 °C; $[\alpha]_D = -314.8$ (*c* 1.06, $CHCl_3$); IR ($CHCl_3$) *v* 1701 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.61 (1H, dd, $^3J = 5.8$ Hz, $^4J = 2.4$ Hz), 7.33–7.12 (5H, m), 6.31 (1H, dd, $^3J = 5.8$ Hz, $^4J = 1.8$ Hz), 5.68–5.62 (1H, m), 5.12–5.01 (2H, m), 3.05–3.01, (1H, m), 2.93–2.86 (1H, m), 2.78–2.70 (1H, m), 0.70 (3H, d, $^3J = 7.5$ Hz); ^{13}C NMR (50.5 MHz, $CDCl_3$) δ 212.6, 168.8, 141.0, 133.3, 133.0, 128.1, 128.0, 126.6, 118.8, 58.2, 46.3, 41.4, 16.5; MS (*m*/*z*, %) 212 (M, 62), 197 (22), 171 (97), 167 (22), 149 (28), 143 (33), 141 (25), 129 (57), 128 (100), 115 (35), 105 (61), 97 (22), 85 (23), 83 (27), 81 (25), 77 (23), 71 (44), 57 (52), 55 (36), 41 (21). Anal. Calcd for $C_{15}H_{16}O$: C, 84.87; H, 7.60. Found: C, 85.08; H, 7.88.

4.2.5. (4*R*,5*S*)-5-Ethoxycarbonylmethyl-4-methyl-5-phenylcyclopentenone, (−)-1e. (+)-**6** (100 mg, 0.53 mmol), NaH (64 mg, 60% mineral oil, 1.59 mmol) and ethyl bromoacetate (71 μL, 0.64 mmol) were reacted as described above to afford (−)-**1e** as a single diastereomer. Yield 110 mg (80%); colourless oil; $[\alpha]_D = -232.5$ (*c* 0.30, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.61 (1H, dd, $^3J = 5.8$ Hz, $^3J = 2.2$ Hz), 7.28–7.23 (3H, m), 7.09–7.06 (2H, m), 6.48 (1H, dd, $^3J = 5.8$ Hz, $^3J = 2.3$ Hz), 4.12 (2H, c, $^3J = 7.2$ Hz), 3.38–3.10 (1H, m), 3.23 (1H, B part of AB system, $^2J = 16.4$ Hz), 3.15 (1H, A part of AB system, $^2J = 16.4$ Hz), 1.25 (3H, t, $^3J = 7.2$ Hz), 0.74 (3H, d, $^3J = 7.6$ Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 211.6, 171.0, 168.1, 140.5, 133.5, 128.2, 127.3, 127.0, 60.7, 55.9, 46.5, 39.7, 15.5, 14.1; MS (*m*/*z*, %) 258 (M, 23), 213 (49), 212 (100), 197 (20), 184 (41), 171 (28), 156 (27), 143 (35), 142 (52), 141 (41), 129 (26), 128 (38), 115 (18), 77 (18). Anal. Calcd for $C_{16}H_{18}O_3$: C, 74.39; H, 7.02. Found: C, 74.51; H, 6.89.

4.3. (2*S*,3*R*,4*S*)-2-Benzyl-3,4-dimethyl-2-phenyl-cyclopentanone, (+)-12

To a solution of CuI (84 mg, 0.44 mmol) in Et_2O (2.9 mL) at 0 °C was added dropwise a 1.6 M solution of MeLi in Et_2O (0.55 mL, 0.88 mmol). After the mixture was stirred for 10 min, a solution of (−)-**1b** (105 mg, 0.4 mmol) in Et_2O (2.9 mL) was added. The mixture was stirred at 0 °C for 2 h and hydrolysed with saturated NH_4Cl solution (6 mL). The organic layer was decanted and the aqueous layer was extracted with Et_2O (3×6 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure to afford an oil that was purified by chromatography (hexane/Et_2O, 9:1). Yield 95 mg (85%); pale yellow oil; $[\alpha]_D = +29.0$ (*c* 1.26, $CHCl_3$); IR ($CHCl_3$) ν 1736 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.36–6.87 (10H, m), 3.40 (1H, B part of AB system, $^2J = 13.3$ Hz), 3.19 (1H, A part of AB system, $^2J = 13.3$ Hz), 2.53 (1H, B part of ABX system, $^2J = 18.7$ Hz, $^3J = 6.7$ Hz), 1.83–1.73 (2H, m), 1.44 (1H, A part of ABX system, $^2J = 18.7$ Hz, $^3J = 11.5$ Hz), 0.92 (3H, d, $^3J = 5.9$ Hz), 0.85 (3H, d, $^3J = 6.4$ Hz); ^{13}C NMR (50.5 MHz, $CDCl_3$) δ 218.7, 140.7, 137.5, 131.3, 131.1, 128.1, 128.0, 127.9, 127.8, 126.6, 126.4, 63.3, 48.7, 44.8, 40.0, 33.8, 17.4, 12.9; MS (*m*/*z*, %) 278 (M, 22), 187 (22), 159 (30), 145 (50), 117 (35), 91 (100). Anal. Calcd for $C_{20}H_{22}O$: C, 86.29; H, 7.97. Found: C, 86.41; H, 8.18.

4.4. (1*S*,2*S*,3*R*,4*S*)-2-Benzyl-3,4-dimethyl-2-phenyl-cyclopentanol, (+)-13

To a suspension of $LiAlH_4$ (6.0 mg, 0.17 mmol) in THF (1.7 mL) at 0 °C, was added dropwise a solution of (+)-**12** (47 mg, 0.17 mmol) in THF (1.7 mL). The mixture was allowed to rt, stirred for 2 h and hydrolysed with saturated NH_4Cl solution (5 mL). The organic layer was decanted and the aqueous layer was extracted with Et_2O (3×5 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure to afford an oil that was purified by chromatography (hexane/Et_2O, 9:1). Yield 35 mg (75%); white solid; mp 68–69 °C; $[\alpha]_D = +46.1$ (*c* 0.5, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$) δ 7.50–7.47 (2H, m), 7.36–7.18 (6H, m), 7.01–6.99 (2H, m), 4.38–4.32 (1H, m), 3.39 (1H, B part of AB system, $^2J = 13.6$ Hz), 2.86 (1H, A part of AB system, $^2J = 13.6$ Hz), 2.10–2.04 (1H, m), 1.83–1.77 (2H, m), 1.59–1.53 (1H, m), 0.99 (3H, d, $^3J = 6.1$ Hz), 0.91 (3H, d, $^3J = 6.6$ Hz); ^{13}C NMR (50.5 MHz, $CDCl_3$) δ 139.8, 138.5, 130.3, 130.2, 128.1, 127.6, 126.4, 126.1, 77.2, 57.7, 49.1, 44.8, 40.4, 36.7, 20.2, 14.9; MS (*m*/*z*, %) 189 (M−Bn, 46), 188 (43), 171 (100), 145 (31), 129 (16), 105 (33), 91 (75), 69 (16). Anal. Calcd for $C_{20}H_{24}O$: C, 85.67; H, 8.63. Found: C, 85.79; H, 8.88.

4.5. General procedure for the synthesis of Mosher's esters

(−)-(*R*)-α-Methoxy-α-trifluormethylphenylacetyl chloride (0.066 mmol), Et_3N (0.075 mmol) and DMAP (10%) were added to a solution of the substrate (0.06 mmol) in anhydrous CH_2Cl_2 (0.3 mL). The mixture was stirred for 18 h at rt, washed with $NaHCO_3$ (1 mL), HCl 5% (1 mL) and again $NaHCO_3$ (1 mL). The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure to afford a yellow oil.

4.5.1. Data of Mosher's ester of (±)-4-hydroxy-2-phenyl-cyclopentenone, (±)-4. ^{19}F NMR (235 MHz, $CDCl_3$) δ −71.89, −71.93.

4.5.2. Data of Mosher's ester of (−)-4-hydroxy-2-phenyl-cyclopentenone, (−)-4. ^{19}F NMR (235 MHz) δ −71.89 (98% ee).

4.5.3. Data of Mosher's ester of (±)-2-benzyl-3,4-dimethyl-2-phenylcyclopentanol, (±)-13. ^{19}F NMR (235 MHz) δ −71.36, −71.55, −71.77, −71.89.

4.5.4. Data of Mosher's ester of (+)-2-benzyl-3,4-dimethyl-2-phenylcyclopentanol, (+)-13. ^{19}F NMR (235 MHz) δ −71.77 (97% ee).

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