Convenient Access to β-Substituted Chiral Phenones

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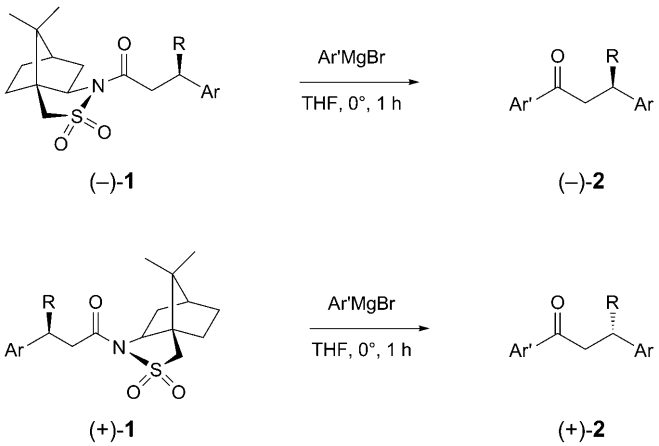
A highly enantioselective approach towards the synthesis of β-substituted chiral ketones by utilizing *Grignard* reagents was achieved. The (*R*)- and (*S*)-antipodes of the target chiral ketones **2a**–**2k** were obtained with up to 100% ee from chiral *N*-alkanoylcamphorsultams **1** (*Scheme*, *Table 2*). This simple, catalyst-free, direct procedure for the formation of chiral ketones is a fascinating method for the practical syntheses of chiral synthons as valuable building blocks and important medicinal intermediates.

Introduction. – Optically active β-substituted ketones (β-chiral ketones) are common subunits in biologically active molecules. They are used as excellent building blocks, which have numerous applications in the enantioselective synthesis of natural products and important medicinal intermediates [1–4]. In recent years, intensive investigations on the synthesis of β-substituted chiral ketones have been reported. For example, enantioselective metal-catalyzed types of the conjugate addition (CA) of organometallic reagents to enones have been extensively studied with *Grignard* [5][6], dialkylzinc [7–12], organocuprate, organoboron, alkyllithium, and silicon reagents [13–18]. Most of these studies, however, involved the use of a catalytic or stoichiometric amount of chiral ligands. Recently, a novel transformation method from *Weinreb* amide to β-substituted chiral ketones has been developed [19–23]. *Weinreb* amide could be further alkylated with *Grignard* reagents to give various ketone derivatives with C(β) as center of chirality. Simultaneously, *Nagao*'s group studied how active monothioester derivatives can be converted to chiral ketones when treated with the *Grignard* reagent and metal-complex catalysts [24]. Furthermore, enzymatic transformations to obtain chiral ketones have also been reported [25–28]. These include the hydrolysis of enol esters and baker-yeast-mediated asymmetric reduction of α,β-unsaturated carbonyl compounds. Nevertheless, almost all of the above-described synthetic methodologies for the synthesis of chiral ketones need expensive chiral ligands and metal catalysts, and the reaction conditions are rigorous (low temperature or long reaction time). Therefore, despite extensive research on the synthesis of chiral ketones, a generally convenient method to obtain β-substituted chiral ketones is still lacking. Recently, we have reported that the highly regioselective and diastereoselective conjugate addition of a series of Ar-substituted α,β-unsaturated carbonyl compounds with various *Grignard* reagents can be achieved by means of a chiral auxiliary [29]. Therefore, in view of our interest in new methods to construct chiral synthons, we would like to report herein a simple, catalyst-free, and direct formation of β-substituted chiral phenones *via* a nucleophilic cleavage reaction of corresponding *N*-alkanoylcamphorsultams with Ar-*Grignard* reagents (*Scheme*).

Results and Discussion. – The synthesis and reaction conditions of the β-substituted chiral ketone derivatives **2a** – **2k** are outlined in the *Scheme*. The key chiral substrates **1** were prepared following the methods outlined in the literature, and their spectral and analytical data were also identical to those stated in [29]. The chiral auxiliary attached to the carbonyl moiety in substrates **1** was then nucleophilically substituted by the aryl group on treatment with a *Grignard* reagent under optimized reaction conditions.

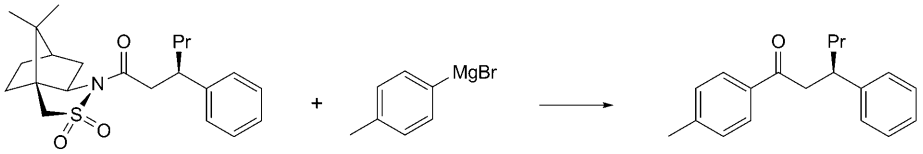
Scheme. *Catalyst-Free Enantioselective Formation of β-Substituted Chiral Phenones* **2a** – **2k** via *Aryl*-Grignard *Reagents* (see *Table 2* for Ar, Ar′, and R)



The reaction conditions were optimized with an investigation of the influence of reaction temperature, reaction time, and the ratio of substrates on the yield and enantioselectivity. At the outset of our study, we selected chiral substrate (–)-**1a** bearing a propyl substituent as a typical substrate to examine the effectiveness of the reaction conditions in the presence of THF (*Table 1*). The ratio of substrate (–)-**1a** to the *Grignard* reagent Ar′MgBr (Ar′ = 4-MeC_6H_4) was examined from 1:1 to 1:2, establishing that the yield of target chiral ketone (–)-**2a** was relatively low (7 – 42%) at the ratio 1:1 and moderate (54%) at the ratio 1:1.5. The highest enantioselectivity (94%) was obtained at $-78°$, but the yield was the lowest, and the reaction required a longer time for completion (*Entry 5*). Among the different reaction conditions, those of *Entry 6* gave the target (–)-**2a** in the best yield and with high enantioselectivity.

High enantioselectivity and convenient access to the β-substituted chiral ketone (–)-**2a** under mild conditions prompted us to extend our investigation to obtain other important chiral building blocks **2**. To explore the generality of the above-described direct transformation, differently β-alkyl-substituted substrates **1** with a variety of aryl groups (Ar) bearing electron-withdrawing groups (such as halogen atoms) or electron-donating substituents (Me and MeO) at the *para*-position were prepared and used as substrates. As shown in *Table 2*, under optimized reaction conditions, the treatment of these substrates **1** with a *Grignard* reagent Ar′MgBr afforded the desired β-chiral phenones **2** with high enantioselectivity (up to 100% ee) in moderate yield. An obvious increase in enantioselectivity for chiral substrates **1** with an unsubstituted phenyl (Ar) and a shorter-chain alkyl group (Pr) at β-position was observed (*Entries 1 – 4*).

Table 1. *Optimization of the Reaction Conditions for the Formation of β-Substituted Chiral Ketone* (–)-**2a**



(–)-**1a** (–)-**2a**

Entry	(–)-**1a**/Ar′MgBr	Temperature [°]	Time [h]	Yield [%][a])	ee of (–)-**2a**[b])
1	1:1	0	1	32	91
2	1:1	0	1.5	33	91
3	1:1	–40	4	42	92
4	1:1	–60	6	11	92
5	1:1	–78	10	7	94
6	1:1.5	0	1	54	91
7	1:1.5	0	1.5	54	91
8	1:2	0	1	52	91

[a]) Yield of isolated material. [b]) The ee values were determined by HPLC analysis with a chiral stationary phase column (*Daicel Chiralpak AD-H*; hexane/i-PrOH 97:3).

However, for substrates **1** with a weakly electron-withdrawing group (Cl) at the *para*-position of Ar, the longer-chain alkyl group (Bu) led to an obvious increase in enantioselectivity and relatively high yields (*Entries 5–10*). As a general trend, an electron-donating group at the *para*-position of Ar provided excellent enantioselectivities (93–97% ee) (*Entries 13–15*). The reaction of chiral substrates **1** with PhMgBr (Ar′ = Ph) afforded the desired product with high enantioselectivity (up to 99%) but the yields of the target chiral ketones **2** were lower (38–42%) (*Entries 16–19*). Electron-donating groups at the *para*-position of Ar′ also provided excellent enantioselectivity (up to 100% ee) and gave moderate yields (*Entries 20* and *21*).

Conclusion. – In summary, we have demonstrated that inexpensive and readily available *Grignard* reagents can be used to provide β-substituted chiral ketones **2** with excellent enantioselectivity. This simple, catalyst-free direct procedure for the formation of chiral ketones is a fascinating method for the practical syntheses of chiral synthons as valuable building blocks and important medicinal intermediates.

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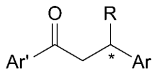
Experimental Part

1. *General.* Unless otherwise noted, all materials were commercially available and were used directly without further purification. HPLC: *Agilent-1100* instrument; *Chiralpak-AD-H* column; hexane/i-PrOH 97:3, 1 ml/min; t_R in min. M.p.: *Büchi B-545* melting-point apparatus; uncorrected. Optical rotations: *Jasco P-1010* polarimeter; enantiomer excesses (ee) by HPLC. ^{1}H- and ^{13}C-NMR Spectra: *Mercury-Plus-*

Table 2. *Enantioselectivity for the Formation of β-Substituted Chiral Ketones* **2**[a])



2

Entry	Ar	Ar′	R	Product	Yield [%][b])	ee [%][c])	Configuration[d])[e])
1	Ph	4-MeC_6H_4	Pr	(−)-**2a**	54	91	(*R*)
2	Ph	4-MeC_6H_4	Pr	(+)-**2a**	53	95	(*S*)
3	Ph	4-MeC_6H_4	Bu	(−)-**2b**	51	86	(*R*)
4	Ph	4-MeC_6H_4	Bu	(+)-**2b**	48	78	(*S*)
5	4-ClC_6H_4	4-MeC_6H_4	Et	(−)-**2c**	46	93	(*R*)
6	4-ClC_6H_4	4-MeC_6H_4	Et	(+)-**2c**	48	89	(*S*)
7	4-ClC_6H_4	4-MeC_6H_4	Pr	(−)-**2d**	48	80	(*R*)
8	4-ClC_6H_4	4-MeC_6H_4	Pr	(+)-**2d**	52	87	(*S*)
9	4-ClC_6H_4	4-MeC_6H_4	Bu	(−)-**2e**	60	97	(*R*)
10	4-ClC_6H_4	4-MeC_6H_4	Bu	(+)-**2e**	56	95	(*S*)
11	4-FC_6H_4	4-MeC_6H_4	Bu	(−)-**2f**	46	79	(*R*)
12	4-FC_6H_4	4-MeC_6H_4	Bu	(+)-**2f**	48	82	(*S*)
13	4-$MeOC_6H_4$	4-MeC_6H_4	Bu	(−)-**2g**	45	97	(*R*)
14	4-$MeOC_6H_4$	4-MeC_6H_4	Bu	(+)-**2g**	52	96	(*S*)
15	4-MeC_6H_4	4-MeC_6H_4	Et	(−)-**2h**	64	93	(*R*)
16	Ph	Ph	Et	(−)-**2i**	40	99	(*R*)
17	Ph	Ph	Et	(+)-**2i**	42	81	(*S*)
18	4-ClC_6H_4	Ph	Et	(−)-**2j**	38	93	(*R*)
19	4-ClC_6H_4	Ph	Et	(+)-**2j**	41	88	(*S*)
20	4-ClC_6H_4	4-$MeOC_6H_4$	Bu	(−)-**2k**	45	80	(*R*)
21	4-ClC_6H_4	4-$MeOC_6H_4$	Bu	(+)-**2k**	50	100	(*S*)

[a]) All reactions were performed with **1** (1.0 mol-equiv.), and Ar′MgBr (1.5 mol-equiv.). [b]) Yield of isolated material. [c]) The ee values were determined by HPLC analysis with a chiral stationary phase column (*Daicel Chiralpak AD-H*; hexane/i-PrOH 97 : 3). [d]) The absolute configuration was assigned by chiroptical comparison with the published value. [e]) The configurations of compounds **2** were assigned *via* the absolute configuration of compounds **1** [29].

400 spectrometer; in $CDCl_3$ at 400 or 600 and 100 MHz, resp.; δ in ppm rel. to Me_4Si as internal standard, *J* in Hz. MS: *TraceMS-2000* organic mass spectrometer; in *m*/*z* (rel. %). Elemental analyses: *Vario-EL-III* elemental analysis instrument.

2. *Synthesis of* **1**: *General Procedure.* The key chiral intermediates (−)-**1** and (+)-**1** were prepared following the literature methods, and the spectral and anal. data of them, except those of (−)-**1g** and (+)-**1g** (see below), were in agreement with published data [29].

(−)-N-*[(3*R*)-3-(4-Methoxyphenyl)heptanoyl]bornane-10,2-sultam* (=*(−)-(3*R*)-3-(4-Methoxyphenyl)-1-[(3a*S*,6*R*,7a*R*)-tetrahydro-8,8-dimethyl-2,2-dioxido-3*H*-3a,b-methano-2,1-benzothiazol-1(4*H*)-yl]-hexan-1-one*; (−)-**1g**): White solid. M.p. 97–99°. $[\alpha]_D^{24} = -73.8$ (*c* = 1.0, CH_2Cl_2). ^{1}H-NMR (400 MHz): 0.81 (*t*, *J* = 7.2, 3 H); 0.96 (*s*, 3 H); 1.08–1.12 (*m*, 2 H); 1.16 (*s*, 3 H); 1.19–1.38 (*m*, 4 H); 1.53–1.61 (*m*, 2 H); 1.85–1.87 (*m*, 3 H); 2.0–2.02 (*m*, 2 H); 2.96–3.08 (*m*, 2 H); 3.15–3.17 (*m*, 1 H); 3.40 (*d*, *J* = 14, 1 H); 3.49 (*d*, *J* = 13.6, 1 H); 3.77–3.81 (*m*, 4 H); 6.77–6.83 (*m*, 2 H); 7.12 (*d*, *J* = 8.8, 2 H). EI-MS: 433 (M^+). Anal. calc. for $C_{24}H_{35}NO_4S$: C 66.48, H 8.14, N 3.23, S 7.39; found: C 66.16, H 7.98, N 3.36, S 7.77.

(+)-N-*[(3*S*)-3-(4-Methoxyphenyl)heptanoyl]bornane-10,2-sultam* (=*(+)-(3*S*)-3-(4-Methoxyphenyl)-1-[(3a*R*,7*S*,7a*S*)-octahydro-8,8-dimethyl-2,2-dioxido-2,1-benzisothiazol-1(4*H*)-yl]heptan-1-one*; (+)-

1g): White solid. M.p. 97–99°. $[\alpha]_D^{24} = +77.5$ ($c = 1.0$, CH_2Cl_2). Spectroscopic data: identical to those of (−)-**1g**.

3. *Synthesis of* **2**: *General Procedure.* To a soln. of **1** (10 mmol) in anh. THF (40 ml) under N_2 at 0°, Ar′MgBr (15 ml, 15 mmol) was added dropwise. The mixture was stirred at 0° for 1 h, and was then quenched with sat. aq. NH_4Cl soln. and extracted with Et_2O (2 × 100 ml). The combined org. phase was washed with brine (100 ml), dried ($MgSO_4$), and concentrated, and the residue purified by flash chromatography (AcOEt/hexane 1:30): **2**.

*(−)-(3*R*)-1-(4-Methylphenyl)-3-phenylhexan-1-one* ((−)-**2a**): White solid. M.p. 44–46°. $[\alpha]_D^{20} = -4.09$ ($c = 1.0$, CH_2Cl_2); 91% ee (HPLC: t_R 8.96 (minor), 12.83 (major)). ^{1}H-NMR (400 MHz): 0.84 (*t*, *J* = 7.2, 3 H); 1.14–1.29 (*m*, 2 H); 1.58–1.70 (*m*, 2 H); 2.38 (*s*, 3 H); 3.21–3.23 (*m*, 2 H); 3.31–3.33 (*m*, 1 H); 7.15–7.29 (*m*, 7 H); 7.79–7.81 (*m*, 2 H). ^{13}C-NMR (100 MHz): 14.0; 20.6; 21.6; 38.4; 41.0; 45.7; 126.1; 126.7; 127.5; 127.8; 128.1; 128.3; 128.6; 129.1; 129.3; 134.6; 143.6; 145.0; 198.8. EI-MS: 266 (M^+). Anal. calc. for $C_{19}H_{22}O$: C 85.67, H 8.32; found: C 85.75, H 8.19.

*(+)-(3*S*)-1-(4-Methylphenyl)-3-phenylhexan-1-one* ((+)-**2a**): White solid. M.p. 44–46°. $[\alpha]_D^{20} = +4.21$ ($c = 0.51$, CH_2Cl_2); 95% ee (HPLC: t_R 9.09 (major), 13.33 (minor)).

*(−)-(3*R*)-1-(4-Methylphenyl)-3-phenylheptan-1-one* ((−)-**2b**): $[\alpha]_D^{19} = -9.55$ ($c = 0.48$, CH_2Cl_2); 86% ee (HPLC: t_R 8.51 (minor), 11.90 (major)). ^{1}H-NMR (400 MHz): 0.80 (*t*, *J* = 7.2, 3 H); 1.09–1.26 (*m*, 4 H); 1.61–1.69 (*m*, 2 H); 2.35 (*s*, 3 H); 3.18–3.21 (*m*, 3 H); 7.10–7.27 (*m*, 7 H); 7.79 (*d*, *J* = 8.4, 2 H). ^{13}C-NMR (100 MHz): 13.9; 21.4; 22.5; 29.6; 35.9; 41.2; 45.7; 125.6; 125.9; 126.1; 127.5; 127.9; 128.3; 128.6; 129.0; 129.1; 134.6; 143.5; 145.0; 198.7. EI-MS: 280 (M^+). Anal. calc. for $C_{20}H_{24}O$: C 85.67, H 8.63; found: C 85.73, H 8.99.

*(+)-(3*S*)-1-(4-Methylphenyl)-3-phenylheptan-1-one* ((+)-**2b**): $[\alpha]_D^{19} = +9.79$ ($c = 0.51$, CH_2Cl_2); 78% ee (HPLC: t_R 8.45 (major), 11.91 (minor)).

*(−)-(3*R*)-3-(4-Chlorophenyl)-1-(4-methylphenyl)pentan-1-one* ((−)-**2c**): $[\alpha]_D^{19} = -4.78$ ($c = 0.9$, CH_2Cl_2); 93% ee (HPLC: t_R 9.33 (minor), 18.33 (major)). ^{1}H-NMR (400 MHz): 0.79 (*t*, *J* = 7.2, 3 H); 1.59–1.61 (*m*, 1 H); 1.73–1.76 (*m*, 1 H); 2.39 (*s*, 3 H); 3.20–3.23 (*m*, 3 H); 7.13–7.27 (*m*, 6 H); 7.79 (*d*, *J* = 8.4, 2 H). ^{13}C-NMR (100 MHz): 11.9; 21.6; 29.2; 42.4; 45.2; 128.0; 128.2; 128.4; 128.9; 129.1; 129.2; 131.7; 134.5; 143.1; 143.8; 198.4. EI-MS: 286 (M^+). Anal. calc. for $C_{18}H_{19}ClO$: C 75.38, H 6.68; found: C 75.29, H 7.02.

*(+)-(3*S*)-3-(4-Chlorophenyl)-1-(4-methylphenyl)pentan-1-one* ((+)-**2c**): $[\alpha]_D^{19} = +11.78$ ($c = 0.9$, CH_2Cl_2); 89% ee (HPLC: t_R 9.25 (major), 18.52 (minor)).

*(−)-(3*R*)-3-(4-Chlorophenyl)-1-(4-methylphenyl)hexan-1-one* ((−)-**2d**): White solid. M.p. 45–46°. $[\alpha]_D^{20} = -4.33$ ($c = 0.9$, CH_2Cl_2); 80% ee (HPLC: t_R 9.35 (minor), 17.97 (major)). ^{1}H-NMR (400 MHz): 0.84 (*t*, *J* = 7.2, 3 H); 1.13–1.21 (*m*, 2 H); 1.55–1.67 (*m*, 2 H); 2.40 (*s*, 3 H); 3.18–3.20 (*m*, 2 H); 3.31–3.34 (*m*, 1 H); 7.11–7.27 (*m*, 6 H); 7.78 (*d*, *J* = 8.4, 2 H). ^{13}C-NMR (100 MHz): 13.9; 20.5; 21.5; 38.4; 40.4; 45.5; 125.8; 128.0; 128.1; 128.4; 128.8; 129.1; 129.2; 131.6; 134.5; 136.1; 143.4; 143.7; 198.3. EI-MS: 300 (M^+). Anal. calc. for $C_{19}H_{21}ClO$: C 75.86, H 7.04; found: C 75.73, H 7.24.

*(+)-(3*S*)-3-(4-Chlorophenyl)-1-(4-methylphenyl)hexan-1-one* ((+)-**2d**): White solid. M.p. 45–46°. $[\alpha]_D^{20} = +3.56$ ($c = 0.9$, CH_2Cl_2); 87% ee (HPLC: t_R 9.56 (major), 19.37 (minor)).

*(−)-(3*R*)-3-(4-Chlorophenyl)-1-(4-methylphenyl)heptan-1-one* ((−)-**2e**): White solid. M.p. 49–51°. $[\alpha]_D^{27} = -5.92$ ($c = 0.5$, CH_2Cl_2); 97% ee (HPLC: t_R 8.87 (minor), 16.47 (major)). ^{1}H-NMR (400 MHz): 0.82 (*t*, *J* = 7.2, 3 H); 1.08–1.30 (*m*, 4 H); 1.59–1.70 (*m*, 2 H); 2.39 (*s*, 3 H); 3.21 (*d*, *J* = 6.4, 2 H); 3.29 (*m*, 1 H); 7.14–7.25 (*m*, 6 H); 7.79 (*d*, *J* = 7.2, 2 H). ^{13}C-NMR (100 MHz): 13.9; 21.5; 22.5; 29.5; 36.0; 40.6; 45.5; 128.1; 128.4; 128.9; 129.2; 131.7; 134.5; 143.5; 143.8; 198.4. EI-MS: 314 (M^+). Anal. calc. for $C_{20}H_{23}ClO$: C 76.29, H 7.36; found: C 76.18, H 7.48.

*(+)-(3*S*)-3-(4-Chlorophenyl)-1-(4-methylphenyl)heptan-1-one* ((+)-**2e**): White solid. M.p. 49–51°. $[\alpha]_D^{27} = +5.84$ ($c = 0.5$, CH_2Cl_2); 95% ee (HPLC: t_R 8.83 (major), 16.99 (minor)).

*(−)-(3*R*)-3-(4-Fluorophenyl)-1-(4-methylphenyl)heptan-1-one* ((−)-**2f**): $[\alpha]_D^{19} = -6.5$ ($c = 0.48$, CH_2Cl_2); 79% ee (HPLC: t_R 9.08 (minor), 14.38 (major)). ^{1}H-NMR (400 MHz): 0.83 (*t*, *J* = 7.2, 3 H); 1.06–1.30 (*m*, 4 H); 1.56–1.72 (*m*, 2 H); 2.39 (*s*, 3 H); 3.18–3.30 (*m*, 3 H); 6.91–6.97 (*m*, 2 H); 7.09–7.28 (*m*, 4 H); 7.79 (*d*, *J* = 8, 2 H). ^{13}C-NMR (100 MHz): 13.9; 21.5; 22.5; 29.5; 36.1; 40.6; 45.8; 115.1; 125.9; 128.0; 128.8; 129.1; 129.2; 134.6; 140.6; 143.7; 161.2; 198.6. EI-MS: 298 (M^+). Anal. calc. for $C_{20}H_{23}FO$: C 80.50, H 7.77; found: C 80.51, H 7.81.

(+)-(3S)-3-(4-Fluorophenyl)-1-(4-methylphenyl)heptan-1-one ((+)-**2f**): $[\alpha]_D^{19} = +4.58$ ($c = 0.46$, CH_2Cl_2); 82% ee (HPLC: t_R 9.02 (major), 14.47 (minor)).

(−)-(3R)-3-(4-Methoxyphenyl)-1-(4-methylphenyl)heptan-1-one ((−)-**2g**): White solid. M.p. 46–48°. $[\alpha]_D^{19} = -4.45$ ($c = 0.47$, CH_2Cl_2); 97% ee (HPLC: t_R 12.22 (minor), 22.16 (major)). ^{1}H-NMR (400 MHz): 0.81 (*t*, *J* = 7.2, 3 H); 1.11–1.26 (*m*, 4 H); 1.59–1.70 (*m*, 2 H); 2.39 (*s*, 3 H); 3.16–3.19 (*m*, 3 H); 6.81 (*d*, *J* = 8.8, 2 H); 7.13 (*d*, *J* = 8.8, 2 H); 7.21 (*d*, *J* = 8, 2 H); 7.79 (*d*, *J* = 8, 2 H). ^{13}C-NMR (100 MHz): 13.9; 21.7; 22.5; 29.6; 36.1; 40.4; 46.0; 55.1; 113.6; 125.9; 127.9; 128.2; 128.3; 128.6; 129.0; 129.1; 134.7; 137.0; 143.5; 157.7; 198.9. EI-MS: 310 (M^+). Anal. calc. for $C_{21}H_{26}O_2$: C 81.25, H 8.44; found: C 81.47, H 8.67.

(+)-(3S)-3-(4-Methoxyphenyl)-1-(4-methylphenyl)heptan-1-one ((+)-**2g**): White solid. M.p. 46–48°. $[\alpha]_D^{19} = +4.58$ ($c = 0.48$, CH_2Cl_2); 96% ee (HPLC: t_R 11.71 (major), 21.35 (minor)).

(−)-(3R)-1,3-Bis(4-methylphenyl)pentan-1-one ((−)-**2h**): $[\alpha]_D^{19} = -5.5$ ($c = 1.2$, CH_2Cl_2); 93% ee (HPLC: t_R 8.37 (minor), 15.42 (major)). ^{1}H-NMR (400 MHz): 0.79 (*t*, *J* = 7.2, 3 H); 1.58–1.63 (*m*, 1 H); 1.73–1.78 (*m*, 1 H); 2.26–2.34 (*m*, 1 H); 2.30 (*s*, 3 H); 2.39 (*s*, 3 H); 7.02–7.15 (*m*, 4 H); 7.21–7.28 (*m*, 2 H); 7.81 (*d*, *J* = 8.4, 2 H). ^{13}C-NMR (100 MHz): 12.0; 20.8; 21.5; 29.1; 42.5; 45.5; 125.5; 125.9; 127.4; 127.8; 128.1; 128.7; 129.0; 129.4; 134.7; 135.9; 141.6; 143.7; 198.9. EI-MS: 266 (M^+). Anal. calc. for $C_{19}H_{22}O$: C 85.67, H 8.32; found: C 85.79, H 8.21.

(−)-(3R)-1,3-Diphenylpentan-1-one ((−)-**2i**): $[\alpha]_D^{23} = -5.6$ ($c = 1.49$, CH_2Cl_2) ([11]: $[\alpha]_D^{25} = -4.3$ ($c = 1.35$, EtOH)); 99% ee (HPLC: t_R 6.74 (minor), 8.57 (major)). ^{1}H-NMR (400 MHz): 0.80 (*t*, *J* = 7.2, 3 H); 1.56–1.67 (*m*, 1 H); 1.76–1.78 (*m*, 1 H); 3.21–3.30 (*m*, 3 H); 7.15–7.26 (*m*, 5 H); 7.41–7.46 (*m*, 2 H); 7.89–7.91 (*m*, 2 H). Other spectral and anal. data: in good agreement with those reported in [8][30–33].

(+)-(3S)-1,3-Diphenylpentan-1-one ((+)-**2i**): $[\alpha]_D^{24} = +5.2$ ($c = 1.5$, CH_2Cl_2) ([12]: $[\alpha]_D^{22} = +4.6$ ($c = 1.26$, EtOH)); 81% ee (HPLC: t_R 6.70 (major), 8.55 (minor)).

(−)-(3R)-3-(4-Chlorophenyl)-1-phenylpentan-1-one ((−)-**2j**): $[\alpha]_D^{25} = -4.7$ ($c = 1.5$, CH_2Cl_2) ([11]: $[\alpha]_D^{25} = -1.8$ ($c = 1.97$, EtOH)); 93% ee (HPLC: t_R 7.32 (minor), 10.72 (major)). ^{1}H-NMR (400 MHz): 0.80 (*t*, *J* = 7.2, 3 H); 1.56–1.67 (*m*, 1 H); 1.76–1.78 (*m*, 1 H); 3.21–3.26 (*m*, 3 H); 7.14–7.26 (*m*, 4 H); 7.52–7.59 (*m*, 2 H); 7.88 (*m*, 2 H). Other spectral and anal. data: identical to those given in [31][33].

(+)-(3S)-3-(4-Chlorophenyl)-1-phenylpentan-1-one ((+)-**2j**): $[\alpha]_D^{25} = +3.8$ ($c = 1.5$, CH_2Cl_2) ([12]: $[\alpha]_D^{24} = +1.5$ ($c = 1.13$, EtOH)); 88% ee (HPLC: t_R 7.32 (major), 10.87 (minor)).

(−)-(3R)-3-(4-Chlorophenyl)-1-(4-methoxyphenyl)heptan-1-one ((−)-**2k**): $[\alpha]_D^{20} = -9.6$ ($c = 1.5$, CH_2Cl_2); 80% ee (HPLC: t_R 9.02 (minor), 15.15 (major)). ^{1}H-NMR (400 MHz): 0.82 (*t*, *J* = 7.2, 3 H); 1.08–1.30 (br., 4 H); 1.57–1.73 (br., 2 H); 3.15–3.18 (*m*, 2 H); 3.27–3.31 (*m*, 1 H); 3.83 (*s*, 3 H); 6.89 (*d*, *J* = 8.8, 2 H); 7.15 (*d*, *J* = 8, 2 H); 7.25 (*d*, *J* = 8.8, 2 H); 7.87 (*d*, *J* = 8.8, 2 H). ^{13}C-NMR (100 MHz): 13.8; 22.5; 29.5; 35.9; 40.7; 45.3; 55.3; 113.6; 128.4; 128.8; 130.1; 130.2; 131.6; 143.5; 163.3; 197.2. EI-MS: 332 ($[M+2]^+$). Anal. calc. for $C_{20}H_{23}ClO_2$: C 72.61, H 7.01; found: C 72.79, H 7.08.

(+)-(3S)-3-(4-Chlorophenyl)-1-(4-methoxyphenyl)heptan-1-one ((+)-**2k**): $[\alpha]_D^{20} = +11.8$ ($c = 1.5$, CH_2Cl_2); 100% ee (HPLC: t_R 8.69 (major)).

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