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Asymmetric Michael Addition of Nitroalkanes to Prochiral Acceptors Catalyzed by Proline Rubidium Salts#

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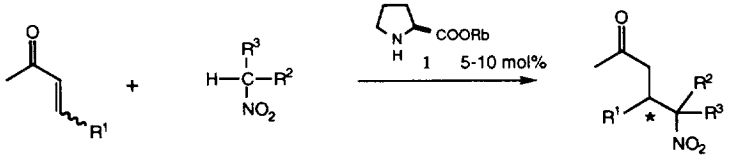
Abstract. Proline rubidium salts catalyze the asymmetric Michael addition of nitroalkanes to prochiral acceptors. When (2*S*)-*L*-prolines were used, acyclic (*E*)-enones gave (*S*)-adducts and cyclic (*Z*)-enones gave (*R*)-adducts predominantly. Enantiomeric excesses exceeding 80% were attained in some reactions of secondary nitroalkanes. Primary nitroalkanes gave mixtures of diastereomers which possess the same configuration at the β-carbon atom. The nitro group of the adducts can be replaced with hydrogen by Bu_3SnH reduction. The overall transformation is equivalent to an asymmetric β-alkylation of the enone. Functionalized nitroalkanes such as nitro alcohol, nitro ester, and nitroalkene may also be utilized in the reaction. © 1997 Elsevier Science Ltd.

Nucleophilic reactions of nitroalkanes are powerful methods of C-C bond formation. These reactions proceed under mild conditions and tolerate various functional groups. In addition, the nitro group can be converted into hydride, amine, carbonyl, *etc.*, by employing well-studied aliphatic nitro chemistry.[1] The Michael reaction is one of the most extensively studied nucleophilic reactions of nitroalkanes, and has been promoted by catalysts such as alkaline metal hydroxide, amine, ammonium hydroxides, alumina, fluoride anion, *etc.*[1] However, only sporadic reports of asymmetric catalysis in these reactions have appeared. Reaction of chalcone and nitromethane was studied to some extent, and 60% ee was attained using chiral amines.[2] In the presence of a nickel-amine catalyst, nitromethane added to 2-cyclohexenone with an enantiomeric excess of 6.5%.[3] The latter was the only example of an asymmetric reaction applied to aliphatic enones, when we started the present work.[4,5] We previously reported nitroalkane additions to prochiral acceptors using *L*-proline rubidium salt (**1**) (Scheme 1).[5] The method substantially broadened the scope of this asymmetric C-C bond formation, details of which are described here.



Scheme 1.

When an enone (1 mol eq) and a nitroalkane (1.5 mol eq) were reacted in chloroform in the presence of *L*-proline rubidium salt (5-10 mol%) at room temperature, an optically active γ-nitro ketone was obtained in a good yield (Table 1). Primary and secondary nitroalkanes reacted faster than nitromethane. It may be due to the lower acidity of nitromethane (p*K*a = 10.2) compared to nitroethane (p*K*a = 8.6) and 2-nitropropane (p*K*a = 7.7).[6] The more substituted nitroalkanes exhibited higher enantiomeric excesses. This asymmetric reaction can be applied to both cyclic and acyclic enones. 2-Cycloheptenone is a good substrate, and

Dedicated to Professor Sam Danishefsky on the occasion of his 60th birthday.

enantiomeric excess as high as 84% ee was attained in its reaction with nitrocyclohexane. An enal also gave an optically active nitro aldehyde in a good chemical yield, though in a meager 29% ee. α,β-Disubstituted enones (2-methyl-2-cyclopentenone and 2-methyl-2-pentenal) and β,β-disubstituted enones (3-methyl-2-cyclohexenone and 4-methyl-3-penten-2-one) were inert.

Table 1. Asymmetric Michael Addition of Nitroalkane to Enone and Enal.

enone/enal	nitroalkane	**1**/mol%	time/h	yield/%[a]	ee/%	config[b]
2-cycloheptenone	CH_3NO_2	5	43	47 [c]	41	(+)
	i-$C_3H_7NO_2$	5	43	79	73	*R*
	cyclo-$C_5H_9NO_2$	10	24	74	67	(+)
	cyclo-$C_6H_{11}NO_2$	10	20	84	84	(+)
2-cyclohexenone	CH_3NO_2	5	51	55 [c]	45	(+)
	n-$C_4H_9NO_2$	5	19	84 [1 : 1.4]	53, 47	*R*, *R*
	i-$C_3H_7NO_2$	5	24	81	59	*R*
(*E*)-3-penten-2-one	CH_3NO_2	5	17	47 [c]	42	(+)
	n-$C_4H_9NO_2$	5	21	64 [1 : 1]	40, 55	*S*, *S*
	i-$C_3H_7NO_2$	5	17	74	68	*S*
	cyclo-$C_5H_9NO_2$	10	24	64	59	(−)
	cyclo-$C_6H_{11}NO_2$	10	62	57	52	(−)
(*E*)-3-nonen-2-one	*i*-$C_3H_7NO_2$	10	39	91	60	(+)
(*E*)-2-hexenal	*i*-$C_3H_7NO_2$	5	24	61	29	(+)

a) Ratio of diastereomer is shown in [:]. b) The absolute configuration at the β-carbon atom of carbonyl group. In case the absolute configuration was not determined, the sign of the optical rotation is shown. c) 10 mol eq of nitromethane were used.

The effect of the catalyst structure in this asymmetric nitroalkane addition is similar to that in the malonate addition, which was reported previously.[4] The following amino acid rubidium salts were not effective with respect to both catalytic activity and stereoselectivity; *L*-piperidinecarboxylate, *N*-methyl-*L*-leucinate, *N*-benzy-*L*-alaninate, *N*-benzyl-*L*-leucinate, *L*-thiazoline-4-carboxylate, and 2-methyl-*L*-thiazoline-4-carboxylate. Since the proline structure appeared to be essential, rubidium salts of several hydroxyproline derivatives were examined; (2*S*,4*R*)-4-(*t*-butyldimethylsilyloxy)prolinate (**2**), (2*R*,4*R*)-4-(*t*-butyldimethylsilyloxy)prolinate (**3**), (2*S*,3*R*,4*S*)-3,4-bis(*t*-butyldimethylsilyloxy)prolinate (**4**), and (2*S*,3*R*,4*S*)-3,4-bis(*t*-butyldiphenylsilyloxy)prolinate (**5**). As shown in Table 2, the stereochemistry is primarily governed by the COORb group at the 2-position. A siloxy group at positions 3 or 4 had only a minor influence on the reaction. Acetonide **7** (R = Me) and cyclohexylidene **7** (R = $(CH_2)_5$) did not promote the addition itself. Rubidium *L*-azetidinecarboxylate (**6**) showed comparable asymmetric induction to **1**.

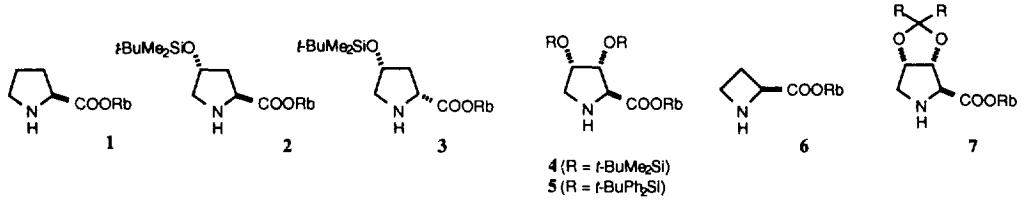
The tertiary nitro derivatives obtained by the addition of the secondary nitroalkanes can readily be denitrated under radical conditions giving β-alkyl ketones.[7] The transformation does not affect the optical purities as shown by reactions of (+)-**8**, (*R*)-(+)-**10**, and (+)-**12** (Scheme 2). The absolute configuration of (*R*)-(+)-**10** was determined by correlation with the known (*R*)-(+)-**11**.[8] The reduction converted (*S*)-(−)-**13** and (*S*)-(−)-**16** to (*S*)-(−)-**14** and (*S*)-(−)-**17**, which were correlated to (*S*)-(−)-**15** and (*R*)-(+)-**18**,[4] respectively. (*R*)-Adducts were obtained from cyclic (*Z*)-enones and (*S*)-adducts from acyclic (*E*)-enones, when (2*S*)-*L*-proline rubidium salts were used. The absolute configurations of the products thus obtained coincide with

those of the products of malonate addition,[4] suggesting that a similar mechanism is involved in both reactions.

Table 2. Effect of Amino Acid Structure on the Asymmetric Michael Addition.

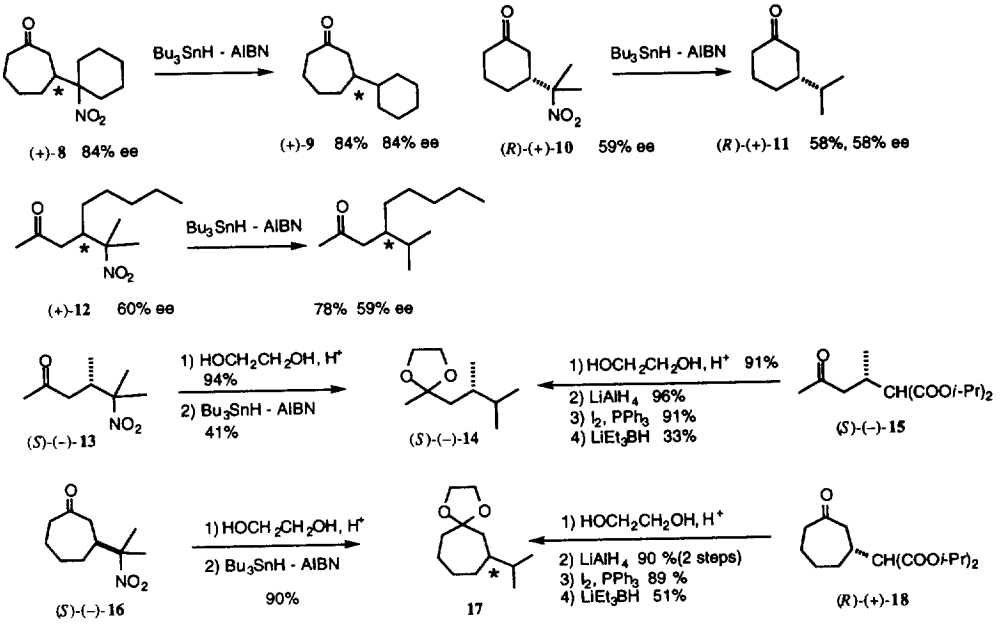
enone	nitroalkane	catalyst	mol%	time/h	yield/%	ee/%	config.[a]
2-cycloheptenone	*i*-$C_3H_7NO_2$	**1**	10	43	79	73	*R*
		2	10	15	70	72	*R*
		3	10	43	70	79	*S*
		4	10	24	73	76	*R*
		5	10	48	41	82	*R*
	cyclo-$C_6H_{11}NO_2$	**1**	10	20	84	84	(+)
		3	10	24	74	86	(–)
2-cyclohexenone	*i*-$C_3H_7NO_2$	**1**	5	24	81	59	*R*
		3	10	24	94	60	*S*
		6	10	23	40	56	*R*
(*E*)-3-penten-2-one	*i*-$C_3H_7NO_2$	**1**	5	17	74	68	*S*
		2	10	15	80	66	*S*
		3	10	14	76	38	*R*
		4	10	17	53	69	*S*
		5	10	17	61	63	*S*
	cyclo-$C_5H_9NO_2$	**1**	10	24	64	59	(–)
		5	10	21	66	63	(–)

a) In case the absolute configuration was not determined, the sign of the optical rotation is shown.

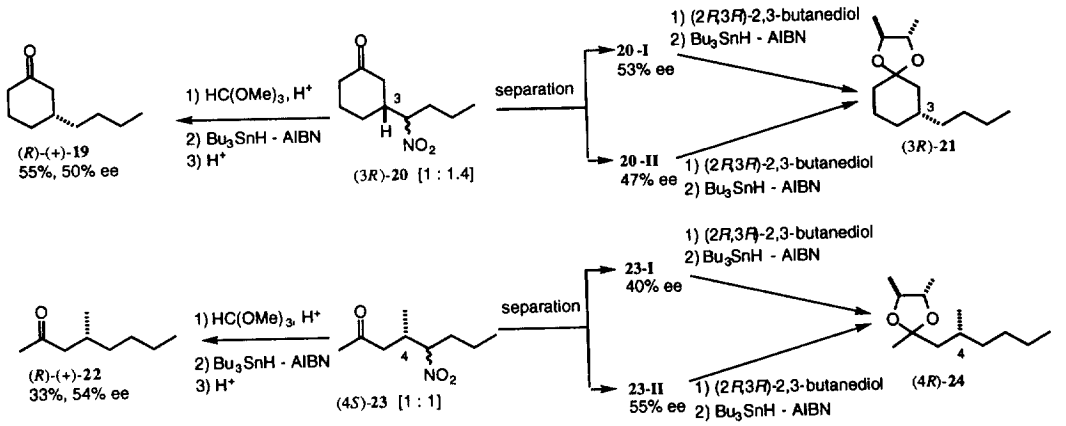


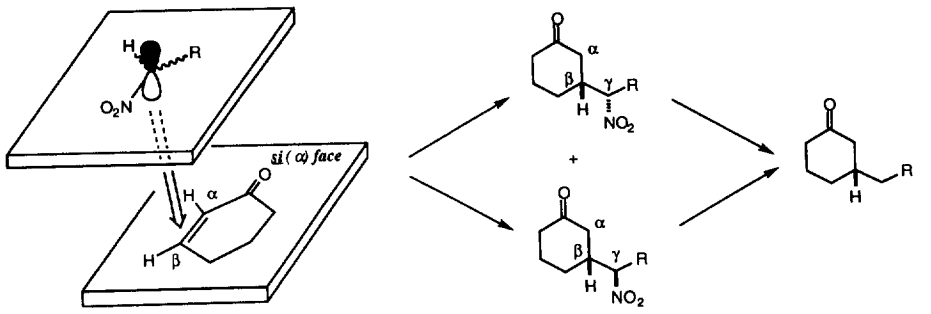
Two diastereoisomers were formed in reaction of primary nitroalkanes. Their ratios are shown in [:] throughout this paper. No epimerization took place when the individual diastereomers of compound **20**, substances **20-I** and **20-II**, were exposed to rubidium prolinate under standard reaction conditions, indicating that the two products were probably formed under kinetic control. Ketalization of each isomer **20-I** and **20-II** with (2*R*,3*R*)-2,3-butanediol showed that the optical purities were comparable (Scheme 3). Radical denitration of these ketals with Bu_3SnH furnished the same end-product, compound **21**. Essentially the same results were obtained with **23**. Thus, the diastereomers formed by the asymmetric addition possess the same configuration at the β-carbon atom, and are isomeric at the γ-carbon atom attached to the nitro group. This implies that the proline catalyst controls the stereochemistry of the C-C bond forming β-carbon atom, and marginally affects that of the γ-carbon atom.

In the previous report,[4] we defined enantiofaces of enones as *si*(α) or *re*(β), which indicate the *si*-face concerning the α-carbon atom and the *re*-face concerning the β-carbon atom, respectively. The underline denotes our proposed sequence rule giving the highest priority to C= group. Based on these, α-enantioface



Scheme 2.



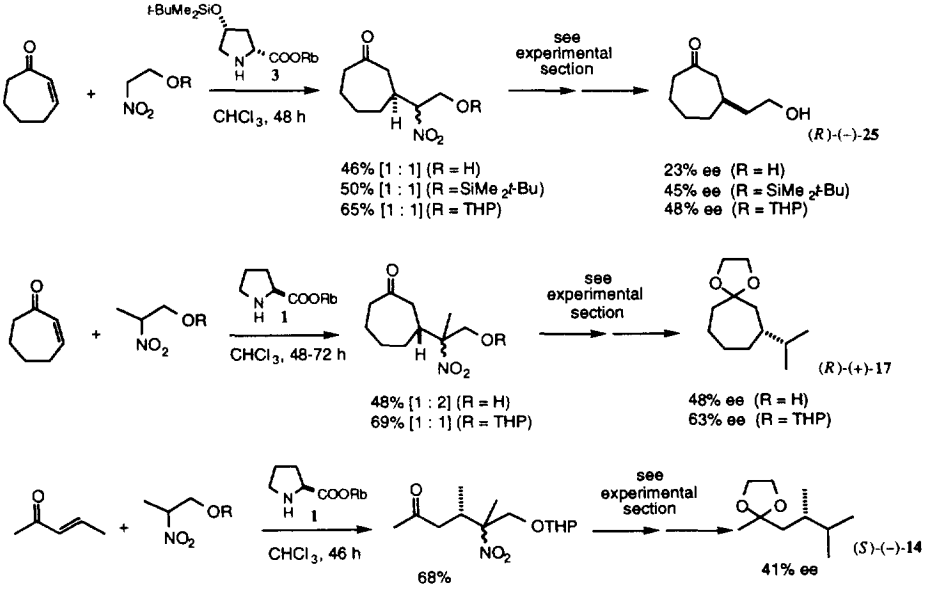


Scheme 3.

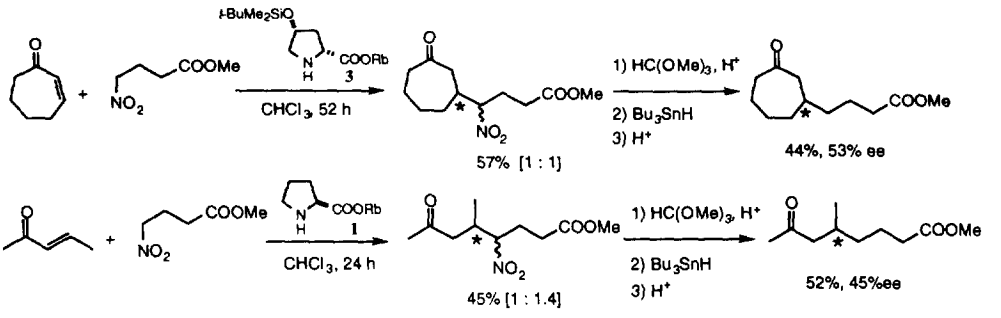
discriminating mechanism and β-enantioface discriminating mechanism were discussed in the asymmetric conjugate addition reactions.[4,9] Reactions can be classified in either of the two enantioselection modes by the absolute configuration of the adducts derived from (*E*)- and (*Z*)-acceptors. The addition of both nitroalkane and malonate gave (*R*)-adducts from (*Z*)-enones and (*S*)-adducts from (*E*)-enones, when *L*-proline rubidium salt was used as catalyst. Since all these reactions proceed *via* *si*(α)-attack of the nucleophiles, they are considered to involve an α-enantioface discriminating mechanism. Probably, the chiral catalyst is located in the vicinity of the α-carbon atom of the acceptors rather than the β-carbon atom in the transition state, and effectively differentiates the enantiofaces of the Michael acceptors. The relative stereochemistry in the asymmetric reactions of primary nitroalkanes mentioned above is consistent with the argument.

The sequence of asymmetric nitroalkane addition and radical denitration introduces primary or secondary alkyl groups at the β-position of enones. The formation of two diastereomers in the reaction of primary nitroalkanes does not impair the overall transformation, since they possess the same configuration at the β-carbon atom. The nitro group therefore can be removed without separation of isomers. The diastereomeric mixtures of (3*R*)-**20** and (4*S*)-**23** were denitrated to give optically active ketones (*R*)-(+)-**19**[10] and (*R*)-(+)-**22**,[11] respectively. Their optical purities were in accordance with the value calculated based on the diastereomer ratios and the enantiomeric excess of each isomer. The secondary nitro derivatives are less reactive compared to the tertiary derivatives towards the radical reduction. *Retro*-Michael addition took place in an attempted reduction of 5-nitro-4-phenyl-2-hexanone. The carbonyl group therefore was protected as dimethyl acetal prior to the Bu_3SnH treatment.

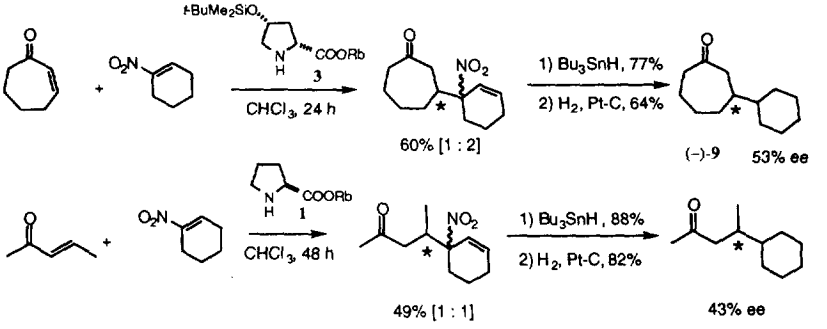
Functionalized nitroalkanes were added to enones using catalysts **1** and **3**. 2-Nitroethanol added smoothly to 2-cycloheptenone giving a hydroxy ketone (*R*)-(−)-**25** after the radical reduction (Scheme 4). The low optical purity was improved by protecting the hydroxyl group as *t*-butyldimethylsilyl ether or as tetrahydropyranyl (THP) ether. Derivatives of 2-nitro-1-propanol showed higher selectivities than those of 2-nitroethanol.



Scheme 4.



Scheme 5.



Scheme 6.

Optically active keto esters were obtained by the reaction of a nitro ester followed by the Bu_3SnH reduction (Scheme 5). 1-Nitro-1-cyclohexene added at the α-carbon atom regioselectively (Scheme 6).[12] The diastereomeric unsaturated γ-nitro ketones were denitrated with Bu_3SnH and then hydrogenated with Pt-C for determination of the stereoselectivity. The absolute configurations of the adducts synthesized from the functionalized nitroalkanes were the same with those of the parent nitroalkanes.

The asymmetric catalytic conjugate addition of organocopper or organozinc reagents[13] to enones is a synthetic equivalent of the present two-steps β-alkylation. The nitroalkane method has several advantages compared to the organometallic method: 1) It is relatively insensitive to air and moisture. 2) It can be applied to both cyclic and acyclic enones. 3) Reasonable enantioselectivity was attained in the introduction of primary and secondary alkyl groups. 4) It tolerates sensitive functionalities.

To summarize, proline rubidium salts promote the catalytic asymmetric Michael addition of nitroalkanes to prochiral acceptors. Although improvement in the enantioselectivity is still needed, the present methodology considerably broadens the scope of this asymmetric synthesis.

Experimental Section

(2*S*,4*R*)-3-(*t*-Butyldimethylsilyloxy)-*L*-proline and (2*R*,4*R*)-3-(*t*-butyldimethylsilyloxy)-*L*-proline are known.[14] See the previous report[4] for other general procedures.

(2*R*,3*R*,4*S*)-(+)-3,4-Bis(*t*-butyldimethylsilyloxy)-*L*-proline. To a solution of methyl (2*R*,3*R*,4*S*)-3,4-dihydroxy-1-benzyl-oxycarbonyl-*L*-prolinate (635 mg, 2.15 mmol)[15] in methanol (4 mL) was added 2 M NaOH (2 mL), and the mixture was stirred for 30 min at room temperature. Then, the solution was cooled to 0 °C, and was acidified by slow addition of 2 M HCl. The organic materials were extracted with ethyl acetate, dried over $MgSO_4$, and concentrated. Under an argon atmosphere, to the residue were added DMF (15 mL), *t*-butyldimethylsilyl chloride (1.12 g, 7.46 mmol), and imidazole (872 mg, 12.8 mmol), and the mixture was stirred at 70 °C for 12 h. After cooled to room temperature, water was added. The organic materials were extracted with ether,

washed with 10% phosphoric acid, with saturated aqueous $NaHCO_3$, and with brine. After dried over $MgSO_4$, the solvents were removed *in vacuo*, and the residue was flash chromatographed over silica gel (hexane : ethyl acetate = 3 : 2) giving (2*R*,3*R*,4*S*)-1-benzyloxycarbonyl-3,4-bis(*t*-butyldimethylsilyloxy)-*L*-proline (488 mg, 45%). Mp 165-166°C (hexane-ethyl acetate). ^{1}H-NMR (200 Hz, $CDCl_3$) δ 0.0-0.2 (12H, m), 0.8-1.0 (18H, m), 3.3-3.8 (2H, m), 4.1-4.4 (3H, m), 5.13 (1H, s), 5.15 (0.5H, d, *J* = 12.3 Hz), 5.23 (0.5H, d, *J* = 12.2 Hz), 7.2-7.5 (5H, m). Recrystallized acid (80 mg, 0.16 mmol) was dissolved in methanol (4 mL), and stirred under hydrogen in the presence of 5% Pd-C (25 mg) for 3 h. After filtration of the insoluble materials, the solvent was removed *in vacuo* to give the amino acid (48 mg, 82%). Mp 178-179 °C (MeOH-water). $[\alpha]_D^{28}$ +3.8 (c 0.66, MeOH). ^{1}H-NMR (200 MHz, CD_3OD) δ 0.13 (6H, s), 0.18 (3H, s), 0.22 (3H, s), 0.94 (9H, s), 0.97 (9H, s), 3.13 (1H, dd, *J* = 9.4, 10.6 Hz), 3.48 (1H, dd, *J* = 6.8, 10.6 Hz), 3.86 (1H, d, *J* = 1.6 Hz), 4.25 (1H, ddd, *J* = 3.4, 6.8, 9.2 Hz), 4.44 (1H, dd, *J* = 1.6, 3.4 Hz). ^{13}C-NMR (125 MHz, CD_3OD) δ -4.8, -4.6, -4.3, 19.0, 19.1, 26.4, 26.4, 48.0, 68.8, 72.7, 76.9, 171.1.

(2*R*,3*R*,4*S*)-(+)-3,4-Bis(*t*-butyldiphenylsilyloxy)-*L*-proline. (2*R*,3*R*,4*S*)-1-Benzyloxycarbonyl-3,4-bis(*t*-butyldiphenyl-silyloxy)-*L*-proline was obtained in 38% yield as above. Mp 72-74 °C. ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1.07 (9H, s), 1.12 (9H, s), 3.07 (0.5H, dd, *J* = 6.4, 10.2 Hz), 3.2-3.6 (1.5H, m), 4.0-4.2 (2H, m), 4.34 (0.5H, brs), 4.52 (0.5H, brs), 4.86 (0.5H, d, *J* = 12.4 Hz), 5.02 (0.5H, d, *J* = 12.4 Hz), 5.03 (1H, s), 7.0-7.5 (17H, m), 7.5-7.8 (8H, m). The protecting group was removed in 67% yield. Mp 202 °C (MeOH-water). $[\alpha]_D^{28}$ +10.7 (c 0.1, MeOH). ^{1}H-NMR (500 MHz, CD_3OD) δ 1.00 (9H, s), 1.16 (9H, s), 2.85 (1H, dd, *J* = 7.5, 10.5 Hz), 3.21 (1H, t, *J* = 10.5 Hz), 3.73 (1H, s), 4.13 (1H, ddd, *J* = 3.4, 7.2, 10.5 Hz), 4.88 (1H, d, *J* = 3.5 Hz), 7.28 (2H, t, *J* = 7.5 Hz), 7.38-7.50 (12H, m), 7.61 (2H, dd, *J* = 1.0, 8.0 Hz), 7.81 (2H, dd, *J* = 1.0, 8.0 Hz), 7.83 (2H, dd, *J* = 1.0, 8.0 Hz).

The Michael Addition of Nitroalkanes. (+)-3-(1-Nitrocyclohexyl)cycloheptanone, (+)-8. Under an argon atmosphere, a mixture of 2-cycloheptenone (0.20 mL, 1.79 mmol), nitrocyclohexane (0.33 mL, 2.71 mmol), and *L*-proline rubidium salt (**1**, 38 mg, 0.18 mmol) was stirred in chloroform (2 mL) at room temperature for 20 h. After quenched with 1 M HCl, the organic materials were extracted twice with ethyl acetate. The combined extracts were washed with water and brine, dried over Na_2SO_4, filtered, concentrated, and flash chromatographed over silica gel giving (+)-**8** (354 mg, 83%). Mp 41-42 °C (acetone-water). $[\alpha]_D^{22}$ +41.7 (c 1.0, $CHCl_3$, 84% ee). ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1.2-2.2 (16H, m), 2.3-2.5 (5H, m). ^{13}C-NMR (50 MHz, $CDCl_3$) δ 22.0, 22.1, 24.4, 24.6, 28.5, 30.6, 30.7, 31.4, 43.1, 44.5, 44.8, 95.0, 212.0. IR (neat) 1707 cm^{-1}. HRMS Calcd for $C_{13}H_{21}NO_3$: 239.1522. Found: 239.1531. Anal. Calcd for $C_{13}H_{21}NO_3$. C; 65.25, H; 8.84, N; 5.85%. Found. C; 64.87, H; 8.59, N; 5.84%. The enantiomeric excess was determined by ^{13}C-NMR (50MHz, $CDCl_3$) of the ketal with (2*R*,3*R*)-2,3-butanediol observing at δ 24.8/26.4, 28.0/28.5, and 109.5/110.3.

(+)-3-(Nitromethyl)cycloheptanone. $[\alpha]_D^{27}$ +25.1 (c 1.0, $CHCl_3$, 41% ee). ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1.30-1.74 (4H, m), 1.84-2.06 (2H, m), 2.40-2.74 (5H, m), 4.31 (2H, d, *J* = 6.8 Hz). ^{13}C-NMR (50 MHz, $CDCl_3$) δ 23.8, 27.8, 33.4, 34.6, 43.6, 46.2, 80.5, 211.0. IR (neat) 1702, 1551 cm^{-1}. Anal. Calcd for $C_8H_{13}NO_3$. C; 56.13, H; 7.65, N; 8.18%. Found. C; 56.11, H; 7.70, N; 8.10%. The enantiomeric excess was determined by ^{13}C-NMR (50MHz, $CDCl_3$) of the ketal with (2*R*,3*R*)-2,3-butanediol observing at δ 22.1/22.3, 40.2/40.4, and 42.2/42.7.

(*R*)-(+)-3-(2-Nitropropan-2-yl)cycloheptanone, (*R*)-(+)-17. $[\alpha]_D^{26}$ +51.8 (c 1.0, $CHCl_3$, 73% ee). ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1.12-1.84 (4H, m), 1.53 (3H, s), 1.55 (3H, s), 1.90-2.10 (2H, m), 2.34-2.70 (5H, m). ^{13}C-NMR (50 MHz, $CDCl_3$) δ 22.1, 23.8, 24.7, 29.0, 31.6, 43.3, 44.1, 45.2, 92.2, 211.8. IR (neat) 1705 cm^{-1}. Anal. Calcd for $C_{10}H_{17}NO_3$. C; 60.28, H; 8.60, N; 7.03%. Found. C; 60.08, H; 8.71, N; 6.97%. The enantiomeric excess was determined by ^{1}H-NMR (600MHz, $CDCl_3$) of the ketal with (2*R*,3*R*)-2,3-butanediol observing at δ 2.37 (ddt, *J* = 11.5, 8.8, 2.5 Hz) and 2.51 (dddd, *J* = 11.0, 9.5, 3.5, 3.0 Hz). Essentially the same enantiomeric excess (79% ee) was obtained when this adduct was reacted with (2*S*,3*S*)-2,3-butanediol. Kinetic resolution during the ketalization is negligible.

(+)-3-(1-Nitrocyclopentyl)cycloheptanone. $[\alpha]_D^{23}$ +34.4 (c 1.0, $CHCl_3$, 67% ee). ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1.2-2.1 (12H, m), 2.2-2.7 (7H, m). ^{13}C-NMR (50 MHz, $CDCl_3$) δ 24.0, 24.1, 24.2, 28.5, 32.1, 34.8, 35.1, 43.1, 43.6, 45.6, 103.9, 211.9. IR (neat) 1705 cm^{-1}. Anal. Calcd for $C_{12}H_{19}NO_3$: C; 63.98, H; 8.50, N; 6.22%. Found: C; 63.80, H; 8.36, N; 6.17%. The enantiomeric excess was determined by ^{13}C-NMR (50MHz, $CDCl_3$) of the ketal with (2*R*,3*R*)-2,3-butanediol observing at δ 21.6/22.2 and 35.2/35.8.

(+)-3-(Nitromethyl)cyclohexanone. $[\alpha]_D^{27}$ +9.4 (c 1.0, $CHCl_3$, 45% ee). Lit.[3] $[\alpha]_D^{20}$ –0.67 (c 2.37, benzene, 6.5% ee). ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1.00-2.80 (9H, m), 4.33-4.41 (2H, m). ^{13}C-NMR (50 MHz, $CDCl_3$) δ 24.0, 28.0, 37.0, 40.7, 44.2, 79.9, 208.2. IR (neat) 1713, 1545 cm^{-1}. Anal. Calcd for $C_7H_{11}NO_3$. C; 53.49, H; 7.05, N; 8.91%. Found. C; 53.29, H; 7.15, N; 8.91%. The enantiomeric excess was determined by ^{13}C-NMR (50MHz, $CDCl_3$) of the ketal with (2*R*,3*R*)-2,3-butanediol observing at δ 21.8/22.1, 34.5/34.9, 35.7/36.5, and 39.5/40.3.

(3*R*)-3-(1-Nitrobutyl)cyclohexanone. (3*R*)-20. Less polar isomer **20-I**: $[\alpha]_D^{28}$ +18.1 (c 1.0, $CHCl_3$, 53% ee). ^{1}H-NMR (200 MHz, $CDCl_3$) δ 0.95 (3H, t, *J* = 7.0 Hz), 1.23-1.41 (2H, m), 1.41-1.78 (4H, m), 1.78-2.58 (7H, m), 4.38 (1H, ddd, *J* = 10.8, 7.6, 3.3 Hz). ^{13}C-NMR (50 MHz, $CDCl_3$) δ 13.3, 19.0, 24.1, 27.3, 32.5, 40.8, 41.6, 43.7, 92.4, 208.5. IR (neat) 1717, 1551 cm^{-1}. Anal. Calcd for $C_{10}H_{17}NO_3$. C; 60.28, H; 8.60, N; 7.03%. Found. C; 60.27, H; 8.47, N; 6.93%. The enantiomeric excess was determined by ^{13}C-NMR (50MHz, $CDCl_3$) of the ketal with (2*R*,3*R*)-2,3-butanediol observing at δ 21.8/22.2, 35.7/36.6, and 39.2/39.7. Polar isomer **20-II**: $[\alpha]_D^{28}$ -7.1 (c 1.0, $CHCl_3$, 47% ee). ^{1}H-NMR (200 MHz, $CDCl_3$) δ 0.96 (3H, t, *J* = 7.2 Hz), 1.22-1.80 (6H, m), 1.90-2.57 (7H, m), 4.44 (1H, ddd, *J* = 10.6, 6.2, 3.6 Hz). ^{13}C-NMR (50 MHz, $CDCl_3$) δ 13.3, 19.1, 24.3, 27.5, 32.5, 40.7, 41.4, 43.3, 92.4, 208.5. IR (neat) 1717, 1549 cm^{-1}. Anal. Calcd for $C_{10}H_{17}NO_3$. C; 60.28, H; 8.60, N; 7.03%. Found. C; 60.21, H; 8.60, N; 7.09%. The enantiomeric excess was determined by ^{13}C-NMR (50MHz, $CDCl_3$) of the ketal with (2*R*,3*R*)-2,3-butanediol observing at δ 22.1/22.5, 35.7/36.6, and 39.2/39.5. Treatment of the each ketal with Bu_3SnH gave the (2*R*,3*R*)-2,3-butanediol ketal of 3-butylcyclohexanone, (3*R*)-**21** with a similar composition. ^{1}H-NMR (200 MHz, $CDCl_3$) δ 0.70-0.86 (3H, m), 1.06-1.72 (21H, m), 3.47-3.62 (2H, m). ^{13}C-NMR (50 MHz, $CDCl_3$, the minor isomer in *italic*) δ 14.0, 17.0, 17.1, 22.9, *23.3*, 29.0, 31.8, *35.0*, 35.5, *36.1*, 36.7, *36.7*, 37.1, 43.0, *43.9*, 77.6, 78.0, 108.5.

(*R*)-(+)-3-(2-Nitropropan-2-yl)cyclohexanone, (*R*)-(+)-10. Mp 63-65 °C (hexane). $[\alpha]_D^{27}$ +15.0 (c 1.0, $CHCl_3$, 59% ee). ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1.22-1.55 (2H, m), 1.57 (3H, s), 1.58 (3H, s), 1.60-1.91 (2H, m), 2.20-2.52 (5H, m). ^{13}C-NMR (50 MHz, $CDCl_3$) δ 22.5, 23.1, 24.2, 25.8, 40.6, 42.5, 46.4, 90.5, 208.8. IR (KBr) 1717, 1537 cm^{-1}. Anal. Calcd for $C_9H_{15}NO_3$. C; 58.36, H; 8.16, N; 7.56%. Found. C; 58.11, H; 8.18, N; 7.50%. The enantiomeric excess was determined by ^{1}H-NMR (600MHz, C_6D_6) of the ketal with (2*R*,3*R*)-2,3-butanediol observing at δ 0.96 (dd, *J* = 6.0, 1.5 Hz)/0.98 (dd, *J* = 5.8, 1.5 Hz).

(+)-4-Methyl-5-nitro-2-pentanone. $[\alpha]_D^{26}$ +2.4 (c 1.0, $CHCl_3$, 42% ee). ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1.07 (3H, dd, *J* = 6.8, 0.7 Hz), 2.17 (3H, s), 2.49 (1H, dd, *J* = 17.8, 6.8 Hz), 2.61 (1H, dd, *J* = 17.8, 6.3 Hz), 2.79 (1H, octet, *J* = 6.6 Hz), 4.34 (1H, ddd, *J* = 11.8, 6.4, 0.7 Hz), 4.43 (1H, ddd, *J* = 11.8, 6.1, 0.7 Hz). ^{13}C-NMR (50 MHz, $CDCl_3$) δ 17.2, 28.0, 30.2, 46.3, 80.1, 206.3. IR (neat) 1717, 1553 cm^{-1}. HRMS Calcd for $C_6H_{11}NO_3$: 145.0739. Found: 145.0739. Anal. Calcd for $C_6H_{11}NO_3$. C; 49.65, H; 7.64, N; 9.65%. Found. C; 48.98, H; 7.66, N; 9.93%. The enantiomeric excess was determined by ^{1}H-NMR (400MHz, C_6D_6) of the ketal with (2*R*,3*R*)-2,3-butanediol observing at δ 4.67 (dd, *J* = 12.0, 4.8 Hz)/4.78 (dd, *J* = 12.0, 4.6 Hz).

(4*S*)-4-Methyl-5-nitro-2-octanone, (4*S*)-23. Less polar isomer **23-I**: $[\alpha]_D^{27}$ -3.0 (c 24, $CHCl_3$, 40% ee). ^{1}H-NMR (200 MHz, $CDCl_3$) δ 0.95 (3H, t, *J* = 8.0 Hz), 0.97 (3H, d, *J* = 6.9 Hz), 1.34 (2H, sextet, *J* = 7.4 Hz), 1.52-1.69 (1H, m), 1.97-2.16 (1H, m), 2.17 (3H, s), 2.37 (1H, dd, *J* = 16.4, 5.8 Hz), 2.43-2.58 (1H, m), 2.65 (1H, dd, *J* = 16.5, 5.8 Hz), 4.53 (1H, dt, *J* = 10.3, 4.2 Hz). ^{13}C-NMR (50 MHz, $CDCl_3$) δ 13.4, 14.8, 19.3, 30.5, 32.0, 32.6, 46.5, 91.1, 206.4. IR (neat) 1717, 1549 cm^{-1}. Anal. Calcd for $C_9H_{17}NO_3$. C; 57.51, H; 9.05, N; 7.40%. Found. C; 57.73, H; 9.15, N; 7.48%. The enantiomeric excess was determined by ^{1}H-NMR (600MHz, $CDCl_3$) of the ketal with (2*R*,3*R*)-2,3-butanediol observing at δ 4.47 (ddd, *J* = 10.5, 6.0, 3.6 Hz)/4.54 (ddd, *J* = 10.5, 6.0, 3.6 Hz). Polar isomer **23-II**: $[\alpha]_D^{23}$ –0.2 (c 25, $CHCl_3$, 55% ee). ^{1}H-NMR (200 MHz, $CDCl_3$) δ 0.94 (3H, t, *J* = 7.2 Hz), 1.01 (3H, d, *J* = 6.5 Hz), 1.22-1.44 (2H, m), 1.55-1.75 (1H, m), 1.85-2.08 (1H, m), 2.15 (3H, s), 2.36 (1H, dd, *J* = 17.9, 9.4 Hz), 2.45-2.72 (2H, m), 4.44 (1H, ddd, *J* = 10.6, 6.5, 3.4 Hz). ^{13}C-NMR (50 MHz, $CDCl_3$) δ 13.4, 16.5, 19.2, 30.4, 32.4, 32.6, 45.7, 92.5, 206.2. IR (neat) 1717, 1549 cm^{-1}. Anal. Calcd for $C_9H_{17}NO_3$. C; 57.70, H; 9.24, N; 7.36%. Found. C; 57.73, H; 9.15, N; 7.48%. The enantiomeric excess was determined by ^{1}H-NMR (600MHz, $CDCl_3$) of the ketal with (2*R*,3*R*)-2,3-butanediol observing at δ 4.57 (ddd, *J* = 10.9, 5.1, 2.8 Hz)/4.69 (ddd, *J* = 10.9, 4.7, 2.7 Hz). Treatment of the each ketal with Bu_3SnH gave the (2*R*,3*R*)-2,3-butanediol ketal of 4-methyl-2-octanone, (4*R*)-**24** with a similar composition. ^{1}H-NMR (200 MHz, $CDCl_3$) δ 0.81-1.01 (6H, m), 1.05-1.73 (15H, m), 1.35 (3H, s), 3.49-3.74 (2H, m). ^{13}C-NMR (50 MHz, $CDCl_3$, the minor isomer in *italic*) δ 14.1, 16.6, 17.1, 21.1, *21.2*, 22.9, 26.0, *26.1*, *28.7*, 28.9, 29.2, *37.8*, 38.0, 46.9, *47.0*, 77.7, *77.9*, *78.4*, 78.5, 109.6.

(*S*)-(–)-4,5-Dimethyl-5-nitro-2-hexanone, (*S*)-(–)-13. $[\alpha]_D^{26}$ -8.7 (c 1.0, $CHCl_3$, 68% ee). ^{1}H-NMR (200 MHz, $CDCl_3$) δ 0.93 (3H, d, *J* = 6.8 Hz), 1.53 (3H, s), 1.54 (3H, s), 2.15 (3H, s), 2.28 (1H, dd, *J* = 17.0, 9.9 Hz), 2.45 (1H, dd, *J* = 17.0, 2.9 Hz), 2.77 (1H, dqd, *J* = 9.9, 6.8, 2.9 Hz). ^{13}C-NMR (50 MHz, $CDCl_3$) δ 15.0, 22.4, 23.8, 30.2, 37.0, 45.5, 91.3, 206.0. IR (neat) 1721 cm^{-1}. Anal. Calcd for $C_8H_{15}NO_3$. C; 55.47, H; 8.73, N; 8.09%. Found. C; 55.18, H; 8.54, N; 7.99%. The enantiomeric excess was determined by ^{1}H-NMR (600MHz, C_6D_6) of the ketal with (2*R*,3*R*)-2,3-butanediol observing at δ 0.96 (d, *J* = 5.7 Hz)/0.98 (d, *J* = 5.7 Hz) and 1.18 (s)/1.19 (s) or by ^{1}H-NMR (500MHz, $CDCl_3$) observing at δ 3.54/3.58 with irradiation at δ 1.23.

(–)-4-(1-Nitrocyclopentyl)-2-pentanone. $[\alpha]_D^{23}$ -1.4 (c 1.0, $CHCl_3$, 59% ee). ^{1}H-NMR (200 MHz, $CDCl_3$) δ 0.95 (3H, dd, *J* = 6.7, 0.7 Hz), 1.56-1.88 (6H, m), 2.16 (3H, s), 2.33 (1H, dd, *J* = 18.0, 10.2 Hz), 2.50-2.84 (4H, m). ^{13}C-NMR (50 MHz, $CDCl_3$) δ 15.9, 23.8, 23.9, 30.4, 34.7, 35.8, 36.5, 46.6, 104.1, 206.5. IR (neat) 1719, 1535 cm^{-1}. Anal. Calcd for $C_{10}H_{17}NO_3$: C; 60.28, H; 8.60, N; 7.03%. Found: C; 60.05, H; 8.60, N; 6.99%. The enantiomeric excess was determined by ^{13}C-NMR (50MHz, $CDCl_3$) of

the ketal with (2*R*,3*R*)-2,3-butanediol observing at δ 36.8/37.0, 42.3/42.6, and 78.9/79.1 or by ^{1}H-NMR (500MHz, $CDCl_3$) at δ 3.54/3.55 with irradiation at δ 1.21.

(–)-4-(1-Nitrocyclohexyl)-2-pentanone. $[\alpha]_D^{22}$ -12.8 (c 1.0, $CHCl_3$, 52 % ee). ^{1}H-NMR (200 MHz, $CDCl_3$) δ 0.92 (3H, dd, *J* = 6.7, 0.8 Hz), 1.05-1.78 (8H, m), 2.15 (3H, s), 2.16-2.72 (5H, m). ^{13}C-NMR (50 MHz, $CDCl_3$) δ 14.9, 22.2, 22.3, 24.6, 30.5, 31.3, 32.3, 37.2, 45.2, 94.2, 206.6. IR (neat) 1721 cm^{-1}. Anal. Calcd for $C_{11}H_{19}NO_3$. C; 61.95, H; 8.98, N; 6.57%. Found. C; 61.70, H; 9.06, N; 6.54%. The enantiomeric excess was determined by ^{13}C-NMR (50MHz, $CDCl_3$) of the ketal with (2*R*,3*R*)-2,3-butanediol observing at δ 26.0/26.2, 38.0/38.2, and 41.2/41.5.

(+)-5-Methyl-5-Nitro-4-pentyl-2-hexanone, (+)-12. $[\alpha]_D^{26}$ +13.2 (c 1.0, $CHCl_3$, 60 % ee). ^{1}H-NMR (200 MHz, $CDCl_3$) δ 0.86 (3H, t, *J* = 6.0 Hz), 1.0-1.5 (8H, m), 1.53 (6H, s), 2.18 (3H, s), 2.35 (1H, dd, *J* = 18.0, 6.3 Hz), 2.53 (1H, dd, *J* = 18.0, 4.2 Hz), 2.68-2.84 (1H, m). ^{13}C-NMR (50 MHz, $CDCl_3$) δ 13.8, 22.3, 23.6, 27.3, 29.8, 31.1, 31.7, 41.2, 44.8, 91.5, 206.0. IR (neat) 1721 cm^{-1}. Anal. Calcd for $C_{12}H_{23}NO_3$. C; 62.85, H; 10.11, N; 6.11%. Found. C; 62.84, H; 9.91, N; 6.13%. The enantiomeric excess was determined by ^{1}H-NMR (400MHz, $CDCl_3$) of the ketal with (2*R*,3*R*)-2,3-butanediol observing at δ 1.68/1.70 with irradiation at δ 2.26.

(+)-3-Propyl-4-methyl-4-nitropentanal. $[\alpha]_D^{23}$ +9.5 (c 1.0, $CHCl_3$, 29% ee). ^{1}H-NMR (200 MHz, $CDCl_3$) δ 0.90 (3H, t, *J* = 6.1 Hz), 1.09-1.45 (4H, m), 1.53 (3H, s), 1.55 (3H, s), 2.36 (1H, ddd, *J* = 17.8, 6.4, 2.0 Hz), 2.50 (1H, ddd, *J* = 17.8, 4.6, 1.2 Hz), 2.75-2.89 (1H, m), 9.76 (1H, dd, *J* = 2.0, 1.2 Hz). ^{13}C-NMR (50 MHz, $CDCl_3$) δ 13.9, 20.9, 23.5, 33.2, 40.2, 45.3, 91.6, 200.0. IR (neat) 1727, 1690 cm^{-1}. Anal. Calcd for $C_9H_{17}NO_3$. C; 57.73, H; 9.15, N; 7.48%. Found. C; 57.83, H; 9.05, N; 7.25%. The enantiomeric excess was determined by ^{13}C-NMR (50MHz, $CDCl_3$) of the ketal with (2*R*,3*R*)-2,3-butanediol observing at δ 22.3/22.4, 24.4/24.5, and 78.0/78.1.

(3*S*)-3-(2-Hydroxy-1-nitroethyl)cycloheptanone. Catalyst **3** was used, and a 1 : 1 mixture of diastereomers was obtained. $[\alpha]_D^{29}$ –9.3 (c 1.1, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.37-1.70 (3H, m), 1.80-2.05 (3H, m), 2.37-2.66 (6H, m), 3.92-4.03 (1H, m), 4.09-4.21 (1H, m), 4.48-4.56 (1H, m). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 23.8, 24.0, 27.6, 28.0, 32.6, 36.1, 36.6, 43.5, 43.5, 45.2, 45.3, 60.8, 61.0, 92.8, 93.0, 211.7, 211.9. IR (neat) 3514, 1702 cm^{-1}. MS *m/e* 201 (M^+, 8), 155 (M^+–NO_2, 72), 137 (M^+–NO_2–H_2O, 43), 125, (M^+–$C_2H_4O_3$, 39), 111 (M^+–$C_2H_4NO_3$, 100). HRMS. Calcd for $C_9H_{15}O_4N$: 201.1001. Found: 201.0999. To determine the stereoselectivity, the mixture was converted to (*R*)-(–)-3-(2-hydroxyethyl)cycloheptanone, (*R*)-(–)-**25** by protection (*t*-$BuMe_2SiCl$, Et_3N, r.t., 10 h; 61%), Bu_3SnH reduction (AIBN, C_6H_6 refl., 6 h; 37%), and deprotection (TBAF, THF, r.t., 1 h; 98%). $[\alpha]_D^{23}$ –10.9 (c 0.1, $CHCl_3$, 23% ee). ^{1}H-NMR (600 MHz, $CDCl_3$) δ 1.28-1.36 (1H, m), 1.40-1.47 (1H, m), 1.50-1.66 (3H, m), 1.76 (1H, br), 1.85-1.92 (4H, m), 2.41 (1H, dd, *J* = 10.6, 14.1 Hz), 2.45-2.53 (3H, m), 3.69 (2H, t, *J* = 6.5 Hz). ^{13}C-NMR (150 MHz, $CDCl_3$) δ 24.2, 28.3, 32.4, 36.9, 39.5, 43.9, 49.4, 60.3, 214.6. IR (neat) 3422, 1698 cm^{-1}. MS *m/e* 156 (M^+, 61), 138 (M^+–H_2O, 15), 111 (M^+–C_2H_5O, 100). HRMS. Calcd for $C_9H_{16}O_2$: 156.1150. Found: 156.1155. The enantiomeric excess was determined by ^{1}H-NMR (500 MHz, $CDCl_3$) of the ketal with (2*R*,3*R*)-2,3-butanediol observing at δ 3.52/3.60 with irradiation at δ 1.23. Since the ketal can possess other than 7-(2-hydroxyethyl)-2,3-dimethyl-1,4-dioxaspiro[4.6]undecane structure, it was acetylated (Ac_2O, pyridine) and the primary alcohol structure was confirmed. ^{1}H-NMR (200MHz, $CDCl_3$) δ 1.1-1.3 (6H, m), 1.3-2.0 (13H, m), 2.04 (3H, s), 3.4-3.6 (2H, m), 4.0-4.2 (2H, m). Known methyl (*R*)-(+)-3-oxocycloheptylacetate[4] was converted to (*S*)-(+)-**25** by ketalization ($HOCH_2CH_2OH$, PTS, toluene refl., 2 h; 92%) and $LiAlH_4$ reduction (THF, refl., 1 h; 79%) followed by acid treatment, which determined the absolute configuration of **25**.

(3*S*)-3-[2-(*t*-Butyldimethylsilyloxy)-1-nitroethyl]cycloheptanone. Catalyst **3** was used, and a 1 : 1 mixture of diastereomers was obtained. $[\alpha]_D^{28}$ –13.6 (c 0.6, $CHCl_3$). ^{1}H-NMR (600 MHz, $CDCl_3$) δ 0.04 (1.5H, s), 0.04 (1.5H, s), 0.05 (1.5H, s), 0.06 (1.5H, s), 0.85 (9H, s), 1.35-1.57 (2H, m), 1.56-1.67 (1H, m), 1.77-2.03 (3H, m), 2.25-2.32 (0.5H, m), 2.36-2.42 (0.5H, m), 2.44-2.63 (4H, m), 3.90 (0.5H, dd, *J* = 3.7, 11.2 Hz), 3.96 (0.5H, dd, *J* = 3.6, 11.1 Hz), 4.08 (0.5H, dd, *J* = 8.6, 11.1 Hz), 4.15 (0.5H, dd, *J* = 8.7, 11.1 Hz), 4.48 (0.5H, dt, *J* = 3.5, 8.5 Hz), 4.52 (0.5H, ddd, *J* = 3.7, 6.5, 8.7 Hz). ^{13}C-NMR (150 MHz, $CDCl_3$) δ -5.7, -5.7, -5.6, 18.0, 23.9, 24.1, 25.6, 27.6, 28.0, 32.6, 32.9, 36.1, 36.5, 43.4, 43.5, 45.3, 45.5, 62.1, 93.3, 93.6, 211.3, 211.4. IR (neat) 1707 cm^{-1}. MS *m/e* 314 (M^+–H, 0.04), 269 (M^+–NO_2, 7), 258 (M^+–C_4H_9, 100). HRMS. Calcd for $C_{15}H_{28}O_4NSi$: 314.1788. Found: 314.1775 (M^+–H). To determine the stereoselectivity, the mixture was converted to (*R*)-(–)-**25** by Bu_3SnH reduction (AIBN, C_6H_6 refl., 4 h) and deprotection (TBAF, THF, r.t., 1 h; 55% in two steps). $[\alpha]_D^{27}$ –15.9 (c 1.0, $CHCl_3$, 45% ee). The enantiomeric excess was determined as above.

(3*S*)-3-[2-(2*H*-Tetrahydropyran-2-yloxy)-1-nitroethyl]cycloheptanone. Catalyst **3** was used, and a mixture of four diastereomers in comparable amounts was obtained. $[\alpha]_D^{28}$ –14.6 (c 1.6, $CHCl_3$). ^{1}H-NMR (500 MHz, $CDCl_3$) δ 1.32-2.04 (12H, m), 2.26-2.64 (5H, m), 3.50-3.56 (1H, m), 3.68-3.84 (1H, m), 3.69 (0.25H, dd, *J* = 3.5, 11.0 Hz), 3.74 (0.25H, dd, *J* = 3.5, 11.0

Hz), 3.94 (0.25H, dd, J = 9.5, 11.5 Hz), 4.00 (0.5H, d, J = 6.5 Hz), 4.04 (0.25H, dd, J = 3.5, 11.5 Hz), 4.22 (0.25H, dd, J = 9, 11 Hz). 4.28 (0.25H, dd, J = 9, 11.0 Hz), 4.52-4.68 (2H, m). ^{13}C-NMR (100 MHz, $CDCl_3$) δ [18.6, 19.1, 19.1], [23.9, 24.0, 24.1], [25.2, 25.2, 25.2], [27.6, 27.7, 28.1, 28.1], [30.1, 30.2, 30.2], [32.6, 32.6, 32.8, 32.8], [36.7, 36.9, 37.2, 37.3], [43.5, 43.6], [45.4, 45.5, 45.6, 45.6], [61.8, 62.4, 62.5], [65.0, 65.1, 66.0, 66.1], [91.0, 91.2, 91.6, 91.7], [98.0, 99.7, 99.8], [211.2, 211.2, 211.3, 211.3]. IR (neat) 1705 cm^{-1}. MS *m/e* 285 (M^+, 0.04), 184 (M^+–$C_5H_9O_2$, 25), 155 (M^+–NO_2–C_5H_8O, 43), 137, (M^+–NO_2–$C_5H_{10}O_2$, 47), 111 (M^+–$C_7H_{12}NO_4$, 25), 101 ($C_5H_9O_2^+$, 100). HRMS. Calcd for $C_{14}H_{23}O_5N$: 285.1576. Found: 285.1566. To determine the stereoselectivity, the mixture was converted to (*R*)-(–)-**25** by Bu_3SnH reduction (AIBN, C_6H_6 refl., 4 h) and deprotection (PTS, MeOH, r.t., 2 h; 59% in two steps). $[\alpha]_D^{23}$ –16.9 (c 0.38, $CHCl_3$, 48% ee). The enantiomeric excess was determined as above.

(3*R*)-3-(1-Hydroxy-2-nitro-2-propyl)cycloheptanone. A 1 : 2 mixture of diastereomers was obtained. $[\alpha]_D^{27}$ +19.6 (c 1.6, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.23-1.32 (1H, m), 1.39-1.68 (3H, m), 1.47 and 1.50 (3H, s), 1.82-2.08 (3H, m), 2.24 (0.6H, dt, J = 11.6, 2 Hz), 2.38 (0.4H, dd, J = 9.6, 12 Hz), 2.46-2.82 (4H, m), 3.81 (1H, d, J = 10 Hz), 3.90 (0.4H, dd, J = 10, 2 Hz), 4.02 (0.6H, dd, J = 10, 2 Hz). ^{13}C-NMR (125 MHz, $CDCl_3$, the minor isomer in *italic*) δ *15.5*, 16.5, 24.3, *24.8*, 28.8, *28.9*, *31.1*, 31.3, *40.2*, 40.9, *43.1*, 43.2, 44.5, *45.0*, 65.8, *66.3*, 95.5, *95.8*, 211.8, *212.0*. IR (neat) 3438, 1700 cm^{-1}. MS *m/e* 215 (M^+, 1), 168 (M^+–HNO_2, 31), 151 (M^+–NO_2–H_2O, 31), 139, (M^+–NO_2–CH_2O, 46), 111 (M^+–$C_3H_6NO_3$, 100). HRMS. Calcd for $C_{10}H_{17}O_4N$: 215.1158. Found: 215.1155. To determine the stereoselectivity, the mixture was converted to (*R*)-(+)-7-isopropyl-1,4-dioxaspiro[4.6]undecane, (*R*)-(+)-**17**, by protection (dihydropyrane, PPTS, $CHCl_3$, r.t., 1 h; 100%), Bu_3SnH reduction (AIBN, C_6H_6 refl., 1 h), deprotection (PTS, MeOH, r.t., 1 h; 82% in two steps), iodination (I_2, PPh_3, C_6H_6, r.t., 1 h),[16] ketalization ($HOCH_2CH_2OH$, PTS, C_6H_6 refl., 4 h; 78% in two steps), and reduction ($LiEt_3BH$, THF, r.t., 4 h; 67%). $[\alpha]_D^{26}$ +2.8 (c 0.5, $CHCl_3$, 48% ee). Removal of the ketal (PTS, MeOH, r.t., 1 h; 90%) gave (*R*)-(+)-3-isopropylcycloheptanone. $[\alpha]_D^{26}$ +27.4 (c 0.3, $CHCl_3$, 48% ee). ^{1}H-NMR (200 MHz, $CDCl_3$) δ 0.86 (6H, d, J = 6.6 Hz), 1.2-2.1 (8H, m), 2.3-2.6 (4H, m). ^{13}C-NMR (50 MHz, $CDCl_3$) δ 19.3, 19.7, 25.1, 29.6, 34.0, 34.1, 42.3, 44.3, 47.5, 215.8. IR (neat) 1702 cm^{-1}. The enantiomeric excess was determined by ^{1}H-NMR (500 MHz, $CDCl_3$) of the ketal with (2*R*,3*R*)-2,3-butanediol observing at δ 3.52/3.61 with irradiation at δ 1.22.

(3*R*)-3-[1-(2*H*-Tetrahydropyran-2-yloxy)-2-nitro-2-propyl]cycloheptanone. A mixture of four diastereomers in comparable amounts was obtained. $[\alpha]_D^{26}$ +36.6 (c 0.8, $CHCl_3$). ^{1}H-NMR (600 MHz, $CDCl_3$) δ 1.24-2.05 (12H, m), 2.22- 2.72 (5H, m), 1.49 (0.75H, s), 1.51 (0.75H, s), 1.53 (0.75H, s), 1.55 (0.75H, s), 3.47-3.52 (1H, m), 3.50 (0.25H, d, J = 10.4 Hz), 3.55 (0.25H, d, J = 10.4 Hz), 3.64-3.75 (1H, m), 3.76 (0.25H, d, J = 10.3 Hz), 3.83 (0.25H, d, J = 10.4 Hz), 3.92 (0.25H, d, J = 10.4 Hz), 3.95 (0.25H, d, J = 10.4 Hz), 4.11 (0.25H, d, J = 10.4 Hz), 4.18 (0.25H, d, J = 10.4 Hz), 4.52-4.62 (1H, m). ^{13}C-NMR (150 MHz, $CDCl_3$) δ [15.4, 15.5, 16.3, 16.4], [18.5, 18.6, 19.0], [24.4, 24.4, 24.7, 24.9], [25.1, 25.1, 25.2, 25.2], [28.7, 28.9, 28.9, 28.9], [30.0, 30.1, 30.1], [31.3, 31.3, 31.5, 31.6], [40.7, 41.1, 41.5, 41.9], [43.1, 43.2], [44.6, 44.7, 45.2, 45.3], [61.6, 61.8, 62.2, 62.2], [70.7, 71.0, 71.1, 71.3], [93.9, 94.3, 94.4, 94.7], [98.6, 98.6, 98.9, 99.1], [211.4, 211.5, 211.6]. IR (neat) 1702 cm^{-1}. MS *m/e* 299 (M^+, 0.2), 216 (M^+–C_5H_7O, 34), 186 (M^+–$C_6H_9O_2$, 30), 137, (M^+–NO_2–C_5H_8O, 79), 151 (M^+–NO_2–$C_5H_{10}O_2$, 100). HRMS. Calcd for $C_{15}H_{25}O_5N$: 299.1733. Found: 299.1735. To determine the stereoselectivity, the mixture was converted to (*R*)-(+)-**17** by Bu_3SnH reduction (AIBN, C_6H_6 refl., 2 h; 98%), deprotection (PTS, MeOH, r.t., 2 h), iodination (I_2, PPh_3, C_6H_6, r.t., 1 h; 83 % in two steps),[16] ketalization ($HOCH_2CH_2OH$, PTS, C_6H_6 refl., 4 h; 95%), and reduction ($LiEt_3BH$, THF, r.t., 4 h; 74%). $[\alpha]_D^{24}$ +5.7 (c 0.8, $CHCl_3$, 63% ee). Removal of the ketal (PTS, MeOH, r.t., 2 h; 88%) gave (*R*)-(+)-3-isopropylcycloheptanone. $[\alpha]_D^{26}$ +53.9 (c 0.9, $CHCl_3$, 63% ee). The enantiomeric excess was determined as above.

(3*S*)-2,3-Dimethyl-2-nitro-1-(2*H*-tetrahydropyran-2-yloxy)-5-hexanone. A 5 : 5 : 1 : 1 mixture of four diastereomers. $[\alpha]_D^{28}$ –12.6 (c 1.0, $CHCl_3$). ^{1}H-NMR (500 MHz, $CDCl_3$, the major two isomers) δ 0.86 (1.5H, d, J = 7.0 Hz), 0.88 (1.5H, d, J = 7.0 Hz), 1.40-1.76 (6H, m), 1.50 (1.5H, s), 1.53 (1.5H, s), 2.11 (3H, s), 2.19-2.30 (1H, m), 2.48-2.54 (1H, m), 2.68-2.84 (1H, m), 3.46 (0.5H, d, J = 9.5 Hz), 3.46-3.51 (1H, m), 3.62-3.76 (1H, m), 3.82 (0.5H, d, J = 10.5 Hz), 3.87 (0.5H, d, J = 10.0 Hz), 4.19 (0.5H, d, J = 10.5 Hz), 4.50-4.55 (0.5H, m), 4.56-4.60 (0.5H, m). ^{13}C-NMR (125 MHz, $CDCl_3$, the major two isomers) δ 14.8, 14.9, 17.2, 17.6, 18.5, 19.0, 25.1, 25.2, 30.0, 30.1, 30.3, 30.3, 34.5, 34.6, 45.6, 45.7, 61.6, 62.2, 70.2, 70.8, 93.2, 93.7, 98.5, 99.1, 205.7, 205.9. IR (neat) 1717 cm^{-1}. MS *m/e* .273 (M^+, 0.03), 172 (M^+–$C_5H_{10}O_2$, 39), 143 (M^+–C_5H_9O–NO_2, 64), 129, (M^+–$C_6H_{10}O_3N$, 20), 125 (M^+–NO_2–$C_5H_{11}O_2$, 100) HRMS. Calcd for $C_{13}H_{23}O_5N$: 273.1577. Found: 273.1548. To determine the stereoselectivity, the mixture was converted to ethylene ketal of (*S*)-4,5-dimethyl-2-hexanone, (*S*)-(–)-**14**, by Bu_3SnH reduction (AIBN, C_6H_6 refl., 4 h; 49%), deprotection (PTS, MeOH, r.t., 2 h; 96%), iodination (I_2, PPh_3, C_6H_6, r.t., 1 h; 66%),[16] ketalization ($HOCH_2CH_2OH$, PTS, toluene, refl., 4 h; 87%), and reduction ($LiEt_3BH$, THF, r.t., 4 h; 46%). $[\alpha]_D^{30}$ –4.6 (c 0.5, $CHCl_3$, 41% ee). The enantiomeric excess was determined by ^{1}H-NMR (500 MHz, $CDCl_3$) of the ketal with (2*R*,3*R*)-2,3-butanediol observing at δ 3.60/3.62 with irradiation at δ 1.23.

Methyl 3-Nitro-3-(3-oxocycloheptyl)butanoate. Catalyst **3** was used, and a 1 : 1 mixture of diastereomers was obtained. $[\alpha]_D^{27}$ –17.4 (c 1.1, $CHCl_3$). ^{1}H-NMR (600 MHz, $CDCl_3$) δ 1.36-1.50 (2H, m), 1.60-1.70 (1H, m), 1.84-2.05 (3H, m), 2.10-2.20 (1H, m), 2.22-2.37 (3H, m), 2.40-2.60 (5H, m), 3.69 (3H, s), 4.47-4.52 (1H, m). ^{13}C-NMR (150 MHz, $CDCl_3$) δ 23.9, 24.1, 25.2, 25.3, 27.8, 28.0, 29.9, 30.0, 32.4, 32.6, 39.3, 39.5, 43.5, 43.5, 45.2, 45.3, 51.9, 51.9, 91.5, 91.5, 172.2, 172.3, 211.3. IR (neat) 1736, 1706 cm^{-1}. MS m/e 226 (M^+–MeO, 54), 211 (M^+–NO_2, 100), 179 (M^+–MeOH–NO_2, 87). HRMS. Calcd for $C_{11}H_{19}O_4N$: 220.1079. Found: 226.1095 (M^+–MeO).

Methyl 5-Methyl-4-nitro-7-oxooctanoate. A 1 : 1.4 mixture of diastereomers. $[\alpha]_D^{23}$ +6.2 (c 0.3, $CHCl_3$). ^{1}H-NMR (600 MHz, $CDCl_3$) δ 0.93 and 0.98 (3H, d, J = 6.8 Hz), 1.97-2.09 (1H, m), 2.11 and 2.13 (3H, s), 2.15-2.23 (1H, m), 2.25-2.40 (3H, m), 2.51-2.55 (1H, m), 2.58-2.66 (1H, m), 3.65 and 3.66 (3H, s), 4.46-4.56 (1H, m). ^{13}C-NMR (150 MHz, $CDCl_3$) δ 14.9, 16.2, 25.3, 25.7, 29.9, 30.1, 30.4, 30.4, 32.0, 32.4, 45.7, 46.4, 51.8, 90.2, 91.3, 172.3, 205.9, 206.2. IR (neat) 1742, 1700 cm^{-1}. HRMS. Calcd for $C_{10}H_{17}O_3$: 185.1177. Found: 185.1167 (M^+–NO_2).

1-Nitro-1-(3-oxocycloheptyl)-2-cyclohexene. Catalyst **3** was used, and a 1 : 2 mixture of diastereomers was obtained. $[\alpha]_D^{26}$ –76.0 (c 1.4, $CHCl_3$). ^{1}H-NMR (600 MHz, $CDCl_3$) δ 1.18-1.47 (2H, m), 1.50-1.72 (4H, m), 1.76-1.82 (1H, m), 1.92-2.05 (3H, m), 2.10-2.17 (1H, m), 2.29-2.62 (6H, m), 5.82-5.86 (1H, m), 6.16-6.21 (1H, m). ^{13}C-NMR (150 MHz, $CDCl_3$, the minor isomer in *italic*) δ 18.52, 24.4, 24 7, *24.8*, *25.0*, 25.9, *27.6*, 28.8, *29.3*, 30.9, *31.3*, *43.2*, 43.4, *44.0*, 44.4, *44.7*, 45.1, 92.6, *92.9*, *124.6*, 125.8, 136.1, *136.2*, *211.8*, 212.1. IR (neat) 1696, 1653 cm^{-1}. MS m/e 191 (M^+–NO_2, 100), 173 (31). HRMS. Calcd for $C_{13}H_{19}O$: 191.1436. Found: 191.1434 (M^+–NO_2). The product was converted to (–)-**9** by Bu_3SnH reduction (AIBN, C_6H_6 refl., 1 h; 77%), and hydrogenation (Pt-C, H_2, 5 atm, EtOAc, r.t., 3 days; 64%). $[\alpha]_D^{21}$ –25.9 (c 0.26, $CHCl_3$, 53% ee). The optical purity was determined by ^{1}H-NMR (500 MHz, $CDCl_3$) of the ketal with (2*R*,3*R*)-2,3-butanediol observing at δ 3.53/3.61 with irradiation at δ 1.23.

1-Nitro-1-(4-oxo-2-butyl)-2-cyclohexene. A 1 : 1 mixture of diastereomers. $[\alpha]_D^{25}$ –17.1 (c 1.1, $CHCl_3$). ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.87 (1.5H, d, J = 6.5 Hz), 0.90 (1.5H, d, J = 6.5 Hz), 1.44-1.69 (3H, m), 1.73-1.80 (1H, m), 1.92-2.02 (1H, m), 2.12 (1.5H, s), 2.13 (1.5H, s), 2.22-2.30 (1H, m), 2.42-2.62 (2H, m), 2.72-2.82 (1H, m), 5.82-5.89 (1H, m), 6.09-6.15 (1H, m). ^{13}C-NMR (125 MHz, $CDCl_3$) δ 14.7, 15.1, 18.6, 18.6, 24.7, 24.8, 27.6, 27.6, 30.3, 30.4, 37.1, 37.1, 45.1, 45.7, 92.1, 124.9, 125.3, 134.9, 135.4, 206.0, 206.1. IR (neat) 1719 cm^{-1}. MS *m/e* 211 (M^+, 0.2), 165 (M^+–NO_2, 64), 147 (M^+–H_2O–NO_2, 50), 107 (M^+–C_3H_6O–NO_2, 100). HRMS. Calcd for $C_{11}H_{17}O_3N$: 211.1208. Found: 211.1213. The product was converted to (+)-5-cyclohexyl-4-methyl-2-hexanone by Bu_3SnH reduction (AIBN, C_6H_6 refl., 1 h; 88%) and hydrogenation (Pt-C, H_2, 5 atm, EtOAc, r.t., 5 days; 82%). $[\alpha]_D^{28}$ +1.1 (c 1.1, $CHCl_3$, 43% ee). ^{1}H-NMR (200 MHz, $CDCl_3$) δ 0.83 (3H, d, J = 6.8 Hz), 0.7-1.3 (6H, m), 1.5-2.0 (6H, m), 2.12 (3H, s), 2.18 (1H, dd, J = 9, 15.6 Hz), 2.46 (1H, dd, J = 4.6, 15.4 Hz). ^{13}C-NMR (50 MHz, $CDCl_3$) δ 17.1, 27.1, 27.2, 29.6, 30.8, 34.7, 43.3, 49.1, 209.9. IR (neat) 1717 cm^{-1}. MS *m/e* 168 (M^+, 7), 110 (M^+–$C_3H_6O_2$, 100), 85 (M^+–C_6H_{11}, 58). HRMS. Calcd for $C_{11}H_{20}O$: 168.1514. Found: 168.1523. The optical purity was determined by ^{1}H-NMR (500 MHz, $CDCl_3$) of the ketal with (2*R*,3*R*)-2,3-butanediol observing at δ 0.89/0.91 with irradiation at δ 1.52.

Reduction of the Tertiary Nitro Compound with Bu_3SnH. (*R*)-(+)-3-Isopropylcyclohexanone, (*R*)-(+)-11. Under an argon atmosphere, a mixture of (*R*)-(+)-**10** (59% ee, 160 mg, 0.87 mmol), Bu_3SnH (0.28 mL, 1.04 mmol), and AIBN (434 mg, 0.26 mmol) in benzene (3 mL) was stirred at reflux for 22 h. After cooling, solvents were removed, and (*R*)-(+)-**11** (86 mg, 58%) was obtained by flash chromatography. $[\alpha]_D^{23}$ +9.0 (c 0.93, $CHCl_3$). Lit.[8] $[\alpha]_D^{20}$ +17.3 (c 6.3, $CHCl_3$). ^{1}H-NMR (200 MHz, $CDCl_3$) δ 0.92 (3H, d, J = 6.4 Hz), 0.93 (3H, d, J = 6.4 Hz), 1.26-1.75 (4H, m), 1.81-1.95 (1H, m), 2.02-2.18 (2H, m), 2.23-2.45 (3H, m). ^{13}C-NMR (50 MHz, $CDCl_3$) δ 19.1, 19.3, 25.3, 28.1, 32.3, 41.3, 45.1, 45.2. IR (neat) 1715 cm^{-1}.

(+)-3-Cyclohexylcycloheptanone, (+)-9. $[\alpha]_D^{22}$ +41.7 (c 1.0, $CHCl_3$, 84 % ee). ^{1}H-NMR (200 MHz, $CDCl_3$) δ 0.9-2.1 (18H, m), 2.3-2.6 (4H, m). ^{13}C-NMR (50 MHz, $CDCl_3$) δ 24.5, 26.6, 28.9, 29.4, 29.6, 33.8, 41.3, 43.6, 44.1, 47.4, 215.1. IR (neat) 1702 cm^{-1}. HRMS. Calcd for $C_{13}H_{22}O$: 194.1671. Found: 194.1688. The optical purity was determined by ^{1}H-NMR (400 MHz, $CDCl_3$) of the ketal with (2*R*,3*R*)-2,3-butanediol observing at δ 3.47-3.54/3.55-3.65.

(+)-4-Isopropyl-2-nonanone. $[\alpha]_D^{23}$ +2.0 (c 1.0, $CHCl_3$, 59% ee). ^{1}H-NMR (200 MHz, $CDCl_3$) δ 0.81 (3H, d, J = 6.1 Hz), 0.84 (3H, d, J = 6.5 Hz), 0.88 (3H, t, J = 5.9 Hz), 1.04-1.38 (8H, m), 1.52-1.92 (2H, m), 2.14 (3H, s), 2.22 (1H, dd, J = 16.1, 7.1 Hz), 2.38 (1H, dd, J = 16.1, 5.8 Hz). ^{13}C-NMR (50 MHz, $CDCl_3$) δ 14.0, 18.4, 19.4, 22.6, 27.0, 29.6, 30.2, 31.2, 32.1, 39.5, 45.5, 209.6. IR (neat) 1717 cm^{-1}. MS (EI) *m/e* 184 (M, 14), 169 (M–CH_3, 6), 141 (M–C_3H_7, 52), 126 (M–C_3H_6O, 100). HRMS. Calcd for $C_{12}H_{24}O$: 184.1827. Found: 184.1825. Anal. Calcd for $C_{12}H_{24}O$. C; 78.20, H; 13.12%. Found. C; 77.69, H; 13.10%. The optical purity was determined by ^{13}C-NMR (50 MHz, $CDCl_3$) of the ketal with (2*R*,3*R*)-2,3-butanediol observing at δ 18.8/19.1, 29.1/29.3, and 40.6/40.8.

Reduction of the Secondary Nitro Compound with Bu_3SnH. (*R*)-(+)-3-Butylcyclohexanone, (*R*)-(+)-19. Under an argon atmosphere, a solution of (3*R*)-**20** (150 mg, 0.76 mmol, a 1 : 1.4 mixture of diastereomers, 53 and 47% ee), a catalytic amount of *p*-toluenesulfonic acid, and methyl orthoformate (0.4 mL, 0.37 mmol) in methanol (2 mL) was stirred for 5 min, when saturated aqueous $NaHCO_3$ was added. Organic materials were extracted with ethyl acetate, washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. To the residue were added benzene (5 mL), Bu_3SnH (1.0 mL, 3.8 mmol) and AIBN (64 mg, 0.39 mmol), and the mixture was heated at reflux for 10 h under an argon atmosphere. Then, Bu_3SnH (1.0 mL, 3.8 mmol) and AIBN (64 mg, 0.39 mmol) were added, and heating was continued for 5 h. After cooled, the mixture was diluted with ether and 4 M HCl, and stirred at room temperature for 3 h. The organic layer was separated, washed with brine, dried over Na_2SO_4, filtered, concentrated, and flash chromatographed over silica gel (3% triethylamine-hexane) giving (*R*)-(+)-**23** (64 mg, 55%). $[\alpha]_D^{23}$ +3.9 (c 1.3, toluene). Lit.[10] $[\alpha]_D^{23}$ +7.23 (c 1.13, toluene, 92 % ee). The optical purity of the product obtained by this optical rotation coincides with the value calculated based on the ee's and the ratio of the two diastereomers, which possess the same configuration at the β-carbon atom of the carbonyl group. ^{1}H-NMR (200 MHz, $CDCl_3$) δ 0.89 (3H, t, *J* = 6.4 Hz), 1.20-1.43 (6H, m), 1.50-2.14 (6H, m), 2.14-2.50 (3H, m). ^{13}C-NMR (50 MHz, $CDCl_3$) δ 13.9, 22.6, 25.2, 28.7, 31.2, 36.1, 38.9, 41.3, 48.0, 211.8. IR (neat) 1717 cm^{-1}. Anal. Calcd for $C_{10}H_{18}O$. C; 77.87, H; 11.76%. Found. C; 78.00, H; 11.70%.

(*R*)-(+)-4-Methyl-2-octanone, (*R*)-(+)-22. Synthesized from a 1 : 1 diastereomer mixture of (4*S*)-**21** (40 and 55% ee). The relatively low yield is due to the volatile nature of the product. $[\alpha]_D^{23}$ +3.5 (c 1.0, $CHCl_3$). Lit.[11] $[\alpha]_D^{25}$ +8.3. ^{1}H-NMR (200 MHz, $CDCl_3$) δ 0.89 (3H, t, *J* = 6.1 Hz), 0.89 (3H, d, *J* = 6.6 Hz), 1.10-1.41 (6H, m), 1.88-2.10 (1H, m), 2.13 (3H, s), 2.21 (1H, dd, *J* = 15.7, 8.0 Hz), 2.42 (1H, dd, *J* = 15.7, 5.8 Hz). ^{13}C-NMR (50 MHz, $CDCl_3$) δ 14.0, 19.8, 22.8, 29.1, 29.2, 30.3, 36.5, 51.3, 209.1. IR (neat) 1717 cm^{-1}. The compound was converted to (*R*)-3-methylheptanoic acid by the haloform reaction.[11] $[\alpha]_D^{24}$ +3.4 (c 1.0, heptane). Lit.[11] $[\alpha]_D^{25}$ +6.3 (c 1, heptane). The optical purity obtained by this optical rotation coincides with the value calculated based on the ee's and the ratio of the two diastereomers, which possess the same configuration at the β-carbon atom of the carbonyl group. ^{1}H-NMR (200 MHz, $CDCl_3$) δ 0.90 (3H, t, *J* = 5.8 Hz), 0.97 (3H, d, *J* = 6.6 Hz), 1.18-1.40 (6H, m), 1.86-2.05 (1H, m), 2.15 (1H, dd, *J* = 14.7, 8.0 Hz), 2.37 (1H, dd, *J* = 14.7, 6.0 Hz). ^{13}C-NMR (50 MHz, $CDCl_3$) δ 14.0, 19.7, 22.8, 29.1, 30.1, 36.3, 41.6, 180.0. IR (neat) 3700-2500, 1711 cm^{-1}. Anal. Calcd for $C_8H_{16}O_2$. C; 66.63, H; 11.18%. Found. C; 66.57, H; 10.74%.

Methyl (–)-3-(3-Oxocycloheptyl)butanoate. $[\alpha]_D^{23}$ -13.7 (c 0.2, $CHCl_3$, 53% ee). ^{1}H-NMR (600 MHz, $CDCl_3$) δ 1.25-1.34 (3H, m), 1.37-1.44 (1H, m), 1.57-1.72 (4H, m), 1.84-1.93 (3H, m), 2.30 (2H, t, *J* = 7.4 Hz), 2.40 (1H, dd, *J* = 10.6, 14.1 Hz), 2.46-2.50 (3H, m), 3.67 (3H, s). ^{13}C-NMR (150 MHz, $CDCl_3$) δ 22.3, 24.3, 28.4, 34.0, 35.8, 36.5, 36.5, 43.8, 49.7, 51.5, 173.9, 214.3. IR (neat) 1742, 1702 cm^{-1}. MS *m/e* 212 (M^+, 30), 129 (M^+–$C_5H_9O_2$, 100). HRMS. Calcd for $C_{12}H_{20}O_3$: 212.1412 Found: 212.1414. The optical purity was determined by ^{1}H-NMR (500 MHz, $CDCl_3$) of the ketal with (2*R*,3*R*)-2,3-butanediol observing at δ 3.54/3.59 with irradiation at δ 1.22.

Methyl (+)-5-Methyl-7-oxooctanoate. $[\alpha]_D^{29}$ +4.1 (c 0.7, $CHCl_3$, 45% ee). ^{1}H-NMR (600 MHz, $CDCl_3$) δ 0.91 (3H, d, *J* = 6.7 Hz), 1.16-1.22 (1H, m), 1.27-1.33 (1H, m), 1.55-1.70 (2H, m), 1.97-2.05 (1H, m), 2.12 (3H, s), 2.24 (1H, dd, *J* = 16.0, 7.9 Hz), 2.29 (2H, dt, *J* = 3.3, 7.8 Hz), 2.41 (1H, dd, *J* = 16.1, 5.8 Hz), 3.66 (3H, s). ^{13}C-NMR (150 MHz, $CDCl_3$) δ 19.6, 22.3, 28.9, 30.4, 34.0, 36.2, 50.9, 51.5, 174.1, 208.8. IR (neat) 1742, 1717 cm^{-1}. MS *m/e* 186 (M^+, 5), 155 (M^+–MeO, 14), 129 (M^+–C_3H_5O, 100). HRMS. Calcd for $C_{10}H_{18}O_3$: 186.1256. Found: 186.1247. The optical purity was determined by ^{13}C-NMR (125 MHz, $CDCl_3$) of the ketal with (2*R*,3*R*)-2,3-butanediol observing the absorption at δ 77.8/77.9 and δ 78.5/78.6.

(*S*)-(–)-2-(2,3-Dimethylbutyl)-2-methyl-1,3-dioxolane, (*S*)-(–)-14. A mixture of (*S*)-(–)-**13** (68% ee, 3.6 g, 21 mmol), ethylene glycol (2.35 mL, 43 mmol), and *p*-toluenesulfonic acid (10 mg, 0.053 mmol) in benzene (100 mL) was heated at reflux for 16 h. After cooling, saturated aqueous $NaHCO_3$ was added. Organic materials were extracted with ethyl acetate, and washed with brine. After drying over Na_2SO_4, the solution was filtered, concentrated, and chromatographed giving (*S*)-(–)-2-(2,3-dimethyl-3-nitrobutyl)-2-methyl-1,3-dioxolane (4.29 g, 94%). $[\alpha]_D^{23}$ -15.5 (c 1.3, $CHCl_3$). ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1.03 (3H, d, *J* = 6.8 Hz), 1.33 (3H, s), 1.51 (3H, s), 1.53 (3H, s), 1.30-1.70 (2H, m), 2.33-2.49 (1H, m), 3.88-4.02 (4H, m). IR (neat) 1539 cm^{-1}. Bu_3SnH reduction as above gave (*S*)-(–)-**14** in 41% yield. $[\alpha]_D^{25}$ -7.5 (c 2.0, $CHCl_3$). ^{1}H-NMR (200 MHz, $CDCl_3$) δ 0.82 (3H, d, *J* = 7.1 Hz), 0.85 (3H, d, *J* = 6.9 Hz), 0.90 (3H, d, *J* = 6.4 Hz), 1.33 (3H, s), 1.35-1.75 (4H, m), 3.88-4.00 (4H, m). ^{13}C-NMR (50 MHz, $CDCl_3$) δ 16.5, 17.8, 19.6, 23.9, 32.9, 34.2, 42.6, 64.1, 64.4, 110.6. IR (neat) 2878, 1466, 1379 cm^{-1}. MS (EI) *m/e* 172 (M, 100), 113 (44), 87 (69).

Synthesis of (*S*)-(–)-14 from (*S*)-(–)-15. Diisopropyl (*S*)-(+)-(4-oxo-2-pentyl)malonate ethylene ketal was obtained from (*S*)-(–)-**15** (76% ee)[4] by ketalization as above. $[\alpha]_D^{27}$ +8.4 (c 1.3, $CHCl_3$). ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1.11 (3H, d, *J* = 7.0 Hz), 1.25

(12H, d, J = 6.3 Hz), 1.35 (3H, s), 1.59 (1H, dd, J = 14.5, 7.7 Hz), 1.88 (1H, dd, J = 14.4, 5.0 Hz), 2.34-2.53 (1H, m), 3.39 (1H, d, J = 6.4 Hz), 3.93 (4H, s), 5.06 (1H, heptet, J = 6.4 Hz), 5.06 (1H, heptet, J = 6.4 Hz). IR (neat) 1729 cm^{-1}. Under an argon atmosphere, the ketal (1.0 g, 3.2 mmol) in THF (5 mL) was added to $LiAlH_4$ (0.24 g, 6.25 mmol) in THF at 0 °C. The mixture was heated at reflux for 1.5 h, and cooled to 0 °C. Ethanol (0.79 mL), 4 M NaOH (0.24 mL), and water (0.72 mL) were added in this order, and the suspension was stirred vigorously to form white solid. The solution was diluted with CH_2Cl_2, decanted, dried over Na_2SO_4, filtered, and concentrated. (*S*)-(–)-2-(4-Hydroxy-3-hydroxymethyl-2-methylbutyl)-2-methyl-1,3-dioxolane (0.62 g, 96%) was obtained by flash chromatography. $[\alpha]_D^{22}$ -8.4 (c 1.1 $CHCl_3$). ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1.15 (3H, d, J = 6.7 Hz), 1.26 (3H, s), 1.48-1.60 (2H, m), 2.09-2.30 (2H, m), 2.67 (2H, s), 3.74 (4H, s), 3.94-4.04 (2H, m), 4.14-4.24 (2H, m). IR (neat) 3406 cm^{-1}. MS (EI) *m/e* 189 (**M**–CH_3, 70), 143 (52), 105 (47), 87 (100). Under an argon atmosphere, a mixture of (*S*)-(–)-diol (118 mg, 0.58 mmol), imidazole (197 mg, 2.9 mmol), triphenylphosphine (761 mg, 2.9 mmol), and iodine (588 mg, 2.3 mmol) in benzene (3 mL) was stirred for 40 min at room temperature.[16] Saturated aqueous $NaHSO_3$ was added, and the organic materials were extracted with ethyl acetate, washed with brine, dried over Na_2SO_4, filtered, and concentrated. (*S*)-(+)-2-(4-Iodo-3-iodomethyl-2-methylbutyl)-2-methyl-1,3-dioxolane (224 mg, 91%) was obtained by flash chromatography. $[\alpha]_D^{24}$ +0.3 (c 1.4, $CHCl_3$). ^{1}H-NMR (200 MHz, $CDCl_3$) δ 0.99 (3H, d, J = 6.9 Hz), 1.34 (3H, s), 1.57 (1H, dd, J = 14.,4, 7.4 Hz), 1.57-1.71 (1H, m), 1.77 (1H, dd, J = 14.4, 4.2 Hz), 1.86-2.05 (1H, m), 3.18 (1H, dd, J = 10.4, 7.5 Hz), 3.37 (2H, d, J = 6.4 Hz), 3.49 (1H, dd, J = 10.2, 4.2 Hz), 3.96 (4H, s). IR (neat) 1289, 1069, 1040 cm^{-1}. MS (EI) *m/e* 424 (**M**, 7), 409 (**M**–CH_3, 36), 298 (**M**–I, 35), 108 (55), 87 (100). Under an argon atmosphere, 1 M $LiHBEt_3$ in THF (3.06 mL, 3.06 mmol) was added to the iodide (217 mg, 0.51 mmol) in THF (7 mL) at 0 °C, and the mixture was stirred at room temperature for 2 h. Water (3 mL), 3 M NaOH, and 30% H_2O_2 were added in this order, and the organic materials were extracted with ether. The organic layer was washed with brine, dried over Na_2SO_4, filtered, concentrated, and chromatographed on silica gel giving (*S*)-(–)-**14** (29 mg, 33%). $[\alpha]_D$ -7.7 (c 0.6, $CHCl_3$). ^{1}H-NMR and IR spectra coincided with the compound obtained from (*S*)-(–)-**13**.

(*S*)-(–)-7-Isopropyl-1,4-dioxaspiro[4.6]undecane, (*S*)-(–)-17. (*S*)-(–)-**16** (79% ee) was ketalized with ethylene glycol and reduced with Bu_3SnH (90% in two steps) as above giving (*S*)-(–)-**17**. $[\alpha]_D^{25}$ –6.3 (c 0.62, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.81 (3H, d, J = 7.2 Hz), 0.82 (3H, d, J = 7.2 Hz), 1.19-1.30 (1H, m), 1.36-1.51 (3H, m), 1.53-1.68 (4H, m), 1.68-1.86 (4H, m), 3.80-3.90 (2H, m), 3.90-3.97 (2H, m). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 18.7, 18.8, 22.5, 28.8, 32.3, 34.1, 38.6, 38.8, 41.4, 63.9, 64.0, 112.7. IR (neat) 2932, 2874 cm^{-1}. MS *m/e* 198 (M^+, 13), 155 (M^+–C_3H_7, 100). HRMS. Calcd for $C_{12}H_{22}O_2$: 198.1619. Found: 198.1614. Diisopropyl (*R*)-(+)-3-oxocycloheptylmalonate, (*R*)-(+)-**18** (59% ee)[4] was also converted to (*R*)-(+)-**17** by ketalization ($HOCH_2CH_2OH$, PTS, C_6H_6 refl., 2 h), reduction ($LiAlH_4$, THF, refl., 1 h; 73% in two steps), iodination (I_2, PPh_3, C_6H_6, r.t., 1 h; 89%),[16] and reduction ($LiEt_3BH$, THF, r.t., 12 h; 51%). $[\alpha]_D^{26}$ +5.7 (c 0.85, $CHCl_3$).

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