Tetrahedron Vol. 37, No. 23, pp 3951 to 3956, 1981
Printed in Great Britain.

0040-4020/81/233951-06$02.00/0

DIASTEREOSELECTIVE AND ENANTIOSELECTIVE SYNTHESIS OF 1,2-DISUBSTITUTED CYCLOALKANECARBOXALDEHYDES[1,2]

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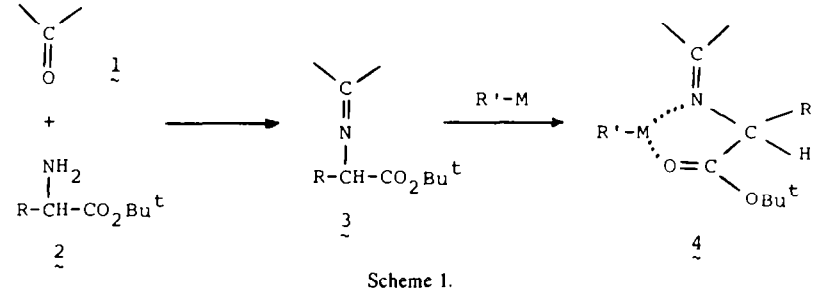
(*Received in USA 24 April, 1981*)

Abstract—A highly useful method for diastereoselective and enantioselective synthesis of *trans*- and *cis*-1,2-disubstituted cycloalkanecarboxaldehydes (*trans*- and *cis*-**10**), useful chiral synthons having asymmetric tertiary and quaternary carbon atoms in vicinal positions in their rings, is devised starting from cycloalkenecarboxaldehydes (**5**). t-Leucine t-butyl ester (**2**, R=Bu^t), a highly effective chiral auxiliary reagent in the present method, can be recovered for recycling without any loss of optical purity. Some mechanistic explanations on the stereochemical courses of the reactions are presented.

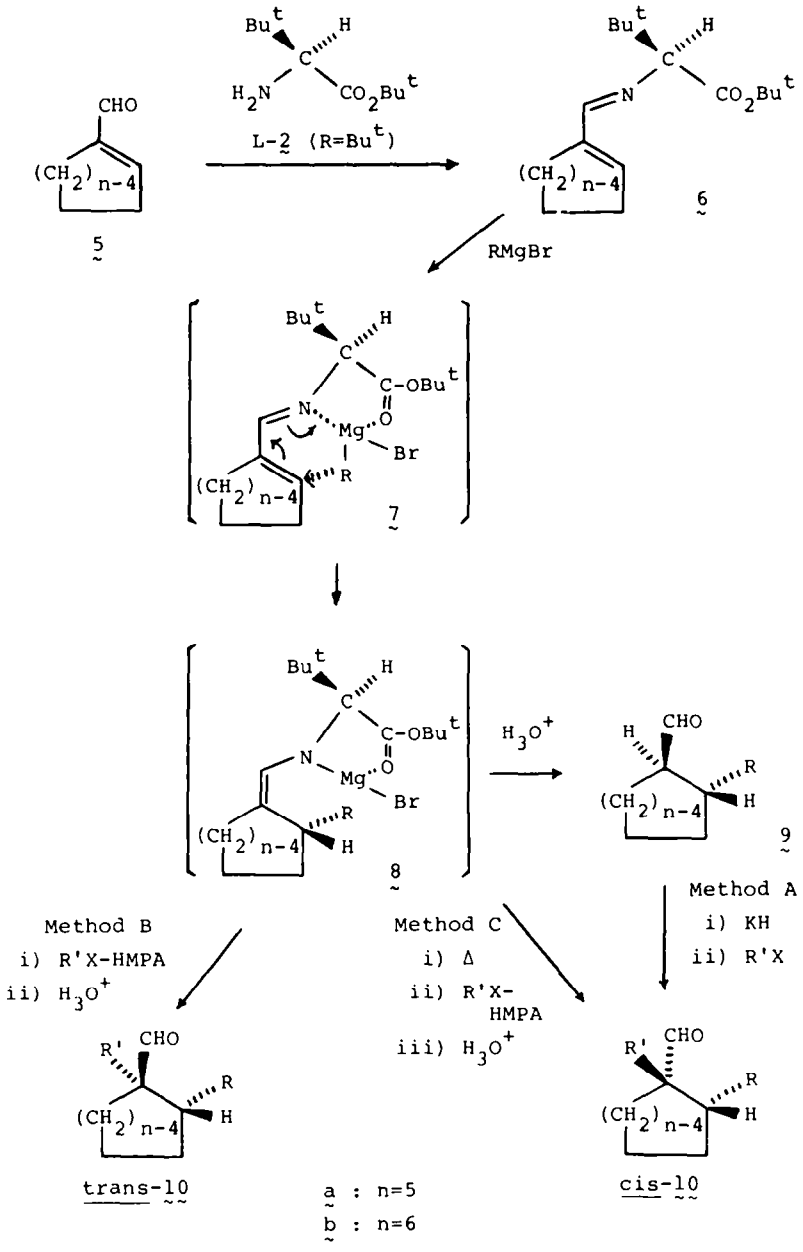
The design of effective asymmetric synthesis has been one of the most attractive and challenging fields in synthetic organic chemistry, and significant progresses are recorded in recent years.[3] As part of our research program directed toward the development of new stereoselective reactions, we have reported a highly efficient method for asymmetric alkylations based on the strategy of controlling conformational freedom of the substrate by chelation.[4] Thus, the conformation of the chiral moiety of the Schiff bases (**3**), prepared from carbonyl compounds (**1**) and optically active α-amino acid esters (**2**), can be effectively fixed as shown in **4** by chelation of appropriate metals with imine nitrogen and ester oxygen suitably situated. It is shown that t-leucine t-butyl ester (**2**, R=Bu^t) is an excellent chiral auxiliary reagent in this method, working as a bidentate ligand during the reaction, and being recovered without any racemization.

Asymmetric synthesis of *trans*-2-substituted cycloalkanecarboxaldehydes (**9**) having two tertiary asymmetric carbon atoms in vicinal positions in their rings was found to proceed by this method with high efficiency via 1,4-addition of Grignard reagents to chiral α,β-unsaturated aldimines (**6**), prepared from the corresponding cycloalkenecarboxaldehydes (**5**) and optically active α-amino acid esters (**2**), followed by hydrolysis.[4g] The present paper describes the extension of the scope of this reaction to diastereoselective asymmetric synthesis of 1,2-disubstituted cycloalkanecarboxaldehydes (**10**) having asymmetric tertiary and quaternary carbon atoms in vicinal positions. It was our object to devise methods to obtain these aldehydes diastereoselectively and enantioselectively because of their high possibility as chiral synthons in synthesis. Thus, the following three methods were examined starting from chiral α,β-unsaturated aldimines as shown in Scheme 2. In method A, optically active aldehydes (**9**), prepared by the above procedure via Grignard 1,4-addition of **6** followed by hydrolysis of the resulting magnesioenamines (**8**),[4g] were metalated and alkylated as usual. In method B, the reaction was performed by one-pot procedure via Grignard 1,4-addition of **6** followed by alkylation of the resulting **8** with alkyl halides. In method C, the reaction was performed as in method B, except that the reaction mixture was heated to reflux for several hours before alkylation. It should be noted that the first conjugate addition step decides the degree of enantioselectivity, while the second alkylation step decides the degree of diastereoselectivity. General procedures are written in the experimental section. The relative configurations of the products were determined by ^{13}C NMR chemical shift values [5] and were further confirmed for some cyclohexane derivatives (**10b**, R=Ph and CH=CH$_2$, R'=Me) by chemical correlation to the known compounds (*trans*-**12**,[6] *cis*-**12**,[6] *trans*-**14**,[7] and *cis*-**14**[8]) using racemates as shown in Scheme 3. The absolute configurations and optical purities of the products (**10**) were based on those of **9** reported previously[4g] by the following facts that **9** was not detected in the reaction products and that the reaction gave one product exclusively except run 5, and therefore, kinetic resolution is expected to be minimum by method B. These values were further confirmed for some cases by ^{1}H NMR using chiral shift reagent, Eu(hfc)$_3$.

The stereochemical course of the first conjugate addition step by Grignard reagents, a common step for



Scheme 1.

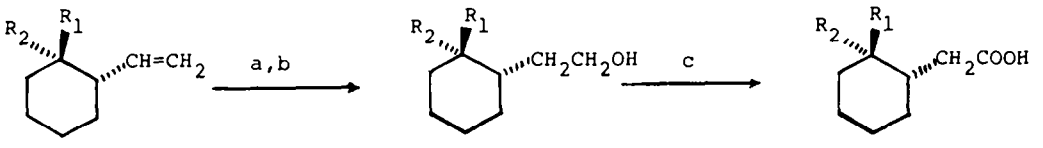


Scheme 2.

methods A, B, and C, is already well known to proceed via *s-cis* conformation as shown in 7.[4g] The point of interest in the present study is the stereochemical course of the second alkylation step with alkyl halides. The results are shown in Table 1. The stereochemical course of the alkylation of the anion of **9** by method A to give *cis*-**10** preferentially is quite reasonable based on the understanding that the reaction occurs from the opposite side of the R group.[9] It is striking to note, therefore, that except run 5 the stereochemical course of the second alkylation step by method B is reversed to give *trans*-**10**, which are isomers that are not readily obtainable under the usual alkylation conditions. It is quite interesting and important from both synthetic and mechanistic viewpoints what is the reason for these reactions to occur from the same side of the R group by method B.

Following the reaction mechanism of the first conjugate addition step proposed earlier,[4a,d,g] the configuration of the double bond of the resulting magnesioenamine should be in *Z*-stereochemistry as shown in **8**. Therefore, the possible reason for reversal of stereochemical course of the second alkylation step by method B is considered to be due to the steric effect of the original chiral center (t-leucine t-butyl ester moiety) in a fixed *Z*-configuration of magnesioenamine. The following experimental evidences support this view.

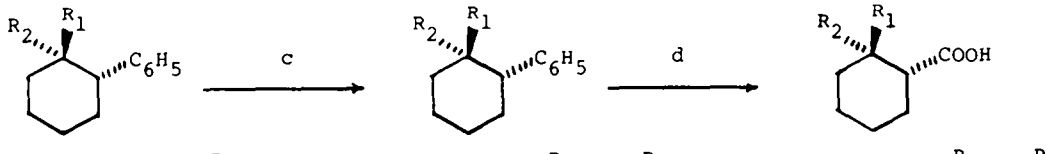
The first evidence came from the examination of the effect of the original chiral center on the diastereoselectivity of the reaction. As shown in Table 2, the reaction of α,β-unsaturated aldimines (**15**), prepared from the corresponding cycloalkenecarboxaldehydes (**5**) and 2-methoxyethylamine, with Grignard reagents followed by methyl iodide by method B afforded the corresponding *cis*-**10** preferentially. This means that the second methyl-



	R_1	R_2
(±)-trans-10b (R=vinyl)	CHO	CH_3
(±)-cis-10b (R=vinyl)	CH_3	CHO

	R_1	R_2
(±)-trans-11	CH_2OH	CH_3
(±)-cis-11	CH_3	CH_2OH

	R_1	R_2
(±)-trans-12	COOH	CH_3
(±)-cis-12	CH_3	COOH



	R_1	R_2
(±)-trans-10b (R=phenyl)	CHO	CH_3
(±)-cis-10b (R=phenyl)	CH_3	CHO

	R_1	R_2
(±)-trans-13	COOH	CH_3
(±)-cis-13	CH_3	COOH

	R_1	R_2
(±)-trans-14	COOH	CH_3
(±)-cis-14	CH_3	COOH

[a] $NaBH_4$-EtOH; [b] B_2H_6-THF, H_2O_2-aq. NaOH; [c] CrO_3-H_2SO_4-acetone; [d] O_3, H_2O_2-AcOH

Scheme 3.

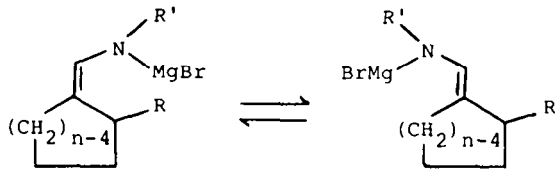
Table 1. Assymetric synthesis of **10**

Run	Method[a]	n	RMgBr	R'X	Isolated yield[b] trans-10	Isolated yield[b] cis-10	% e.e.[a,c]
1	A[d]	5	C_6H_5MgBr	CH_3I	0	65	82
2	A[d]	5	CH_2=CHMgBr	CH_3I	0	61	92
3	A[d]	6	C_6H_5MgBr	CH_3I	1	62	91
4	A[d]	6	CH_2=CHMgBr	CH_3I	11	51	93
5	B	5	C_6H_5MgBr	CH_3I	15	62	82[e]
6	B	5	CH_2=CHMgBr	CH_3I	62	0	92
7	B	6	C_6H_5MgBr	CH_3I	55	0	91
8	B	6	CH_2=CHMgBr	CH_3I	67	0	93
9	B	6	CH_2=CHMgBr	$C_6H_5CH_2I$	67	0	93
10	B	6	CH_2=CHMgBr	CH_2=CH-CH_2Br	63	0	93
11	B	6	CH_2=CHMgBr	C_2H_5I	65	0	93
12	B	6	CH_2=CHMgBr	CH_3OCH_2Cl	52	0	93
13	C	5	C_6H_5MgBr	CH_3I	2	44	82
14	C	6	C_6H_5MgBr	CH_3I	0	49	91

a) See text. b) After column chromatography. c) Corrected value for the optical purity of 2 (R=Bu^t) used. d) Some O-methylated product was also isolated. e) This value was obtained for cis-isomer by comparison of its rotation with that obtained in run 1.

ation occurs from the opposite side of the initially introduced R group, as in the reaction of **9** by method A as described above. As the 2-methoxyethylamine moiety of **15** is established to work as a bidentate ligand[10] like t-leucine t-butyl ester moiety of **6** during the Grignard 1,4-addition step, it is highly probable that the magnesioenamine (**16**), having similar structure with the corresponding magnesioenamine (**8**) but having no chiral center at the chelated ring, is produced. The fact that the reaction of methyl iodide gave *cis*-**10** preferentially with **16**, while *trans*-**10** preferentially with **8** (except run 5 in Table 1) clearly suggests that the original chiral center at the chelated ring of **8** exhibits strong steric influence on the second alkylation step.

The second evidence came from the examination of the effect of *Z*-configuration on the diastereoselectivity of the reaction by method B. It is reported that *E*-*Z*-isomers of metalloenamines do not equilibrate under the condition like that employed in method B, but do equilibrate in THF under reflux.[11] Assuming that magnesioenamine (**17**) of *Z*-configuration is a less stable isomer compared with the corresponding *E*-isomer (**18**), it is probable that equilibration between **17** and **18** prior to alkylation will change the diastereoselectivity of the reaction. Although the chemical yields became lower probably due to the instability of magnesioenamines at higher temperatures, methylation of magnesioenamines after heating was found to give *cis*-isomer preferentially as shown in Table 1 (runs 13 and 14). Additional support for the existence of *E*-*Z* isomerization of metalloenamines in this case was observed by ^{13}C NMR studies by the method similar to that reported by Bergbreiter, Newcomb[11a] and Meyers.[11b] Thus, starting from cyclohexenecarboxaldehyde (**5b**) whose aldehyde carbon was enriched with ^{13}C, magnesioenamine (**8b**, R=Ph) was prepared with phenylmagnesium bromide in THF-d_8 at −23°. ^{13}C NMR spectrum of this magnesioenamine showed a single peak of enriched carbon at 146.0 ppm before heating, but a new peak at 147.5 ppm appeared after heating at 70°. The intensity of the new peak relative to the initial peak increased gradually, and the signals became complex after 3 hr at 70°, probably due to partial decomposition.



17 18

Scheme 4.

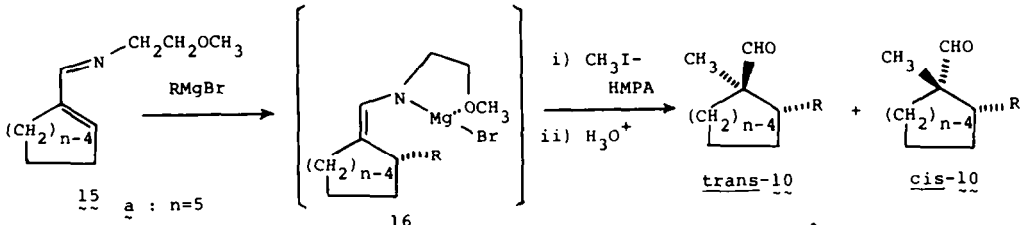
These data clearly show that the formation of magnesioenamine having *Z*-configuration and attack of alkyl halide under the steric influence of the original chiral center of t-leucine t-butyl ester moiety are responsible for the preferred formation of *trans*-isomer in method B. However, as shown in the results by method A, substituent R introduced initially is expected to show steric hindrance at the second alkylation step in method B also. Therefore, assuming that the configuration of magnesioenamine is retained in *Z*-configuration throughout the reaction, stereochemical course of the second alkylation step by method B is considered to be determined by the sum of the two opposing steric effects. In all cases examined, the results can be rationalized by evaluating the steric effect by the original chiral center as shown above except one example (Table 1, run 5). This situation was verified by the results of cyclopentenecarboxaldehyde (**5a**) with Grignard reagents having R group of different steric size followed by methyl iodide by method B as shown in Table 3. Thus, in cyclopentane series, *trans*-isomer predominates in cases where steric size of R group is not so bulky, while *cis*-isomer predominates in cases where steric size is reasonably bulky.

The present procedures for the synthesis of *trans*- and *cis*-1,2-disubstituted cycloalkanecarboxaldehydes (**10**) in high diastereomeric and enantiomeric purities are expected to be highly valuable in providing useful chiral synthons in the synthesis of various optically active compounds.

EXPERIMENTAL

All m. and bo. ps are uncorrected. IR spectra were recorded with a JASCO DS-402G or with a JASCO IRA-1 grating IR spectrometer. NMR spectra were recorded with a JEOL JNM-PS

Table 2. The reaction of **15** to **10** by method B

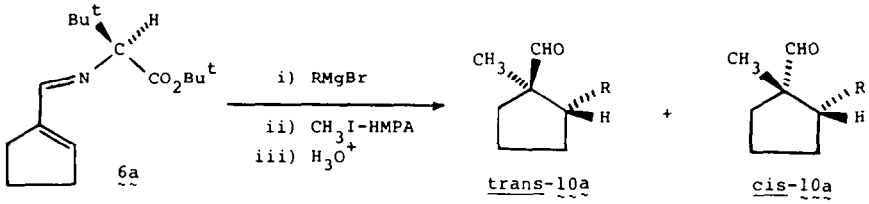


15 a : n=5 b : n=6 16

Run	n	RMgBr	Isolated yield[a] trans-10	cis-10
1	5	C_6H_5MgBr	0	17
2	5	CH_2=CHMgBr	8	25
3	6	C_6H_5MgBr	0	52
4	6	CH_2=CHMgBr	0	45

a) After column chromatography

Table 3. The reaction of **6a** to **10a** by method B



6a

trans-10a cis-10a

Run	RMgBr	Chem. yield (%)	trans-10a : cis-10a[a]	
1	CH_2=CHMgBr	62	>95	<5
2	CH_2=C(CH$_3$)MgBr	71	20	80
3	C_6H_5MgBr	82	18	82

a) The ratio was determined by ^{1}H NMR.

100 or with a Hitachi R-24 spectrometer for ^{1}H, with a JEOL JNM-FX 100 spectrometer for ^{13}C. Chemical shift values are expressed in ppm relative to internal standard (TMS or ^{13}C-enriched TMS). Mass spectra were recorded with a JEOL JMS-01 SG-2 mass spectrometer. Optical rotations were measured with a JASCO DIP-181 automatic polarimeter.

General procedure for the synthesis of **10**

Method A. KH (22.7% in oil) (1.76 g, corresponding to be 400 mg of KH, 10.0 mmol) was washed with hexane, and was suspended in THF (25 ml). A soln of **9** (5.0 mmol) in THF (2.5 ml) was added to the above suspension, and the whole was stirred under Ar at room temp until gas evolution ceased, and was then cooled to −23°.[13] A soln of alkyl halide (20 mmol) in THF (1 ml) was added and then the whole was stirred for 30 min. After addition of satd. aq. NH_4Cl (20 ml), the mixture was extracted twice with ether (30 ml, 20 ml). The combined ethereal extracts were washed successively with 5% aq. $Na_2S_2O_3$, 10% aq. HCl, satd. aq. $NaHCO_3$, satd aq. NaCl, and dried ($MgSO_4$). Evaporation of the solvent afforded the product mixture, which was subjected to silica gel column chromatography. The results are summarized in Table 1. Typical example is as follows:

Run 1. Starting from(-)-*trans*-**9a** (R=Ph) (o.p. 82%),[4g] (+)-*cis*-**10a** (R=Ph, R'=Me) of $[\alpha]_D^{20}$ +3.4° (*c* = 3.99, benzene) was obtained as a colorless liquid (612 mg, 65%). IR (film) cm^{-1}: 1725 (CHO). ^{1}H NMR ($CDCl_3$) δ:1.18 (3H, s, CH_3), 1.24–2.35 (6H, m, CH_2-CH_2-CH_2), 2.76–3.00 (1H, m, *CH*), 7.03–7.31 (5H, m, C_6H_5), 9.15 (1H, s, *CHO*). ^{13}C NMR ($CDCl_3$) δ:21.2 (CH_3), 56.0 (quarternary *C*), 56.7 (tertiary *C*), 126.7, 128.2, 138.8 (C_6H_5), 205.2 (*CHO*). MS m/e: 188 (M^+). 2,4-Dinitrophenylhydrazone: m.p. 123–125° (dec). Anal. ($C_{19}H_{20}N_4O_4$)C, H, N.

Method B. A soln of Grignard reagent (40 mmol) in THF was added to a soln of 6 (prepared from **5** and L-2 (R=Bu^t) of 91.3% optical purity[4d] for runs 5 through 8, and of 99% optical purity[4d] for runs 9 through 12 in Table 1) (10 mmol) in THF (the volume of THF solution was adjusted to be 70 ml after addition) at −23° under Ar, the whole was stirred at the same temp for 5 hr.

(i) From the above mixture, a portion (21 ml, 30% of the total) was removed, and was poured into 10% aq. citric acid (20 ml). After stirring at room temp for 1 hr, the whole was extracted twice with ether (50 ml × 2). The ethereal extracts were combined, washed successively with satd. aq. $NaHCO_3$, satd. aq. NaCl, dried ($MgSO_4$), and evaporated to give a residue, which was subjected to silica gel column chromatography to isolate **9** for the confirmation of optical rotations.[4g]

(ii) To the rest (70% of the total) of the above mixture was added a soln of alkyl halide (42 mmol, 6 equivs) and HMPA (6.27 g, 35 mmol, 5 equivs) in THF (5 ml), and the whole was stirred at −23° for 30 min, and then at room temp for 15 hr. The mixture was poured into 10% aq. citric acid (60 ml). After stirring at room temp for 1 hr, the whole was extracted twice with ether (100 ml × 2). The ethereal extracts were combined, washed with 10% aq. $Na_2S_2O_3$ satd. aq. $NaHCO_3$, satd. aq. NaCl, dried ($MgSO_4$), and evaporated to give a residue, which was subjected to silica gel column chromatography to obtain all isolable products. Typical example is as follows:

Run 7. (i) (−)-*trans*-**9b** (R=Ph) was isolated as colorless liquid (298 mg, 53%) of $[\alpha]_D^{20}$ −38.1° (*c* = 1.07, benzene) ($[\alpha]_D^{20}$ −41.7° (benzene), or 95% e.e.[4g] after correction of the optical purity of **6b** used). (ii) (−)-*trans*-**10b** (R=Ph, R'=Me) was isolated as colorless liquid (775 mg, 55%). IR (film) cm^{-1}: 1722 (CHO). ^{1}H NMR ($CDCl_3$) δ: 1.01 (3H, s, CH_3), 1.17–2.08 (8H, m, CH_2–CH_2–CH_2–CH_2), 3.30 (1H, dd, J = 11.5 and 4.4 Hz, *CH*), 6.94 7.37 (5H, m, C_6H_5), 9.47 (1H, s, *CHO*). ^{13}C NMR ($CDCl_3$) δ: 13.0 (CH_3), 46.7 (tertiary *C*), 50.5 (quarternary *C*), 127.9, 128.4, 129.4, 142.0 (C_6H_5), 205.5 (*CHO*). $[\alpha]_D^{20}$ −12.7° (*c* = 4.03, benzene) ($[\alpha]_D^{20}$ −13.9° (benzene) after correction of the optical purity of **6b** used). MS m/e: 202 (M^+). 2,4-Di-nitrophenylhydrazone: m.p. 167.5–169°. Anal. ($C_{20}H_{22}N_4O_4$) C, H, N. From the above aq. citric acid phase, L-2 (R=Bu^t) was recovered without any loss of optical purity.

Method C. A soln of PhMgBr (6.0 mmol) in THF (3.75 ml) was added to a soln of **6** (5.0 mmol) in THF (25 ml) at −23° under Ar, and the whole was stirred at the same temp for 5 hr, and then was refluxed for 3 to 6 hr. The mixture was cooled to −23° again, and was mixed with a soln of MeI (1.87 ml, 30 mmol) and HMPA (3.5 ml, 20 mmol) in THF (5 ml). The whole was stirred at −23° for 2 hr, and then at room temp for 16 hr. The mixture was poured into 10% aq. citric acid (60 ml), and the whole was treated as written in method B-ii above to give an oil, which was subjected to column chromatography. Typical example is as follows:

Run 14. (+)-*cis*-**10b** (R=Ph, R'=Me) was isolated as a colorless liquid (462 mg, 49%) of $[\alpha]_D^{20}$ +41.9° (*c* = 1.13, benzene) ($[\alpha]_D^{20}$ +45.8° (benzene) after correction of the optical purity of **6b** used). IR (film) cm^{-1}: 1722 (CHO). ^{1}H NMR ($CDCl_3$) δ: 0.97 (3H, s, CH_3), 1.12–2.08 (8H, m, CH_2–CH_2–CH_2–CH_2), 2.58 (1H, dd, J = 12.0 and 3.7 Hz, *CH*), 7.08–7.43 (5H, m, C_6H_5), 9.75 (1H, s, *CHO*). ^{13}C NMR ($CDCl_3$) δ: 22.9 (CH_3), 48.9 (quarternary *C*), 53.0 (tertiary *C*), 126.6, 127.9, 129.2, 141.6 (C_6H_5), 206.7 (*CHO*). MS *m/e*: 202 (M^+). 2,4-dinitrophenylhydrazone: m.p. 178.5–179.5° (for (±)-isomer). Anal. ($C_{20}H_{22}N_4O_4$) C, H, N.

(±)-trans-2-*Methyl*-2-*hydroxymethyl*-*cyclohexaneethanol* ((±)-trans-11). (±)-*trans*-**10b** (R=vinyl) (prepared from **5b** and (±)-**2** (R=Bu^t) by method B) was reduced with $NaBH_4$ to the corresponding alcohol, which was subjected to hydroboration followed by oxidation as usual to give (±)-*trans*-**11** in 69% yield as colorless prisms of m.p. 53–55°. Anal. ($C_{10}H_{20}O_2$), C, H.

(±)-cis-2-*Methyl*-2-*hydroxymethyl*-*cyclohexaneethanol* ((±)-cis-11). (±)-*cis*-**10b** (R = vinyl) (prepared from (±)-**9b** (R=vinyl) by method A) gave (±)-*cis*-**11** in 50% yield as colorless prisms of m.p. 113.5–114°. Anal. ($C_{10}H_{20}O_2$) C, H.

(±)-trans-2-*Carboxy*-2-*methylcyclohexaneacetic acid* ((±)-trans-12). (±)-*trans*-**11** was oxidized with Jones reagent in

acetone as usual to give (±)-*trans*-**12** in 68% yield as colorless prisms of m.p. 174–177.5° (reported[6] m.p. 175–177.8°). IR (KBr) cm^{-1}: 1705 (COOH). ^1H NMR ($CDCl_3$) δ: 0.93–1.87 (9H, m), 1.23 (3H, s, CH_3), 2.03–2.41 (2H, m, CH_2COOH), 9.05–11.5 (2H, broad, two COO*H*). Anal. ($C_{10}H_{16}O_4$) C, H.

(±)-cis-2-*Carboxy*-2-*methylcyclohexaneacetic acid* ((±)-cis-12). (±)-*cis*-**11** gave (±)-**12** in 36% yield as colorless prisms of m.p. 165–166° (reported[6] m.p. 163–165°). IR (KBr) cm^{-1}: 1720 (COOH). ^{1} NMR ($CDCl_3$) δ: 1.05–2.21 (9H, m), 1.29 (3H, s, CH_3), 2.54–2.67 (2H, m, CH_2COOH), 10.22–11.66 (2H, broad, two COO*H*). Anal. ($C_{10}H_{16}O_4$) C, H. This sample was identified with the authentic sample prepared by the reported method[6] by IR, NMR, and mixed m.p. determination.

(±)-trans-1-*Methyl*-2-*phenylcyclohexanecarboxylic acid* ((±)-trans-13). (±)-*trans*-**10b** (R=Ph) (prepared from **5b** and (±)-**2** (R=Bu^t) by method B) was oxidized with Jones reagent in acetone as usual to give (±)-*trans*-**13** as a crude solid of m.p. 124–141° in almost quantitative yield and was used in the next step without further purification. IR (KBr) cm^{-1}: 1691 (COOH). MS *m/e*: 218 (M^+).

(±)-cis-1-*Methyl*-2-*phenylcyclohedanecarboxylic acid* ((±)-cis-13). (±)-*cis*-**10b** (R=ph) (prepared from (±)-**9b** (R=Ph) by method A) gave (±)-*cis*-**13** as a crude solid of m.p. 82–89° in almost quantitative yield and was used in the next step without further purification. IR (KBr) cm^{-1}: 1687 (COOH). MS *m/e*: 218 (M^+).

(±)-trans-1-*Methylcyclohexane*-1,2-*dicarboxylic acid* ((±)-trans-14). (±)-*trans*-**13** was oxidized with ozone in acetic acid followed by treatment with 30% aq. H_2O_2 as usual to give (±)-*trans*-**14** as colorless prisms of m.p. 213–214° (reported[7] m.p. 213°). IR (KBr) cm^{-1}: 1690 (COOH). ^1H NMR (DMSO-d_6) δ: 1.13 (3H, s, CH_3). Anal. ($C_9H_{14}O_4$) C, H.

(±)-cis-1-*Methylcyclohexane*-1,2-*dicarboxylic acid* ((±)-cis-14). (±)-*cis*-**13** gave (±)-*cis*-**14** as colorless prisms of m.p. 159–160° (reported[8] m.p. 159.5–160°). IR (KBr) cm^{-1}: 1700 (COOH). ^1H NMR (DMSO-d_6) δ: 1.19 (3H, s, CH_3). Anal. ($C_9H_{14}O_4$) C, H.

N-(*Cyclopentenylmethylidene*)-2-*methoxyethyamine* (**15a**. Prepared from **5a** and 2-methoxyethylamine as usual as a pale yellow liquid. IR (film) cm^{-1}: 1645, 1610 (C=N, C=C). ^1H NMR ($CDCl_3$) δ: 1.71–2.83 (6H, m), 3.35 (3H, s, OCH_3), 3.64 (4H, S, N-CH_2-CH_2-O), 6.11–6.37 (1H, m, C*H*=C), 8.13 (1H, s, C*H*=N). MS *m/e* : 153 (M^+).

N(*Cyclohexenylmethylidene*) - 2 - *methoxyethylamine* (**15b**). Prepared from **5b** and 2-methoxyethylamine as a pale yellow liquid. IR (film) cm^{-1}: 1645, 1630 (C=N, C=C). ^1H NMR ($CDCl_3$) δ: 1.36–2.67 (8H, m), 3.35 (3H, s, OCH_3), 3.60 (4H, s, N-CH_2-CH_2-O), 5.97–6.31 (1H, m, C*H*=C), 7.80 (1H, s, C*H*=N). MS *m/e*: 167 (M^+).

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