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Distinction of Diastereofaces at the α-Position of Chiral Cyclic Acetals

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Key words: chiral acetal; asymmetric 1,2-addition; asymmetric 1,4-addition; C_2 symmetry; determination of optical purity; chiral carboxylic acid

Abstract: *Asymmetric 1,2- and 1,4-additions to substrates with an acetal as a chiral auxiliary have been studied. Among the tested substrates, C_2-symmetrical 5c was most effective for 1,2-addition with $MeTi(O\text{-}iPr)_3$. Furthermore, C_2-symmetrical carbinol 5b has been found to be a potent ^{1}H-NMR reagent for determination of optical purity of carboxylic acids with a chiral center at the α-position.*

In connection with our previous study on the diastereoselective preparation of chiral 1,3-dioxane derivatives (**1-4a,b**),[1] we wish to report here asymmetric 1,2- and 1,4-additions at the α-position of chiral cyclic acetals, in addition to an application of related compounds as ^{1}H-NMR reagents for the determination of the optical purity of carboxylic acids with a chiral center at the α-position.

1. Asymmetric 1,2-addition Asymmetric 1,2-additions based on a chiral acetal auxiliary has been studied by Alexakis[2a] and Tamura.[2b] In the course of our preliminary studies on asymmetric reactions using chiral acetals,[3] 1,2-addition of MeMgBr to various aldehydes (**1-7c**) has been investigated. Substrates **1-7c** were prepared by the sequence of reactions: i) acetalization of α-keto esters (methyl pyruvate and methyl benzoylformate) with chiral diols such as (*R*)-butane-1,3-diol, (*R,R*)-pentane-2,4-diol, (*R,R*)-butane-2,3-diol, and (*R,R*)-1,4-dibenzyloxybutane-2,3-diol; ii) $LiAlH_4$ reduction of esters (**1-7a**) to carbinols (**1-7b**); and iii) Swern's oxidation[4] of **1-7b** to **1-7c**. The stereochemistry of **1-4a,b** was unambiguously determined as depicted in Fig. 1 based on 270 MHz two-dimensional NOESY spectra.[1] For example, in the NOESY spectrum of the acetate of **2b**, a cross peak between 2-CH_2O- and 4-H was observed. In **3b**, cross peaks between 2-Me and 4-H, 6-Hax were observed. Aldehydes **1-4c** were assumed to keep the configuration of the corresponding carbinols **1-4b**. For the conformation of the C_2-symmetrical **5a,b**, a bulky phenyl group seems to have an equatorial orientation based on the observation of a cross peak between 2-CH_2O- and 4-Haxial of **5b** in the NOESY spectrum.

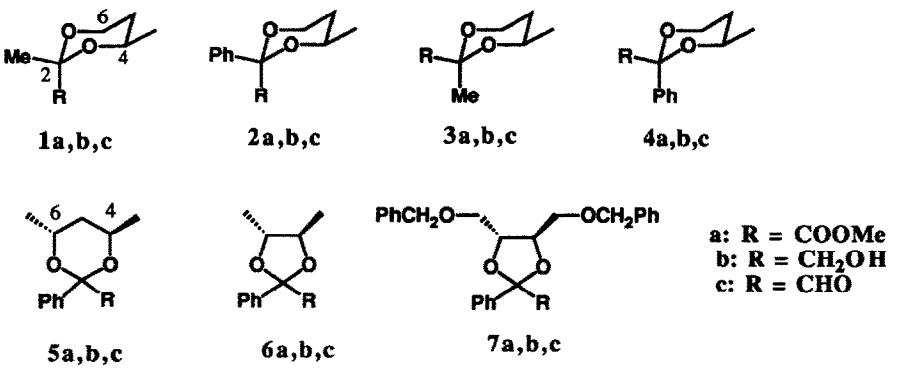


Fig. 1

The reaction of **1-7c** with MeMgBr (3 eq.) in THF was carried out at -15°C for 8-15 h, and addition products were obtained in fair to good yields (60-83%)(Table I). Although the diastereomeric ratios of products were unsatisfactory (up to 77 : 23 in entry 3), their absolute configuration suggests the following: 1) Aldehydes of equatorial orientation (entries 3 and 4) gave better diastereoselectivity than those of axial orientation (entries 1 and 2). Concerning the absolute configuration of the newly generated stereogenic center, the former gave predominantly (*R*)-products and the latter gave (*S*)-products. 2) In the cases of C_2-symmetrical substrates (entries 5-7), six-membered **5c** (entry 5) gave a better result than five-membered **6,7c** (entries 6 and 7). The diastereomeric ratio of the addition products was estimated by ^{1}H-NMR spectra based on the intensity of 1'-Me signals. In the cases of entries 1 and 2, two diastereomeric products could be easily separated by silica-gel column chromatography.

The absolute configuration of the newly generated stereogenic center of products in entries 1 and 3 was determined after conversion into the chiral α-ketol (3-hydroxy-2-butanone) by comparison of specific rotations with those reported.[5] For the product in entry 5, the absolute configuration was determined by Mosher's method[6] after conversion into the corresponding (-)-MTPA ester of α-ketol (2-hydroxy-1-phenyl-1-propanone).

Next, a C_2-symmetrical **5c** was submitted to 1,2-addition with another methylated metal species such as Me_2CuLi, MeMgBr-CuI, and $MeTi(O\text{-}iPr)_3$. Results are summarized in Table II. The diastereomeric excess of addition product in entries 1-5 was similar in all cases (46-60 % d.e.).

Table I. Asymmetric 1,2-addition of MeMgBr to 1-7c

RCHO —(MeMgBr, -15°C, THF)→ RCH(OH)CH$_3$ (1')

Entry	Substrate	Yield (%)	Diastereomeric Ratio (1'*R* : 1'*S*)
1	**1c**	65	43 : 57
2	**2c**	60	39 : 61
3	**3c**	70	77 : 23
4	**4c**	78	74 : 26
5	**5c**	83	75 : 25
6	**6c**	67	68 : 32
7	**7c**	80	72 : 28

The best result (62% yield, 88% d.c.) was obtained in entry 6 by the reaction with $MeTi(O\text{-}iPr)_3$ in ether at room temperature. A similar reaction at -15°C was so slow that the addition product was afforded in only 3% yield (86% d.e.)(85% recovery of **5c**).

The stereochemical course of reactions in Table II was considered to be as follows. Taking into consideration the conformational property of the axial aldehyde function in **5c**, two kinds of stable conformations (**A** and **B**) were presumed. Based on local conformational analysis of **A** and **B**, the former might allow an addition of reagent from the *si*-face of the carbonyl and the latter from the *re*-face. But, the reaction from the *si*-face seems to be hindered by a C_6-axial methyl group in the case of **A**. Consequently, addition from the *re*-face was considered to be favorable in both cases of **A** and **B** (Fig. 2).

Table II. Asymmetric 1,2-addition to 5c

5c

Entry	Reagents and Conditions	Yield (%)	D.e. (%)
1	MeMgBr/THF/-15°C/10h	83	50
2	MeMgBr/Ether/-15°C/8h	89	58
3	Me_2CuLi/Ether/-78°C/2h	95	46
4	Me_2CuLi/HMPA/Ether/-78°C/3h	91	52
5	MeMgBr/CuI/Ether/-78°C/10h	76	60
6	$MeTi(O\text{-}iPr)_3$/Ether/r.t./20h	62	88

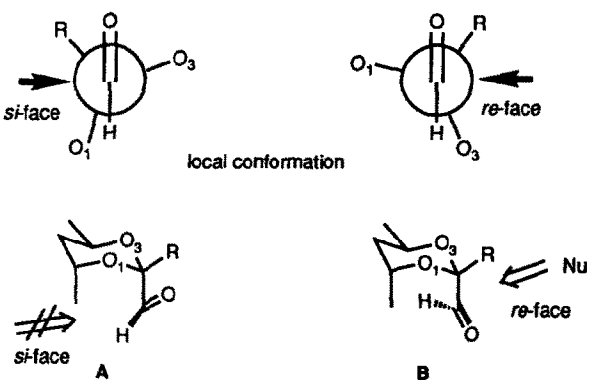
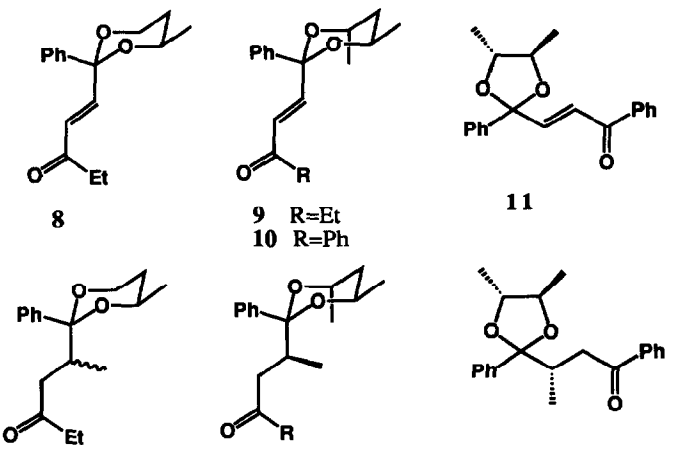


Fig. 2

2. Asymmetric 1,4-addition In connection with the asymmetric 1,4-addition to α,β-unsaturated carbonyl compounds with an acetal moiety as a chiral auxiliary, several studies have been reported utilizing various types of substrates by other groups.[2a,7] In these cases, diastereoselectivity was not satisfactory (0-34 % d.e.). These results prompted us to study the asymmetric 1,4-addition to α,β-unsaturated ketones (**8-11**) with a chiral acetal function at the γ-position. In our work, 1,4-addition of Me_2CuLi to **8-11**, prepared by Wittig-Horner reactions of corresponding aldehydes (**2c**, **5c** and **7c**), was employed in ether at -30 °C. Conjugate addition products (**12-15**) were obtained in good yields (82-91 %). The diastereoselectivity of these reactions was unsatisfactory (8-48 % d.e.)(Fig. 3). The best result (91% yield, 48% d.e.) among them was obtained utilizing **10** as a substrate in the presence of trimethylsilyl chloride.[8] This selectivity seems to be

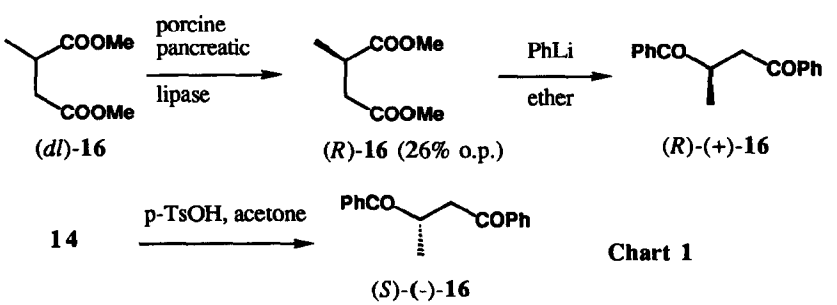
the best result at present among the aforementioned similar asymmetric conjugate additions.[2a,7] D.e. values were estimated based on doublet signals attributable to a methyl group on the newly generated stereogenic center in the ^{1}H-NMR spectra. The absolute configuration of products (**14** and **15**) was determined by comparison of the specific rotation with that of an authentic sample after conversion into 2-methyl-1,4-diphenyl-1,4-butanedione (**16**). The authentic sample of (+)-**16** was synthesized as follows. Dimethyl (*R*)-2-methylsuccinate (26 % o.p.) prepared in accordance with Rousseau's procedure[9] was employed to a reaction with phenyl lithium to afford (+)-**16** ($[\alpha]_D^{24}$ +15.3 (*c* 0.10, $CHCl_3$)). Deacetalization of **14** and **15** afforded (-)-**16** in 90-99% yield. These results suggest the absolute configuration of **14** and **15** to be *S* (Chart 1). The absolute stereochemistry of **13** was assumed by comparison of the ^{1}H-NMR spectrum with that of **14**. The stereochemical reaction process was considered to be similar to that of 1,2-addition (Fig. 2).



8 **9** R=Et **10** R=Ph **11**

12: 8% d.e. **13**: R=Et 38% d.e. **14**: R=Ph 48% d.e. **15**: 12% d.e.

Fig. 3



(*dl*)-**16** (*R*)-**16** (26% o.p.) (*R*)-(+)-**16**

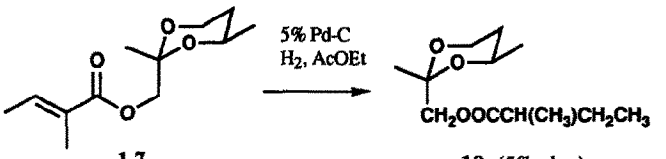
14 (*S*)-(-)-**16**

Chart 1

3. Application of chiral 1,3-dioxanes as a ^{1}H-NMR reagent for determination of e.e.

Our previous attempt for asymmetric hydrogenation of **17** afforded the saturated product (**18**) with a poor d.e (Chart 2). In the ^{1}H-NMR spectrum of **18**, the diastereotopic 2'-Ha,b were observed as two sets of doublet signals, respectively. This result prompted us to study a ^{1}H-NMR spectroscopic application of chiral

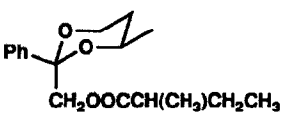
acetals to determine the e.e. of carboxylic acids with a stereogenic center at the α-position. Mosher's method[6] is so far the most widely accepted for the determination of e.e. for chiral alcohols and amines, but there has been no general NMR spectroscopic method for chiral carboxylic acids. At first, a ^{1}H-NMR spectroscopic study was employed utilizing five types of carbinols (**1b**, **2b**, **4b**, **5b**, and **6b**) as chiral acetal derivatives (Table III).



17 18 (5% d.e.)

Chart 2

Table III. Chemical shifts of α-protons of cyclic acetals



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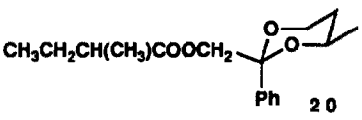

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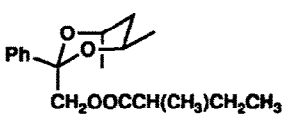

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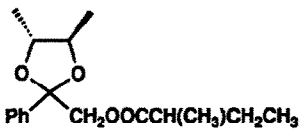

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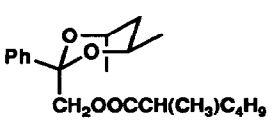
Entry	Substrates	δ Ha	(δ Ha')	(δ Hb')	δ Hb	$\Delta\delta_A$	$\Delta\delta_B$	$\Delta\delta_C$
1	**18**	4.33	(4.36)	(4.43)	4.46	0.03	0.13	0.07
2	**19**	4.46	(4.50)	(4.63)	4.67	0.04	0.21	0.13
3	**20**	4.09	(4.11)	(4.16)	4.18	0.02	0.09	0.05
4	**21**	4.01	(4.05)	(4.39)	4.43	0.04	0.42	0.34
5	**22**	4.20	(4.23)	(4.29)	4.32	0.03	0.12	0.06

$\Delta\delta_A$ = δHb-δHb' = δHa'-δHa, $\Delta\delta_B$ = δHb-δHa, $\Delta\delta_C$ = δHb'-δHa'

For estimating the ability to distinguish corresponding diastereomers, three types of $\Delta\delta_{A,B,C}$ values seem to be useful: $\Delta\delta_A$= δHb-δHb'=δHa'-δHa, $\Delta\delta_B$= δHb-δHa, $\Delta\delta_C$= δHb'-δHa'. $\Delta\delta_A$ value shows directly the effectiveness for differentiating the two diastereomers. In addition $\Delta\delta_B$ and $\Delta\delta_C$ show ease in assignment of

each signal. Among the substrates tested, **21** showed the largest $\Delta\delta$ values ($\Delta\delta_A$= 0.04, $\Delta\delta_B$= 0.42, $\Delta\delta_C$= 0.34). The ^{1}H-NMR spectroscopic generality of **21**-type compounds was studied as shown in Table IV. In all cases, $\Delta\delta_A$ value is larger than 0.04; especially in cases of substrates with a phenyl group (**24** and **25**), $\Delta\delta_A$ is 0.19 and 0.22, respectively. Furthermore, $\Delta\delta_B$ and $\Delta\delta_C$ values are large enough to be observed as isolated signals. These results suggest that **5b** is a potent reagent for the determination of the e.e. of chiral carboxylic acids with the stereogenic center at the α-position. The correlation between each peak (Ha,a',b,b') and absolute stereochemistry was studied based on compound **25**. As shown in entries 5 and 6 of Table IV, signals at δ 4.11 and 4.29 could be assigned to Ha,b of (2'*R*)-**25** and signals at δ 3.90 and 4.51 to Ha,b of (2'*S*)-**25**, respectively. These assignments were based on a principle similar to that of Mosher's method.[6] That is to say, by assuming a stable conformation of **25** to be as shown in Table IV, Hb' in (2'*R*)-**25** might be observed at upper field than Hb in (2'*S*)-**25**, and Ha' in (2'*R*)-**25** at lower field than Ha in (2'*S*)-**25**.

Table IV. Chemical shifts of α-protons of cyclic acetal derivatives



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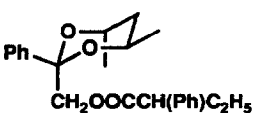

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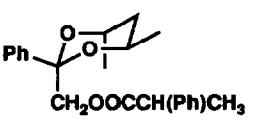

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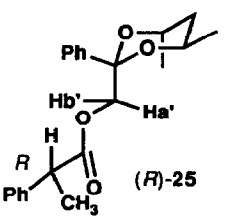
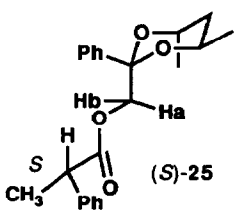


(*R*)-**25**



(*S*)-**25**

Entry	Substrates	δ Ha	(δ Ha')	(δ Hb')	δ Hb	$\Delta\delta_A$	$\Delta\delta_B$	$\Delta\delta_C$
1	**21**	4.01	(4.05)	(4.39)	4.43	0.04	0.42	0.34
2	**23**	4.00	(4.04)	(4.38)	4.42	0.04	0.42	0.34
3	**24**	3.90	(4.09)	(4.32)	4.51	0.19	0.61	0.23
4	**25**	3.90	(4.11)	(4.29)	4.51	0.22	0.61	0.18
5	(2'*R*)-**25**		4.11	4.29				
6	(2'*S*)-**25**	3.90			4.51			

$\Delta\delta_A$ = δHb-δHb' = δHa'-δHa, $\Delta\delta_B$ = δHb-δHa, $\Delta\delta_C$ = δHb'-δHa'

To develop the method utilizing **5b** as a ^{1}H-NMR reagent, it is necessary to establish a suitable method for ester bond formation between the chiral alcohol and the carboxylic acid. To this end, three kinds of method were investigated: I) Transesterification with the sodium salt of **5b** and the corresponding methyl ester of the substrate (100 °C in toluene). II) Esterification by Mitsunobu's method.[10] III) Esterification with **5b** and the acid chloride prepared from the carboxylic acid ($(COCl)_2$ in refluxing benzene). Method I afforded ester in 60-80 % yields, but this method needed the very severe reaction conditions of heating at 100°C for 5 h. Method II resulted in poor yields (13-21 %) because of steric hindrance. Method III, the best route at present, afforded esters in 70-85 % yields.[11]

Experimental

Infrared (IR) spectra were measured on a JASCO A-202 spectrometer, ^{1}H-NMR spectra on a JEOL GX-270 spectrometer, and mass spectra (MS) on a JEOL JMS-D-300 spectrometer. Specific rotation was measured on a JASCO DIP-360 polarimeter. For column chromatography, silica gel 70-230 mesh (Merck, Kieselgel 60) was used. All organic solvent extracts were washed with brine, and dried over anhydrous sodium sulfate.

Preparation of 5-7a,b Compounds **5-7a,b** were prepared by a similar manner to those of **1-4a,b.**[1]

(4*R*,6*R*)-2-Methoxycarbonyl-4,6-dimethyl-2-phenyl-1,3-dioxane (5a) Colorless solid, mp. 50-52°C (haxane-ether), 65% yield, $[\alpha]_D^{22}$ +9.0 (*c* 1.03, $CHCl_3$). IR (Nujol): 1742, 1450, 1380, 1240, 1100 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.32, 1.34 (3H each, d, *J*=6.3 Hz, 4,6-Me), 1.64-1.73 (2H, m, 5-H), 3.70 (3H, s, COOMe), 3.92, 4.20 (1H each, m, 4,6-H), 7.32-7.40 (3H, m, Ar-H), 7.62-7.67 (2H, m, Ar-H). MS *m/z*:191 (M^+-COOMe), 123, 105.

(4*R*,5*R*)-2-Methoxycarbonyl-4,5-dimethyl-2-phenyl-1,3-dioxolane (6a) Colorless oil, 67% yield, $[\alpha]_D^{23}$ -46.8 (*c* 1.22, $CHCl_3$). IR (neat): 1743, 1440, 1250, 1095 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.32, 1.36 (3H each, d, *J*=5.9 Hz, 4,5-Me), 3.70, 3.94 (1H each, dq, *J*=2.3, 5.9 Hz, 4,5-H), 3.74 (3H, s, COOMe), 7.32-7.41 (3H, m, Ar-H), 7.57-7.64 (2H, m, Ar-H). MS *m/z*: 177 (M^+-COOMe), 105.

(4*R*,5*R*)-4,5-Dibenzoyloxymethyl-2-methoxycarbonyl-2-phenyl-1,3-dioxolane (7a) Colorless oil, 83% yield, $[\alpha]_D^{23}$ +20.9 (*c* 1.66, $CHCl_3$). IR (neat): 1743, 1450, 1100 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.63 (3H, s, COOMe), 4.22, 4.44 (1H each, m, 4,5-H), 4.51, 4.59 (2H each, s, OCH_2Ph), 7.21-7.38 (13H, m, Ar-H), 7.59-7.63 (2H, m, Ar-H). MS *m/z*: 448 (M^+), 389, 105, 91.

(4*R*,6*R*)-2-Hydroxymethyl-4,6-dimethyl-2-phenyl-1,3-dioxane (5b) Colorless oil, 91% yield, $[\alpha]_D^{20}$ +9.5 (*c* 1.02, $CHCl_3$). IR (neat): 3480, 1450, 1380, 1120 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.20 (3H, d, J=6.6 Hz, 4-Me), 1.26 (3H, d, *J*=6.6 Hz, 6-Me), 1.45-1.71 (2H, m, 5-H), 2.04 (1H, t, *J*=6.8 Hz, OH), 3.57 (2H, m, 2-CH_2), 3.88, 4.34 (1H each, m, 4,6-H), 7.28-7.40 (3H, m, Ar-H), 7.50-7.54 (2H, m, Ar-H). MS *m/z*: 204 (M^+-18), 191, 105.

(4*R*,5*R*)-2-Hydroxymethyl-4,5-dimethyl-2-phenyl-1,3-dioxolane (6b) Colorless oil, 97% yield, $[\alpha]_D^{23}$ -32.0 (*c* 1.18, $CHCl_3$). IR (neat): 3450, 1445, 1380, 1240, 1090 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.21, 1.33 (3H each, d, *J*=5.9 Hz, 4,5-Me), 2.10 (1H, t, *J*=6.8 Hz, OH), 3.53-3.75 (3H, m, 2-CH_2, 4 or 5-H), 3.86 (1H, dq, *J*=2.3, 5.9 Hz, 5- or 4-H), 7.28-7.39 (3H, m, Ar-H), 7.49-7.54 (2H, m, Ar-H). MS *m/z*: 190 (M^+-18), 177, 105.

(4*R*,5*R*)-4,5-Dibenzoyloxymethyl-2-hydroxymethyl-2-phenyl-1,3-dioxolane (7b) Colorless oil, 85% yield, $[\alpha]_D^{21}$ -0.66 (*c* 1.47, $CHCl_3$). IR (neat): 3450, 1450, 1240, 1070 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.79 (1H, t, *J*=5.6 Hz, OH), 3.40 (2H, m, 2-CH_2), 3.64-3.85 (4H, m, 4,5-CH_2), 4.02, 4.45 (1H each, m, 4,5-H), 4.44, 4.62 (2H each, s, OCH_2Ph), 7.16-7.39 (13H, m, Ar-H), 7.46-7.53 (2H, m, Ar-H). MS *m/z*: 402 (M^+-18), 389, 105, 91.

Preparation of 1-7c Oxalyl chloride (1.5 eq) was added to a solution of dimethyl sulfoxide (1.5 eq) in CH_2Cl_2 at -78°C under an Ar atmosphere. After being stirred for 5 min, carbinol (**1-7b**, 1.0 eq) in CH_2Cl_2 was added and the whole was stirred for 0.5 h. A solution of triethylamine (3 eq) in CH_2Cl_2 was added, and for additional 0.5 h the whole was stirred. Reaction was quenched by addition of brine and the whole was extracted with ether. Ether extracts were washed and dried. Solvent was removed *in vacuo* and oily residue was purified by silica gel column chromatography.

(2*R*,4*R*)-2-Formyl-2,4-dimethyl-1,3-dioxane (1c) Colorless oil, 32% yield, $[\alpha]_D^{24}$ +19.6 (*c* 1.66, $CHCl_3$). IR (neat): 2800, 1740, 1370, 1100 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.26 (3H, d, *J*=5.9 Hz, 4-Me), 1.35 (3H, s, 2-Me), 1.44, 1.68 (1H each, m, 5-H), 3.80-4.02 (3H, m, 4,6-H), 9.59 (1H, s, CHO). MS *m/z*: 145 (M^+-1), 115.

(2*R*,4*R*)-2-Formyl-4-methyl-2-phenyl-1,3-dioxane (2c) Colorless oil, 84% yield, $[\alpha]_D^{22}$ +45.1 (*c* 1.35, $CHCl_3$). IR (neat): 2800, 1750, 1440, 1380, 1090 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.37 (3H, d, *J*=6.3 Hz, 4-Me), 1.55, 1.71 (1H each, m, 5-H), 4.04-4.23 (3H, m, 4,6-H), 7.33-7.43 (3H, m, Ar-H), 7.57-7.63 (2H, m, Ar-H), 9.49 (1H, s, CHO). MS *m/z*: 207 (M^++1), 177, 105.

(2*S*,4*R*)-2-Formyl-2,4-dimethyl-1,3-dioxane (3c) Colorless oil, 58% yield, $[\alpha]_D^{24}$ -9.0 (*c* 1.68, $CHCl_3$). IR (neat): 2800, 1750, 1380, 1090 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.24 (3H, d, *J*=5.9 Hz, 4-Me), 1.48 (3H, s, 2-Me), 1.43-1.76 (2H, m, 5-H), 3.93-4.22 (3H, m, 4,6-H), 9.28 (1H, s, CHO). MS *m/z*: 129 (M^+-15), 115.

(2*S*,4*R*)-2-Formyl-4-methyl-2-phenyl-1,3-dioxane (4c) Colorless oil, 52% yield, $[\alpha]_D^{22}$ -77.7 (*c* 1.11, $CHCl_3$). IR (neat): 2800, 1755, 1450, 1380, 1100 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.32 (3H, d, *J*=6.3 Hz, 4-Me), 1.40, 1.78 (1H each, m, 5-H), 3.84-4.13 (3H, m, 4,6-H), 7.36-7.53 (5H, m, Ar-H), 9.24 (1H, s, CHO). MS *m/z*: 206 (M^+), 177, 105.

(4*R*,6*R*)-2-Formyl-4,6-dimethyl-2-phenyl-1,3-dioxane (5c) Colorless oil, 87% yield, $[\alpha]_D^{22}$ +21.4 (*c* 1.04, $CHCl_3$). IR (neat): 2800, 1742, 1450, 1380, 1120 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.33, 1.35 (3H each, d, J=6.3 Hz, 4,6-Me), 1.64-1.75 (2H, m, 5-H), 3.97-4.22 (2H, m, 4,6-H), 7.33-7.44 (3H, m, Ar-H), 7.54-7.60 (2H, m, Ar-H), 9.39 (1H, s, CHO). MS *m/z*: 191 (M^+-CHO), 122, 105.

(4*R*,5*R*)-2-Formyl-4,5-dimethyl-2-phenyl-1,3-dioxolane (6c) Colorless oil, 61% yield, $[\alpha]_D^{23}$ -31.0 (*c* 1.27, $CHCl_3$). IR (neat): 2800, 1745, 1450, 1380, 1080 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.33, 1.36 (3H each, d, *J*=5.9 Hz, 4,5-Me), 3.71-3.92 (2H, m, 4,5-H), 7.29-7.45 (3H, m, Ar-H), 7.50-7.58 (2H, m, Ar-H), 9.48 (1H, s, CHO). MS *m/z*: 206 (M^+), 177, 105.

(4*R*,5*R*)-4,5-Dibenzoyloxymethyl-2-formyl-2-phenyl-1,3-dioxolane (7c) Colorless oil, 96% yield, $[\alpha]_D^{22}$ +14.6 (*c* 1.63, $CHCl_3$). IR (neat): 2800, 1740, 1450, 1260, 1100 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.51-3.75 (4H, m, 4,5-CH_2), 4.20, 4.37 (1H each, m, 4,5-H), 4.51, 4.59 (2H each, s, OCH_2Ph), 7.14-7.40 (13H, m, Ar-H), 7.50-7.57 (2H, m, Ar-H), 9.48 (1H, s, CHO). MS *m/z*: 418 (M^+), 389, 105, 91.

Reaction of 1-7c with MeMgBr (Table I) MeMgBr (3.0 M ether solution, 3 eq) was added to a stirred solution of aldehydes **1-7c** (1 eq) in THF at -15°C under an Ar atmosphere. After being stirred for 8-15 h, 5% aqueous NH_4Cl solution was added to a reaction mixture, and the whole was extracted with ether. Ether extracts were washed with brine and dried. After removal of solvent *in vacuo*, oily residue was chromatographed over silica gel.

Entry 1: **(2*R*,4*R*)-2-[(*S*)-1-Hydroxyethyl]-2,4-dimethyl-1,3-dioxane** Less polar and major product. Colorless oil, 37% yield, $[\alpha]_D^{24}$ -11.7 (*c* 0.24, $CHCl_3$). IR (neat): 3480, 1440, 1380, 1100 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.18 (3H, d, *J*=6.3 Hz, 1'-Me), 1.22 (3H, d, *J*=5.9 Hz, 4-Me), 1.27 (3H, s, 2-Me), 1.44-1.71 (2H, m, 5-H), 1.97 (1H, br.s, OH), 3.78-4.14 (3H, m, 4,6-H), 4.53 (1H, q, *J*=6.3 Hz, 1'-H). MS *m/z*: 145 (M^+-Me), 115. **Determination of absolute configuration**: Product (80 mg) and *p*-TsOH (10 mg) in

acetone (2 ml) was stirred at room temperature for 7 h. Usual work-up and purification by silica gel cromatography afforded (*S*)-3-hydroxy-2-butanone (20 mg, 45 %) as a colorless oil. $[\alpha]_D^{27}$ +75.3 (*c* 1.1, H_2O), lit.[5] for (*S*)-3-hydroxy-2-butanone $[\alpha]_D$ +80 (*c* 1.18, H_2O), for (*R*)-3-hydroxy-2-butanone $[\alpha]_D$ -82 (*c* 0.84, H_2O). **(2*R*,4*R*)-2-[(*R*)-1-Hydroxyethyl]-2,4-dimethyl-1,3-dioxane** More polar and minor product. Colorless oil, 28% yield, $[\alpha]_D^{24}$ +13.8 (*c* 0.10, $CHCl_3$). IR (neat): 3460, 1440, 1380, 1100 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.17 (3H, d, *J*=5.9 Hz, 4-Me), 1.18 (3H, d, *J*=6.6 Hz, 1'-Me), 1.28 (3H, s, 2-Me), 1.46-1.71 (2H, m, 5-H), 1.92 (1H, br.s, OH), 3.83-4.08 (3H, m, 4,6-H), 4.59 (1H, q, *J*=6.6 Hz, 1'-H). MS *m/z*: 145 (M^+-Me), 115.

Entry 2: **(2*R*,4*R*)-2-[(*S*)-1-Hydroxyethyl]-4-methyl-2-phenyl-1,3-dioxane** Less polar and major product. Colorless oil, 37% yield, $[\alpha]_D^{22}$ +21.6 (*c* 0.11, $CHCl_3$). IR (neat): 3450, 1450, 1380, 1110 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.96 (3H, d, *J*=6.3 Hz, 1'-Me),1.28 (3H, d, *J*=6.3 Hz, 4-Me), 1.47, 1.82 (1H each, m, 5-H), 2.39 (1H, br.s, OH), 3.78 (1H, m, 6-Heq), 3.95 (1H, m, 6-Hax), 4.09 (1H, q, *J*=6.3 Hz, 1'-H), 4.34 (1H, m, 4-H), 7.27-7.38 (3H, m, Ar-H), 7.47-7.52 (2H, m, Ar-H). MS *m/z*: 204 (M^+-18), 177, 123, 105. **(2*R*,4*R*)-2-[(*R*)-1-Hydroxyethyl]-4-methyl-2-phenyl-1,3-dioxane** More polar and minor product. Colorless oil, 23% yield, $[\alpha]_D^{22}$ +73.7 (*c* 0.10, $CHCl_3$). IR (neat): 3480, 1440, 1380, 1110 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.99 (3H, d, *J*=6.3 Hz, 1'-Me),1.22 (3H, d, *J*=6.3 Hz, 4-Me), 1.47, 1.78 (1H each, m, 5-H), 2.04 (1H, br.s, OH), 3.86-4.08 (2H, m, 6-H), 4.16 (1H, q, *J*=6.3 Hz, 1'-H), 4.26 (1H, m, 4-H), 7.27-7.39 (3H, m, Ar-H), 7.47-7.56 (2H, m, Ar-H). MS *m/z* 204 (M^+-18), 177, 105.

Entry 5: **(4*R*,6*R*)-2-[(*R*)-1-Hydroxyethyl]-4,6-dimethyl-2-phenyl-1,3-dioxane** 50% d.e. at C-1'. Colorless oil, 83% yield, IR (neat): 3480, 1450, 1380, 1120 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ for 1'*R*-isomer: 0.97 (3H, d, *J*=6.3 Hz, 1'-Me), 1.15 (3H, d, *J*=6.6 Hz, 4- or 6-Me), 1.26 (3H, d, *J*=6.6 Hz, 6- or 4-Me), 2.38 (1H, br.s, OH); δ for 1'*S*-isomer: 1.22 (d, *J*=6.6 Hz, 4- or 6-Me), 1.25 (d, *J*=6.3 Hz, 6- or 4-Me), 2.64 (br. s, OH), (See Table II, entry 6). MS *m/z*: 218 (M^+-18), 191, 105. **Determination of absolute configuration:** Product in entry 5 (80 mg) and *p*-TsOH (20 mg) in acetone (2 ml) was stirred at room temperature for 3 days. Usual work-up and purification by silica gel chromatography afforded (*R*)-2-hydroxy-1-phenyl-1-propanone (44.3 mg, 87 %) as a colorless oil. $[\alpha]_D^{27}$ +42.0 (*c* 0.83, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ : 1.46 (3H d, *J*=6.9 Hz, CH_3), 3.80 (1H, br, OH), 5.17 (1H, q, *J*=6.9 Hz, CH), 7.50-7.66 (3H, m, Ar-H), 7.91-7.96 (2H, m, Ar-H). The obtained ketol was converted into corresponding (-)-MTPA ester in usual manner. 48% d.e. ^{1}H-NMR ($CDCl_3$) δ for major (minor) isomer: 1.64 (1.56) (d, *J*=7.3 (6.8) Hz, CH_3), 3.58 (3.66) (s, OCH_3). By comparing with these chemical shifts based on Mosher's rule,[6] absolute configuration of the major isomer was deduced to be *R* and that of the minor isomer to be *S*.

Reaction of 5c with MeTi(O-iPr)$_3$ (Table II, entry 6) Compound **5c** (132 mg, 0.6 mmol) in ether (2 ml) was added at 0°C to a solution of $MeTi(O\text{-}iPr)_3$ prepared with $ClTi(O\text{-}iPr)_3$ (0.42 ml, 1.8 mmol) and MeMgBr (3 M in ether, 0.6 ml, 1.8 mmol) under an Ar atmosphere. After being stirred for 20 h at room temperature, Reaction was quenched by addition of 5% aqueous NH4Cl solution, and the whole was extracted with ether. Ether extracts were washed with brine and dried. After removal of solvent *in vacuo*, oily residue was chromatographed over silica gel. 88% d.e. at C-1'. ^{1}H-NMR ($CDCl_3$) δ for 1'*R*-isomer: 0.97 (3H, d, *J*=6.3 Hz, 1'-Me), 1.15 (3H, d, *J*=6.6 Hz, 4- or 6-Me), 1.26 (3H, d, *J*=6.6 Hz, 6- or 4-Me), 1.44 (1H, ddd, *J*=5.6, 7.3, 13.2 Hz, 5-H), 1.63 (1H, ddd, *J*=4.9, 7.9, 13.2 Hz, 5-H), 2.38 (1H, br.s, OH), 3.78-3.93 (2H, m, 4,6-H), 4.30 (q, J=5.9 Hz, 1'-H), 7.27-7.37 (3H, m, Ar-H), 7.46-7.51 (2H, m, Ar-H).

Preparation of 8-11 To a stirred suspension of NaH (60% oil suspension, 56 mg, 1.4 mmol) in THF (1 ml), phosphonate (1.4 mmol) in THF (0.5 ml) was added at 0°C under an Ar atmosphere. After 10 min, aldehyde (1 mmol) in THF (1 ml) was added, and reaction mixture was stirred for 1 h at room temperature. 5% Aqueous NH_4Cl was added to reaction mixture, and the whole was extracted with ether. Ether extracts were washed with brine and dried. After removal of solvent *in vacuo*, oily residue was chromatographed over silica gel.

(2*R*,4*R*)-4-Methyl-2-[3-oxo-(1*E*)-penten-1-yl]-2-phenyl-1,3-dioxane (8) Colorless oil, 62% yield, IR (neat): 1675, 1630, 1450, 1380, 1120 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.09 (3H, t, *J*=7.3 Hz, 5'-H),

1.30 (3H, d, *J*=6.3 Hz, 4-Me), 1.53 (1H, m, 5-Heq), 1.77 (1H, m, 5-Hax), 2.60 (2H, q, *J*=7.3 Hz, 4'-H), 4.02-4.20 (3H, m, 4,6-H), 6.41, 6.79 (1H each, d, *J*=16.2 Hz, olefinic-H), 7.25-7.37 (3H, m, Ar-H), 7.52-7.60 (2H, m, Ar-H). MS *m/z*: 260 (M^+), 177, 105.

(4*R*,6*R*)-4,6-Dimethyl-2-[3-oxo-(1*E*)-penten-1-yl]-2-phenyl-1,3-dioxane (9) Colorless oil, 89% yield, ^{1}H-NMR ($CDCl_3$) δ: 1.06 (3H, t, *J*=7.3 Hz, 5'-H), 1.25 (3H, d, *J*=6.3 Hz, 4- or 6-Me), 1.28 (3H, d, *J*=6.6 Hz, 6- or 4-Me), 1.62-1.71 (2H, m, 5-H), 2.58 (2H, q, *J*=7.3 Hz, 4'-H), 3.80, 4.03 (1H each, m, 4,6-H), 6.39, 6.65 (1H each, d, *J*=15.8 Hz, olefinic-H), 7.27-7.39 (3H, m, Ar-H), 7.49-7.54 (2H, m, Ar-H).

(4*R*,6*R*)-4,6-Dimethyl-2-[3-oxo-3-phenyl-(1*E*)-propen-1-yl]-2-phenyl-1,3-dioxane (10) Colorless oil, 85% yield, IR (neat): 1680, 1630, 1450, 1380, 1120 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.28 (3H, d, *J*=6.6 Hz, 4-Me), 1.32 (3H, d, *J*=6.3 Hz, 6-Me), 1.60-1.75 (2H, m, 5-H), 3.84, 4.11 (1H each, m, 4,6-H), 6.89, 7.19 (1H each, d, *J*=15.5 Hz, olefinic-H), 7.28-7.59 (8H, m, Ar-H), 7.88-7.92 (2H, m, Ar-H). MS *m/z*: 322 (M+), 191, 105.

(4*R*,5*R*)-4,5-Dimethyl-2-[3-oxo-3-phenyl-(1*E*)-propen-1-yl]-2-phenyl-1,3-dioxolane (11) Colorless oil, 44% yield. IR (neat): 1675, 1620, 1450, 1380, 1080 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.31, 1.35 (3H each, d, *J*=5.9 Hz, 4,5-Me), 3.70, 3.84 (1H each, m, 4,5-H), 7.04, 7.19 (1H each, d, *J*=15.5 Hz, olefinic-H), 7.27-7.61 (8H, m, Ar-H), 7.87-7.97 (2H, m, Ar-H). MS *m/z*: 308 (M+), 177, 105.

Conjugate Addition of Me_2CuLi to 8-11 MeLi (1.4 M in ether, 10 eq) was added to a stirred suspension of CuI (5 eq) in ether at -30°C under an Ar atmosphere, then enone (**8-11**, 1 eq)[12] in ether was added. The whole was stirred for 1 h. Usual work-up and silica gel column chromatography afforded **12-15**.

(4*R*,6*R*)-4,6-Dimethyl-2-[(*S*)-4-oxohexan-2-yl]-2-phenyl-1,3-dioxane (13) 38% d.e. at C-2', Colorless oil, 82% yield, IR (neat): 1710, 1450, 1380, 1110 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ for 2'*S*-isomer: 0.78 (3H, d, J=6.3 Hz, 1'-H), 1.00 (3H, t, *J*=7.3 Hz, 6'-H), 1.13, 1.19 (3H each, d, *J*=6.3 Hz, 4,6-Me), 1.35-1.59 (2H, m, 5-H), 2.01 (1H, dd, J=15.7, 6.6 Hz, 3'-H), 2.63 (1H, dd, J=15.7, 4.3 Hz, 3'-H), 3.73, 4.16 (1H each, m, 4,6-H), 7.24-7.36 (3H, m, Ar-H), 7.41-7.47 (2H, m, Ar-H); δ for 2'*R*-isomer: 0.73 (d, J=6.9 Hz, 1'-H), 1.04 (t, *J*=7.3 Hz, 6'-H), 1.97 (dd, J=16.2, 7.9 Hz, 3'-H), 2.79 (1H, dd, J=16.2, 5.3 Hz, 3'-H), 3.64 (m, 4- or 6-H). MS *m/z*: 276 (M^+), 177, 105.

(4*R*,6*R*)-4,6-Dimethyl-2-[(*S*)-4-oxo-4-phenylbutan-2-yl]-2-phenyl-1,3-dioxane (14) 48% d.e. at C-2',[12] Colorless oil, 91% yield, IR (neat): 1690, 1450, 1380, 1080 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ for 2'*S*-isomer: 0.86 (3H, t, J=6.9 Hz, 1'-H), 1.14 (3H, d, *J*=6.6 Hz, 4- or 6-Me), 1.21 (3H, d, *J*=6.3 Hz, 6- or 4-Me), 1.37-1.61 (2H, m, 5-H), 2.51 (1H, dd, J=15.8, 8.9 Hz, 3'-H), 2.68 (1H, m, 2'-H), 3.29 (1H, dd, J=15.8, 3.3 Hz, 3'-H), 3.77, 4.18 (1H each, m, 4,6-H), 7.27-7.57 (8H, m, Ar-H), 7.87-7.97 (2H, m, Ar-H); δ for 2'*R*-isomer: 0.80 (d, J=6.9 Hz, 1'-H), 1.15 (d, *J*=6.3 Hz, 4- or 6-Me), 1.20 (d, *J*=6.6 Hz, 6- or 4-Me), 2.45 (1H, dd, J=15.8, 8.9 Hz, 3'-H), 3.68 (m, 4- or 6-H). MS *m/z*: 338 (M^+), 252, 191, 105.

(*S*)-2-Methyl-1,4-diphenylbutane-1,4-dione (16) An acetone solution (3 ml) of compound **14** (79 mg, 0.23 mmol) and *p*-TsOH (10 mg) was stirred at room temperature for 3 days. The reaction mixture was diluted with AcOEt and washed with brine, then dried. Removal of solvent *in vacuo* and subsequent purification by silica gel column chromatography afforded **16** (58 mg, 99%). Colorless solid. $[\alpha]_D^{20}$ -42.7 (*c* 2.29, $CHCl_3$)(48% e.e.). IR (Nujol): 1680, 1450, 1380 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.29 (3H, d, J=7.3 Hz, 2-Me), 3.13 (1H, dd, *J*=17.8, 5.0 Hz, 3-H), 3.74 (1H, dd, *J*=17.8, 8.3 Hz, 3-H), 4.16 (1H, m, 2-H), 7.43-7.61 (6H, m, Ar-H), 7.95-8.08 (4H, m, Ar-H). MS *m/z*: 252 (M^+), 234, 105. Determination of absolute configuration of **16**: The authentic sample of (*R*)-**16** was synthesized in 20% yield by a reaction of (*R*)-dimethyl 2-methylsuccinate (26% o.p.)[9] and phenyl lithium (2 eq) in ether at -78°C. $[\alpha]_D^{24}$ +15.3 (*c* 0.10, $CHCl_3$). This result suggests the absolute configuration of **16** is *S*.

Preparation of 19-25: A mixture of oxalyl chloride (2 mmol) and carboxylic acid (1 mmol) in benzene (3 ml) was refluxed for 2 h. After removal of solvent and excess oxalyl chloride *in vacuo*, benzene (1 ml) and alcohol (2 mmol) in pyridine (1 ml) were added. The whole was stirred for 1 h at room temperature. Usual work-up and purification by silica gel afforded corresponding esters **19-25**.

(2*R*,4*R*)-4-Methyl-2-[(*RS*)-2-methylbutanoyloxymethyl]-2-phenyl-1,3-dioxane (19) Colorless oil, 72% yield, IR (neat): 1730, 1440, 1380, 1120 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ : 0.80, 0.81 (1.5H each, d, J=7.4 Hz, CH_2CH_3), 1.04 (3H, d, *J*=7.1 Hz, $OCOCHCH_3$), 1.26 (3H, d, *J*=6.1 Hz, 4-Me), 2.30 (1H, m, OCOCH), 3.95, 4.13, 4.28 (1H each, m, 4,6-H), 4.46, 4.67 (0.5H each, *J*=11.6 Hz, 2-CHaHb), 4.50, 4.63 (0.5H each, *J*=11.6 Hz, 2-CHa'Hb'), 7.27-7.38 (3H, m, Ar-H), 7.54-7.59 (2H, m, Ar-H).

(2*S*,4*R*)-4-Methyl-2-[(*RS*)-2-methylbutanoyloxymethyl]-2-phenyl-1,3-dioxane (20) Colorless oil, 70% yield, IR (neat): 1730, 1450, 1380, 1110 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ : 0.79, 0.81 (1.5H each, d, J=7.4 Hz, CH_2CH_3), 1.04, 1.06 (1.5H each, d, *J*=6.9 Hz, $OCOCHCH_3$), 1.24 (3H, d, *J*=6.3 Hz, 4-Me), 2.35 (1H, m, OCOCH), 3.79-4.06 (3H, m, 4,6-H), 4.09, 4.18 (0.5H each, *J*=11.4 Hz, 2-CHaHb), 4.11, 4.16 (0.5H each, *J*=11.4 Hz, 2-CHa'Hb'), 7.30-7.50 (5H, m, Ar-H).

(4*R*,6*R*)-4,6-Dimethyl-2-[(*RS*)-2-methylbutanoyloxymethyl]-2-phenyl-1,3-dioxane (21) Colorless oil, 76% yield, IR (neat): 1740, 1450, 1380, 1120 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ : 0.81, 0.83 (1.5H each, d, J=7.3 Hz, CH_2CH_3), 1.05, 1.07 (1.5H each, d, *J*=6.9 Hz, $OCOCHCH_3$), 1.22 (3H x 2, d, *J*=6.3 Hz, 4,6-Me), 2.33 (1H, m, OCOCH), 3.73, 4.28 (1H each, m, 4,6-H), 4.01, 4.43 (0.5H each, *J*=11.2 Hz, 2-CHaHb), 4.05, 4.39 (0.5H each, *J*=11.2 Hz, 2-CHa'Hb'), 7.26-7.38 (3H, m, Ar-H), 7.52-7.57 (2H, m, Ar-H). MS *m/z*: 306 (M^+), 191, 105.

(4*R*,5*R*)-4,5-Dimethyl-2-[(*RS*)-2-methylbutanoyloxymethyl]-2-phenyl-1,3-dioxolane (22) Colorless oil, 74% yield, IR (neat): 1740, 1450, 1380, 1240, 1090 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ : 0.83, 0.85 (1.5H each, d, J=7.3 Hz, CH_2CH_3), 1.09, 1.10 (1.5H each, d, *J*=6.9 Hz, $OCOCHCH_3$), 1.23, 1.31 (3H each, d, *J*=5.9 (6.3) Hz, 4,5-Me), 2.38 (1H, m, OCOCH), 3.55, 3.86 (1H each, m, 4,6-H), 4.20, 4.32 (0.5H each, *J*=11.9 Hz, 2-CHaHb), 4.23, 4.29 (0.5H each, *J*=11.9 Hz, 2-CHa'Hb'), 7.28-7.38 (3H, m, Ar-H), 7.52-7.57 (2H, m, Ar-H). MS *m/z*: 294 (M^+), 215, 177.

(4*R*,6*R*)-4,6-Dimethyl-2-[(*RS*)-2-methylhexanoyloxymethyl]-2-phenyl-1,3-dioxane (23) Colorless oil, 70% yield, IR (neat): 1740, 1450, 1380, 1240, 1120 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ : 0.85, 0.86 (1.5H each, d, J=7.3 Hz, CH_2CH_3), 1.05, 1.06 (1.5H each, d, *J*=7.3 (6.9) Hz, $OCOCHCH_3$), 1.22 (3H x 2, d, *J*=6.3 Hz, 4,6-Me), 2.38 (1H, m, OCOCH), 3.74, 4.29 (1H each, m, 4,6-H), 4.00, 4.42 (0.5H each, *J*=11.2 Hz, 2-CHaHb), 4.04, 4.38 (0.5H each, *J*=11.2 Hz, 2-CHa'Hb'), 7.27-7.38 (3H, m, Ar-H), 7.52-7.57 (2H, m, Ar-H). MS *m/z*: 334 (M^+), 257, 249, 191.

(4*R*,6*R*)-4,6-Dimethyl-2-[(*RS*)-2-phenylbutanoyloxymethyl]-2-phenyl-1,3-dioxane (24) Colorless oil, 78% yield, IR (neat): 1740, 1445, 1380, 1120 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ : 0.82, 0.85 (1.5H each, d, *J*=7.3 Hz, CH_2CH_3), 1.11, 1.13, 1.15, 1.18 (1.5H each, d, *J*=6.3 Hz, 4,6-Me), 3.41, 3.89 (0.5H each, t, *J*=7.3 (7.6) Hz, OCOCH), 3.65, 4.13 (1H each, m, 4,6-H), 3.90, 4.51 (0.5H each, *J*=11.6 Hz, 2-CHaHb), 4.09, 4.32 (0.5H each, *J*=11.2 Hz, 2-CHa'Hb'), 7.19-7.47 (10H, m, Ar-H). MS *m/z*: 291 (M^+-Ph), 191, 105.

(4*R*,6*R*)-4,6-Dimethyl-2-[(*R*)-2-phenylpropanoyloxymethyl]-2-phenyl-1,3-dioxane [(2'*R*)-25] 95% d.e.[11] Colorless oil, 75% yield, $[\alpha]_D^{24}$ -25.1 (*c* 1.05, $CHCl_3$). IR (neat): 1740, 1445, 1380, 1120 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ : 1.10, 1.18 (3H each, d, *J*=6.3 Hz, 4,6-Me), 1.45 (3H, *J*=7.3 Hz, $OCOCHCH_3$), 3.59-3.73 (2H, m, OCOCH, 4- or 6-H), 4.10 (1H, m, 6- or 4-H), 4.11, 4.29 (1H each, *J*=11.2 Hz, 2-CH_2), 7.19-7.36 (8H, m, Ar-H), 7.40-7.47 (2H, m, Ar-H). MS *m/z*: 277 (M^+-Ph), 191, 105.

(4*R*,6*R*)-4,6-Dimethyl-2-[(*S*)-2-phenylpropanoyloxymethyl]-2-phenyl-1,3-dioxane [(2'*S*)-25] 95% d.e.[11] Colorless oil, 78% yield, $[\alpha]_D^{24}$ +3.5 (*c* 0.94, $CHCl_3$). IR (neat): 1740, 1445, 1380, 1120 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ : 1.13, 1.16 (3H each, d, *J*=6.3 Hz, 4,6-Me), 1.44 (3H, *J*=7.3 Hz, $OCOCHCH_3$), 3.60-3.71 (2H, m, OCOCH, 4- or 6-H), 4.08 (1H, m, 6- or 4-H), 3.90, 4.51 (1H each, *J*=11.2 Hz, 2-CH_2), 7.21-7.45 (10H, m, Ar-H). MS *m/z*: 277 (M^+-Ph), 191, 105.

References and Notes

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11. On preparation of (*R*)-**25** and (*S*)-**25** by means of method III, products were slightly epimerized at benzylic asymmetric center (95% d.e. each).
12. Reaction of compound **9** with Me_2CuLi was employed by addition of a mixture of **9** (1 eq) and TMSCl (5 eq). Reaction in the absence of TMSCl afforded **14** of 40% d.e.