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Asymmetric Synthesis with Sugar Derivatives. II.*[1], 1)
Asymmetric Syntheses by Methoxy-Mercuration of Cinnamic Esters of Sugar Derivatives

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The methoxy-mercurations of cinnamic esters of 1, 2; 5, 6-di-*O*-isopropylidene- and -cyclohexylidene-D-glucose, 5-deoxy-1, 2-*O*-isopropylidene-D-xylose, (−)-menthol, and (+)-borneol with mercuric acetate in methanol, followed by the reductive demercuration of the 3-acetoxymercuri-2-methoxyhydrocinnamic esters with sodium borohydride, gave, after the hydrolysis of the demercurated esters, IV, with alkali, 3-methoxy-3-phenylpropionic acid (V) in 1—27% optical yields, depending on the methoxy-mercuration time. When the methoxy-mercuration time was extended, the specific rotation of V decreased, but there was no corresponding decrease in the synthetic yield in the presence of nitric acid as a catalyst. This shows that an equilibrium in the methoxy-mercuration has been completed. The demercurated esters, IV, were reduced with lithium aluminum hydride to afford 3-methoxy-3-phenylpropan-1-ol (IX) in 6—22% optical yields. The absolute configurations of both V and IX were established to be (S)(−)-configurations. In the methoxy-mercuration, it seems likely that no oxygen atoms of sugar derivatives act as a co-ordinating group to keep the acetoxymercuri-group onto one side of the carbon-carbon double bond of cinnamate.

In a previous paper1) dealing with the conjugate addition of phenylmagnesium bromide to crotonates, it was shown that 3-phenylbutyric acids derived from some sugar crotonates gave much better optical yields than the acid from (−)-menthyl crotonate. This indicated that the oxygen atoms of the sugar played an important role in hindering the free rotation of the sugar part by holding the magnesium atom, which co-ordinated with the ester carbonyl. The present investigation was undertaken to examine, by means of an asymmetric synthesis, whether a similar effect could be observed in the course of the methoxy-mercuration2) of an acyclic unsaturated system such as that of the cinnamic ester of the sugar derivative.

The methoxy-mercurations of methyl,3) ethyl,4) and (−)-menthyl5) cinnamates (I; R=methoxy, ethoxy, and (−)-menthoxy) and the demercuration6,7) of the adduct, III (R=methoxy), to IV have been reported. As to a cyclic unsaturated system, Henbest *et al.*8) found that cyclohexenes substituted by an oxygen-containing group such as the methoxy group at the 4-position, on treatment with mercuric acetate in methanol, gave the corresponding single adduct, in which the new anionic substituent (OMe) and the mercuri-group were placed in a trans 1, 4- and a cis 1, 3-relation to the original oxygen-containing group respectively. It has been pointed out, therefore, that the reaction proceeds through a trans addition9) (OMe and HgOAc) and that the mercuri-group enters into the same side of the original oxygen-containing group.

The present paper will describe asymmetric syntheses of 3-methoxy-3-phenylpropionic acid (V) and 3-methoxy-3-phenylpropan-1-ol (IX) by the methoxy-mercuration of cinnamic esters and will discuss the steric course of the reaction.

Procedure and Results

Methoxy-mercurations of 3-*O*-cinnamoyl-1, 2; 5, 6-di-*O*-isopropylidene-D-glucose (Ia), 3-*O*-cinnamoyl-1, 2; 5, 6-di-*O*-cyclohexylidene-D-glucose (Ib), 3-*O*-cinnamoyl-5-deoxy-1, 2-*O*-isopropylidene-D-xylose (Ic), (−)-menthyl cinnamate (Id), and (+)-bornyl cinnamate (Ie) were carried out with

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*[1] Presented at the 19th Annual Meeting of the Chemical Society of Japan, Tokyo, April, 1966.

1) Part I: M. Kawana and S. Emoto, This Bulletin, **39**, 910 (1966).

2) J. Chatt, *Chem. Revs.*, **48**, 7 (1951).

3) W. Schrauth, W. Schoeller and R. Struensee, *Ber.*, **43**, 695 (1910); **44**, 1048 (1911).

4) A. K. Chaudhuri, K. L. Mallik and M. N. Das, *Tetrahedron*, **19**, 1981 (1963).

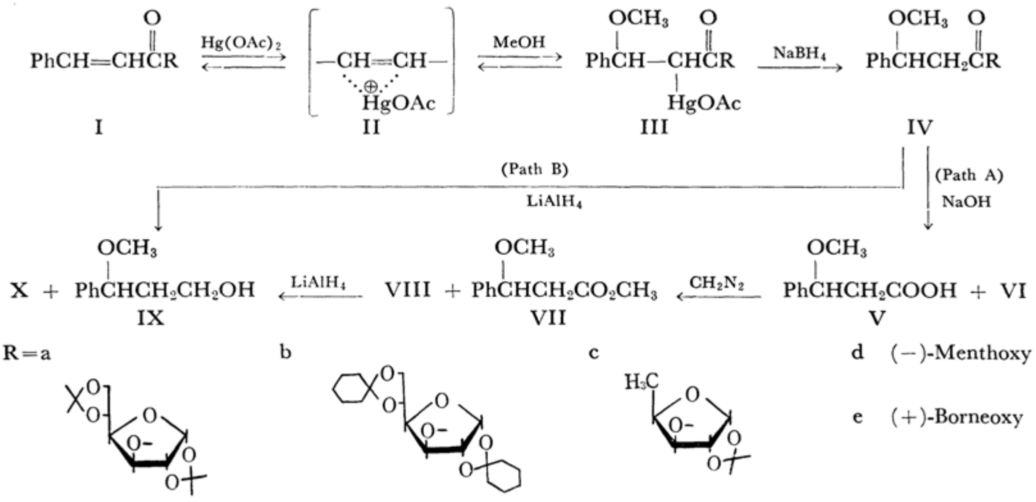
5) L. T. Sandborn and C. S. Marvel, *J. Am. Chem. Soc.*, **48**, 1409 (1926).

6) G. F. Wright, *ibid.*, **57**, 1993 (1935).

7) W. Schrauth, W. Schoeller and R. Struensee, *Ber.*, **44**, 1432 (1911).

8) a) H. B. Henbest and B. Nicholls, *J. Chem. Soc.*, **1959**, 227; b) H. B. Henbest and R. S. McElhinney, *ibid.*, **1959**, 1834.

9) A. G. Brook and G. F. Wright, *Acta Cryst.*, **4**, 50 (1951); J. Bain and M. M. Harding, *J. Chem. Soc.*, **1965**, 4025.



VI: Cinnamic acid
X: Cinnamyl and hydrocinnamyl alcohols
VIII: Methyl cinnamate
Ph: Phenyl group

TABLE 1. ASYMMETRIC SYNTHESIS OF 3-METHOXY-3-PHENYLPROPIONIC ACID (V)

Ester	Expt. No.	Reaction time hr	Malar ratio V : VI		$[\alpha]_D^{20}$ (*c*, benzene)		Yield of V, %	
					V+VI	V	Opt.*1	Syn.*2
Ia	1	(10 min)	55	45	−8.3° (0.69)	−14°	21	43
	2	1.5	90	10	−13.6° (1.40)	−14°	21	76
	3	5	95	<5	−12.9° (1.58)	−13°	19	88
	4	8	95	<5	−11.6° (1.37)	−12°	18	87
	5	24	95	<5	−8.2° (1.42)	−9°	13	82
	6	72	95	<5	−3.1° (1.27)	−3°	4	80
	7*3	114	84	16	−13.1° (1.62)	−15°	22	77
Ib	8	5	86	14	−16.2° (1.80)	−18°	27	81
	9	8	95	<5	−15.4° (1.34)	−16°	24	81
	10	24	95	<5	−12.0° (1.30)	−12°	18	90
	11	48	95	<5	−8.2° (1.58)	−9°	13	84
Ic	12	1.5	90	10	−14.6° (1.34)	−15°	22	85
	13	5	95	<5	−14.1° (1.40)	−15°	22	89
	14	48	95	<5	−9.1° (1.54)	−9°	13	86
Id	15	1.5	39	61	−5.7° (1.45)	−13°	19	36
	16	5	32	68	−4.0° (1.90)	−11°	16	33
	17	8	35	65	−2.8° (1.56)	−7°	10	29
	18	24	39	61	−1.0° (1.43)	−2°	3	39
	19	48	39	61	+0.6° (1.63)	+1°	1	36
	20	72	40	60	+1.3° (1.44)	+3°	4	41
Ie	21	5	65	35	+2.4° (1.96)	+3°	4	67

*1 Calculated on the basis of $[\alpha]_D$ −67° estimated for the optically pure V.
*2 Calculated from the corresponding ester, I.
*3 The catalyst of nitric acid was not used.

mercuric acetate in methanol in the presence of a catalytic amount of nitric acid[6)] at 20°C for various reaction times. The crude adduct, III, was demercurated without isolation with sodium borohydride[8a)] to yield the crude ester, IV. When the mercuration time was more than 5 hr, the infrared spectrum of every crude ester, IV, except IVb (see "Experimental Section") showed a trace of an absorption band characteristic of the carbon-carbon double bond of the starting ester, indicating that the methoxy-mercuration had been almost completed, but that the demethoxy-mercuration[10] might have occurred to a small extent in the demercuration with sodium borohydride. The crude ester, IV, was completely hydrolyzed (Path A) without isolation to yield V and cinnamic acid (VI); under the same conditions, V was optically stable. The sugar esters, IVa—IVc, were more easily hydrolyzed to V than were IVd or IVe.

The NMR signals[11] for the protons on C-3 of V and on C-2 of VI were clearly separated from each other; hence, the integration of each signal provided a direct measure of the amounts of V and VI. The results are shown in Table 1. The absolute configurations and a method of calculating optical yields for the optically active compounds obtained in the present experiments will be described further below.

The methoxy-mercurations of Ia—Id for 5 hr gave, predominantly, (S) (−)-V *via* the corresponding III and IV; in contrast with these, (R) (+)-V was obtained in the case of Ie (Expt. Nos. 3, 8, 13, 16, and 21). The specific rotation of V decreased for the extended time of the methoxy-mercuration without, however, decreasing the synthetic yield (Fig. 1); when the reaction was more than 37 hr, V derived from Id came to possess an opposite sign of rotation, but its extent was small. This shows that an equilibrium in the methoxy-mercuration had been completed.

The formation of the undesirable compound, VI, results from one or more of the following causes: (a) incomplete methoxy-mercuration in an equilibrium state, (b) demethoxy-mercuration with sodium borohydride, and (c) the elimination of methanol in the hydrolysis. However, it was difficult to determine the exact extent of (a), (b), or (c). If (b), (c), or both of them proceeded asymmetrically, the molar ratio of the two diastereomeric adducts, III, prepared by the asymmetric methoxy-mercuration might differ considerably from that of the enantiomers, V, derived from III. In the case of the sugar esters, however, (b) or (c) exerted only a minor influence upon the molar ratio of the two diastereomers, IV, or the enantiomers, V, judging from the infrared spectroscopic observation of the crude ester, IV, and of the molar ratio of the final product, V, to VI respectively; even if the two diastereomers, III, had been produced in an equal amount by the complete methoxy-mercuration and (b), (c), or both of them, had occurred stereoselectively, the optical yield of V calculated on the basis of the found molar ratio of V to VI (95 : 5) would have been only 5.2%. In the case of the (−)-menthyl and (+)-bornyl esters, the formation of a large amount of VI was mainly due to (c), because the crude product, IV, had contained only a negligible amount of the corresponding I after the demercuration. In this case, it is doubtful that an asymmetric hydrolysis occurs in the step from IV to V.

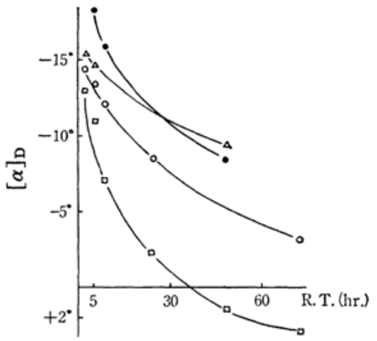


Fig. 1. Change in the specific rotation of 3-methoxy-3-phenylpropionic acid (V) prepared from Ia—Id for the various reaction time of methoxy-mercuration.

○: Ia ●: Ib △: Ic □: Id

Thus, the crude ester, IVa, IVd, or IVe (the methoxy-mercuration time was 5 hr), was reduced to 3-methoxy-3-phenylpropan-1-ol (IX) with lithium alminum hydride (Path B), little elimination of methanol from IV being observed. The results are shown in Table 2. A comparison of the optical yield of V (Path A) with that of IX (Path B) will show that a little of the asymmetric-center of IV was lost in the hydrolysis (Expt. Nos. 16, 21, 24, and 25). Therefore, it can be concluded that the optical activity of V derived from Id or Ie is, for the most part, to be attributed to the asymmetric methoxy-mercuration. The crude ester, IVa, afforded V and IX in almost the same optical yields through Path A and Path B respectively (Expt. Nos. 3 and 23).

In order to ascertain the absolute configurations and the estimated specific rotations of V and IX, the following chemical conversion was carried out: a mixture ($[\alpha]_D$ −12.9°, Expt. No. 3) of V and VI was esterified with diazometane to yield the crude ester, VII ($[\alpha]_D$ −11.7°), which was then further reduced with lithium alminum hydride to the crude alcohol, IX ($[\alpha]_D$ −23.0°)

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[10] F. G. Bordwell and M. L. Douglass, *J. Am. Chem. Soc.*, **88**, 993 (1966); Dr. Y. Inouye has written us that the demercuration of IIId with sodium borohydride in an aqueous alkaline medium gave the starting cinnamic ester by the retrogressive elimination reaction. We are grateful to Dr. Inouye for communicating his results.

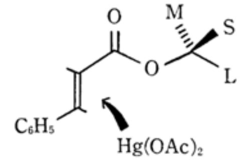
[11] The following signals in the NMR spectrum were assigned to each proton of V: an AB portion of the ABX spectrum centered at τ 7.43 (A) and τ 7.11 (B) (multiplet, $J_{AB}=15.6$ cps, $J_{AX}=5.4$ cps and $J_{BX}=7.8$ cps), with an X portion at τ 5.38 (quartet) arising from 2H (AB) on C-2 and 1H (X) on C-3, and three singlets, at τ 6.79, 2.68 and −0.95, due to 3H of the methoxy group, 5H of the phenyl group, and 1H of the hydroxycarbonyl group respectively. The signal of 1H on C-2 of cinnamic acid showed a doublet centered at τ 3.58 ($J=15.0$ cps).

Table 2. Asymmetric synthesis of 3-methoxy-3-phenylpropan-1-ol (IX)

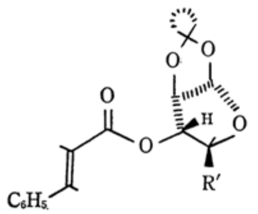
Ester	Expt.*1 No.	Path	Crude IX $[\alpha]^{20}_D$ (c, benzene)	Yield, % Opt.*2	Yield, % Syn.*3
Ia	22	A	−23.0° (0.86)	19	74
	23	B	−24.3° (0.63)	20	72
Id	24	B	−25.8° (0.85)	22	60
	24*4	B	−26.6° (0.53)	22	57
Ie	25	B	+6.7° (1.40)	6	84

*1 The reaction time was 5 hr.
*2 Calculated on the basis of $[\alpha]_D$ −120° estimated for the optically pure IX.
*3 Calculated from the corresponding ester, I.
*4 Pure IX.

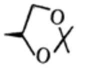
(Table 2. Expt. No. 22). As the absolute configuration[12] of (+)-VII ($[\alpha]_D$ +61.0°) prepared by the reaction of the optically pure methyl (+)-3-hydroxy-3-phenylpropionate with methyl iodide and silver oxide has been known to be (R), it was found that both (−)-V and (−)-IX have the (S)-configuration. On the basis of the above experimental results, if a small amount of the optically inactive compound, VI (the molar ratio of V to VI was 95 : 5), VIII, or X, does not affect the optical activity of V, VII, or IX respectively, the specific rotations of the pure compounds, V and IX, may be estimated to be 67° and 120° respectively. The optical yields in the present experiments were calculated on the basis of these values.

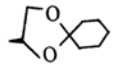


XI



XII

R′ =  = Ia

R′ =  = Ib

R′ = CH_3 = Ic

Discussion

It has been known that the methoxy-mercuration[4] of ethyl cinnamate proceeds through an ionic mechanism involving a rigid three-membered mercurinium ion, II, in the rate-determining step, and that the presence of a catalytic amount of nitric acid as well as perchloric acid appreciably accelerates the rate of methoxy-mercuration. As the degradation of olefin-mercuric salt-addition compounds to the original components in acidic media is well known,[13] it is expected that the methoxy-mercuration of cinnamates may reach an equilibrium.[14] This is true in the present experiments (Fig. 1).

At the early stage of the methoxy-mercuration, however, if asymmetric induction arises from the step of the formation of a mercurinium ion and not from the step of the attack of methanol, Prelog's rule[15] can be applied to the reactions of (−)-menthyl and (+)-bornyl cinnamates. An asymmetric center binding the hydroxy group in (−)-menthol can be depicted as in XI (S=the smallest group, M=the medium-sized group, and L=the largest group). Mercuric acetate would enter from the least-hindered side (the S-side) of Id, followed by the rapid attack of methanol from the M-side, resulting in the formation of (S)(−)-V in excess; IVe, in which the relation between S and M groups is opposite to (−)-menthol, gives (R)(+)-V predominantly.

The configurational relation among S, M, and L-groups in the sugar derivatives used in the present experiment is the same as that in (−)-menthol (see XII). However, the 5,6-*O*-iso-propylidene or -cyclohexylidene group (the L-group) on the five-membered ring has a fair chance of covering the S-side of the carbon-carbon double bond of the ester. That is, it is expected that IVa and IVb will give (R)(+)-V in excess

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[12] K. Balenovec, B. Urbas and A. Deljac, *Croat. Chem. Acta,* **31**, 153 (1959).

[13] See, for example, M. M. Kreevoy, L. L. Schaleger and J. C. Ware, *Trans. Faraday Soc.,* **58**, 2433 (1962); K. Ichikawa, H. Ouchi and S. Araki, *J. Am. Chem. Soc.,* **88**, 3880 (1960).

[14] K. L. Mallik and M. N. Das, *ibid.,* **82**, 4296 (1960).

[15] V. Prelog, *Helv. Chim. Acta,* **36**, 308 (1953).

if the asymmetric induction arises from only the steric effect of these groups, by which phenylmagnesium bromide is prevented from entering into the carbon-carbon double bond from the S-side in the conjugate addition of the Grignard reagent to the sugar crotonate. Contrary to this expectation for IVa and IVb, (S)(−)-V was practically produced in a 27% (maximum) optical yield, in agreement with Prelog's rule. On the basis of these observations, however, it could not be concluded that the oxygen atom on C-5 of glucose was effective in holding the acetoxymercuri-group onto the S-side because of the poor optical yields of V and because of the fact to be described below. In a recent experiment,[16] we found that the reaction of 1, 2 ; 5, 6-di-*O*-cyclohexylidene-3-*O*-phenylglyoxyl-D-glucose, as well as (−)-menthyl glyoxylate[17] with methylmagnesium iodide yielded, after saponification, (R)(−)-2-hydroxy-2-phenylpropionic acid (atrolactic acid) in a poor optical yield by the S-side attack of the Grignard reagent.

In discussing a Prelog model in a previous paper,[1] we applied a less probable conformer of 1, 2-*O*-isopropylidene-D-xylose as the most stable model, for which the model, XII ($R'=CH_3$) had been assumed to be appropriate. Therefore, the methoxy-mercuration of Ic also provided (S)(−)-V, in accordance with Prelog's rule.

Figure 1 shows that the predominant diastereomeric adduct, III, at the early period of the methoxy-mercuration, would be preferentially decomposed with nitric acid to I through a mercurinium ion, II, whose preferred conformation is not clear. If the predominant diastereomer, III, had been stable in the acid-catalyzed equilibrium reaction, the asymmetric methoxy-mercuration of I would have afforded V in a higher optical yield *via* III and IV.

Experimental[18]

Starting Materials. 3-*O*-Cinnamoyl-1, 2 ; 5, 6-di-*O*-isopropylidene-D-glucose (Ia), 3-*O*-cinnamoyl-1, 2 ; 5, 6-di-*O*-cyclohexylidene-D-glucose (Ib), and 3-*O*-cinnamoyl-5-deoxy-1, 2-*O*-isopropylidene-D-xylose (Ic) were prepared by the reaction[1] of cinnamoyl chloride with the corresponding sugar derivatives in a mixture of pyridine and benzene at −5—0°C; (+)-bornyl cinnamate (Ie), $[\alpha]_D^{20}$ +26.7° (*c* 1.93, chloroform) (lit.[19] $[\alpha]_D^{21}$ +28.40° ($\alpha=+1.42°$, chloroform)), was similarly prepared from (+)-borneol. (−)-Menthyl cinnamate (Id), $[\alpha]_D^{20}$ −64.3° (*c* 1.42, acetone) (lit.[19] $[\alpha]_D^{21}$ −63.60° ($\alpha=-3.18$, acetone)), was synthesized by the reaction[20] of cinnamoyl chloride with (−)-menthol at 130°C.

The Asymmetric Synthesis of 3-Methoxy-3-phenylpropionic Acid (V). To a solution of the cinnamic ester (0.01 mol) in absolute methanol (30 m*l*), was successively added mercuric acetate (0.011 mol) and a solution of 60% nitric acid (50 mg) in absolute methanol (10 m*l*); the mixture was then occasionally shaken at 20°C for 5 hr. However, the treatment of Ib, which is sparingly soluble in methanol, was carried out under mechanical stirring for 8 hr. Anhydrous sodium bicarbonate (2.5 g) was suspended in the resulting clear solution under cooling at 0°C, and solid sodium borohydride (400 mg) was added little by little with shaking. After the mixture had stood at room temperature for 15 min, acetone (5 m*l*) was added to decompose the excess sodium borohydride. The mixture was then diluted with water (40 m*l*) and extracted with a large volume of ether. The extract was washed with a little water and dried. The evaporation of the solvent afforded the crude reduction product, IV, whose infrared spectrum showed the presence of a faint trace of the starting ester but no hydroxy groups.[21] The crude product, IVa, IVb, or IVc, was then completely hydrolyzed with sodium hydroxide (0.8 g, 0.02 mol) in a mixture of ethanol (20 m*l*) and water (4 m*l*) at room temperature for 4 hr; a longer reaction time (96 hr) was necessary for the complete hydrolysis of IVd or IVe. Cold water (60 m*l*) was added to the resulting solution, and the solution was extracted with a large volume of chloroform; 1, 2; 5, 6-di-*O*-isopropylidene-D-glucose, 1, 2 ; 5, 6-di-*O*-cyclohexylidene-D-glucose or 5-deoxy-1, 2-*O*-isopropylidene-D-xylose was recovered in a 90—95% yield from the extract.

The water layer was acidified with 6 N hydrochloric acid and extracted with ether, and the extract was dried. The evaporation of the solvents gave a mixture of V and cinnamic acid (VI), which were identified by comparing their infrared and NMR spectra with those of the corresponding authentic sample.[7] Their molar ratio was calculated on the basis of the integrated NMR signals.

All the results are listed in Table 1.

A change in the specific rotation of V at various reaction times of the methoxy-mercuration is shown in Fig. 1.

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[16] The results will be described in detail elsewhere.

[17] V. Prelog and H. L. Meier, *Helv. Chim. Acta*, **36**, 320 (1953).

[18] Optical rotations were measured with a Perkin-Elmer Model 141 photoelectric polarimeter (direct reading to ±0.002°) in a 1 dm tube. The infrared spectra were obtained using either a Perkin-Elmer Model 521 grating infrared spectrophotometer or a Shimadzu IRS-27 Model D. The NMR spectra were recorded on a Nippon Denshi Model C-60 at 60 Mc in deuteriochloroform, with tetramethylsilane ($\tau=10$) as the internal standard. All boiling points are uncorrected. The normal extraction procedure involved drying over anhydrous sodium sulfate and evaporating under reduced pressure by a water aspirator at 60°C. Thin layer chromatography was performed using the ascending technique, with a 250 μ layer of silica gel G (E. Merck, Darmstadt, Germany) or basic aluminum oxide (M. Woelm, Eschwege, Germany) activated for 2 hr at 120°C. The developed layers were visualized by spraying them with a mixture of methanol, sulfuric acid, and *p*-methoxybenzaldehyde (8.5 : 1 : 0.5, v/v) and then heating them to 120°C.

[19] T. P. Hilditch, *J. Chem. Soc.*, **93**, 1 (1908).

[20] K. L. McCluskey and B. C. Sher, *J. Am. Chem. Soc.*, **49**, 452 (1927).

[21] The 5, 6-*O*-isopropylidene group in the sugar derivative was gradually destroyed with the acids during the extended methoxy-mercuration time, thus showing the absorption band of hydroxy group in the infrared spectrum.

In order to test the optical stability of V in an alkaline solution, the crude acid, V ($[\alpha]_D^{20}$ $-16.2°$), was allowed to stand for 97 hr under the same conditions as were used in the hydrolysis of IV. The starting material, $[\alpha]_D^{20}$ $-15.0°$ (*c* 1.29, benzene), was thus recovered in a 95% yield.

(−)-Methyl 3-Methoxy-3-phenylpropionate (VII). A solution of diazomethane, which had been prepared from *N*-methyl-*N*-nitrosourea (4.0 g) in ether (250 m*l*), was added at room temperature to a solution of the crude acid V (1.4 g, $[\alpha]_D^{20}$ $-12.9°$, Expt. No. 5) in ether (25 m*l*) until the solution assumed a yellow color. After 1 hr, the excess diazomethane was decomposed by adding acetic acid, and the resulting solution was washed with saturated aqueous sodium bicarbonate and then with water, and dried. The evaporation of ether gave (−)-VII (1.3 g) (*ca.* 86% yield), $[\alpha]_D^{20}$ $-11.7°$ (*c* 0.91, benzene), whose NMR and infrared spectra were identical with those of rac.-VII, an authentic sample.[6,7] The signals for methyl cinnamate (VIII) had almost disappeared in both the spectra.

NMR: a multiplet of the AB portion in an ABX spectrum centered at τ 7.48 (A) and τ 7.14 (B) (2H on C-2, $J_{AB}=15.0$ cps, $J_{AX}=5.4$ cps, $J_{BX}=8.4$ cps), with a quartet of the X portion centered at τ 5.37 (1H on C-3), a singlet at τ 6.80 (3H of the methoxy group), a singlet at τ 6.33 (3H of the methoxy carbonyl group), and a singlet at τ 2.66 (5H of the phenyl group).

The Asymmetric Synthesis of 3-Methoxy-3-phenylpropan-1-ol (IX). The yields and specific rotations of the products are shown in Table 2.

The starting material, IVa, IVd, or IVe, was derived from the corresponding I (0.01 mol) by methoxymercuration for 5 hr.

A solution of the crude compound, IV or (−)-VII ($[\alpha]_D^{20}$ $-11.7°$) from Ia (0.01 mol), in anhydrous ether (25 m*l*) was added slowly, with shaking under cooling at 25°C, to a suspension of lithium aluminum hydride (300 mg, 0.008 mol) in anhydrous ether (25 m*l*). After 30 min, the excess lithium aluminum hydride was decomposed with ethyl acetate (10 m*l*). The mixture was treated with water and then with 6 N hydrochloric acid, and the resulting clear solution was extracted with ether. The extract was washed with water and dried, and then ether was evaporated.

The products from IVd (3.3 g), whose thin layer chromatogram[22] showed two spots (R_f 0.55, mainly due to IX, and 0.84, due to (−)-menthol) on basic aluminum oxide with chloroform, and two main spots (R_f 0.29, due to IX, and 0.79, due to (−)-menthol) and a faint spot (R_f 0.48, due to cinnamyl and hydrocinnamyl alcohols) on silica gel with ether - petroleum ether (3 : 7, v/v), were chromatographed three times on a basic activated alumina column. Elution with chloroform gave the crude compound, IX (1.0 g), which, on distillation, afforded IX (940 mg), bp 73—75°C/0.5—1 mmHg, n_D^{20} 1.5157 (lit.[23] bp 106—107°C/2 mmHg, n_D^{20} 1.5156).

Found: C, 71.95; H, 8.35%. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49%.

The NMR spectrum of the product agreed with that to be expected for IX.

NMR: a multiplet centered at τ 8.04 (2H on C-2), a singlet at τ 7.31 (1H of the hydroxyl group), a singlet at τ 6.78 (3H of the methoxy group), a triplet centered at τ 6.26 (2H on C-1, $J=6.0$ cps), a quartet centered at τ 5.62 (1H on C-3), and a singlet at τ 2.71 (5H of the phenyl group).

The signals of the protons of the hydroxy and the methoxy groups shifted depending on the concentration of IX in deuteriochloroform.

The products from IVa (4.2 g) were dissolved in a mixture of methanol (6 m*l*), ether (9 m*l*), and 6 N hydrochloric acid (3 m*l*) in order to remove the sugar, and the resulting solution was allowed to stand at room temperature for 1.5 hr. The solution was diluted with water and extracted with a large volume of ether, and the ethereal extract was washed with water and dried. The evaporation of the solvents gave the crude compound, $[\alpha]_D^{20}$ $-23.4°$ (*c* 1.40, benzene), which, after column chromatography on basic activated alumina by elution with chloroform, afforded the crude compound, IX (1.2 g.). A thin layer chromatogram of the compound showed a single spot (R_f 0.56) and the absence of glucose on basic aluminum oxide with chloroform, and a main spot (R_f 0.28) and a faint spot (R_f 0.46) on silica gel with ether - petroleum ether (3 : 7, v/v).

The products from IVe (3.1 g), whose thin layer chromatogram showed two spots (R_f 0.27, due to IX, and 0.75, due to (+)-borneol) and a faint spot (R_f 0.47) on silica gel with ether - petroleum ether (3 : 7, v/v), were chromatographed on a silica gel column. Elution with the same solvent gave the crude compound, IX (1.4 g).

The products (570 mg) from VII (780 mg 0.004 mol) were not purified with chromatography.

The NMR spectra of all the crude compounds, IX, were identical with those of IX, but their thin layer chromatograms showed a faint trace of optically inactive alcohols on silica gel with ether - petroleum ether (3 : 7, v/v).

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22) The thin layer chromatograms of cinnamyl alcohol and hydrocinnamyl alcohol showed a spot at R_f 0.55 and a spot at R_f 0.58 respectively on basic aluminum oxide with chloroform, while they showed a spot at R_f 0.48 on silica gel with ether - petroleum ether (3 : 7, v/v).

23) S. Mamedov and D. Khydyrov, *Zh. Obshch. Khim.*, **33**, 457 (1963); *Chem. Abstr.*, **59**, 488 (1963).