The Stereochemistry of Nucleophilic Addition. V.[1] The Reformatsky Reaction of 2-Phenylpropanal with Methyl α-Bromopropionate

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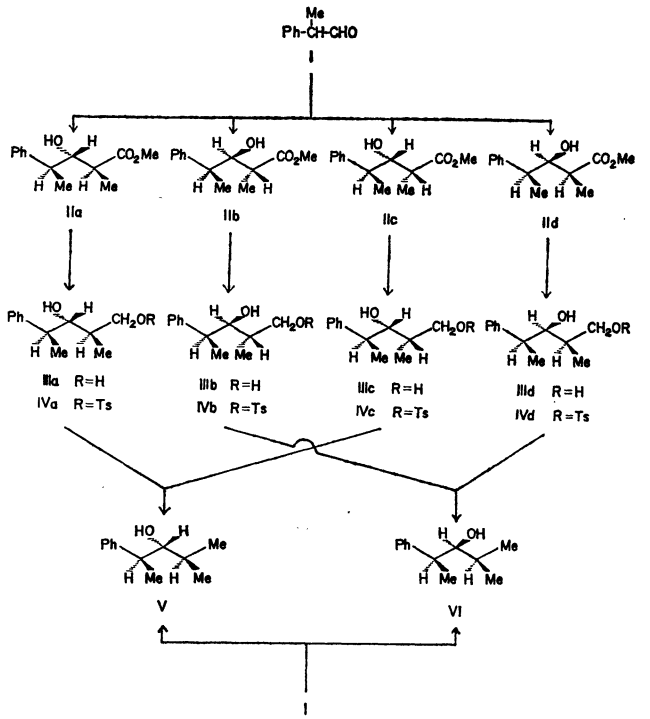
(Received January 24, 1972)

The Reformatsky reaction of 2-phenylpropanal (I) with methyl α-bromopropionate gave the diastereomeric methyl 3-hydroxy-2-methyl-4-phenylvalerates, IIa, IIb, IIc, and IId, in a 5 : 24 : 16 : 55 ratio. The configurations of these β-hydroxy esters were assigned by the following experiments. The reduction of IIa—IId with $LiAlH_4$ gave the corresponding diols, IIIa—IIId, which were then converted to the monotosylates, IVa—IVd. The further reduction of IVa or IVc and IVb or IVd with $LiAlH_4$ gave the epimeric 2-methyl-4-phenyl-3-pentanols, V and VI respectively. Since V and VI were also obtained as minor and major products (20 : 80 ratio) of the Grignard reaction of I with isopropylmagnesium iodide, the configurations of the C-3 and C-4 positions in IIa—IId were assigned. The Wittig reaction of I with carbomethoxyethylidenetriphenylphosphorane gave methyl 2-methyl-4-phenyl-2-*cis*-pentenoate (VII) and its *trans*-isomer (VIII), which were then reduced to the corresponding alcohols, IX and X respectively. The *cis*-hydration of IX gave IIIc and IIId, while a similar treatment of X gave IIIa and IIIb. From this experiments, the relative configurations from the C-2 position to the C-3 position in IIa—IId were also assigned. These configurational assignments of IIa—IId were further confirmed by the ozonization of IIa—IId.

In previous papers,[2-4] we reported on the stereochemistry of the Reformatsky reaction of carbonyl compounds possessing an asymmetric α-carbon atom with methyl (or ethyl) bromoacetate. In these reactions the products had two vicinally-situated asymmetric carbon atoms, which led to two epimeric racemates. On the other hand, if methyl α-bromopropionate is used as a nucleophilic reagent in place of the bromoacetate, the product can be expected to have three asymmetric carbon atoms; therefore, four racemic isomers will be present. The present paper will describe the stereochemistry of the Reformatsky reaction of 2-phenylpropanal (I) with methyl α-bromopropionate.

The condensation of I with methyl α-bromopropionate in dry benzene in the presence of zinc gave a mixture of diastereomeric methyl 3-hydroxy-2-methyl-4-phenylvalerates in a 75% yield. The separation of these esters was subsequently carried out by means of column chromatography on silica gel to give, in the order of elution, the IIa, IIb, IIc, and IId esters in a 5 : 24 : 16 : 55 ratio. The configurations of these β-hydroxy esters (IIa—IId) were assigned in the following manner. The reduction of IIa, IIb, IIc, and IId with $LiAlH_4$ in ether afforded the corresponding 2-methyl-4-phenylpentane-1,3-diols, IIIa, IIIb, IIIc, and IIId respectively. Subsequently, the IIIa—IIId diols were subjected to tosylation with *p*-toluenesulfonyl chloride in pyridine to give the corresponding monotosylates, IVa, IVb, IVc, and IVd respectively. The reduction of IVa and IVc in dry tetrahydrofuran with $LiAlH_4$ gave the same alcohol, 2-methyl-4-phenyl-3-pentanol (V). Therefore, it is clear that IIa and IIc possess the same configuration at the C-3 and C-4 positions. On the other hand, the tosylates, IVb and IVd, were also reduced to another alcohol (VI). These findings mean that the configurations of IIb and IId at the C-3 and C-4 positions are the same. Furthermore, the Grignard reaction of I with isopropylmagnesium iodide gave the epimeric alcohols in a 20 : 80 ratio; these minor and major alcohols were shown to be identical with the above V and VI respectively by a comparison of their IR spectra.



Since the stereochemistry of the Grignard reaction is well known as Cram's rule[5,6] of asymmetric induction, the configurations of the C-3 and C-4 positions in

1) Part IV. T. Matsumoto, G. Sakata, Y. Tachibana, and K. Fukui, This Bulletin, **45**, 1147 (1972). Although the formula depicted represent only one enantiomer, they are taken to indicate a racemate.

2) T. Matsumoto and K. Fukui, *ibid.* **44**, 1090 (1971).

3) T. Matsumoto, I. Tanaka, and K. Fukui, *ibid.*, **44**, 3378 (1971).

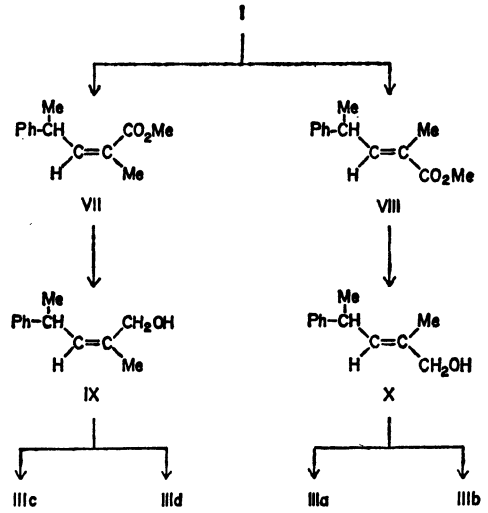
4) T. Matsumoto, Y. Tachibana, T. Ohno, and K. Fukui, *J. Sci. Hiroshima Univ. Ser. A*, **35**, 231 (1971).

5) D. J. Cram and F. A. Abd Elhafez, *J. Amer. Chem. Soc.*, **74**, 5828 (1952).

6) G. J. Karabatsos, *ibid.*, **89**, 1367 (1967).

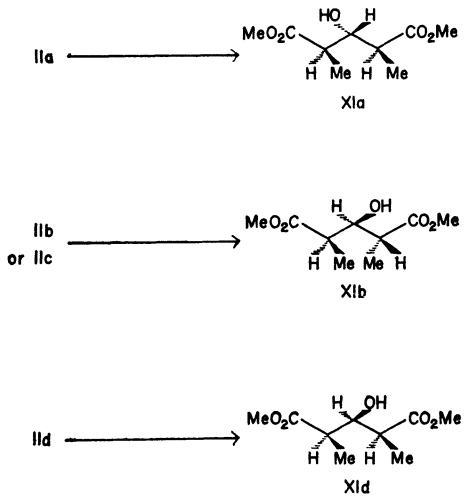
the β-hydroxy esters were assigned to as is shown in IIa—IId. To obtain the data on the configuration of the C-2 position relative to the C-3 position in IIa–IId, the following experiments were carried out.

The Wittig reaction of I with carbomethoxyethylidene triphenylphosphorane in dry benzene gave an 87% yield of a mixture of geometric isomers, which were then successfully separated by means of column chromatography on silica gel into two oily esters in a 3 : 97 ratio. It is well known[7,8] that the ylids stabillized by an adjacent carbonyl function yield, as the predominant product, an isomer in which the carbonyl function is *trans* to the larger group at the beta carbon atom. In the NMR spectra it is also known that the signal of a *cis*-vinyl proton to the methoxycarbonyl group appeares in a field lower than that of the corresponding *trans*-vinyl proton.



The chemical shifts of the vinyl protons in the above minor and major esters were observed at δ 5.88 ppm and at δ 6.78 ppm respectively. Therefore, the structures of the minor and major esters were identified as methyl 2-methyl-4-phenyl-2-*cis*-pentenoate (VII) and its *trans*-isomer (VIII) respectively. These assignments were further supported by the chemical shifts of the methine protons at the C-4 position in VII and VIII. That is, VII showed the signal of the methine proton at δ *ca.* 4.5 ppm, suggesting the presence of a *cis*-methoxycarbonyl group relative to the methine proton, because VIII showed the corresponding signal at δ *ca.* 3.7 ppm. The VII and VIII esters were then reduced with $LiAlH_4$ in ether to give the corresponding alcohols, IX and X respectively. The hydroboration of the *cis*-alcohol (IX), followed by oxidation with alkaline hydrogen peroxide, gave the diols (IIIc and IIId). This result means that the configurations of the IIIc and IIId diols differ only at the C-4 position. On the other hand, a similar treatment of the *trans*-alcohol (X) gave the IIIa and IIIb diols. Therefore, the difference between the configurations of the IIIa and IIIb diols is also at the C-4 position. Further, it is well known[9] that the hydration of the carbon-carbon double bond by the hydroboration-oxidation procedure proceeds in a *cis* manner.

On the basis of the above experiments, the configurations of all the asymmetric carbon atoms in the β-hydroxy esters were assigned as is shown in IIa—IId. These configurational assignments of IIa—IId were further confirmed by the following experiments. If the phenyl group in IIa—IId could be converted to the methoxycarbonyl group, it might be expected that IIa and IId would afford, respectively, two meso isomers, XIa and XId, while IIb or IIc would afford a racemate, XIb. Therefore, the ozonization of IIb and IIc in acetic acid, followed by the methylation of the resulting acids with diazomethane, was carried out; as would be expected, the same diester, XIb, was obtained. However, a similar treatment of IIa and IId afforded the corresponding diesters, XIa and XId.



An attempt will now be made to explain the ratio of IIa–IId. It is known[3] that the stereochemistry of the Reformatsky reaction of the carbonyl compound possessing an asymmetric α-carbon atom has been explained by Cram's rule of asymmetric induction. Further, the stereochemistry of this reaction has also been explained on the hypothesis of an enolate-anion mechanism[10] involving a cyclic transition state, as in the case of the Ivanov reaction.[11] Therefore, the four models (A, B, C, and D) of transition states for the Reformatsky reaction of I with methyl α-bromopropionate in the presence of zinc are as is shown in Fig. 1. The conformation of I in A and B is more stable than that in C and D, as has been reported by Karabatsos.[6] For the steric interaction between the methyl group at the C-2 position and the hydrogen at the C-3 position, the B and D transition states should be less stable than the corresponding A and C transition states. Thus, the stability of these transition states decreases in the order of A, B, C, and D, leading to the IId, IIb, IIc, and IIa esters respectively.

7) A. Maercker, "Organic Reactions," Vol. 14, Wiley, New York (1965), p. 270.

8) T. Matsumoto, K. Hidaka, T. Nakayama, and K. Fukui, *Chem. Lett.*, **1972**, 1.

9) G. Zweifel and H. C. Brown, "Organic Reactions," Vol. 13, Wiley, New York (1963), p. 1.

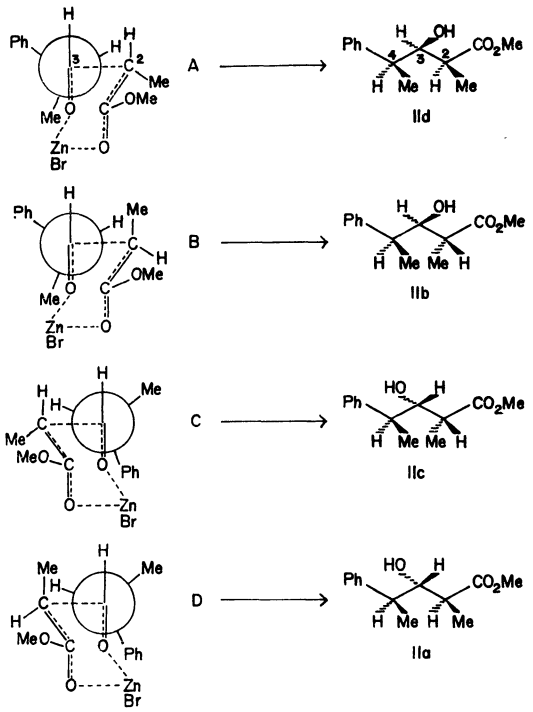


Fig. 1

Experimental

All the melting and boiling points are uncorrected. The NMR spectra were taken on a Hitachi Model R-20 NMR spectrometer (60 MHz), using tetramethylsilane as the internal standard. The chemical shifts are presented in terms of δ values; s: singlet, bs: broad singlet, d: doublet, bd: broad doublet, dd: double doublet, t: triplet, dqa: double quartet, qi: quintet, m: multiplet. The column chromatography was performed on Merck silica gel (0.08 mm).

Methyl 3-Hydroxy-2-methyl-4-phenylvalerates (IIa, IIb, IIc, and IId). A solution of methyl α-bromopropionate (6.01 g) and 2-phenylpropanal (I: 3.22 g) in dry benzene (10 m*l*) was added, drop by drop at 80°C and over a period of 20 min, to a stirred suspension of purified zinc powder[12] (2.35 g) in dry benzene (3.0 m*l*); the temperature was kept at 80—85°C during the addition. After the addition was complete, the mixture was refluxed for 70 min, cooled, decomposed with dilute hydrochloric acid, and then extracted with benzene. The extract was successively washed with aqueous sodium hydrogen carbonate and water, dried over sodium sulfate, and then evaporated. The residue was distilled to give a mixture of methyl 3-hydroxy-2-methyl-4-phenylvalerates (IIa—IId) as an oil; bp 115—125°C/1 mmHg; yield, 4.80 g. The above oil was purified by means of column chromatography on silica gel (500 g), using benzene containing 1% ether and then 7% ether as the eluents. The first fraction gave IIa as a solid (199 mg) which was recrystallized from petroleum ether to give colorless crystals; mp 59—59.6°C. NMR in CCl_4: 1.13(d, J=6.5 Hz, $-CH(C\underline{H}_3)CO_2CH_3$), 1.31 (d, J=7 Hz, $-CH(C\underline{H}_3)C_6H_5$), 2.32(qi, J=6.5 Hz, $-C\underline{H}CO_2CH_3$), 2.75 (s, $-O\underline{H}$), *ca.* 2.8 (m, overlap, $-C\underline{H}C_6H_5$), 3.53 (s, $-CO_2C\underline{H}_3$), *ca.* 3.6 (m, overlap, $-C\underline{H}OH$), 7.18 (s, $-C_6\underline{H}_5$).

Found: C, 70.32; H, 8.17%. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16%.

The second fraction gave IIb as an oil; yield, 954 mg. NMR in CCl_4: 1.15 (d, J=7 Hz, $-CH(C\underline{H}_3)CO_2CH_3$), 1.32 (d, J=7 Hz, $-CH(C\underline{H}_3)C_6H_5$), *ca.* 2.3 (m, $-C\underline{H}CO_2CH_3$), *ca.* 2.75 (m, overlap, $-C\underline{H}C_6H_5$), 2.85 (s, $-O\underline{H}$), *ca.* 3.4 (m, overlap, $-C\underline{H}OH$), 3.60 (s, $-CO_2C\underline{H}_3$), 7.16 (s, $-C_6\underline{H}_5$

Found: C, 70.22; H, 8.16%. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16%.

The third fraction gave IIc as an oil; yield, 636 mg. NMR in CCl_4: 1.12 (d, J=7 Hz, $-CH(C\underline{H}_3)CO_2CH_3$), 1.24 (d, J=5 Hz, $-CH(C\underline{H}_3)C_6H_5$), 1.83 (d, J=5 Hz, $-C\underline{H}CO_2CH_3$), *ca.* 2.2—3.0 (m, $-C\underline{H}C_6H_5$), *ca.* 2.7 (overlap, $-O\underline{H}$), 3.60 (s, $-CO_2C\underline{H}_3$), *ca.* 3.9 (m, $-C\underline{H}OH$), 7.17(s, $-C_6\underline{H}_5$).

Found: C, 70.22; H, 8.17%. Calcd for $C_3H_{18}O_3$: C, 70.24; H, 8.16%.

The fourth fraction gave IId as an oil; yield, 2185 mg. NMR in CCl_4: 1.09 (d, J=7 Hz, $-CH(C\underline{H}_3)CO_2CH_3$, 1.32 (d, J=6.5 Hz, $-CH(C\underline{H}_3)C_6H_5$), 2.22 (m, $-C\underline{H}CO_2CH_3$), *ca.* 2.7 (m, overlap, $-O\underline{H}$ and $-C\underline{H}C_6H_5$), 3.58 (s, $-CO_2C\underline{H}_3$), 3.95 (m, $-C\underline{H}OH$), 7.12 (s, $-C_6\underline{H}_5$).

Found: C, 70.31; H, 8.18%. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16%.

The total yield of IIa—IId was 3.974 g (75% from I).

Reduction of IIa, IIb, IIc, and IId with $LiAlH_4$. *a)*: A solution of IIa (523 mg) in dry ether (5.0 m*l*) was added, drop by drop over a period of 30 min, to a suspension of $LiAlH_4$(200 mg) in dry ether (15 m*l*) at room temperature, and then the mixture was refluxed for 2.5 hr. After cooling, the mixture was decomposed with dilute hydrochloric acid and extracted with ether. The extract was washed with an aqueous sodium chloride solution, dried over sodium sulfate, and then evaporated. The residue was chromatographed on silica gel (30 g), using benzene containing 20% ether as the eluent, to give 2-methyl-4-phenylpentane-1,3-diol (IIIa) as an oil; yield, 245 mg. NMR in $CDCl_3$: 0.90 (d, J=6.5 Hz, $-CH(C\underline{H}_3)CH_2OH$), 1.24 (d. J=7 Hz, $-CH(C\underline{H}_3)C_6H_5$), 1.55 (m, $-C\underline{H}CH_2OH$), 2.86 (qi, J=6.5 Hz, $-C\underline{H}C_6H_5$), 3.41 (s, $-O\underline{H}$), *ca.* 3.55 (m, overlap, $-C\underline{H}OH$ and $-CH_2\underline{O}H$), 7.23 (s, $-C_6\underline{H}_5$).

Found: C, 74.28; H, 9.57%. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34%).

b): The IIb ester (400 mg) was reduced with $LiAlH_4$ by a method similar to that used for IIIa. The crude product was recrystallized from petroleum ether to give IIIb as colorless crystals; mp 52—53°C; yield, 275 mg. NMR in $CDCl_3$: 0.95 (d, J=7 Hz, $-CH(C\underline{H}_3)CH_2OH$), 1.29 (d, J=7 Hz, $-CH(C\underline{H}_3)C_6H_5$), 1.75 (m, $-C\underline{H}CH_2OH$), 2.90 (s, $-O\underline{H}$), 3.0 (m, overlap, $-C\underline{H}C_6H_5$), *ca.* 3.7 (m, overlap, $-C\underline{H}OH$ and $-CH_2\underline{O}H$), 7.28 (s, $-C_6\underline{H}_5$).

Found: C, 74.36; H, 9.47%. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34%.

c): The IIc ester (749 mg) was also reduced with $LiAlH_4$ to give IIIc as colorless crystals (from petroleum ether); mp 70.5—71°C; yield, 452 mg. NMR in $CDCl_3$: 1.02 (d, J=7 Hz, $-CH(C\underline{H}_3)CH_2OH$), 1.19(d, J=7 Hz, $-CH(C\underline{H}_3)C_6H_5$), *ca.* 2.0 (m, overlap, $-C\underline{H}CH_2OH$), 2.02 (s, $-OH$), 2.84 (m, $-C\underline{H}C_6H_5$), 3.73 (d, J=5 Hz, $-CH_2\underline{O}H$),

10) Ref. 3 and the references cited therein.

11) H. E. Zimmerman and M. D. Traxler, *J. Amer. Chem. Soc.*, **79**, 1920 (1957).

12) R. L. Shriner, "Organic Reactions," Vol. 1, Wiley, New York (1942). p. 16.

3.88 (dd, overlap, J=9.5 and 2 Hz, -CHOH), 7.30 (s, -C_6H_5).

Found: C, 74.29; H, 9.48%. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34%.

d): Similarly, the IId ester (2.20 g) was reduced to IIId; colorless crystals (1.30 g); mp 98—98.5°C (from *n*-hexane containing ether). NMR in $CDCl_3$: 0.92 (d, J=6.5 Hz, -CH(CH_3)CH_2OH), 1.34 (d, J=6.5 Hz, -CH(CH_3)C_6H_5), *ca.* 1.4 (m, overlap, -CHCH$_2$OH), 2.39 (s, -OH), 2.8 (m, -CHC$_6$H$_5$), 3.62 (d, J=4 Hz, -CH$_2$OH), 3.97 (dd, J=9.5 and 2 Hz, -CHOH), 7.24 (s, -C_6H_5).

Found: C, 74.28; H, 9.53%. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34%.

The Tosylates (IVa, IVb, IVc, and IVd). a): A mixture of the IIIa diol (189 mg) and *p*-toluenesulfonyl chloride (186 mg) in dry pyridine (3.0 m*l*) was allowed to stand at room temperature for 72 hr. After a usual work-up, the crude product was chromatographed on silica gel (15 g). Elution with benzene containing 5% ether was then carried out to give IVa as an oil; yield, 133 mg.

Found: C, 65.72; H, 7.08%. Calcd for $C_{19}H_{24}O_4S$: C, 65.50; H, 6.94%.

b): The other tosylates (IVb, IVc, and IVd) were also prepared from the corresponding diols (IIIb, IIIc, and IIId) by a method similar to that used for IVa.

IVb; Found: C, 65.70; H, 7.04%. Calcd for $C_{19}H_{24}O_4S$: C, 65.50; H, 6.94%.

IVc; Found: C, 65.48; H, 6.95%. Calcd for $C_{19}H_{24}O_4S$: C, 65.50; H, 6.94%.

IVd; Found: C, 65.80; H, 7.15%. Calcd for $C_{19}H_{24}O_4S$: C, 65.50; H, 6.94%.

2-Methyl-4-phenyl-3-pentanols (V and VI). a) By the Grignard Reaction: A solution of I (1.960 g) in dry ether (5.0 m*l*) was added, drop by drop over a period of 30 min, to a Grignard reagent, prepared from magnesium (0.660 g) and isopropyl iodide (3.950 g) in dry ether (20 m*l*). The mixture was refluxed for 90 min, cooled, decomposed with a mixture of ice and dilute hydrochloric acid, and then extracted with ether. The extract was successively washed with aqueous sodium thiosulfate and water. After drying over sodium sulfate, the solvent was evaporated; the residue (2.032 g) was then chromatographed on silica gel (200 g), using benzene containing 3% ether as the eluent. The first fraction gave a minor alcohol (V) as an oil (327 mg).

Found: C, 80.64; H, 10.21%. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18%.

The second fraction gave a major alcohol (VI) as an oil (1142 mg).

Found: C, 80.81; H, 10.14%. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18%.

b) From the Tosylates (IVa and IVc): The tosylate (IVa: 133 mg) was reduced with $LiAlH_4$ (50 mg) in dry tetrahydrofuran (3.0 m*l*) by a method similar to that used for IIIa. The crude product was purified by column chromatography on silica gel (30 g), using benzene containing 2% ether as the eluent, to give an oil (36 mg); this oil was shown to be identical with the above minor alcohol (V) of the Grignard reaction by an IR spectral comparison.

By a similar reduction, IVc was converted to V; its identity was also confirmed by an IR spectral comparison.

c) From the Tosylates (IVb and IVd): The tosylates (IVb and IVd) were treated with $LiAlH_4$ by a method similar to that used in *b*). After chromatographic purification, the two products were shown by a spectral comparison to be identical with the major alcohol (VI) of the Grignard reaction.

*Methyl 2-Methyl-4-phenyl-2-*cis*-pentenoate (VII) and Its* trans*-Isomer (VIII)*. A mixture of I (2.68 g), carbomethoxyethylidene triphenylphosphorane (6.96 g), and dry benzene (50 m*l*) was refluxed for 2 hr under a stream of nitrogen; the solvent was then evaporated under a vacuum. The residue was extracted with ether. The extract, after the removal of the ether, was chromatographed on silica gel (500 g), using benzene containing 1% ether as the eluent. The first fraction gave methyl 2-methyl-4-phenyl-2-*cis*-pentenoate (VII) as an oil (0.12 g). NMR in CCl_4: 1.31 (d, J=7 Hz, -CHCH_3), 1.83 (d, J=1.5 Hz, =CCH_3), 3.66 (s, -CO_2CH_3), *ca.* 4.5 (m, -CHCH_3), 5.88 (dqa, J=10 and 1.5 Hz, =CH), 7.15 (s, -C_6H_5).

Found: C, 76.66; H, 7.96%. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90%.

The second fraction gave methyl 2-methyl-4-phenyl-2-*trans*-pentenoate (VIII) as an oil (3.41 g), NMR in CCl_4: 1.36 (d, J=7 Hz, -CHCH_3), 1.83 (d, J=1.5 Hz, =CCH_3), 3.65 (s, -CO_2CH_3), *ca.* 3.65 (m, overlap, -CHCH_3), 6.78 (dqa, J=9 and 1.5 Hz, =CH), 7.18 (s, -C_6H_5).

Found: C, 76.35; H, 7.87%. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90%.

*2-Methyl-4-phenyl-2-*cis*-pentenol (IX) and Its* trans*-Isomer (X)*. *a)*: A solution of VII (225 mg) in dry ether (5.0 m*l*) was added, drop by drop over a period of 10 min at —10—0°C, to a stirred suspension of $LiAlH_4$ (100 mg) in dry ether (4.0 m*l*). The mixture was further stirred for 1.5 hr at this temperature and then decomposed with a mixture of ice and dilute hydrochloric acid. The mixture was extracted with ether. The extract was washed with an aqueous sodium chloride solution, dried over sodium sulfate, and then evaporated. The residual oil was purified by column chromatography on silica gel (30 g). Elution with benzene containing 15% ether gave IX as an oil (118 mg). NMR in CCl_4: 1.24 (d, J=7 Hz, -CHCH_3), 1.71 (d, J=1.5 Hz, =CCH_3), 2.33 (s, -OH), 3.66 (m, -CHCH_3), 3.99 (s, -CH_2-), 5.31 (bd, J=9 Hz, =CH), 7.10 (s, -C_6H_5).

Found: C, 81.79; H, 9.21%. Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.15%.

b): By a method similar to that used for IX, the ester (VIII: 1.36 g) was also reduced with $LiAlH_4$ to give X as an oil (0.97 g). NMR in CCl_4: 1.26 (d, J=7 Hz, -CHCH_3), 1.58 (d, J=1.5 Hz, =CCH_3), 3.00 (bs, -OH), *ca.* 3.6 (m, overlap, -CHCH_3), 3.78 (s, -CH_2-), 5.44 (bd, J=9 Hz, =CH), 7.12 (s, -C_6H_5).

Found: C, 81.98; H, 9.27%. Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.15%.

*Hydroboration of 2-Methyl-4-phenyl-2-*cis*-pentenol (IX) and 2-Methyl-4-phenyl-2-*trans*-pentenol (X)*. *a)*: A solution of the *cis*-alcohol (IX: 380 mg) in dry tetrahydrofuran (5.0 m*l*) was added to a solution of sodium borohydride (150 mg) in dry tetrahydrofuran (3.0 m*l*) at 0—5°C over a 10-min period. To the stirred and cooled solution, a solution of freshly-distilled boron trifluoride etherate (0.7 m*l*) in dry tetrahydrofuran (3.0 m*l*) was added at this temperature over a period of 5 min. After the sitrring had been continued for 3 hr at 0—10°C, a few drops of water, aqueous sodium hydroxide (12%: 3.0 m*l*), and then hydrogen peroxide (30%: 0.7 m*l*) were added successively. The mixture was stirred for 30 min, poured into an aqueous sodium hy-

droxide solution, and then extracted with ether. The extract was washed successively with aqueous sodium hydroxide and water. After the removal of the dried ether, the residue (368 mg) was chromatographed on silica gel (35 g), using benzene containing 15% ether as the eluent. The first fraction gave the recovered IX (150 mg). The second fraction gave colorless crystals (50 mg), which were shown to be identical with the above IIIc by a comparison of their IR spectra. The third fraction gave colorless crystals (88 mg), which were also shown to be identical with the above IIId by a comparison of their IR spectra.

b): The *trans*-alcohol (X: 3.75 g) was treated by a method similar to that used in *a)*. The crude product was purified by means of column chromatography on silica gel to give IIIa (256 mg) and IIIb (1787 mg), which were shown to be identical with the authentic samples by a comparison of their IR spectra.

Ozonolyses of IIa—IId. *a)* The ozone gas stream from a laboratory ozonator (Nihon Ozon Co.) was passed through a solution of IId (1.755 g) in acetic acid (40 m*l*) for 40 hr at room temperature. The mixture was allowed to stand at room temperature with hydrogen peroxide (30%: 10 m*l*). After the decomposition of the excess reagent with aqueous sodium hydrogen sulfite (25%: 40 m*l*), the solution was evaporated under a vacuum. The residue was extracted with ether, after which the extract was methylated with diazomethane. The crude ester, after the removal of the ether, was purified by means of column chromatography on silica gel (200 g). Elution with benzene containing 3% ether gave the recovered IId (574 mg). Further elution with benzene containing 7% ether gave XId (221 mg) as an oil. NMR in CCl_4: 1.19 (d, J=7 Hz, 2-$\underset{|}{C}HC\underline{H}_3$), 2.48 (qi, J=7 Hz, 2-$C\underline{H}CH_3$), 3.0 (bs, -O$\underline{H}$), 3.67 (s, 2-$CO_2C\underline{H}_3$), 3.98 (t, J=7 Hz, -$\underset{|}{C}\underline{H}OH$).

Found: C, 52.78; H, 8.07%. Calcd for $C_9H_{16}O_5$: C, 52.93; H, 7.90%,

b) The ozonization of the IIa ester (215 mg) was carried out, by a method similar to that used for XId, to give XIa (15 mg) as an oil. NMR in CCl_4: 1.18 (d, J=7 Hz, 2-$\underset{|}{C}HC\underline{H}_3$), 2.58 (qi, J=7 Hz, 2-$\underset{|}{C}\underline{H}CH_3$), 3.03 (bs, -O$\underline{H}$), *ca.* 3.6 (m, overlap, -$\underset{|}{C}\underline{H}OH$), 3.65 (s, 2-$CO_2C\underline{H}_3$).

Found: C, 52.91; H, 7.98%. Calcd for $C_9H_{16}O_5$: C, 52.93; H, 7.90%.

c) The IIb ester (497 mg) was treated, by a method similar to that used for XId, to give XIb (56 mg) as an oil. NMR in CCl_4: 1.18 (d, J=7 Hz 2-$\underset{|}{C}HC\underline{H}_3$), 2.48 (qi, J=7 Hz, 2-$\underset{|}{C}\underline{H}CH_3$), 2.81 (bs, -O$\underline{H}$), 3.67 (s, 2-$CO_2C\underline{H}_3$), 3.78 (m, overlap, -$\underset{|}{C}\underline{H}OH$).

Found: C, 52.81; H, 7.96%. Calcd for $C_9H_{16}O_5$: C, 52.93; H, 7.90%.

Similarly, the IIc ester (290 mg) was also treated by a method similar to that used for XId, thus giving an oil (43 mg) which was shown to be identical with XIb by a comparison of their IR spectra.