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The Stereochemistry of Nucleophilic Addition. II.[1] The Reformatsky Reaction of Methyl (+)-α-Bromopropionate, 2-Phenylpropanal, and 3-Phenyl-2-butanone

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The Reformatsky reaction of methyl (+)-α-bromopropionate with benzaldehyde was carried out in order to study the reaction mechanism, and two epimeric methyl 3-hydroxy-2-methyl-3-phenylpropionates (IIa and IIb) were obtained in a 59 : 41 ratio. From a comparison of the optical activity of IIb with that of pure (−)-IIb, it was estimated that IIb consists only seven percent of an optically-active compound; this results supports the hypothesis of the enolate anion mechanism. Subsequently, the stereochemistry of this reaction with 2-phenylpropanal (IV) and 3-phenyl-2-butanone (VIII) was studied. The condensation of IV with methyl bromoacetate gave a mixture of the epimeric methyl 3-hydroxy-4-phenylvalerates (Va and Vb), which were separated in a 26 : 74 ratio by means of column chromatography on silica gel. Similarly, VIII was also condensed with methyl bromoacetate to give the epimeric methyl 3-hydroxy-3-methyl-4-phenylvalerates (IXa and IXb) in a 31 : 69 ratio. The configurations of these esters were assigned by correlation with the products of the Grignard reaction, the stereochemistry of which is well known. From the present study, it is clear that the Reformatsky and the Grignard reactions of the carbonyl compound having an asymmetric α-carbon atom proceed in a similar fashion; that is, the entering group predominantly approaches the carbonyl group from the least-hindered side. Therefore, Cram's rule of asymmetric induction can be applied in the stereochemistry of the Reformatsky reaction.

The Reformatsky reaction[2] has long been recognized as a convenient method for preparing β-hydroxy esters, and the stereochemistry of this reaction, as well as that of the Ivanov reaction, has been explained by the hypothesis of an enolate anion mechanism[3–6] involving a cyclic transition state. If the reaction proceeds through the enolate anion intermediate, the condensation of the optically-active α-haloester possessing an asymmetric α-carbon atom, with a carbonyl compound which has no asymmetric carbon atom might be expected to yield a racemate of the corresponding β-hydroxy ester. To obtain further information on this reaction mechanism, we have now studied the condensation of benzaldehyde with methyl (+)-α-bromopropionate (I) in a benzene solution in the presence of zinc. The product (methyl 3-hydroxy-2-methyl-3-phenylpropionate) was separated by means of column chromatography on silica gel to give two epimeric esters; IIa (liquid), $[\alpha]_D^{25}+1.5°$ ($CHCl_3$) and IIb (mp 50.5—51.5°C), $[\alpha]_D^{25}-3.9°$ ($CHCl_3$), in a 59 : 41 ratio. The configurations of the racemates of these major (IIa) and minor (IIb) products had already been identified by Zimmerman and English[7] and Canceill *et al.*[8] as *erythro*- and *threo*-compounds respectively. In order to compare them with the above IIb, optically-pure (−)-IIb was prepared from (±)-*threo*-3-hydroxy-2-methyl-3-phenylpropionic

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1) Part I of this series: T. Matsumoto and K. Fukui, This Bulletin, **44**, 1090 (1971). Although the formulas depicted represented only one enantiomer, they are taken to mean a racemate unless otherwise stated.

2) S. Reformatsky, *Ber.*, **20**, 1210 (1887).

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

4) E. Toromanoff, *Bull. Soc. Chim. Fr.*, **1962**, 1190.

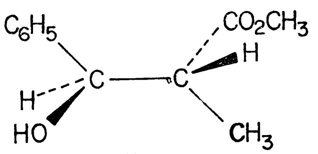
5) M. Mousseron, M. Mousseron, J. Neyrolles, and Y. Beziat, *ibid.*, **1963**, 1483.

6) H. O. House, "Modern Synthetic Reactions," W. A. Benjamin, New York, N. Y. (1965), p. 242.

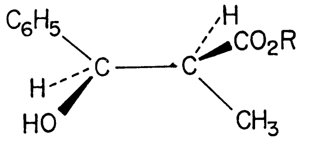
7) H. E. Zimmerman and J. English, Jr., *J. Amer. Chem. Soc.*, **76**, 2291 (1954).

8) J. Canceill, J-J. Basselier, and J. Jacques, *Bull. Soc. Chim. Fr.*, **1963**, 1906.

acid (IIIb), mp 97—98°C, in the following manner. (±)-IIIb was resolved by means of cinchonidine, and one of the diastereomeric salts, mp 170—172°C; $[\alpha]^{25}_{D}-87.6°$ (EtOH), was decomposed with dilute sulfuric acid to give (−)-IIIb, mp 106—107°C; $[\alpha]^{25}_{D}-19.7°$ (EtOH), which was then further converted by diazomethane to (−)-IIb ($[\alpha]^{25}_{D}-57.1°$ ($CHCl_3$)). Since (+)-I was recovered with an unchanged specific rotation after it had been refluxed in dry benzene with zinc for 2 hr (the time required for the reaction), it was estimated that a ninety-three-percent racemization occurred in the above condensation. In view of this racemization and the ratio, which was not 50 : 50 in the *erythro*- and *threo*-isomers, the main reaction seems to proceed through the enolate anion mechanism. However, since only a small degree of the optical activity is observed in the products, it is apparent that the reaction partially proceeds by a different reaction mechanism, such as the carbanion mechanism.



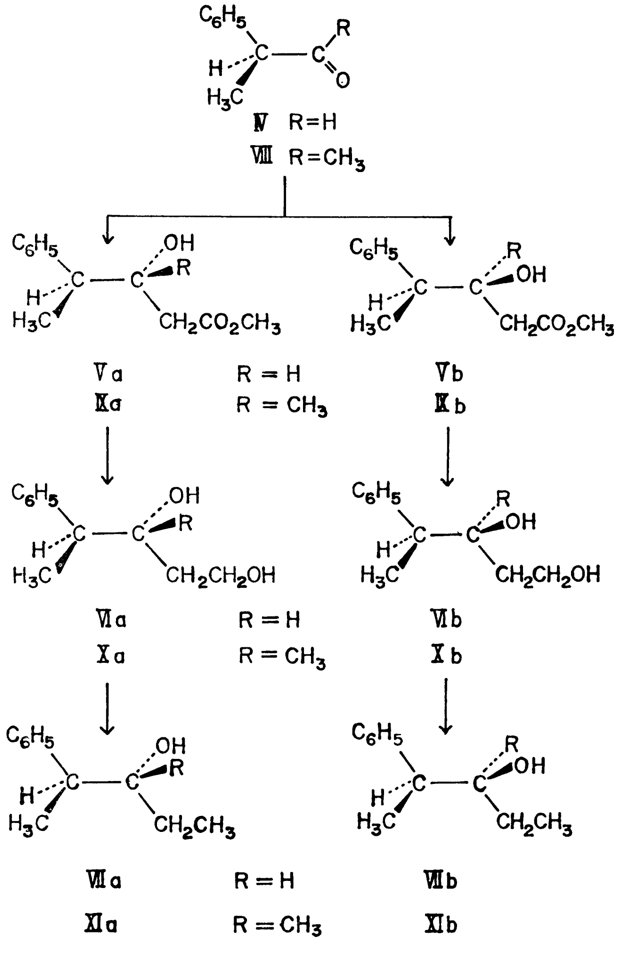
IIa



IIb R=CH_3
IIIb R=H

Subsequently, we turned our attention to the study of the stereochemistry of the Reformatsky reaction with carbonyl compounds possessing an asymmetric α-carbon atom, because this type of reaction has been little studied.[9–11] In a previous paper[11] we reported on the stereochemistry of the Reformatsky reaction with 2-alkylcyclohexanones. In this paper we wish to extend the scope of it to non-cyclic carbonyl compounds.

The condensation of 2-phenylpropanal (IV) with methyl bromoacetate in dry benzene in the presence of zinc gave a mixture of epimeric methyl 3-hydroxy-4-phenylvalerates, which were separated by column chromatography to give two oily esters (Va and Vb) in a 26 : 74 ratio. The configurations of these minor (Va) and major (Vb) products were assigned by correlation with the products of the Grignard reaction, the stereochemistry of which is well known. The reduction of Va and Vb with $LiAlH_4$ in ether afforded the corresponding diols, VIa and VIb, respectively. Subsequently, VIa and VIb were subjected to the tosylation with *p*-toluenesulfonyl chloride in pyridine, followed by the reduction of the resulting monotosylates with $LiAlH_4$ in tetrahydrofuran, to give the epimeric 2-phenyl-3-pentanols, VIIa (liquid) and VIIb (mp 39—40°C) respectively. Since Cram and Elhafez[12] had reported the preparation of *threo*- and *erythro*-2-phenyl-3-pentanols by the Grignard reaction of IV with ethylmagnesium bromide or by the reduction of 2-phenyl-3-pentanone with $LiAlH_4$, the condensation of IV with ethylmagnesium iodide was carried out for purposes of direct comparison; the mixture of epimers thus obtained was successfully separated by column chromatography[13] into the *threo* and *erythro* isomers in a 19 : 81 ratio. The alcohols, VIIa and VIIb, were shown to be identical with the authentic *threo* (minor) and *erythro* (major) isomers respectively by comparisons of their IR and NMR spectra.



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[9] W. W. Epstein and A. C. Sonntag, *Tetrahedron Lett.*, **1966**, 791.

[10] M. Perry and Y. Maroni-Barnaud, *Bull. Soc. Chim. Fr.*, **1969**, 3574.

[11] T. Matsumoto and K. Fukui, This Bulletin, **44**, 1090 (1971).

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

[13] The diastereomers were separated by Cram and Elhafez[12] through the use of the phthalic acid ester for the *threo* isomer and the 3-nitrophthalic acid ester of the *erythro* isomer.

Similarly, 3-phenyl-2-butanone (VIII)[14] was also condensed with methyl bromoacetate to give the epimeric methyl 3-hydroxy-3-methyl-4-phenylvalerates (IXa and IXb) in a 31 : 69 ratio. The reduction of the minor (IXa) and major (IXb) esters with LiAlH$_4$ gave the corresponding diols (Xa, mp 76.5—77.5°C and Xb, mp 76—76.5°C), which were

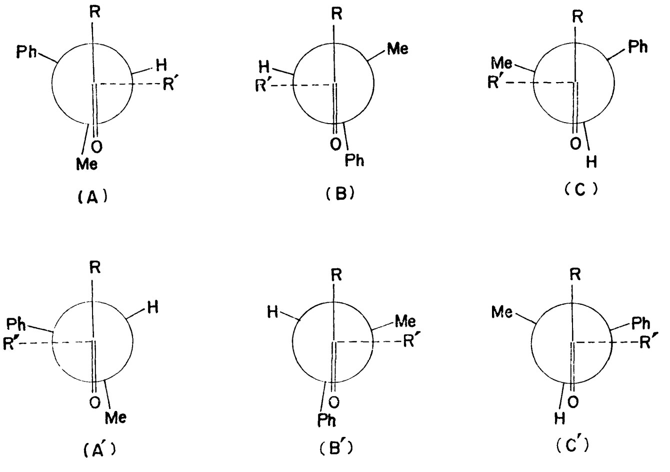


Fig. 1

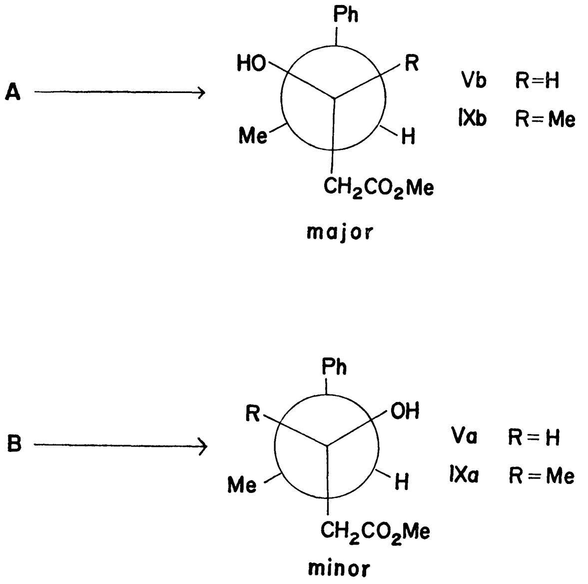
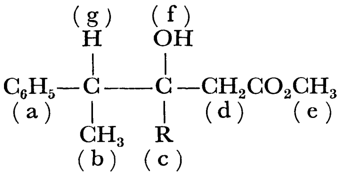


Fig. 2

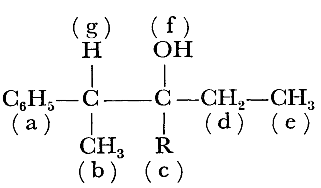
TABLE 1. THE NMR SPECTRA OF Va, Vb, IXa, AND IXb IN $CDCl_3$



$$\underset{(a)}{C_6H_5}-\underset{\underset{(b)}{CH_3}}{\overset{\overset{(g)}{H}}{C}}-\underset{\underset{(c)}{R}}{\overset{\overset{(f)}{OH}}{C}}-\underset{(d)}{CH_2}\underset{(e)}{CO_2CH_3}$$

	a	b	c	d	e	f	g
Va R=H	7.33 (s)	1.32 (d, J=7 Hz)	4.2 (m)	2.39 (d, J=5 Hz)	3.67 (s)	2.49 (s)	2.86 (m)
Vb R=H	7.27 (s)	1.38 (d, J=7 Hz)	4.1 (qa, J=6.5 Hz)	2.31 (d, J=6 Hz)	3.63 (s)	2.98 (s)	2.78 (m)
IXa R=CH_3	7.14 (s)	1.33 (d, J=7 Hz)	1.23 (s)	2.37 (s)	3.57 (s)	3.36 (s)	2.80 (qa, J=7 Hz)
IXb R=CH_3	7.11 (s)	1.33 (d, J=7 Hz)	1.17 (s)	2.34 (s)	3.58 (s)	3.44 (s)	2.90 (qa, J=7 Hz)

TABLE 2. THE NMR SPECTRA OF VIIa, VIIb, XIa AND XIb IN $CDCl_3$



$$\underset{(a)}{C_6H_5}-\underset{\underset{(b)}{CH_3}}{\overset{\overset{(g)}{H}}{C}}-\underset{\underset{(c)}{R}}{\overset{\overset{(f)}{OH}}{C}}-\underset{(d)}{CH_2}-\underset{(e)}{CH_3}$$

	a	b	c	d	e	f	g
VIIa R=H	7.26 (s)	1.25 (d, J=7 Hz)	3.54 (m)	*ca.* 1.5 (overlap)	0.94 (t, J=6.5 Hz)	1.63 (s)	2.72 (qi, J=7 Hz)
VIIb R=H	7.27 (s)	1.31 (d, J=7 Hz)	3.53 (m)	*ca.* 1.5 (overlap)	0.91 (t, J=6.5 Hz)	1.68 (s)	2.77 (qi, J=7 Hz)
XIa R=CH_3	7.28 (s)	1.28 (d, J=7 Hz)	1.09 (s)	*ca.* 1.4 (overlap)	0.91 (t, J=6.5 Hz)	1.37 (s)	2.83 (qa, J=7 Hz)
XIb R=CH_3	7.26 (s)	1.31 (d, J=7 Hz)	1.03 (s)	*ca.* 1.4 (overlap)	0.91 (t, J=7 Hz)	1.32 (s)	2.81 (qa, J=7 Hz)

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[14] C. M. Suter and A. W. Weston, *J. Amer. Chem. Soc.*, **64**, 533 (1942).

then further converted to the corresponding 2-phenyl-3-methyl-3-pentanols (XIa and XIb) *via* monotosylates. The Grignard reaction of VIII with ethylmagnesium iodide gave the epimeric alcohols in a 20 : 80 ratio, these minor and major alcohols were also shown by the spectral comparison to be identical with the above XIa and XIb respectively. The six models of transition states for the addition to the carbonyl group directly bonded to asymmetric carbon atom are shown in Fig. 1. The A, B, and C conformations should be more stable than the corresponding A′, B′, and C′ conformations. Of the three (A, B, and C), A is the most stable, while the second most stable conformation is B, as has been reported by Karabatsos.[15] Thus, A and B, where the incoming group, R′, is closest to the smallest group, hydrogen, lead to the major and minor products respectively, as is shown in Fig. 2.

From the present study, it is clear that the Reformatsky and the Grignard reactions with the carbonyl compound possessing an asymmetric α-carbon atom proceed in a similar fashion. Therefore, it may be suggested that Cram's rule[12,15] of asymmetric induction can be applied in the stereochemistry of the Reformatsky reaction. The stereoselectivity of the Reformatsky reaction observed is slightly less than that of the Grignard reaction.

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, dd: double doublet, t: triplet, qa: quartet, qi: quintet, m: multiplet. The column chromatography was performed on Merck silica gel (0.08 mm).

Methyl (+)-α-Bromopropionate (I). (+)-I (bp 55–56°C/31 mmHg, $[\alpha]^{25}_{D}+68.8°$ (neat)) was prepared from (+)-lactic acid (30% aqueous solution) by the method of Cowdrey *et al.*[16] The reported physical properties[16] of (+)- and (−)-I are bp 46°C/14 mmHg, $[\alpha]_D$ +19.17°[17] and bp 44°C/12 mmHg, $[\alpha]_D$ −68.57°, respectively.

The Reformatsky Reaction of Benzaldehyde with Methyl (+)-α-Bromopropionate. This reaction was carried out by a method similar to that used with ethyl (±)-α-bromopropionate by Zimmerman and English.[7] The crude product (1.123 g) was directly purified by means of column chromatography on silica gel (80 g). Elution with benzene containing 7% and then 15% ether gave two fractions. The first fraction gave methyl *erythro*-3-hydroxy-2-methyl-3-phenylpropionate (IIa: 503 mg), $[\alpha]^{25}_{D}+1.5°$ (*c* 0.152, $CHCl_3$) as a colorless oil. NMR in $CDCl_3$: 1.10 (d, J=7 Hz, $-\overset{|}{C}HC\underline{H}_3$), 2.74 (m, $-\overset{|}{C}\underline{H}CH_3$), 3.21 (d, J=4 Hz, $-O\underline{H}$), 3.52 (s, $-CO_2C\underline{H}_3$), 4.93 (dd, J=4 and 5.5 Hz, $-\overset{|}{C}\underline{H}OH$), 7.18 (s, $-C_6\underline{H}_5$).

Found: C, 68.11; H, 7.20%. Calcd for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27%.

The second fraction gave the *threo*-isomer (IIb: 356 mg), $[\alpha]^{25}_{D}$ −3.9° (*c* 0.198, $CHCl_3$) as a colorless solid. This was recrystallized from ether containing *n*-pentane to give colorless crystals, mp 50.5—51.5°C, which were shown to be identical with authentic (±)-IIb by a mixed-melting-point determination and by a comparison of their IR spectra. NMR in $CDCl_3$: 0.92 (d, J=7 Hz, $-\overset{|}{C}HC\underline{H}_3$), 2.74 (qi, J=7 Hz, $-\overset{|}{C}\underline{H}CH_3$), 3.35 (s, $-O\underline{H}$), 3.60 (s, $-CO_2C\underline{H}_3$), 4.61 (d, J=8 Hz, $-\overset{|}{C}\underline{H}OH$), 7.18 (s, $-C_6\underline{H}_5$).

Found: C, 68.20; H, 7.33%. Calcd for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27%.

*The Resolution of (±)-*threo*-3-Hydroxy-2-methyl-3-phenylpropionic Acid (IIIb) with Cinchonidine.* A solution of (±)-IIIb (1.20 g), mp 97—98°C (lit,[7] mp 96.5—97.5°C) in ethyl acetate was added to a hot solution of cinchonidine (1.96 g) in ethyl acetate (100 m*l*), and then the solution was concentrated to *ca.* 40 m*l*. After the solution had stood at room temperature, the precipitates were collected and then recrystallized from ethyl acetate to give cinchonidine salt as colorless crystals; mp 170—172°C, $[\alpha]^{25}_{D}$ −87.6° (*c* 0.083, EtOH); yield, 1.22 g.

Found: C, 73.66; H, 7.28; N, 5.80%. Calcd for $C_{29}H_{34}O_4N_2$: C, 73.39; H, 7.22; N, 5.90%.

The cinchonidine salt (1.36 g) was decomposed with dilute sulfuric acid (5%: 20 m*l*) and extracted with ether, and the extract was washed with a saturated sodium chloride solution. After it had been dried over sodium sulfate and the ether had been removed, the residue (425 mg) was recrystallized from benzene to give (−)-IIIb as colorless crystals; mp 106—107°C; $[\alpha]^{25}_{D}$ −19.7° (*c* 0.094, EtOH).

Found: C, 66.87; H, 6.65%. Calcd for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71%.

The acid, (−)-IIIb, was methylated with ethereal diazomethane to give (−)-IIb, $[\alpha]^{25}_{D}$ −57.1° (*c* 0.123, $CHCl_3$) or −41.6° (*c* 0.114, EtOH). The IR spectrum was identical with that of authentic (±)-IIb.

The Reformatsky Reaction of 2-Phenylpropanal (IV) with Methyl Bromoacetate. A few drops of a solution of IV (3.22 g) and methyl bromoacetate (5.47 g) in dry benzene (10 m*l*) were stirred, at 80°C, into a mixture of purified zinc powder (2.35 g) and dry benzene (3.0 m*l*). When the exothermic reaction started, the heating bath was removed; the liquid reactants were then added at a rate to maintain the refluxing without further external heating. The total addition required 15 min. The mixture was refluxed for an additional 90 min, cooled, decomposed with a mixture of ice and 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 under a vacuum to give a mixture of epimeric β-hydroxy esters as a colorless oil; bp 147—151°C/10 mmHg; yield, 3.90 g.

The above ester (2.027 g) was chromatographed on silica gel (200 g); subsequently elution with benzene containing 7% and then 10% ether was carried out to give two fractions. The first fraction gave Va (459 mg).

Found: C, 69.15; H, 7.80%. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74%.

The second fraction gave Vb (1301 mg).

Found: C, 69.25; H, 7.86%. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74%.

Reduction of Va and Vb with $LiAlH_4$. *a)* A solution of Vb (1.300 g) in dry ether (10 m*l*) was added, drop by drop over a 20-min period, to a suspension of $LiAlH_4$ (490 mg)

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

16) W. A. Cowdrey, E. D. Hughes, and C. K. Ingold, *J. Chem. Soc.*, **1937**, 1227.

17) It seems that the low specific rotation value for (+)-I is due to the contamination of racemate.

in dry ether (5.0 m*l*). The mixture was refluxed for 2 hr, cooled, poured into a mixture of ice (*ca.* 50 g) and dilute hydrochloric acid (5%: 30 m*l*), and then extracted with ether. The extract was washed with a saturated sodium chloride solution, dried over sodium sulfate, and then evaporated to give VIb (1.106 g) as an oil which showed no carbonyl absorption band in its IR spectrum and which could be used for the next step without purification. For analysis this was chromatographed on silica gel; elution with benzene containing 50% ether was then carried out.

Found: C, 73.48; H, 9.14%. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95%.

b) A solution of Va (343 mg) in dry ether (6.0 m*l*) was reduced with $LiAlH_4$ (130 mg) by a method similar to that used for VIb; a diol (VIa: 274 mg) was thus obtained as an oil.

Found: C, 73.02; H, 9.22%. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95%.

threo- *and* erythro-*2-Phenyl-3-pentanols (VIIa and VIIb). a) By the Grignard Reaction*: The Grignard reaction of IV with ethylmagnesium iodide was carried out by a method similar to that of Cram and Elhafez.[12] The crude product (1.054 g: bp 88—107°C/8 mmHg) was purified by means of column chromatography on silica gel (200 g), after which elution was carried out with benzene containing 4% ether to give two fractions. The first fraction gave *threo*-2-phenyl-3-pentanol (VIIa) as an oil (110 mg).

Found: C, 80.31; H, 9.68%. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.83%.

The second fraction gave a solid (457 mg) which was then recrystallized from petroleum ether to give the *erythro*-isomer (VIIb) as colorless crystals; mp 39—40°C.

Found: C, 80.20; H, 9.93%. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.83%.

b) From VIa and VIb: A mixture of VIb (0.977 g), *p*-toluenesulfonyl chloride (1.034 g), and dry pyridine (10 m*l*) was allowed to stand at room temperature for 24 hr and was then poured into a mixture of ice and dilute hydrochloric acid (10%: 50 m*l*). The mixture was extracted with ether, and the extract was washed successively with dilute hydrochloric acid and a saturated sodium chloride solution. After the extract had been dried over sodium sulfate and the ether had been removed, the crude product (0.778 g) was purified by column chromatography on silica gel (60 g) to give monotosylate as an oil; yield, 0.388 g. NMR in $CDCl_3$: 1.28 (3H, d, *J*=7 Hz, $-\overset{|}{C}HC\underline{H}_3$), 2.42 (3H, s, $-C_6H_4C\underline{H}_3$), 7.22 (5H, s, $-C_6\underline{H}_5$), 7.28 and 7.76 (each 2H, d, *J*=8.5 Hz, $-C_6\underline{H}_4CH_3$).

Found: C, 64.46; H, 6.66%. Calcd for $C_{18}H_{22}O_4S$: C, 64.65; H, 6.63%.

A solution of the above tosylate (350 mg) in dry tetrahydrofuran (5.0 m*l*) was stirred, drop by drop over a 20-min period, into a suspension of $LiAlH_4$ (171 mg) in dry tetrahydrofuran (5.0 m*l*). The mixture was then refluxed for 3 hr, poured into a mixture of ice and dilute hydrochloric acid (5%: 30 m*l*), and extracted with ether. The extract was washed with a saturated sodium chloride solution, dried, and then evaporated to give an oil (275 mg) which was chromatographed on silica gel (30 g). Elution with benzene containing 3% ether was subsequently carried out to give a solid (138 mg) which was shown to be identical with the above authentic *erythro*-isomer (VIIb) by an IR spectral comparison.

Similarly, the diol VIa was also converted to the *threo*-isomer (VIIa).

The Reformatsky Reaction of 3-Phenyl-2-butanone (VIII) with Methyl Bromoacetate. A ketone (VIII: 4.05 g) was condensed with methyl bromoacetate (4.10 g) in dry benzene in the presence of zinc (1.77 g) by a method similar to that used for V. The product was distilled under a vacuum to give an oil; bp 148—151°C/9 mmHg; yield, 3.37 g.

A portion (2.604 g) of the above product was chromatographed on silica gel (230 g) and separated into two epimeric *β*-hydroxy esters (IXa: 694 mg and IXb: 1524 mg).

IXa; Found: C, 70.49; H, 8.31%. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16%.

IXb; Found: C, 70.45; H, 8.21%. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16%.

Reduction of IXa and IXb with LiAlH₄. *a)* IXa (1.00 g) was reduced with $LiAlH_4$ by a method similar to that used for VIb. The crude product was recrystallized from *n*-hexane to give Xa as colorless crystals; mp 76.5—77.5°C; yield, 700 mg. NMR in $CDCl_3$: 1.17 (s, $-\overset{|}{\underset{|}{C}}C\underline{H}_3$), 1.32 (d, *J*=7 Hz, $-\overset{|}{C}HC\underline{H}_3$), 1.78 (qa, *J*=5 Hz, $-C\underline{H}_2CH_2OH$), 2.64 (s, $-O\underline{H}$), 2.91 (qa, *J*=7 Hz, $-\overset{|}{C}\underline{H}CH_3$), 3.86 (t, *J*=5 Hz, $-C\underline{H}_2OH$), 7.32 (s, $-C_6\underline{H}_5$).

Found: C, 74.29; H, 9.45%. Calcd for $C_{11}H_{14}O_3$: C, 74.19; H, 9.34%.

b) IXb was also reduced with $LiAlH_4$ to give Xb as colorless crystals; mp 76—76.5°C (after crystallization from *n*-hexane). The mixed melting point with Xa (mp 76.5—77.5°C) was 59—61°C. NMR in $CDCl_3$: 1.18 (s, $-\overset{|}{\underset{|}{C}}C\underline{H}_3$), 1.33 (d, *J*=7 Hz, $-\overset{|}{C}HC\underline{H}_3$), *ca.* 1.70 (m, $-C\underline{H}_2CH_2OH$), 2.55 (bs, -OH), 2.81 (qa, *J*=7 Hz, $-\overset{|}{C}\underline{H}CH_3$), 3.77 (m, $-C\underline{H}_2OH$), 7.15 (s, $-C_6\underline{H}_5$).

Found: C, 74.40; H, 9.44%. Calcd for $C_{11}H_{14}O_3$: C, 74.19; H, 9.34%.

2-Phenyl-3-methyl-3-pentanols (XIa and XIb). a) By the Grignard Reaction: A solution of VIII (9.00 g) in dry ether (20 m*l*) was added, drop by drop at 0—5°C over a 30-min period, to a Grignard reagent, prepared from magnesium (1.48 g) and ethyl iodide (9.48 g) in dry ether (30 m*l*). The mixture was stirred at room temperature for 30 min and was then refluxed for 1 hr. After a usual work-up, the product was distilled under a vacuum to give an oil; bp 103—113°C/7 mmHg; yield, 7.92 g. A portion (2.051 g) of the above oil was chromatographed on silica gel (200 g). The elution was carried out with benzene containing 1% and then 5% ether to give the epimeric alcohols (XIa, 225 mg and XIb, 908 mg).

XIa: Found: C, 80.89; H, 10.38%. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18%.

XIb: Found: C, 80.60; H, 10.41%. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18%.

b) From Xa and Xb: By a method similar to that used for VIIb, the two diols (Xa and Xb) were converted to XIa, and XIb respectively, which later substances were shown by a spectral comparison to be identical with the above epimeric alcohols of the Grignard reaction.