fluoride (200 g.) as in the preparation of 4-ketotetrahydrophenanthrene. The crude ketone was purified by recrystallization from methanol. There was obtained 5.7 g. (61%) of product which melted at 148–148.5°.

Anal. Calcd. for $C_{19}H_{16}O_2$: C, 82.58; H, 5.84. Found: C, 82.59; H, 5.91.

The 2,4-dinitrophenylhydrazone melted at 286–287° after recrystallization from xylene.

Anal. Calcd. for $C_{26}H_{20}O_5N_4$: C, 65.78; H, 4.42. Found: C, 65.99; H, 4.59.

The 2,4,7-trinitrofluorenone molecular complex was prepared and recrystallized from absolute ethanol in the form of orange-red needles which melted at 194.5–195.0°.

Anal. Calcd. for $C_{32}H_{21}O_9N_3$: N, 7.10. Found: N, 7.20.

1-Hydroxy-11-methoxychrysene (V).—The dehydrogenation of ketone IV (500 mg.) was carried out using palladium black (75 mg.) with α-methylnaphthalene as the solvent. The crude base-soluble product was sublimed to yield 53 mg. (10%) of V which melted at 147–148° after one recrystallization from benzene–petroleum ether.

Anal. Calcd. for $C_{19}H_{14}O_2$: C, 83.19; H, 5.14. Found: C, 83.08; H, 5.12.

The melting point of a mixture of ketone IV and its dehydrogenation product V was 104–117°.

5-Methoxychrysene.—A mixture of ketone IV (1.5 g.), amalgamated zinc (4 g.) water (3 ml.), concentrated hydrochloric acid (9 ml.) and toluene (2 ml.) was refluxed for 90 hours; during this time six 3-ml. portions of hydrochloric acid were added. The crude product obtained by toluene extraction of the diluted reaction mixture was remethylated as in the preparation of III. The crude product thus obtained was purified by allowing a benzene solution to stand over sodium for 24 hours and then passing it through a column of alumina. Evaporation of the benzene eluates yielded as the first fraction a colorless solid[9] (m.p. above 200° with decomposition) which was not further characterized, then a solid, m.p. 108–115°, and finally a yellow oil. The second solid fraction (130 mg.) was dehydrogenated over palladium-on-charcoal (35 mg.) using α-methylnaphthalene as a solvent. The reaction mixture was diluted with petroleum ether, the catalyst filtered and the solution chilled to yield a pale yellow solid. This was recrystallized from benzene–petroleum ether to yield nearly colorless needles which melted at 139–141°. A mixture of this sample with authentic 5-methoxychrysene (m.p. 142–143°)[5] melted at 139–142°.

4-Methoxy-1-phenanthrenecarboxylic Acid (VI).—Acid II (320 mg.) was added to a suspension of calcium hypochlorite (1.5 g.) in water (145 ml.) and sodium carbonate (1.5 g.). The mixture was refluxed for five hours and filtered while hot. Sodium thiosulfate (7 g.) was added to the cold filtrate which then was acidified to yield a mixture of sulfur and crude acid VI. The acid was separated by extraction with sodium bicarbonate solution and reacidification of the clear extract. After recrystallization from toluene the pure acid melted at 237–239° (reported[8] melting point of 4-methoxy-*x*-phenanthrenecarboxylic acid was 238–239°). The methyl ester prepared by the action of diazomethane on VI melted at 91–92° after one recrystallization from methanol (reported[8] m.p. 93–94°).

4-Methoxy-3-phenanthrenecarboxylic Acid (VII).—A solution of butyllithium was prepared from lithium (0.35 g.), dry ether (25 ml.) and butyl chloride (3 g.). 4-Methoxyphenanthrene (0.5 g.) was added, the solution stirred for 12 hours and finally refluxed for 3 hours. The reaction mixture was poured into a slurry of Dry Ice (20 g.) in dry ether (50 ml.). The ether solution was warmed to room temperature, dilute hydrochloric acid was added and the ether layer separated. The acidic products were removed by sodium bicarbonate extraction. Acidification of the extracts yielded crude acid VII contaminated with valeric acid. The product was purified by recrystallization from benzene-ligroin, sublimation and recrystallization again, m.p. 154–155°.

Anal. Calcd. for $C_{16}H_{12}O_3$: C, 76.17; H, 4.80. Found: C, 76.12; H, 4.87.

NEW BRUNSWICK, NEW JERSEY

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[9] D. Thomas and A. Nathan, THIS JOURNAL, **70**, 331 (1948), have obtained a diene, 7,7'-dimethoxy-3,3',4,4'-tetrahydro-1,1'-binaphthyl as a by-product in the Clemmensen reduction of 7-methoxy-1-tetralone. The similarity in structure between this ketone and ketone IV suggests that an analogous diene might be formed from IV.

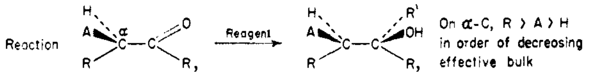
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA, LOS ANGELES]

Studies in Stereochemistry. X. The Rule of "Steric Control of Asymmetric Induction" in the Syntheses of Acyclic Systems

BY DONALD J. CRAM AND FATHY AHMED ABD ELHAFEZ

RECEIVED MARCH 12, 1952

A rule is proposed to correlate and predict the stereochemical direction of asymmetric induction in reactions of acyclic systems in which a new asymmetric center is created adjacent to an old: "In non-catalytic reactions of the type shown (Formulas), that diastereomer will predominate which would be formed by the approach of the entering group from the *least hindered side* of the double bond when the rotational conformation of the C–C bond is such that the double bond is flanked by the two least bulky groups attached to the adjacent asymmetric center." This rule successfully correlates the configurations of thirty-five compounds prepared by six different reactions of the above type, in each case the stereochemical relationships between the asymmetric carbons of the substances having been demonstrated by some independent means. This rule has been used to predict the configurations of fifty compounds whose stereochemical structures have been hitherto unknown.



The phenomenon of asymmetric induction in the synthesis of compounds that already contain one or more asymmetric carbon atoms has been recognized for many years, the classic work in acyclic systems being that of McKenzie.[1] Recently, four types of asymmetric synthesis have been reported in which symmetrical ketones have been reduced to optically active alcohols utilizing optically active reducing agents. Mosher, *et al.*, reduced methyl *t*-butyl ketone to active alcohol with active 2-methylbutylmagnesium chloride.[2] Doering, *et al.*, reduced isobutyrophenone with active 2-methyl-1-butanol (catalyzed with sodium ethoxide),[3a] 6-methyl-2-heptanone with active aluminum 2-

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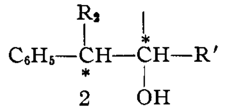
[1] (a) A. McKenzie, *J. Chem. Soc.*, **85**, 1249 (1904), and later papers. Other pertinent references are: (b) E. E. Turner and M. M. Harris, *Quarterly Reviews*, **1**, 299 (1947); (c) D. M. Bovey and E. E. Turner *J. Chem. Soc.*, 3223 (1951).

[2] H. S. Mosher and E. La Combre, THIS JOURNAL, **72**, 3994, 4991 (1950).

[3] (a) W. E. Doering and T. C. Aschner, *ibid.*, **71**, 838 (1949); (b) W. E. Doering and R. W. Young, *ibid.*, **72**, 631 (1950).

butoxide[3b] and methyl cyclohexyl ketone with active aluminum 3-methyl-2-butoxide[3b] to give in each case optically active products. Bothner-By reduced a series of ketones to active alcohols using lithium aluminum hydride-*d*-camphor as an asymmetric reducing agent.[4] The unique feature in two of these investigations[2,3b] is that all of the relative configurations of all of the asymmetric carbon atoms were known beforehand in each particular system, and in every case that enantiomorph predominated in the product which would be predicted on steric grounds from a comparison of models of the diastereomerically related transition states (cyclic) involved. Prelog, *et al.*,[5] making use of the same concepts has attempted to *predict* the relative configurations of the asymmetric carbon atoms in the α-hydroxy esters produced by the reaction of Grignard reagents with α-keto esters of *l*-menthol.

The present investigation reports eight cases of asymmetric induction in the syntheses of simple secondary alcohols that contain two asymmetric centers of type I, the relative configurations of which have been determined. In each synthesis,



$$C_6H_5-\overset{R_2}{\underset{2}{\overset{|}{\underset{*}{C}}}}H-\overset{1}{\underset{OH}{\overset{*}{\underset{|}{C}}}}H-R'$$

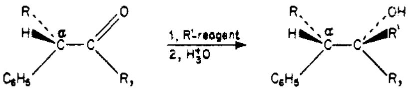
I

carbon-1 was made asymmetric in the presence of an asymmetric center (carbon-2) already in the molecule. This type of system was chosen to study the stereochemical direction of asymmetric induction because: (a) the two asymmetric centers are on adjacent carbon atoms; (b) carbon-2 does not carry any groups capable of complexing with reagents involved in the creation of asymmetry at carbon-1; (c) the structures of the diastereomeric alcohols can be readily demonstrated.

Results

Table I reports the results of the treatment of various aldehydes with Grignard reagents and various ketones with lithium aluminum hydride to give mixtures of diastereomerically related products. In runs 1–6, the diastereomers were separated through their acid phthalate and 3-nitro acid phthalate esters in such a way as to obtain a crude estimate of the balance of each component in the product. In runs 7 and 8 the two diastereomers were separated utilizing the facts that one diastereomer was a crystalline solid, and the other formed a *p*-nitrobenzoate of suitable solubility characteristics. The configurations of the diastereomers of 3-phenyl-2-butanol, 2-phenyl-3-pentanol and 3-phenyl-2-pentanol (runs 1–6) have all been determined in previous studies.[6] The fact that the stereochemical course of the Chugaev reaction is predominantly *cis* in acyclic systems[6a] (and in cyclic systems whenever possible)[7] coupled with the

TABLE I



On α-C, $C_6H_5 > R > H$ in order of decreasing effective bulk

Run no.	R	R_1	Reagent	Config. product rule predicts[a]	Balance of isomers found *erythro*	*threo*
1	CH_3	H	CH_3MgI	*erythro*	2	1
2	CH_3	CH_3	$LiAlH_4$	*threo*	1	2.5
3	C_2H_5	H	CH_3MgI	*erythro*	2.5	1
4	C_2H_5	CH_3	$LiAlH_4$	*threo*	1	3
5	CH_3	H	C_2H_5MgBr	*erythro*	3	1
6	CH_3	C_2H_5	$LiAlH_4$	*threo*	1	2
7	CH_3	H	C_6H_5MgBr	*threo*	1	>4
8	CH_3	C_6H_5	$LiAlH_4$	*erythro*	>4	1
9[b]	CH_3	C_6H_5	Na·EtOH	*erythro*	*erythro* predominates	

[a] In most compounds that contain two adjacent asymmetric carbon atoms, at least two of the groups attached to one of the asymmetric centers are the same or similar to two of the groups attached to the other. The term *erythro* always names that diastereomer whose configuration is such that in one of its three eclipsed conformations at least *two sets of substituents of identical or like composition are side by side*. The term *threo* names the other diastereomer. An illustration is

erythro *threo*

[b] Taken from data of F. Kayser, *Ann. chim.*, **6**, 145 (1936).

observation that the xanthate of one diastereomer of 1,2-diphenyl-1-propanol gave predominantly *cis*-α-methylstilbene and the other *trans*-α-methylstilbene allows an assignment of configuration to these starting carbinols. The structures of these *cis*- and *trans*-olefins are assigned on the basis of their ultraviolet absorption spectra (Fig. 1).

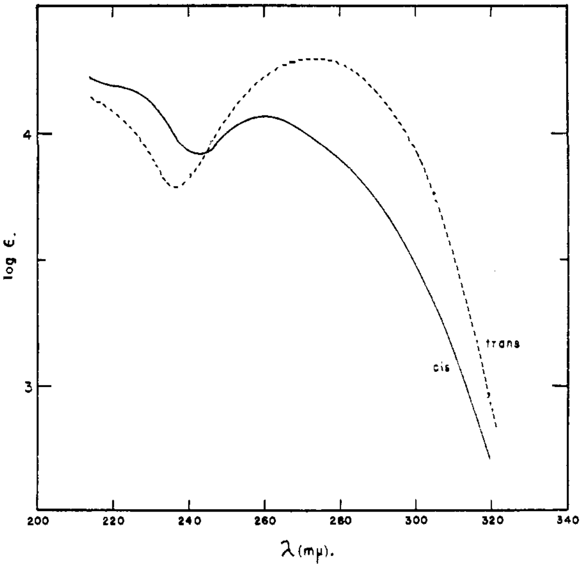


Fig. 1.—Ultraviolet absorption spectra of *cis*- and *trans*-α-methylstilbene in ethanol (Beckman quartz spectrophotometer).

Discussion

The Chugaev Reaction—The high degree of stereospecificity observed in the Chugaev reac-

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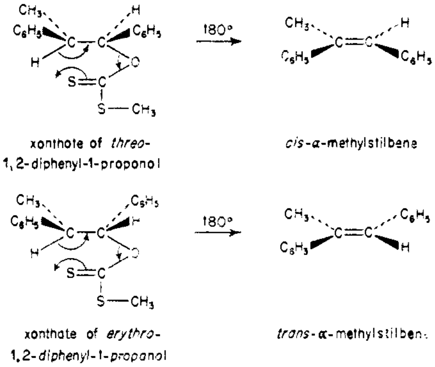
(4) A. Bothner-By, THIS JOURNAL, **73**, 846 (1951).

(5) V. Prelog and W. Dauben, Abstract of Papers, XIIth International Congress of Pure and Applied Chemistry, Sept., 1951, p. 401.

(6) (a) D. J. Cram, THIS JOURNAL, **71**, 3863, 3871, 3875, 3883 (1949); (b) D. J. Cram, *ibid.*, **74**, 2149 (1952).

(7) W. Hückel, W. Tappe and G. Legutke, *Ann.*, **543**, 191 (1940); and E. R. Alexander and A. Mudrak, THIS JOURNAL, **72**, 3196 (1950); **73**, 61 (1951).

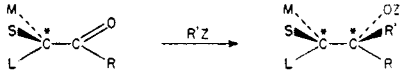
tion[8] as applied to the *threo* isomer of the 1,2-diphenyl-1-propanol system is interesting because in the transition state two phenyl groups are brought into a rather constrained configuration. In several other cases, reactions that involve similar steric constraints are suppressed in favor of other competing reactions.[9] As would be expected, the activation energies for the decomposition of the xanthate of *threo* configuration appeared to be considerably higher than that for the decomposition of the *erythro* isomer. A similar but smaller effect was observed in the pyrolyses of the xanthates of the stereoisomers of 3-phenyl-2-butanol,[6a] in which the reaction of the *erythro* isomer (methyl and phenyl groups *cis* in the transition state) required a higher temperature than that of the *threo* isomer. A kinetic investigation of the Chugaev reaction in these systems is in progress.



The assignment of structures to the olefinic products upon which the assignment of configuration to the carbinols ultimately depends was made on the basis that one olefin absorbed light at longer wave lengths and higher intensities than the other (see Fig. 1). Coplanarity of the two benzene rings and the ethylene group is sterically less compatible in the *cis* than the *trans* isomer, and therefore resonance is more damped in the *cis* than in the *trans* olefin. Such damping usually leads to absorption of light at shorter wave lengths, since the excited states are usually more resonance stabilized than the ground states of this type of molecule.[10]

The Rule of Steric Control of Asymmetric Induction.—The nine cases of asymmetric induction reported in Table I illustrate the well established principle[11] that in the creation of a new asymmetric center in the presence of old, *the configuration at the new asymmetric center of the predominant diastereomeric product can be inverted by inverting the order in which substituents are attached to that new center.* This principle is generally applicable, and the fundamental basis of its operation seems to be associated with the different steric limitations that the substituents attached to the asymmetric carbon atom already in the molecule must place on the various possible avenues of approach of an entering group to the carbon atom that is becoming asymmetric.[12] The question arises as to whether a correlation can be made of the *stereochemical direction of asymmetric induction* and the arrangement of groups according to their effective bulk at the asymmetric carbon atom of the starting materials in the reactions at hand.

Such a correlation has been found to apply to the data of Table I. In the starting materials the groups attached to the asymmetric carbon atom can in each case be unambiguously arranged as $C_6H_5 > R(CH_3 \text{ or } C_2H_5) > H$ with regard to their effective bulk. The configuration of the predominant diastereomeric product can be most *conveniently* predicted on the basis of the following rule. "In reactions of the following type, that diasteromer will predominate which would be formed by the approach of the entering group from the *least hindered side* of the double bond when the rotational conformation of the C–C bond is such that the double bond is flanked by the two least bulky groups attached to the adjacent asymmetric center."[13]



L > M > S in effective bulk

The general applicability of this rule is demonstrated by the data of Table II taken from the literature.[14] The twenty-seven cases listed are all

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[8] The mechanism of this reaction has been discussed previously (ref. 7 and 6a).

[9] G. Fodor, V. Bruckner, J. Kiss and G. Ohegyi, *J. Org. Chem.*, **14**, 337 (1949); L. H. Welsh, THIS JOURNAL, **71**, 3500 (1949); P. I. Pollak and D. Y. Curtin, *ibid.*, **72**, 961 (1950). See also W. G. Young and D. Pressman, *ibid.*, **61**, 1640 (1939) and S. Winstein and D. Seymour, *ibid.*, **68**, 119 (1946).

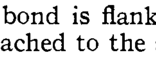
[10] These assignments of configuration are in harmony with those of E. Ellingboe and R. C. Fuson [*ibid.*, **55**, 2964 (1933)] made on the basis that the *trans* isomer should be the more stable (more resonance of stabilization). These authors demonstrated that the lower melting olefin isomerized completely to the higher melting olefin when treated with acid.

[11] See references in Tables II and III, particularly to the extensive work of McKenzie, *et al.*, and Tiffeneau, *et al.*.

[12] The concept that asymmetric induction is sterically controlled has been employed by numerous investigators (*e.g.*, Mosher[2] and Doering[3]) in correlating the results of asymmetric syntheses with the relative bulks and dispositions of groups in the systems involved. The most far reaching correlation has been applied to reactions involving ring systems by D. H. R. Barton, *Experientia*, **6**, 316 (1950).

[13] An explanation for the existence of such a correlation is suggested in the statement of this rule. Thus the reagents involved in these reactions (RMgX or $LiAlH_4$) probably coördinate with the carbonyl group of the starting material as well as with a mole of ether [see H. L. Cohen and B. F. Wright, Abstracts Papers Presented at Buffalo Meeting American Chemical Society, p. 32K (1952)]. The oxygen therefore becomes effectively the bulkiest group in the molecule and tends to orient itself between the two least bulky groups attached to the adjacent asymmetric carbon atom.

[14] D. Y. Curtin, *et al.* [see references (1), (2) and (4) of Table II] in the course of their elegant work on pinacol-like rearrangements provided eight cases (see Table II) which fit into the correlation stated in this rule. Although not explicitly stated, these authors appeared to recognize that a correlation existed between the *order* in which R_1 and R_2 were introduced



$$R-\underset{NH_2}{\overset{*}{C}H}-\underset{OH}{\overset{R_1}{\overset{*}{C}}}-R_2$$

in the synthesis of molecules of the above type and the *configurations* of the two asymmetric carbon atoms relative to each other in the product.

NOTE ADDED IN PROOF.—Between the time that this article was accepted and published, the contribution of D. Y. Curtin, E. E. Harris, and E. K. Meislich [THIS JOURNAL, **74**, 2901 (1952)] appeared which deals with some of the same subject matter approached from a somewhat different point of view. The compatibility of the configurational assignments made in the previous and current papers would tend to support the generalizations made in each article.

consistent with, and no cases were found that were in conflict with, the rule. The types of reactions listed in Tables I and II are the following: the reactions of Grignard reagents with both ketones and aldehydes; the reductions of ketones to alcohols with lithium aluminum hydride, sodium and alcohol, sodium amalgam and water, and aluminum isopropoxide; the reduction of oximes to amines with sodium amalgam.[15] In every case the configurations of the products have been demonstrated by some independent means.

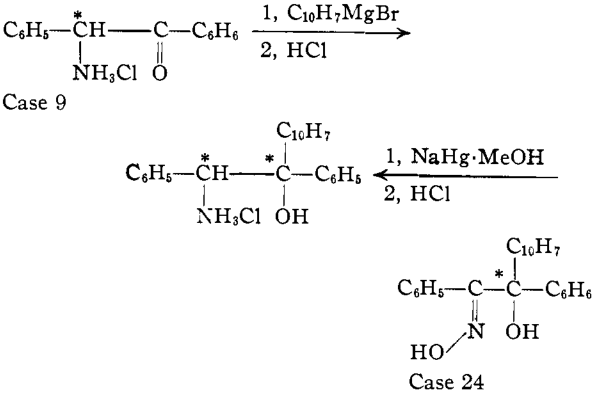
Of these six types of transformations, all but the aluminum isopropoxide reduction reaction are irreversible, and the balance between the diastereomeric products is kinetically determined. The reduction of carbonyl groups with aluminum isopropoxide is clearly reversible, and the chance of obtaining an equilibrium mixture is greater. However, the reaction is usually run for a relatively short time and with a large excess of reducing agent, and it is improbable in the cases listed (Table II) that thermodynamic equilibration occurred. The rule might be violated in some cases should the diastereomers produced become equilibrated.

In catalytic reductions of ketones to alcohols, although in some cases the predominant diastereomer is that predicted by the rule, a number of exceptions have been found.[16] Such results are not unexpected since it has often been observed in cyclic systems that catalytic and chemical reductions give different stereochemical results, and even the stereochemistry of catalytic reductions changes radically with the conditions of the experiment.

Two possible difficulties arise in deciding whether or not a piece of data is consistent with the rule. The first has to do with low or unreported yields of the product or products isolated. In many cases, one member of a diastereomeric pair was prepared by introducing the groups attached to the second asymmetric carbon atom into the molecule in a given order, and the other isomer was prepared by simply inverting that order. In these cases, even though the yield in the final reaction was low or unreported, it seems safe to assume that the isomer isolated was the predominant isomer formed. In Table II, cases 1 and 2, 3 and 4, 5 and 6, 7 and 8, 18 and 25, and 26 and 27 are of this type. In cases 9, 10, 12, 16, 17, 19, 20 and 24, either the yields of the predominant isomer are over 50% or the yield data was presented in such a way as to indicate the relative yields of both isomers. Therefore in the nine cases of Table I and in twenty out of the twenty-seven cases listed in Table II, the predicted isomer has been demonstrated to predominate, whereas in six of the other seven cases (11, 13, 14, 21, 22 and 23) the correct isomer has been either the only one isolated or the one isolated in the larger amount.

The second difficulty in applying the rule stems from having to arrange the groups attached to the initially asymmetric carbon atom in decreasing order of their *effective* bulk. The nine cases of Table I present no problem since a phenyl is unambiguously more bulky than a methyl or ethyl which are more bulky than a hydrogen. In Table II more difficult choices had to be made. In cases 3 and 4 a methyl group was chosen as having a greater *effective* bulk than an amine hydrochloride group because the latter was undoubtedly converted to an ion-pair ($\underset{H}{\underset{|}{-N^{\ominus}}}{}^{\oplus}MgX$) by the Grignard reagent, and the geometry of such an ion-pair is probably relatively non-rigid, and is more adaptable to its steric environment. In case 12 a choice had to be made between a phenyl and a dodecylamino as the effectively larger group. In spite of the fact that the latter occupies a larger total volume, the phenyl was picked as the larger effective group because its volume must be concentrated in the vicinity of the carbonyl group whereas the chain of the dodecylamino group could be spread out away from the carbonyl group. A phenyl was picked as effectively larger than a benzylamino group in case 14 for essentially the same reasons. Case 15 is interesting because of the presence of a phenyl and a piperidyl group on the asymmetric carbon of the starting material. These two groups should be of approximately equal effective bulk and the two isomers were isolated in about equal amounts from the reaction.

A comparison of cases 9 and 24 of Table II reveals the interesting situation in which the *roles* of the two carbon atoms that are asymmetric in the products are *inverted* in the starting materials. Thus in case 9 the carbon carrying the phenyl, the amino and hydrogen groups directs the attachment of an α-naphthyl to a benzoyl group whereas in case 24 the carbon carrying the phenyl, α-naphthyl and hydroxyl groups directs the attachment of hydrogen to the oxime function. An analogous situation is found in cases 10 and 20.



$$C_6H_5-\underset{NH_3Cl}{\underset{|}{\overset{*}{C}H}}-\underset{O}{\underset{\|}{C}}-C_6H_6 \xrightarrow[2,\ HCl]{1,\ C_{10}H_7MgBr}$$

Case 9

$$C_6H_5-\underset{NH_3Cl}{\underset{|}{\overset{*}{C}H}}-\underset{OH}{\underset{|}{\overset{C_{10}H_7}{\overset{|}{\overset{*}{C}}}}}-C_6H_5 \xleftarrow[2,\ HCl]{1,\ NaHg\cdot MeOH} C_6H_5-\underset{HO\diagup N}{\underset{\|}{C}}-\underset{OH}{\underset{|}{\overset{C_{10}H_7}{\overset{|}{\overset{*}{C}}}}}-C_6H_6$$

Case 24

The rationale for the operation of the rule may be quite different for different cases.[13] In the cases of Table II, the asymmetric carbon atom of the starting material carries a hydroxyl or amino group which can possibly react with the reagent (*e. g.*, a Grignard) to form a complex such as II. This complex would have the geometry of a five-membered ring, and R′ would be expected to approach the carbon atom carrying the carbonyl group from

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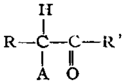
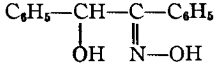
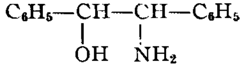
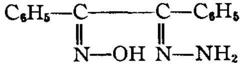
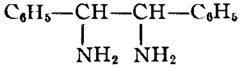
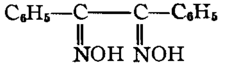
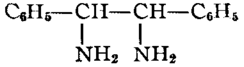
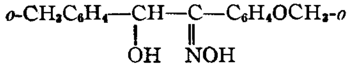
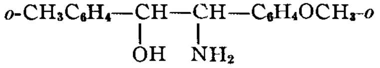
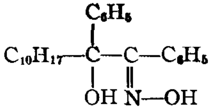
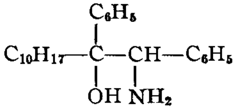
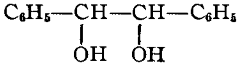
(15) Papers XI and XII of this series [THIS JOURNAL, **74**, 5835, 5839 (1952)] report two cases in which alkyl lithiums are added to ketones to form diastereomeric mixtures of teritary alcohols in which the predicted isomer predominated.

(16) For instance see J. F. Hyde, E. Browning and R. Adams, *ibid.*, **50**, 2288 (1928).

TABLE II

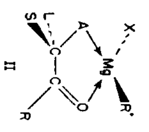
REACTIONS WHOSE STEREOCHEMISTRY HAVE BEEN DEMONSTRATED TO BE CONSISTENT WITH RULE

Case no.	 $R-\overset{H}{\overset{\vert}{\underset{A}{\underset{\vert}{C}}}}-\underset{O}{\underset{\Vert}{C}}-R'$		(Starting material)		Groups on α-C arranged in order effective bulk	Config. predom. product[a]	Yield, %	Lit. ref.[b]
	A	R	R'	Reagent				
1	NH_3Cl	C_6H_5	C_6H_5	p-ClC_6H_4MgBr	R > A > H	*erythro*	30	1, 2
2	NH_3Cl	C_6H_5	p-ClC_6H_4	C_6H_5MgBr	R > A > H	*threo*	36	1, 2
3	NH_3Cl	CH_3	C_6H_5	p-$CH_3C_6H_4MgBr$	R > A > H	*erythro*	..[c]	2, 3, 4
4	NH_3Cl	CH_3	p-$CH_3C_6H_4$	C_6H_5MgBr	R > A > H	*threo*	..[c]	2, 3, 4
5	NH_3Cl	C_6H_5	C_6H_5	p-$CH_3OC_6H_4MgBr$	R > A > H	*erythro*	60	4, 5, 6
6	NH_3Cl	C_6H_5	p-$CH_3OC_6H_4$	C_6H_5MgBr	R > A > H	*threo*	..[c]	4
7	NH_3Cl	C_6H_5	C_6H_5	p-$CH_3C_6H_4MgBr$	R > A > H	*erythro*	23	4, 5, 6
8	NH_3Cl	C_6H_5	p-$CH_3C_6H_4$	C_6H_5MgBr	R > A > H	*threo*	18	4, 5, 6
9	NH_3Cl	C_6H_5	C_6H_5	α-NaphthylMgBr	R > A > H	*erythro*	45	5, 7
10	NH_3Cl	C_6H_5	C_6H_5	$NaHg\cdot H_2O$	R > A > H	*erythro* *threo*	Predom. Small amt.	8, 9, 10
11	n-$C_4H_9NH_2Cl$	C_6H_5	C_6H_5	Al(i-prop.)$_3$	R > A > H	*erythro*	26	11
12	n-$C_{12}H_{25}NH_2Cl$	C_6H_5	C_6H_5	Al(i-prop.)$_3$	R > A > H	*erythro*	56	11
13	$C_6H_5CH_2CH_2NH_2Cl$	C_6H_5	C_6H_5	Al(i-prop.)$_3$	R > A > H	*erythro*	41	11
14	$C_6H_5CH_2NH_2Cl$	C_6H_5	C_6H_5	Al(i-prop.)$_3$	R > A > H	*erythro*	38	11
15	Piperidyl·HCl	C_6H_5	C_6H_5	Al(i-prop.)$_3$	R = A > H	*erythro* *threo*	26 25	11
16	$HOCH_2CH_2NH_2Cl$	p-ClC_6H_4	p-ClC_6H_4	Al(i-prop.)$_3$	R > A > H	*erythro*	77	12
17	OH	C_6H_5	C_6H_5	NaHg·EtOH	R > A > H	*meso*	85	13
18	OH	C_6H_5	C_6H_5	Al(i-prop.)$_3$	R > A > H	*meso*	90	14
19	CH_3CONH	CH_2OH	p-$NO_2C_6H_4$	Al(i-prop.)$_3$	A > R > H	*threo*	90	15
20	 $C_6H_5-\underset{OH}{\underset{\vert}{CH}}-\underset{N-OH}{\underset{\Vert}{C}}-C_6H_5$	NaHg·EtOH	 $C_6H_5-\underset{OH}{\underset{\vert}{CH}}-\underset{NH_2}{\underset{\vert}{CH}}-C_6H_5$		C_6H_5 > OH > H	*erythro* > *threo*	10 parts 1 part	8, 9 16
21	 $C_6H_5-\underset{N-OH}{\underset{\Vert}{C}}-\underset{N-NH_2}{\underset{\Vert}{C}}-C_6H_5$	NaHg·EtOH	 $C_6H_5-\underset{NH_2}{\underset{\vert}{CH}}-\underset{NH_2}{\underset{\vert}{CH}}-C_6H_5$		C_6H_5 > NH_2 > H	*meso*	..[c]	17, 18
22	 $C_6H_5-\underset{NOH}{\underset{\Vert}{C}}-\underset{NOH}{\underset{\Vert}{C}}-C_6H_5$	NaHg·EtOH Na·EtOH	 $C_6H_5-\underset{NH_2}{\underset{\vert}{CH}}-\underset{NH_2}{\underset{\vert}{CH}}-C_6H_5$		C_6H_5 > NH_2 > H	*meso* *dl*	23% ..[c]	18, 19
23	 $o\text{-}CH_3C_6H_4-\underset{OH}{\underset{\vert}{CH}}-\underset{NOH}{\underset{\Vert}{C}}-C_6H_4OCH_3\text{-}o$	Na·EtOH	 $o\text{-}CH_3C_6H_4-\underset{OH}{\underset{\vert}{CH}}-\underset{NH_2}{\underset{\vert}{CH}}-C_6H_4OCH_3\text{-}o$		C_6H_5 > OH > H	*erythro*	~13%[d]	20
24	 $C_{10}H_{17}-\overset{C_6H_5}{\overset{\vert}{\underset{OH}{\underset{\vert}{C}}}}-\underset{N-OH}{\underset{\Vert}{C}}-C_6H_5$	NaHg·MeOH	 $C_{10}H_{17}-\overset{C_6H_5}{\overset{\vert}{\underset{OH}{\underset{\vert}{C}}}}-\underset{NH_2}{\underset{\vert}{CH}}-C_6H_5$		$C_{10}H_{17}$ > C_6H_5 > OH	*erythro* *threo*	~40% ~10%	6
25	$O{=}CH-CH{=}O$	C_6H_5MgBr	 $C_6H_5-\underset{OH}{\underset{\vert}{CH}}-\underset{OH}{\underset{\vert}{CH}}-C_6H_5$		C_6H_5 > OH > H	*dl*	..[c]	21

26[e]	$C_6H_5\text{—}\underset{O}{\underset{\Vert}{C}}\text{—}\underset{O}{\underset{\Vert}{C}}\text{—}C_6H_5$	CH_3MgBr	$C_6H_5\text{—}\overset{CH_3}{\overset{\vert}{\underset{OH}{\underset{\vert}{C}}}}\text{—}\overset{CH_3}{\overset{\vert}{\underset{OH}{\underset{\vert}{C}}}}\text{—}C_6H_5$	$C_6H_5 > CH_3 > OH$	*dl*(87°)	..[c]	22
27[e]	$CH_3\text{—}\underset{O}{\underset{\Vert}{C}}\text{—}\underset{O}{\underset{\Vert}{C}}\text{—}CH_3$	C_6H_5MgBr	$C_6H_5\text{—}\overset{OH_3}{\overset{\vert}{\underset{OH}{\underset{\vert}{C}}}}\text{—}\overset{CH_3}{\overset{\vert}{\underset{OH}{\underset{\vert}{C}}}}\text{—}C_6H_5$	$C_6H_5 > CH_3 > OH$	*meso* (122°)	..[c]	22

[a] See footnote *a* of Table I. [b] These literature references report both the determination of configuration of the products of the reactions of the table as well as the results of the reactions themselves. These references are as follows: (1) D. Y. Curtin, E. E. Harris and P. I. Pollak, THIS JOURNAL, **73**, 3453 (1951); (2) D. Y. Curtin and P. I. Pollak, *ibid.*, **73**, 992 (1951); (3) M. Tiffeneau, J. Levy and E. Ditz, *Bull. soc. chim. France*, [5] 2, 1871 (1935); (4) P. I. Pollak and D. Y. Curtin, THIS JOURNAL, **72**, 961 (1950); (5) A. McKenzie and A. Wood, *Ber.*, **71**, 358 (1938); (6) A. McKenzie and W. S. Denmler, *J. Chem. Soc.*, **125**, 2105 (1924); (7) A. McKenzie and A. K. Mills, *Ber.*, **62**, 1784 (1929); (8) A. McKenzie and D. J. C. Pirie, *ibid.*, **39B**, 876 (1936); (9) J. Read and C. C. Steele, *J. Chem. Soc.*, 910 (1927); (10) J. Read and I. G. Campbell, *ibid.*, 2377 (1930); (11) R. E. Lutz, J. A. Freak and R. S. Murphey, THIS JOURNAL, **70**, 2018 (1948); (12) R. E. Lutz, and R. S. Murphey, *ibid.*, **71**, 478 (1949); (13) J. C. Irvine and J. Weir, *J. Chem. Soc.*, **91**, 1390 (1907); (14) H. Lund, *Ber.*, **70B**, 1520 (1937); (15), L. M. Long and H. D. Troutman, THIS JOURNAL, **71**, 2473 (1949); (16) H. G. Söderbaum, *Ber.*, **28**, 2523 (1895); (17) A. Darapsky and H. Spannagel, *J. prakt. Chem.*, **92**, 289 (1915); (18) F. Feist, *Ber.*, **27**, 213 (1894); (19) J. A. McRae and A. S. Townshend, *Can. J. Research*, 11, 628 (1934); (20) N. A. B. Wilson and J. Read, *J. Chem. Soc.*, 1120 (1935); (21) H. Wren and C. J. Still, *ibid.*, **103**, 1772 (1913); (22) M. Tiffeneau and J. Levy, *Bull. soc. chim. France*, 41, 1356 (1927). [c] Yield not reported. [d] Most of the starting material went to product in which the OH group had been removed from the molecule. [e] Configurations are assigned to the products of these reactions on the basis of melting point comparisons. The symmetry properties of *meso* isomers of compounds containing a dibenzyl-like structure have in all known cases (eight) resulted in a melting point higher than that found for the corresponding *dl*-isomer.

the least hindered side (in II, from above the plane of the page).[17] In all of the reactions of Table II,



II

the correct steric result could be predicted on the basis of model II except in cases 24, 26 and 27. In these three cases, although the experimental results are consistent with the rule, the above model does not appear to apply.

Table III gives representative illustrations of the results of fifty reactions found in the literature in which the configurations of the products are unknown (see Tables II and III for references.) In all of these cases the two diastereomers were prepared by introducing the groups attached to one of the asymmetric carbons into the molecule in two different chronological orders. The configurations of the fifty products should all be predictable on the basis of the rule of steric control of asymmetric induction. It is hoped that many new tests of this rule will be brought forward in the future.

Experimental

Preparation of 3-Phenyl-2-butanone, 3-Phenyl-2-pentanone and 2-Phenyl-3-pentanone.—These compounds were all prepared by the oxidation of the corresponding alcohols[6a] with chromic acid. The following procedure used for 3-phenyl-2-butanol is illustrative.

The secondary alcohol (150 g.) dissolved in 1 liter of benzene was added slowly (six hours) to a thoroughly stirred solution of 476 g. of sodium chromate in a mixture of 350 ml. of acetic acid, 630 ml. of concentrated sulfuric acid and 2100 ml. of water. The temperature was kept at 25–30° during the addition. The layers were separated, the benzene layer was washed successively with water, sodium carbonate solution and water. The benzene was evaporated and the resulting ketone was distilled, wt. 125 g., b.p. 97–8° (11 mm.).

Preparation of 1,2-Diphenyl-1-propanone.—This substance was prepared from methylhydrobenzoin (m.p. 103–105°)[18] by the method of McKenzie, *et al.*,[19] in 70% yield, m.p. 50–52°.

The Reduction of 3-Phenyl-2-butanone, 3-Phenyl-2-pentanone, 2-Phenyl-3-pentanone and 1,2-Diphenyl-1-propanone to the Corresponding Secondary Alcohols.—The procedures are all illustrated by that employed for 1,2-diphenyl-1-propanone. A solution of this ketone (210 g. in 500 ml. of dry ether) was added dropwise to a well-stirred mixture of 13.3 g. of lithium aluminum hydride and 500 ml. of ether. After the addition was complete, the mixture was refluxed for 20 minutes, cooled and mixed with 1 *N* sulfuric acid and cracked ice. The layers were separated, the organic layer was washed successively with ice-water, sodium carbonate solution, water, and the solution was dried and evaporated to an oil. Distillation of this oil (b.p. 139–142° (1–2 mm.)) gave 202 g. (95% yield) of a mixture of diastereomeric 1,2-diphenyl-1-propanols.

When cooled this mixture solidified, and the solid was collected and recrystallized three times from pentane to give 154 g. (76% yield) of *erythro*-1,2-diphenyl-1-propanol, m.p. 50–51°.[20]

Anal. Calcd. for $C_{15}H_{16}O$: C, 84.87; H, 7.60. Found: C, 84.90; H, 7.69.

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[17] This model is in some respects like those of Mosher (ref. 2) and Doering (ref. 3) who developed a somewhat analogous explanation for their steric results.

[18] M. Tiffeneau and Dorlencourt, *Ann. chim. phys.*, [8] **16**, 252 (1909), and A. McKenzie and H. Wren, *J. Chem. Soc.*, **97**, 473 (1910).

[19] A. McKenzie and R. Roger, *ibid.*, **125**, 844 (1924).

[20] F. Kayser (footnote *b*, Table I) reported m.p. 48° for this isomer and m.p. 122° for its phenylurethan. He reported m.p. 116° for the phenylurethan of the *threo* isomer.

TABLE III

ILLUSTRATION OF KNOWN COMPOUNDS WHOSE CONFIGURATIONS ARE UNKNOWN AND CAN PROBABLY BE PREDICTED BY THE RULE

Case no.	R	A	α-Isomer predominates[a]		β-Isomer predominates[a]		Lit.[b] ref.
			R_1	Reagent (R')	R_1	Reagent (R')	
1	C_6H_5	OH	CH_3	C_2H_5MgX	C_2H_5	CH_3MgX	22
2	C_6H_5	OH	C_2H_5	C_6H_5MgX	C_6H_5	C_2H_5MgX	22, 23
3	C_6H_5	OH	C_2H_5	p-$CH_3OC_6H_4MgX$	p-$CH_3OC_6H_4$	C_6H_5MgX	24
4	C_6H_5	C_2H_5	H	n-C_4H_9MgX	n-C_4H_9	Na·EtOH(R' = H)	25
5	C_6H_6	C_2H_5	H	C_6H_5MgX	C_6H_5	Na·EtOH(R' = H)	26
6	p-$CH_3OC_6H_4$	OH	C_2H_5	p-$CH_3OC_6H_4MgX$	p-$CH_3OC_6H_4$	C_2H_5MgX	27
7	CH_3	NH_3Cl	C_6H_5	p-$CH_3OC_6H_4MgX$	p-$CH_3OC_6H_4$	C_6H_5MgX	3
8	α-Tetrahydroisoquinolinobenzyl	Piperidyl	CH_3	C_6H_5MgX	C_6H_5	CH_3MgX	28

[a] The general practice of calling the α-isomer that substance prepared from the lower molecular weight starting carbonyl compound seems to be well established in the French and English literature. [b] See Table I, footnote *b* for references 22 and 3. The other references are as follows: (23) R. Roger, *Helv. Chim. Acta.* **12,** 1060 (1929), *Biochem. J.*, [2] **230,** 320 (1931); (24) A. KcKenzie, E. M. Luis, M. Tiffeneau and P. Weill, *Bull. soc. chim. France*, [4] **45,** 419 (1929); (25) P. Jullien and F. Kayser, *ibid.*, [4] **53,** 700 (1937); (26) F. Kayser, *Ann. chim.*, **6,** 145 (1936); (27) P. Weill, *Bull. soc. chim. France*, [4] **49,** 1804. 1816 (1931); (28) N. H. Cromwell and D. J. Cram, THIS JOURNAL, **71,** 2579 (1949).

The phenylurethan was prepared in the usual way, m.p. 130–131°.

Anal. Calcd. for $C_{22}H_{21}O_2N$: C, 79.72; H, 6.38. Found: C, 79.94; H, 6.49.

The *p*-nitrobenzoate was prepared in the usual way, m.p. 106–107°.

Anal. Calcd. for $C_{22}H_{19}NO_4$: C, 73.11; H, 5.29. Found: C, 73.15; H, 5.47.

The filtrates from the crystallizations of the solid alcohol were combined, the solvent was evaporated, and the resulting oil was distilled to give 48 g. of an oil, b.p. 139–141° (2–3 mm.). A portion of this material (10.6 g.) was converted to a *p*-nitrobenzoate derivative which after seven crystallizations from ethyl acetate amounted to 1.8 g., m.p. 143–144° (undepressed by admixture with *p*-nitrobenzoate of the *threo* isomer).

The Separation of the Diastereomers in the 3-Phenyl-2-butanol, the 3-Phenyl-2-pentanol, the 2-Phenyl-3-pentanol Systems.—The diastereomers were separated in these three systems through the use of the phthalic acid esters for the *threo* isomers and the 3-nitrophthalic acid esters of the *erythro* isomers. The procedures for these separations are identical with those reported in papers I and II of this series[5a] for the separations of the diastereomeric mixtures obtained by the action of the appropriate Grignard reagents on the appropriate aldehydes. The preparations of the alcoholic mixtures through the Grignard reaction were repeated, and the separations of diastereomers were carried out in parallel with the corresponding separations of alcohols prepared by the reductions of the ketones. In each case the acid phthalate esters were prepared first followed by the 3-nitrophthalic acid esters. Two complete cycles of reactions were employed. The results are given in Table I.

The Preparation of 1,2-Diphenyl-1-propanol from 2-Phenylpropionaldehyde and the Separation of Diastereomers in This System.—To a Grignard reagent prepared from 60.5 g. of magnesium, 391 g. of bromobenzene and 1500 ml. of dry ether was added 268 g. of 2-phenylpropionaldehyde.[6a] The reaction mixture was worked up in the usual way to give 394 g. (94% yield) of a colorless oil, b.p. 139–143° (2–3 mm.). This mixture could not be induced to crystallize.

A solution of 212 g. of this oil in 350 ml. of dry pyridine was treated with 186 g. of freshly prepared *p*-nitrobenzoyl chloride, and the resulting mixture was heated on the steam-bath for two hours. The mixture was then added to ice and dilute sulfuric acid, and the solid that separated was collected, dried and recrystallized seven times from ethyl acetate, wt. 252 g. (74% yield), m.p. 143–144°. This material is the *p*-nitrobenzoate of the *threo* isomer.

Anal. Calcd. for $C_{22}H_{19}NO_4$: C, 73.11; H, 5.29. Found: C, 73.10; H, 5.61.

The filtrates from the above crystallizations were combined, the solvent was evaporated, and the material crystallized, wt. 88 g., m.p. 111–125°. This material was hydrolyzed to alcohol, and the resulting mixture of diastereomers could be crystallized only with difficulty. This fact shows that only minor amounts of *erythro* isomer were produced in this reaction.

Pure *threo* alcohol was obtained as follows. A mixture of 252 g. of ester, 39 g. of potassium hydroxide, 28 g. of sodium hydroxide, 500 ml. of methanol and 500 ml. of water was refluxed for 12 hours. The product was recovered from the reaction mixture in the usual way, wt. 141 g. (95% yield), b.p. 136–137° (1–2 mm.), $n^{25}D$ 1.5718.

Anal. Calcd. for $C_{15}H_{16}O$: C, 84.87; H, 7.60. Found: C, 84.95; H, 7.79.

The phenylurethan was prepared, m.p. 117–118°.[20]

Anal. Calcd. for $C_{22}H_{21}O_2N$: C, 79.72; H, 6.38. Found: C, 79.63; H, 6.44.

The Chugaev Reaction as Applied to the Isomeric 1,2-Diphenyl-1-propanols.—The xanthate of *erythro*-1,2-diphenyl-1-propanol was prepared as follows. A mixture of 21.2 g. of carbinol, 110 ml. of dry toluene and 4 g. of potassium was heated at reflux for 24 hours, cooled to room temperature and 14 g. of carbon disulfide was added to the solution. The resulting mixture was stirred at reflux temperature for ten hours, cooled and excess methyl iodide was added. After again stirring at reflux temperature (eight hours), the mixture was cooled and shaken with a mixture of water and ether. The organic layer was washed with water, dried and the solvent was evaporated first at atmospheric pressure and finally at 25 mm. The concentrated solution was cooled; the crystals that appeared were collected and recrystallized from absolute ethanol, wt. 21.5 g. (70% yield), m.p. 77–78°.

Anal. Calcd. for $C_{17}H_{18}OS_2$: C, 67.57; H, 6.00. Found: C, 67.41; H, 5.99.

The xanthate of the *threo* isomer was prepared by a similar procedure. From 21.2 g. of alcohol was obtained 22.1 g. (71% yield) of xanthate as a yellow oil. This material had been purified by precipitating it from pentane at Dry Ice temperature. An attempt to distil it at 200 μ led to decomposition and therefore it was used directly in the pyrolysis experiment.

The xanthate of *erythro*-1,2-diphenyl-1-propanol (6.04 g.) was heated at 20–22 mm. of pressure and at a temperature starting at 130° and ending at 195°. The decomposition started at 130°, and the olefin that distilled was collected and recrystallized from hot ethanol, wt. 3.0 g. (77% yield), m.p. 80–82°, m.m.p. with an authentic sample of *trans*-α-methylstilbene,[21] 81–82°.

Anal. Calcd. for $C_{15}H_{14}$: C, 92.74; H, 7.26. Found: C, 92.75; H, 7.02.

From the filtrates was recovered 55 mg. of an unidentified oil.

The dibromide of the *trans*-olefin was prepared in the usual way, m.p. 125–126°. Melting points of 127°[22a] and 134°[22b] have been reported for this derivative.

Anal. Calcd. for $C_{15}H_{14}Br_2$: C, 50.88; H, 3.99. Found: C, 50.70; H, 4.03.

The xanthate of the *threo*-1,2-diphenyl-1-propanol (12.1

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(21) H. Ley, *Ber.*, **50,** 249 (1917).

(22) (a) J. Levy, P. Gallais and D. Abragam, *Bull. soc. chim. France*, **43,** 873 (1928); (b) M. C. Hell, *Ber.*, **37,** 457 (1904).

g.) was pyrolyzed by the same method as its isomer. Decomposition of this xanthate did not set in until a temperature of 145° was reached. The distillate (6.75 g.) was crystallized from pentane, and the crystals obtained were recrystallized from pentane. By carrying through second crops, a total of 5.03 g. of *cis*-α-methylstilbene was obtained (65% yield), m.p. 47–48° (lit.[10] 48°).

Anal. Calcd. for $C_{15}H_{14}$: C, 92.74; H, 7.26. Found: C, 92.75; H, 7.23.

From the combined filtrates was isolated by distillation 1.65 g. of a yellow oil. This oil (1.4 g.) was heated with hydrobromic acid (1 ml. of 48%) and 50 ml. of glacial acetic acid for two hours at 100° and the resulting mixture was poured onto ice. From the oil that separated only 0.15 g. of *trans*-α-methylstilbene was isolated. The rest of the material was probably some sulfur-containing compound.

Since *cis*-olefin can be readily converted to the *trans* isomer by the above procedure,[10] this experiment demonstrates that the yellow oil contained only minor amounts of either *cis*- or *trans*-olefin.

The dibromide of *cis*-α-methylstilbene was prepared in the usual way (45% yield), m.p. 132–133° (dec.), m.p. with dibromide from the *trans*-olefin, 119–131°.

Anal. Calcd. for $C_{15}H_{14}Br_2$: C, 50.88; H, 3.99. Found: C, 50.86; H, 4.16.

LOS ANGELES, CALIF.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

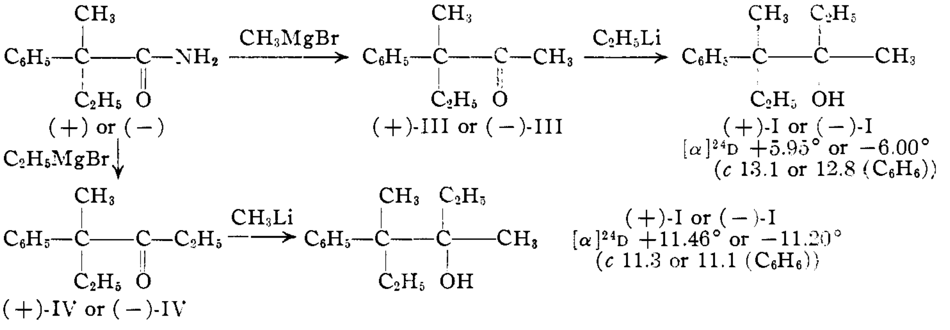
Studies in Stereochemistry. XI. The Preparation and Complete Resolution of the 3,4-Dimethyl-4-phenyl-3-hexanol System

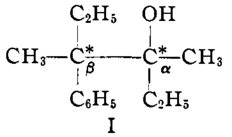
BY DONALD J. CRAM AND JACK D. KNIGHT

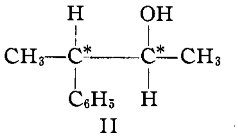
RECEIVED MARCH 12, 1952

Optically pure (+)- and (−)-methylethylphenylacetic acids were converted through their respective amides to the corresponding (+)- and (−)-3-methyl-3-phenyl-2-pentanones and (+)- and (−)-4-methyl-4-phenyl-3-hexanones. The addition of ethyl lithium to each of the methyl ketones gave carbinol in which one diastereomer predominated whereas the addition of methyl lithium to each of the ethyl ketones gave carbinol in which the other diastereomer predominated. All four isomers of 3,4-dimethyl-4-phenyl-3-hexanol as well as their *p*-bromobenzoates were isolated in optically pure state. Correlations of the configurations of these substances with their rotations and modes of preparation are made.

A considerable amount of interest has developed recently in the resolution of optically active tertiary alcohols for purposes of studying the stereochemistry and mechanism of the S_N1 reaction.[1,2] A number of other investigations of the effect of steric and electronic factors on the course of the solvolysis and rearrangement reactions in sterically strained tertiary systems have also been reported.[3] The 3,4-dimethyl-4-phenyl-3-hexanol system (I) combines the feature of asymmetry with that of steric strain at the two reactive centers (C_α and C_β) of this molecule. Moreover, this quaternary–tertiary system (I) is somewhat analogous to the tertiary–secondary 3-phenyl-2-butanol system (II), whose symmetry properties proved valuable in the study of the Wagner–Meerwein,[4] substitution[4] and elimination reactions.[5] This paper reports the preparation, resolution and characterization of I, and Paper XII in this series reports the results of the solvolysis of esters of this carbinol.




I


II

Results

Methylethylphenylacetic acid[2] was resolved into its two optical antipodes, the (+)-isomer being separated as its brucine salt and the (−)-isomer as its quinine salt. Table I reports the rotations, physical properties and analyses of these acids as well as the other intermediates in the synthesis.[6,7] The amides of the (+)- and (−)-acids were each

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(1) (a) W. Doering and H. Zeiss, THIS JOURNAL, **72**, 147 (1950), Abstracts of Meeting of the American Chemical Society, Philadelphia, Pa., April, 1950, p. 7L. (b) H. Zeiss, Abstracts of Meeting of the American Chemical Society, Chicago, Ill., Sept., 1950, p. 50N; (c) H. Zeiss, THIS JOURNAL, **73**, 2391 (1951); (d) E. Hughes, C. Ingold, R. Martin and D. Meigh, *Nature*, **166**, 679 (1950).

(2) Probably the first tertiary system to be prepared in an optically active state is the methylethylbenzylcarbinyl chloride of E. Wallis and P. Bowman, *J. Org. Chem.*, **1**, 383 (1936).

(3) (a) P. D. Bartlett and A. Schneider, THIS JOURNAL, **67**, 141 (1945), and P. D. Bartlett, *Bull. soc. chim. France*, **18**, 100C (1951); (b) H. C. Brown and R. Fletcher, THIS JOURNAL, **71**, 1845 (1949); (c) F. Brown, T. Davis, I. Dostrovsky, O. Evans and E. Hughes, *Nature*, **167**, 987 (1951).

(4) D. J. Cram, THIS JOURNAL, **71**, 3863, 3875 (1949); **74**, 2129, 2159 (1952).

(5) D. J. Cram, *ibid.*, **71**, 3871 (1949); *ibid.*, **74**, 2149, 2152 (1952).

(6) E. Wallis and P. Bowman (ref. 2) prepared the (−)-isomer of this substance ([α]²⁰D −23.28°, benzene) but apparently did not obtain optically pure material.

(7) Evidence for the optical purity of all the active compounds reported in Table I is found in the facts that the magnitudes of the rotations of enantiomorphically related materials are in each case almost equivalent, and that samples of the same materials prepared in different runs had the same rotations.