Sodium Borohydride Reduction of Substituted *trans*-Decalones

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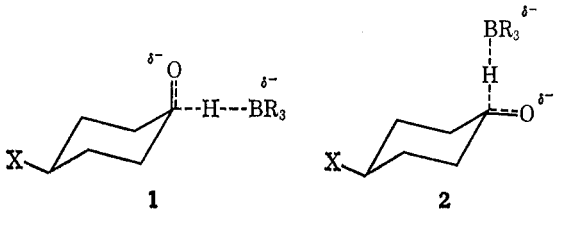
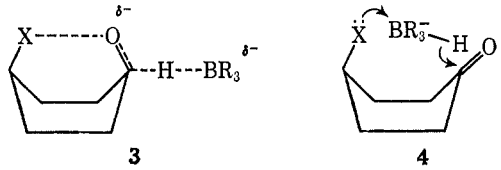
There has been considerable interest for some time in evaluating the effects of remote polar substituents on the course of ionic reactions. One such group of studies has been directed to the question of the stereochemical influence that a remote polar substituent can exert on the outcome of the sodium borohydride reduction of cyclohexanones.[2-5] In general, two visualizations of the mechanism by which such effects may operate have been proposed. The first describes the effect as purely electrostatic. The transition state is pictured in **1** and **2**, leading, respectively, to *cis* and *trans* product. When X is an electron-withdrawing group, the cisoid form (**1**) is electrostatically more



1 **2**

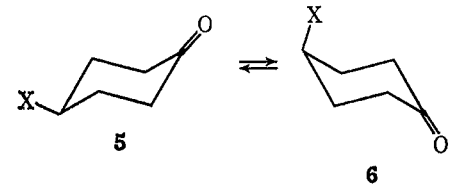
stable than the transoid form (**2**) because the negative oxygen is closer to the electron-deficient carbon at C_4 in form **1** than it is in form **2**.[6]

The second mechanistic proposal requires the direct participation of the remote substituent with either the keto group[3] (as in **3**) or with the borohydride moiety[4] (as in **4**). As is apparent from the representation, this second mechanism requires that the cyclohexane ring be capable of passing through a boat form.



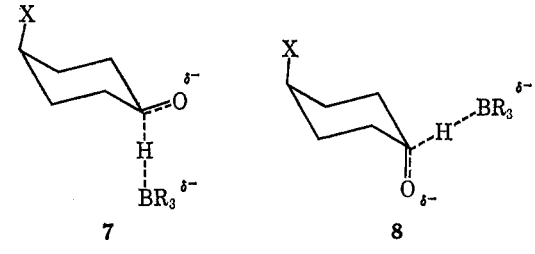
3 **4**

We view the first mechanistic proposal as an oversimplification for the following reasons. As has been amply demonstrated,[7,8] cyclohexane compounds with two polar substituents may show conformational abnormalities that are wholly unpredictable on steric grounds alone. For example,[8] 4-hydroxycyclohexanone-2,2,6,6-d_4 has been found to exist in the conformation analogous to **6** (*i.e.*, with an axial substituent) to the extent of 39% in D_2O, 53% in pyridine,



5 **6**

and 54% in chloroform. There is no reason why the factors influencing the conformational equilibrium in the case of the 4-hydroxy compound cannot be reasonably extended to any relatively unbulky polar substituent including chloro or carboxy, since it has been shown that intramolecular hydrogen bonding (which might be mentioned to explain the hydroxy case) is relatively minor in 4-hydroxycyclohexanone.[9] If the foregoing argument is valid, then one is not justified in considering electrostatic influences in only the two forms **1** and **2**, but one must also consider the likely existence of two additional forms **7** and **8**. If it is further noted that forms **1** and **7** both lead to *cis* product while forms **2** and **8** both lead to *trans* product,



7 **8**

it should be apparent that drawing conclusions as to the nature of electrostatic interactions in the transition state based only on analyses of the products of the reaction may be seriously misleading.

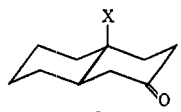
Our approach to the problem of evaluating the directing effects of remote polar substituents has been to employ as model substrates *trans*-1- and *trans*-2-decalones appropriately substituted. Since, of the possible conformations in the *trans*-decalin system, there is only a single chair–chair conformation, the question of conformational equilibrium of the type **5** ⇄ **6** does not enter. Our data are summarized in Table I.

The differences in the two sets of substrates are obvious: the compounds of type **9** are *trans*-2-decalones while those of type **10** are *trans*-1-decalones; the substituents in the case of **9** are axial while those in the case of **10** are equatorial. Despite these differences, the presence of a polar substituent in the (relatively speaking) 4 position was in all cases accompanied by an increase in the proportion of product oriented *cis* to the substituent, regardless of whether the resultant hydroxyl is itself oriented axially or equatorially.

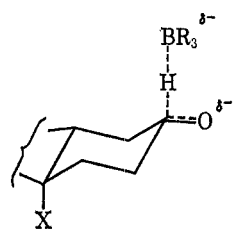
There are two likely mechanistic pictures that will account for the increased proportion of *cis*-oriented products in the presence of the polar substituent. The first suggests that the most favored transition states in the cases of type **9** and type **10** systems should

(1) To whom inquiries should be addressed.
(2) M. G. Combe and H. B. Henbest, *Tetrahedron Lett.*, 404 (1961).
(3) H. Kwart and T. Takeshita, *J. Amer. Chem. Soc.*, **84**, 2833 (1962).
(4) H. O. House, *et al.*, *J. Org. Chem.*, **27**, 4141 (1962).
(5) D. M. S. Wheeler and M. M. Wheeler, *ibid.*, **27**, 3796 (1962).
(6) Combe and Henbest (*cf.* ref 2) calculate the distances for **1** and **2** to be 3.40 and 4.12 Å, respectively.
(7) (a) K. Kozina and T. Yoshino, *J. Amer. Chem. Soc.*, **75** 166 (1953); (b) P. Groth and O. Hassel, *Acta Chem. Scand.*, **19**, 1709 (1965).
(8) W. F. Trager, B. J. Nist, and A. C. Huitric, *Tetrahedron Lett.*, 2931 (1965).
(9) R. D. Stolow, *J. Amer. Chem. Soc.*, **84**, 686 (1962).

TABLE I
RATIOS OF EQUATORIAL/AXIAL ALCOHOLS ARISING FROM THE SODIUM BOROHYDRIDE REDUCTION (METHANOL) OF *trans*-DECALONES

	Equatorial/axial hydroxyl orientation
 9	
a, X = H	76:24
b, X = COOH	92:8
c, X = $COOCH_3$	100:0
 10	
a, X = H	68:32
b, X = COOH	36:64
c, X = $COOCH_3$	56:44

be represented as in **11** and **12**, respectively. In these representations, the negative oxygen achieves its



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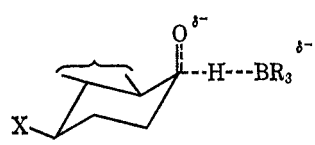

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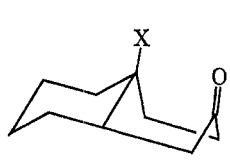
closest proximity to the *substituent* (which in the present cases has a markedly electron-deficient center adjacent to the ring) rather than to the electron-deficient carbon at C_4.

The second mechanistic picture that accounts for *cis*-oriented product requires intramolecular participation and is essentially that shown in **3**. Its relevance for the present case depends on the fact that the decalones **9** and **10** are capable of existing in half-boat conformations as in **13** and **14**, respectively. Compound



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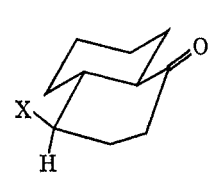

14

9 (in the form **13**) clearly satisfies the geometrical requirements necessary for intramolecular participation. Our examination of models suggests, however, that compound **10** (in the form **14**) cannot achieve suitable geometry for intramolecular participation.

In order to resolve the "electrostatic effect" *vs.* "participation effect" uncertainty, we are presently preparing for reduction additional decalones in which, it is hoped, the polar substituent is not capable of participation.

Experimental Section[10]

trans-**1-Decalone** (**10a**).—Pure *trans-trans*-1-decalol was prepared according to the published procedure.[11] The product was recrystallized from pentane, mp 59–60° (lit.[11] mp 59.5°). The alcohol (5.0 g, 0.032 mol) was dissolved in acetone (10 ml) and treated with Jones reagent (6.8 ml, prepared from 27 g of chromium trioxide, 23 ml of concentrated sulfuric acid, and 100 ml of water). The oxidation proceeded at room temperature for 0.5 hr. The reaction mixture was then extracted four times with ether; the ether extracts were washed with water and then dried over anhydrous sodium sulfate. Distillation afforded *trans*-1-decalone, bp 80–85° (3 mm) [lit.[11] bp 80–85° (3 mm)], yield 3.6 g (72%).

trans-anti-**4-Carboxy-1-decalone** (**10b**).—The compound was prepared according to the procedure of Nazarov, Kucherov, and Segal,[12] mp 154–155° (lit.[12] mp 156°).

trans-anti-**4-Carbomethoxy-1-decalone** (**10c**).—*trans-anti*-4-Carboxy-1-decalone (**10b**) was dissolved in absolute methanol containing 2% concentrated sulfuric acid. The solution was refluxed for 3 hr. Methanol was distilled away and the residue was dissolved in ether. The ethereal solution was washed with water, bicarbonate solution, and water and dried over anhydrous sodium sulfate. Evaporation of the solvent gave the required ester, which was recrystallized from petroleum ether (bp 60–90°). It had mp 66–67° (lit.[12] mp 68°).

trans-cis-**2-Decalol**.—$\Delta^{1,9}$-2-Octalone[13] was reduced according to the procedure of Van Tamelen and Proost[14] by lithium in anhydrous ammonia. Further reduction of this product by sodium borohydride in methanol followed by recrystallization from hexane gave the desired alcohol, mp 74° (lit.[11] mp 72.1–74.8°).

trans-**2-Decalone** (**9a**).—*trans-cis*-2-Decalol (5.0 g, 0.032 mol) was oxidized with Jones reagent as before. Distillation of the product afforded the alcohol-free ketone, bp 78–80° (3.2 mm) [lit.[14] bp 106° (12 mm)], yield 3.9 g (78%).

trans-cis-**2-Hydroxy-10-decalincarboxylic Acid**.—*trans-cis*-2-Hydroxy-10-decalincarboxylic acid lactone[15] (42 g, 0.23 mol) was mixed with aqueous sodium hydroxide (40 g of NaOH in 200 ml of water) and the mixture was refluxed for several hours. The homogeneous solution was cooled, acidified (concentrated HCl), and then continuously extracted with ether. Evaporation of the ether and recrystallization from hexane–ethanol gave the desired carboxy alcohol, mp 162–163° (lit.[16] mp 160–161°), yield 40 g (86%).

trans-**10-Carboxy-2-decalone** (**9b**).—*trans-cis*-2-Hydroxy-10-decalincarboxylic acid (3.5 g, 0.018 mol) was oxidized with Jones reagent as before. Recrystallization of the product from ether–petroleum ether afforded the desired carboxy ketone, mp 90–91° (lit.[16] mp 91.5–93°), yield 1.9 g (54%).

Methyl *trans-cis*-**2-Hydroxy-10-decalincarboxylate**.—*trans-cis*-2-Hydroxy-10-decalincarboxylic acid (1.0 g, 0.005 mol) was methylated with ethereal diazomethane. The ether was allowed to evaporate and the product was recrystallized from petroleum ether (bp 60–90°), mp 82–84° (lit.[16] mp 82–83°), yield 0.96 g (89%).

trans-**10-Carbomethoxy-2-decalone** (**9c**).—Methyl *trans-cis*-2-hydroxy-10-decalincarboxylate (0.67 g, 0.0031 mol) was oxidized with Jones reagent as before. The product, which could not be crystallized, was shown by its infrared spectrum to be free of alcohol and was therefore used in the subsequent reduction without further purification. The authenticity of the product was verified by comparison with the published[16] infrared spectrum.

Borohydride Reduction of *trans*-**Decalones** (**9a and 10a**).—The ketone (0.178 mol) was added to a stirred solution of sodium borohydride (0.178 mol) in methanol at room temperature. The reaction was continued for 24 hr. Sodium hydroxide solution (150 ml, 2 *N*) was added and the solution was refluxed for 2 hr. The resulting solution was continuously extracted with ether overnight. The ether extract was dried (anhydrous so-

(10) All melting points and boiling points are uncorrected. Melting points were determined on a Fisher-John apparatus. The infrared spectra were recorded on a Perkin-Elmer Model 337 spectrophotometer.

(11) W. G. Dauben, R. C. Tweit, and C. Mannerskantz, *J. Amer. Chem. Soc.*, **76**, 4420 (1954).

(12) I. N. Nazarov, V. F. Kucherov, and G. M. Segal, *Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1215 (1956).

(13) G. Stork, *et al.*, *J. Amer. Chem. Soc.*, **85**, 207 (1963).

(14) E. E. Van Tamelen and W. C. Proost, Jr., *ibid.*, **76**, 3632 (1954).

(15) W. G. Dauben, R. C. Tweit, and R. L. MacLean, *ibid.*, **77**, 48 (1955).

(16) A. S. Dreiding and A. J. Tomasewski, *ibid.*, **77**, 411 (1955).

dium sulfate) and the ether was removed. The residual mixed alcohols were directly subjected to glpc analysis or were acetylated with a 30% molar excess of acetyl chloride in benzene solution, and the undistilled acetates were subjected to glpc analysis.

Borohydride Reduction of Substituted Decalones (9b, 9c, 10b, and 10c).—The ketone (0.012 mol) was added to a stirred solution of sodium borohydride (0.012 mol) in methanol at 0°. The reaction was continued for 4 hr, whereupon dilute hydrichloric acid was added to bring the solution to pH 4. Methanol was evaporated and the residue was continuously extracted with ether. After drying and evaporation of the ether, the mixed alcohols were methylated with ethereal diazomethane if appropriate (*i.e.*, in the case of **9b** and **10b**). The mixed ester–alcohols were acetylated as before with acetyl chloride and the analysis was carried out on the undistilled acetates.

Analysis.—Analyses were performed on an Aerograph Model 600 HyFi with flame ionization detector. The columns were either 15 ft by 1/8 in. stainless steel packed with 10% Carbowax 20M on acid-washed Chromosorb, 80–100 mesh, or 20 ft by 1/8 in. stainless steel packed with FFAP on acid-washed Chromosorb, 80–100 mesh. The oven was operated at constant temperatures varying from 180 to 230° ± 2°.

The composition of the product mixtures was compared before and after acetylation only for *trans*-1-decalone (**10a**) and *trans*-2-decalone (**9a**). In these cases, agreement was ±2%—within experimental error—and thereafter only the acetates were determined. The calibration of the column was carried out using authentic samples of *trans-trans*-1-decalyl acetate, *trans-cis*-2-decalyl acetate, and the acetate of methyl *trans-cis*-2-hydroxy-10-decalincarboxylate. In cases where authentic samples were not available, the identifications of equatorial hydroxyl (as acetate) and axial hydroxyl (as acetate) was made by relative retention times.

No attempt was made to isolate the products of the reductions. Reductions of all ketones were essentially complete as shown by the absence of other than trace amounts of unreduced ketone in the infrared spectra. The percentages reported in all cases are relative percentages of reduced materials.

Registry No.—Sodium borohydride, 16940-66-2; **9a**, 23646-48-2; **9b**, 23595-68-8; **9c**, 23595-69-9; **10a**, 21370-71-8; **10b**, 23595-70-2; **10c**, 23595-71-3.

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A Simple and Quantitative Method of Preparation of *cis*-Stilbene and Its Deuterated Analog, Ph—CD=CD—Ph

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In the course of studies of the chemistry of radical ions and dianions of diphenylacetylene, we discovered a simple and quantitative method for synthesis of *cis*-stilbene and of its deuterated analog, Ph—CD=CD—Ph. To our knowledge, no method which yields quantitatively pure *cis* isomer, without admixture of the *trans*-stilbene, has been yet described in the literature.[1]

Ten milliliters of 10^{-2} *M* solution of diphenylacetylene in tetrahydrofuran is treated with metallic lithium at −78°. The chunks of lithium metal used for the reduction are previously washed with a cold (−78°) solution of diphenylacetylene which is subsequently decanted in a high-vacuum system. The reaction is over in *ca.* 1–2 hr and yields a slurry which is removed from the excess of metal by pouring it through a narrow tube into another container. Thereafter a solution of methanol, or deuterated methanol, is added and the protonated products are allowed to warm to room temperature. It should be stressed that all the operations, including the protonation, have to be performed at −78°, preferentially on a high-vacuum line. Whenever the reacting mixture is allowed to warm, even to −60°, other products, including *trans*-stilbene, are formed.

The alkali is extracted with water and the organic layer is extracted with carbon tetrachloride. The alkali-free layer is then dried with anhydrous $MgSO_4$, the solvent is evaporated, and the residual *cis*-stilbene (or deuterated *cis*-stilbene) is then isolated. The yield is quantitative. No difficulties are expected in scaling up this preparation.

The product was identified by its uv spectrum, a single sharp peak at 280 mμ characteristic of the *cis* isomer (the *trans* isomer gives a double peak at 298 and 310 mμ and a shoulder at 322 mμ). Its identity was also proved by vpc using a silicone column which separates the isomers (checked with original samples). Finally, the nmr spectrum gives two sharp peaks, one at 393.5 cps, the other at 428 cps, intensities being in the expected ratio 1:5. The deuterated product gives only one peak at 428 cps with no other peaks visible in the spectrum. The nmr spectrum of the *trans* isomer is much more complex, with seven peaks in the range 430–447 cps and the olefinic peak at 421 cps.

It is interesting to point out that the reduction with sodium under similar conditions gives several products, including the *trans* isomer, but none of the *cis* isomer. Apparently, the alkali salts of the dianions of diphenylacetylene have well-defined geometry, namely, the lithium salts being *cis* while the sodium salt appears to be of *trans* form.

The addition of LiCl to the cold (−80°) solution of the sodium salt in THF precipitates the red lithium salt which, on protonation, gives pure *cis*-stilbene.

The organolithium salts often are dimeric,[2] and we tentatively suggest that this tendency of forming quadrupoles may be responsible for the *cis* structure of the dilithium salt. Thus the two lithium cations could be located one above and the other below the plane of the hydrocarbon framework, each interacting with *both* lone electron pairs of the carbanions and with one half of the π-electron cloud. Of course, this geometry requires a *cis* form of the salt.

Registry No.—*cis*-Stilbene, 645-49-8; deuterated *cis*-stilbene, 3947-91-9.

Acknowledgment.—We gratefully acknowledge the support of this investigation by the National Science Foundation and by the Petroleum Research Fund, administered by the American Chemical Society.

(1) (a) O. H. Wheeler and H. N. Battle de Pabon, *J. Org. Chem.*, **30**, 1473 (1965). (b) K. N. Campbell and E. E. Young, *J. Amer. Chem. Soc.*, **65**, 965 (1943). Electrolytic reduction of tolane on spongy Ni cathode yields 80% *cis* isomer. (c) It is claimed that hydrogenation of acetylene on 5% palladium on $BaSO_4$ gives excellent yields of *cis* olefins: R. L. Augustine, "Catalytic Hydrogenation," Marcel Dekker, Inc., New York, N. Y., 1965, p 69. However, this reaction was not checked for the tolane reduction.

(2) M. Szwarc, "Carbanions, Living Polymers and Electron-Transfer Processes," Interscience Publishers, New York. N. Y., 1968, Chapter VIII.