potassium carbonate and extracted with three 100-ml portions of ether. The combined ether extracts were dried over anhydrous potassium carbonate, the ether was removed by distillation, and the remaining colorless oil was distilled through a Vigreux column [bp 130–132° (0.5 mm)] to give 4.15 g (75%) of 1-phenylindolizidine (**4b**).

A picrate, mp 172–173°, was prepared from picric acid in ethanol.

Anal. Calcd for $C_{14}H_{19}N \cdot C_6H_3N_3O_7$ (**4b·picrate**): C, 55.81; H, 5.15. Found: C, 55.64; H, 4.94.

Preparation of Iminium Salts and Enamines.—With the one exception noted below, the iminium salts whose properties, analyses and yields are listed in Table IV were prepared according to previously published procedures.[16,17] The corresponding enamines were obtained from these salts by basification and purified for infrared and nmr measurements by vapor phase chromatography except for **13** which was vacuum distilled.

The product obtained by oxidation of 1-methylquinolizidine with mercuric acetate was separated by crystallization into two fractions with melting points of 219–220° (5% yield) and 253–255° dec (49% yield). Although these melting points are in agreement with the reported values[24] for **22** and **21**, respectively, the nmr spectrum of the latter compound contains three peaks in the C-methyl region at such positions and relative areas as to suggest an *ca.* 3–4:1 mixture of **21**:**22**. An elemental analysis of the salt, mp 253–255° dec, was obtained.

Anal. Calcd for 80% $C_{10}H_{18}ClNO_4$ (**21**) and 20% $C_{10}H_{18}ClNO_5$ (**22**): C, 47.14; H, 7.13. Found: C, 47.22; H, 6.99.

Vapor phase chromatography of the free base obtained from this salt substantiated the above composition and provided a sample of the enamine **11** which was converted to authentic $\Delta^{5(10)}$-dehydroquinolizidinium perchlorate (**21**).

Acknowledgment.—This research was supported in part by funds from the Research Committee of the University of California. The assistance of Mr. Robert Francis in obtaining some of the spectra is gratefully acknowledged.

Reduction of 1,2-Cyclohexanedione by Aluminum Isopropoxide. Stoichiometric Control of Stereochemistry[1]

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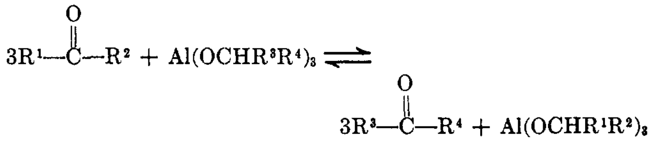
1,2-Cyclohexanedione has been reduced to 1,2-cyclohexanediol by aluminum isopropoxide in toluene at 105°. The isomeric product composition has been observed to vary from 57 ± 2% *cis* (68 ± 5% total 1,2-cyclohexanediols) with a dione/Al(O-*i*-Pr)$_3$ molar ratio of 0.25, to 75 ± 2% *cis* (18 ± 7% glycols) with a molar ratio of 2.0. Dependence of the reductive path on reagent stoichiometry is suggested to explain this stoichiometric control of stereochemistry.

The equilibrium consisting of the Meerwein–Ponndorf–Verley (MPV) reduction of ketones and the Oppenauer oxidation of secondary alcohols is of significant interest to organic chemists and has been the subject of two major reviews[2] and several recent publications.[3] Although monofunctional ketones and alcohols have received considerable attention, vicinal diones, diols, and hydroxyketones appear to have been relatively neglected. Reported MPV studies indicate that reduction by aluminum isopropoxide in isopropyl alcohol converts benzil to 90–94%,[4,5] and benzoin to 90%[4] *meso*-hydrobenzoin, that reduction of benzoin with aluminum ethoxide produces both *meso-* and *rac*-hydrobenzoin in a temperature-dependent (or temperature- and solvent-dependent) ratio,[6] and that Oppenauer oxidation of benzoin and the isomeric hydrobenzoins proceeds in 74–87% yield.[7]



$$3R^1\!-\!\overset{\overset{\displaystyle O}{\|}}{C}\!-\!R^2 + Al(OCHR^3R^4)_3 \rightleftharpoons 3R^3\!-\!\overset{\overset{\displaystyle O}{\|}}{C}\!-\!R^4 + Al(OCHR^1R^2)_3$$

Rather high stereoselectivities seem to occur generally in hydridic reductions of benzil to hydrobenzoin, regardless of the nature of the reductant. The following yields of *meso*-hydrobenzoin have been reported in reductions of benzil: 90% with Al(O-*i*-Pr)$_3$;[4] 84–87%, $(C_6H_5)_2SnH_2$;[8,9] 93%, $(n\text{-}C_4H_9)_2SnH_2$;[9] 95%, $LiAlH_4$–$AlCl_3$;[10] 70–81%, $NaBH_4$ (82–92% hydrobenzoin)[11] and 56% (89% hydrobenzoin);[12] 81–90%, $LiAlH_4$ (86–90% hydrobenzoin).[13] These variable, but frequently high stereoselectivities may be rationalized by a variety of reductive pathways and suggest the desirability of a comprehensive study of the stereochemistry of the Meerwein-Ponndorf-Verley-Oppenauer (MPVO) equilibria of vicinal diones, diols, and hydroxy ketones. Initial results of such a study, including an apparently unique stoichiometric control of stereochemistry, are reported here.

Results

Dione Reduction.—Hydridic reductions of benzil appear to produce predominantly *meso*-hydrobenzoin. Free rotation about the carbonyl–carbonyl bond permits at least two reductive routes to this isomer: in one, both carbonyls of a cisoid dicarbonyl system are reduced by a single metal hydride molecule; in the other each carbonyl of a transoid system is reduced by

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[1] Presented at the 151st National Meeting of the American Chemical Society, Pittsburgh, Pa., March 1966.

[2] A. L. Wilds, *Org. Reactions*, **2**, 178 (1944); C. Djerassi, *ibid.*, **6**, 207 (1951).

[3] E. W. Warnhoff and P. Reynolds-Warnhoff, *J. Org. Chem.*, **28**, 1431 (1963); B. J. Yager and C. K. Hancock, *ibid.*, **30**, 1174 (1965), and references contained therein.

[4] H. Lund, *Ber.*, **70**, 1520 (1937).

[5] W. L. Truett and W. N. Moulton, *J. Am. Chem. Soc.*, **73**, 5913 (1951).

[6] H. Meerwein and R. Schmidt, *Ann.*, **444**, 221 (1925).

[7] J. Staněk and J. Žemlička, *Chem. Listy*, **51**, 493 (1957); *Chem. Abstr.*, **51**, 10448*h* (1957).

[8] H. G. Kuivila and O. F. Beumel, Jr., *J. Am. Chem. Soc.*, **80**, 3798 (1958).

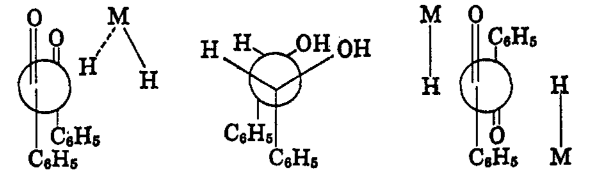
[9] H. G. Kuivila and O. F. Beumel, Jr., *ibid.*, **83**, 1246 (1961).

[10] R. F. Nystrom and C. R. A. Berger, *ibid.*, **80**, 2896 (1958).

[11] J. Dale, *J. Chem. Soc.*, 910 (1961).

[12] S. W. Charkin and W. G. Brown, *J. Am. Chem. Soc.*, **71**, 122 (1949).

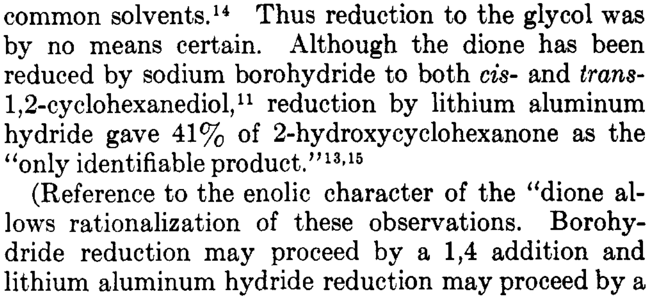
[13] L. W. Trevoy and W. G. Brown, *ibid.*, **71**, 1675 (1949).

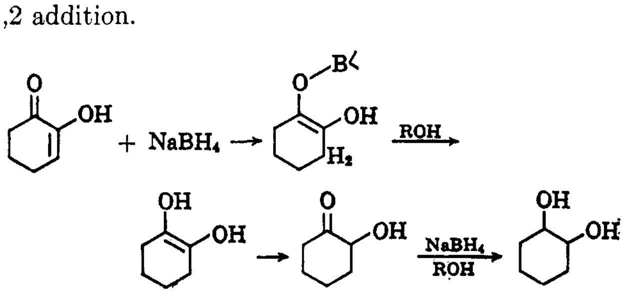


a separate moleule, one on either face of the benzil plane.

In an attempt to remove free rotation as a source of ambiguity, and to initiate a study of the stereochemistry of MPV reductions of vicinal diketones, the MPV reduction of 1,2-cyclohexanedione was investigated. Although many reports refer to the chemistry of 1,2-cyclohexanedione, several studies indicate that this material exists predominantly as the monoenol in common solvents.[14] Thus reduction to the glycol was by no means certain. Although the dione has been reduced by sodium borohydride to both *cis*- and *trans*-1,2-cyclohexanediol,[11] reduction by lithium aluminum hydride gave 41% of 2-hydroxycyclohexanone as the "only identifiable product."[13,15]

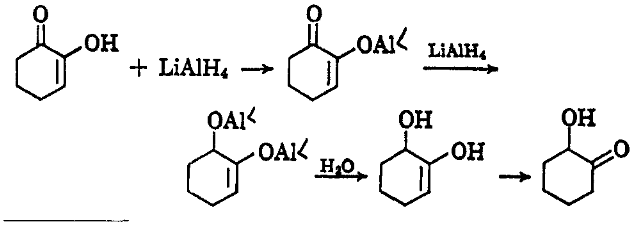
(Reference to the enolic character of the "dione allows rationalization of these observations. Borohydride reduction may proceed by a 1,4 addition and lithium aluminum hydride reduction may proceed by a 1,2 addition.

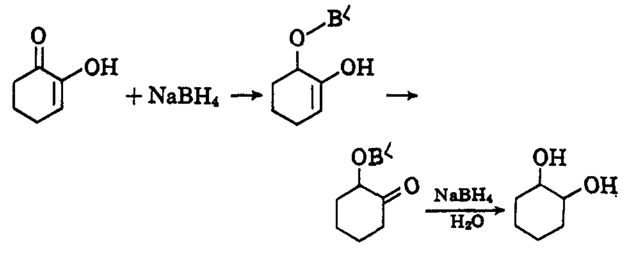




Since lithium aluminum hydride reductions are carried out in aprotic media, rapid tautomerism of the enol aluminate to a keto aluminate, thus permitting complete reduction, would not be expected.

Alternatively, lithium aluminum hydride, the more hydridic reagent, may react rapidly with the acidic enolic hydrogen of the monoenol to produce an aluminum enolate which could undergo carbonyl reduction, then tautomerize during hydrolysis to the observed acyloin. Rapid removal of the monoenol from the tautomeric equilibrium could preclude reaction of the dione as such. Conversely, the borohydride, less strongly hydridic, may react initially with the carbonyl(s) of either tautomer and, with reduction of one carbonyl, permit a shift of equilibrium from the enol to the keto tautomer, in a protic solvent, for complete reduction.[15])





Gas chromatography, the principal analytical technique, indicated that MPV reduction of 1,2-cyclohexanedione did indeed produce both *cis*- and *trans*-1,2-cyclohexanediol. However, a report that benzoin disproportionates to benzil and benzyl phenyl ketone during gas chromatography[16] made verification desirable. Column chromatography of a typical reaction mixture gave fractions identified by mixture melting point as the expected isomeric glycols. In addition, gas chromatography of 2-hydroxycyclohexanone, an analog to benzoin, gave no evidence of glycol formation. Finally, use of a blank reaction containing the dione but no aluminum isopropoxide gave no trace of glycol. There seems no doubt that glycols observed during gas chromatography are produced in the MPV reduction.

The reductions themselves were accomplished by heating to gentle reflux or to 105.0° (the approximate pot temperature of gently refluxing mixtures) for 5 hr a mixture of 10 mmoles of dione, 25 ml of toluene, and varying amounts of aluminum isopropoxide. No attempts were made to determine optimum reaction conditions. After decomposition with aqueous potassium sodium tartrate and extraction of the aqueous phase with chloroform, combined organic phases were examined by gas chromatography. Application of the standard procedure to the individual isomeric cyclohexanediols produced essentially quantitative recovery (95% or more) of each. Results of 18 reductions are presented in Table I and summarized in Table II.

Isomeric Glycols.—The most remarkable feature of the data in Tables I and II is the clear dependence of the isomeric glycol proportions on reagent stoichiometry. As shown in Figure 1, the relative isomeric composition of the glycols appears to be linearly related to the dione/alkoxide molar ratio.

To investigate possible thermodynamic product control as a complicating factor, individual mixtures of 10 mmoles of each isomer, 20 mmoles of acetone, 40 mmoles of aluminum isopropoxide, and 25 ml of toluene were refluxed for 5 hr and examined by the usual procedure. From the *trans* isomer was obtained 92% 1,2-cyclohexanediols: 87.5% *trans*, 4.5% *cis*; from the *cis* isomer, 96%: 95% *cis*, about 1% *trans*. Since the larger observed isomerization corresponds to less than

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[14] (a) C. W. N. Cumper, G. B. Leton, and A. I. Vogel, *J. Chem. Soc.*, 2067 (1965); (b) R. Bakule and F. A. Long, *J. Am. Chem. Soc.*, **85**, 2309 (1963); (c) G. Hesse and G. Krehbiel, *Ann.*, **593**, 35 (1955); (d) G. Schwarzenbach and C. Wittwer, *Helv. Chim. Acta*, 663 (1947); (e) the nmr spectrum of 1,2-cyclohexanedione, 5% in CCl_4, clearly contains a vinylic triplet of the enol at τ 3.37: Neal T. Campbell, private communication, Department of Chemistry, University of Delaware. Because the material has been consistently referred to as the dione, and because its enolic character is not evident in the present work, the dione nomenclature shall be continued here.

[15] Such a difference in modes has been observed by W. R. Jackson, and A. Zurqiyah, *J. Chem. Soc.*, 5280 (1965).

[16] D. L. Banbury and M. S. Osyany, *J. Chromatog.*, **19**, 12 (1965).

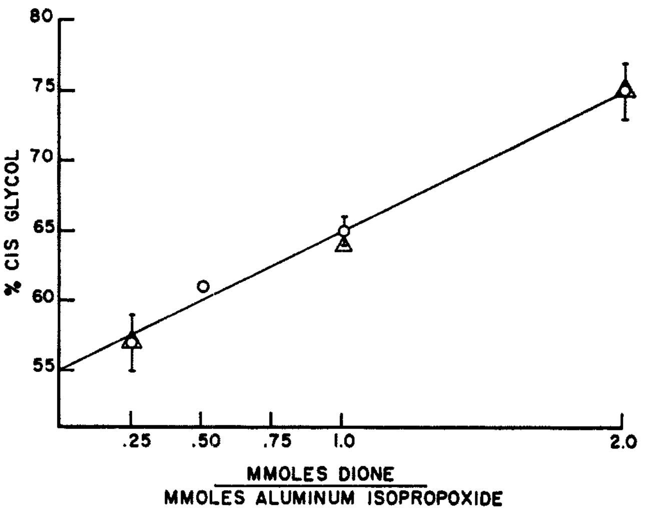

Figure 1.—Isomeric glycol composition as a function of $Al(O\text{-}i\text{-}Pr)_3$ stoichiometry: averages of all runs (○) and of runs at 105.0° (△).

TABLE I

YIELDS AND STEREOCHEMICAL COMPOSITIONS OF 1,2-CYCLOHEXANEDIOLS AS A FUNCTION OF $Al(O\text{-}i\text{-}Pr)_3$ STOICHIOMETRY

Run	$Al(O\text{-}i\text{-}Pr)_3$,[a] mmoles	1,2-Cyclohexanediols, %	*cis*,[b] %	Solids, g
1[c]	40	72	57	None
2	40	74	56	None
3	40	71	56	None
4	40	69	56	None
5	40	68	55	None
6	40	64	57	None
7	40	59	60	None
8	20	54	61	. . .
9[c]	10	42	64	0.60
10	10	55	66	. . .
11[c]	5	31	77	0.85
12[c]	5	23	75	0.85
13[c]	15[d]	19	73	2.20[e]
14	5	15	75	0.90
15	5	17	72	1.2
16	5	16	77	. . .
17	5	8	76	. . .
18	2.5	None observed	. .	0.95

[a] Ten mmoles of dione was used in each run except 13. [b] As per cent total glycol. [c] At 105.0°; runs without superscript were at gentle reflux. [d] Thirty mmoles of dione and 15 mmoles of $Al(O\text{-}i\text{-}Pr)_3$. [e] For 30 mmoles of dione.

TABLE II

A SUMMARY OF THE EFFECT OF ALUMINUM ISOPROPOXIDE STOICHIOMETRY IN THE REDUCTION OF 1,2-CYCLOHEXANEDIONE

No. of runs	Mmoles of dione/mmoles of $Al(O\text{-}i\text{-}Pr)_3$	Glycol yield, %	*cis*, %	Solids, g
7	0.25	68 ± 5[a]	57 ± 2[a]	None
1	0.50	54	61	. . .
2	1.0	49 ± 7	65 ± 1	0.6
7	2.0	18 ± 7	75 ± 2	0.7–1.2[b]
1	4.0	None	. . .	0.95

[a] Standard deviations. [b] Per 10 mmoles of dione.

5% of recovered glycols, *cis/trans* ratios observed here must be reflections of overwhelming kinetic control. Further, thermodynamic control would necessarily involve equilibria utilizing acetone. Not only were reaction temperatures well above the boiling point of acetone, but evidence has been obtained for the removal of acetone from the reaction mixture by a reductive dimerization.[17] Finally, three reactions were carried out with 5 mmoles of aluminum isopropoxide. After 5 hr at 105.0° an additional 35 mmoles of the alkoxide was added to each and heating was continued for 5 more hr. Results are presented in Table III.

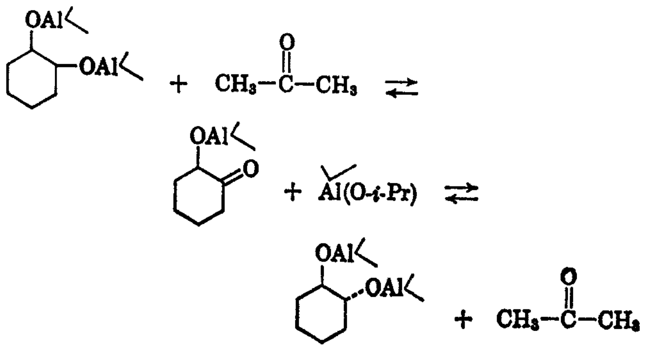

TABLE III

1,2-CYCLOHEXANEDIOLS OBTAINED FROM TWO-STAGE REDUCTIONS

Run	Glycols, %	*cis*, %	Solids, g
1	35	70	0.07
2	31	70	0.50
3	24	66	0.25

If the isomeric differences obtained with variations in alkoxide stoichiometry were thermodynamic in origin, the average result of these three runs (69 ± 2% *cis* glycol) should equal the average obtained in the seven one-stage runs with 40 mmoles of alkoxide (57 ± 2% *cis*). Clearly, it does not. Indeed, a comparison of the average total yield of glycols from these three stepwise runs (30 ± 5%) with that obtained with 5 mmoles (Tables I and II) (18 ± 7%) suggests that the observed decrease in the relative amount of *cis* glycol here may be due to enrichment in the *trans* isomer by reaction of residual dione with the added 35 mmoles of aluminum isopropoxide.

A second factor which might have influenced isomer proportions, variations in reaction temperature,[6,11] can be ruled out by results obtained at 105.0°. The differences in isomeric ratios (% cis, Table I) in runs 1, 9, and 11–13, and the similarities in runs 1 and 2–7, and in 11–13 and 14–17 suggest that temperature variations are not a contributing factor, even under simple reflux. The equalities of the average of runs 2–7 with run 1, and the average of runs 11–13 with the average of runs 14–17 support this conclusion.

A third potential source of isomeric variations may be in the formation of yellow-orange, amorphous solids appearing in many reaction mixtures. As noted in Table II, the solids were observed in reductions employing dione/isopropoxide molar ratios of 4.0, 2.0, and 1.0, but not 0.25. Preferential inclusion of the *trans* diol, or an immediate precursor, in these solids could produce the observed variations in product stereochemistry.

The structure of these solids has not yet been established. They are high melting (above 350°), give a positive aluminon test for aluminum, leave a basic residue on ignition, are essentially water insoluble,

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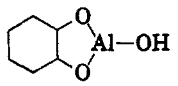
[17] Manuscript in preparation.

but are soluble in concentrated alkali, and are apparently recovered on neutralization. The infrared spectrum (Nujol mull) of solids dried over phosphorus pentoxide contains a broad, strong absorption band at 3600–3000 cm^{-1} (C–H cutoff) suggesting a free hydroxyl group. Because the solids appear in largest quantities with low stoichiometries of alkoxide, a structure similar to



seemed reasonable to explain both spectral and stoichiometric observations. This appears unlikely, however, because reflux of 10 mmoles of each stereoisomeric glycol, individually, with 5 mmoles of aluminum isopropoxide gave copious, gelatinous material which yielded less than 5 mg of solids on hydrolysis.

Although the structure of these solids is unknown, their effect on this study would seem to depend on inclusion of 1,2-cyclohexanediol, an immediate precursor, or a derivative. To determine whether the solids contained cyclohexanediol aluminates which might be unusually resistant to hydrolysis, various portions of solids were refluxed with 50 ml of aqueous potassium sodium tartrate; to determine whether they might contain a precursor, additional portions were refluxed with aluminum isopropoxide in toluene. Results are presented in Table IV.

Table IV

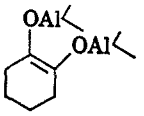
Examination of Reaction Solids

Source[a]	Reagent[b]	Reflux time, hr	Glycols, %	*cis*, %	Correction,[c] %	Residual solids, mg
9	A	1	4	55	−1	2
12	A	1	7	67	−2	2
13	A	5	2.5	76	0	5
13	A	25	1.9	73	−2	5
13	A	138	1.8	81	+2	5
11	B	5	4.5	67	−2	171
8	B	5	0.4	83	. . .	1

[a] Run number of Table I. Solids recovered from run 13 were divided into three equal portions; solids from other runs were used *in toto*. [b] A, 50 ml of concentrated potassium sodium tartrate; B, 8 g of Al(O-*i*-Pr)$_3$ in 25 ml of toluene. [c] To be added to *cis*, % in Table I.

The data of Table IV indicate clearly that no significant amounts of glycols or their closely related derivatives or precursors are contained in the solids. In no case does the correction for glycol composition amount to more than experimental errors of Table II.

The possibility that the solids consist of a structure similar to



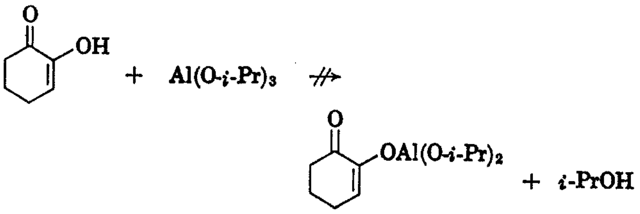
obtained by a 1,4 addition seems unlikely. Not only does the commonly accepted six-membered cyclic transition state[2,3] for the MPV reduction seem incompatible with the geometric requirements of a 1,4 addition in this cyclohexanedione system, but further it is difficult to understand why such a 1,4 addition might be obtained at low aluminum stoichiometries when clearly 1,2 addition is obtained at high stoichiometries. Finally, hydrolysis of such a structure should give 2-hydroxycyclohexanone; no more than traces of peaks potentially attributable to this acyloin appear in chromatograms of hydrolysates.

The conclusion seems reasonable that, while the solids may contain a cyclohexyl moiety, their formation does not induce the observed stereoisomeric variations. The data of Table III suggest that their formation under reaction conditions may be irreversible, but the last two entries in Table IV seem to contradict this. Studies of these solids are being continued.

Discussion

Two significant conclusions seem clear: (1) 1,2-cyclohexanedione, predominantly a monoenol, is reduced to a glycol by aluminum isopropoxide, and (2) the product stereochemistry is determined by reagent stoichiometry.

Dione Reduction.—The very fact of reduction to glycols rules out significant preliminary exchange to produce the aluminum enolate since reduction of its carbonyl should produce acyloin, but not glycol, on hydrolysis. No simple mechanism seems available for reduction of the aluminum enolate to a glycol in an aprotic medium. In addition, because the reductions were carried out in an aprotic medium, observation of glycols in reaction products[18] argues for a 1,2 rather than a 1,4 addition.



Any mechanism for the reduction must require that tautomerism be more rapid than enol–alkoxide exchange.[19] One attractive mechanism would involve a rapid coordination (or actual reduction) of the single carbonyl of the monoenol, followed by a slower enol-to-keto tautomerism, with enol–alkoxide exchange too slow to be significant. If the exchange is considered an "enolysis" of the aluminum isopropoxide, the proposal is consistent with the report that the hydride transfer step in MPV reductions can be sufficiently rapid so that alcoholysis of the resulting mixed aluminum alkoxide is rate determining.[20] Two alternative routes would also involve reduction of the true dione: (1) a rapid, preliminary shift in the tautomeric equilibrium, under reaction conditions, to favor the dione, and (2) rapid reduction of a small equilibrium concentration of dione with a concomitant shift of the equilibrium toward the dione.

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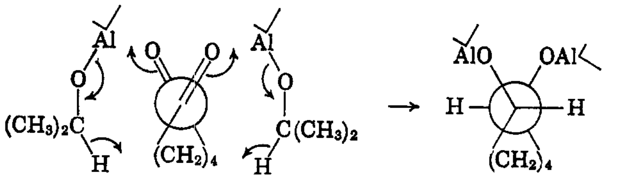
(18) Reaction mixtures were not examined systematically for 2-hydroxycyclohexanone. Conclusions in this study are based on observation of the glycol as the major reaction product with high aluminum alkoxide stoichiometries. Presence of small amounts of the acyloin, even in reactions with high aluminum alkoxide stoichiometries cannot be ruled out. Thus minor aluminum enolate formation, either through exchange with the monoenol or through a 1,4 addition cannot be ruled out entirely by this study.

(19) Rates of keto–enol tautomerism of 1,2-cyclohexanedione in aqueous media have been studied by F. A. Long and R. Bakule, *J. Am. Chem. Soc.*, **85**, 2313 (1963); see also ref 14b.

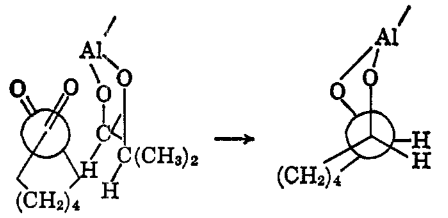
(20) V. J. Shiner, Jr. and D. Whittaker, *ibid.*, **85**, 2337 (1963).

Isomeric Glycols.—These data appear to represent the first example of an effect of reagent stoichiometry on the stereoselectivity of a reaction. No significant effects on product stereochemistries have been produced by variations in stoichiometry of sodium borohydride (twofold)[21] or lithium aluminum hydride (sevenfold and greater)[22] in the reduction of 3,3,5-trimethylcyclohexanone, by variations in lithium aluminum hydride (16-fold) in the reduction of tropinone,[23] or by variations in aluminum isopropoxide (sixfold and greater) in the reduction of (−)-menthone.[24] A profound solvent effect on the borohydride reduction of 3,3,5-trimethylcyclohexanone has been reported.[21] It seems unlikely that the stoichiometric effect observed in the present work operates by a change in solvent characteristics. The dipole moments of both toluene (μ = 0.31 to 0.35 D.)[25] and aluminum isopropoxide (μ = 1.4 D.)[26] are both low; an increasing concentration of aluminum isopropoxide should not produce large *differences* in solvation energies for ground and transition states leading to the isomeric glycols.

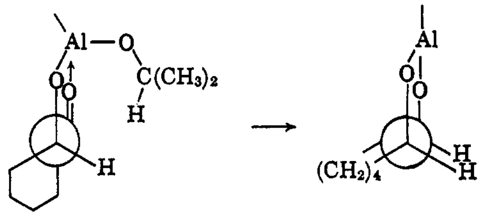
The simplest explanation consistent with the data suggests that at high aluminum isopropoxide stoichiometries two aluminum atoms coordinate with the dione before significant hydride transfer occurs. Since simple coordination presumably requires a smaller activation energy than hydride transfer, this appears reasonable. If the maximum permitted carbonyl–carbonyl dihedral angle in a 1,2-cyclohexanedione system is 60°,[27] the steric requirements of the two aluminum isopropoxide molecules should place them on opposite faces of the ring and produce a *trans* glycol. This process need not be synchronous, but the stereochemical consequences must be determined during or before hydride transfer.

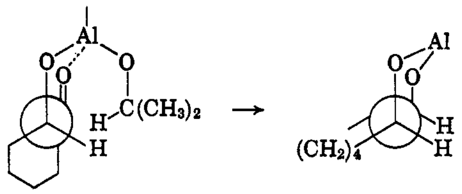


Competing with this process, and *becoming more important with decreasing alkoxide stoichiometry*, are several other routes utilizing one aluminum species and leading to predominant or exclusive *cis* product. First, a single aluminum alkoxide species may reduce both carbonyls, simultaneously or in rapid succession. An approximation of the usual transition state[2,3] should require the aluminum to be on one side of the ring, rather than in its average plane, thus requiring a *cis* product.

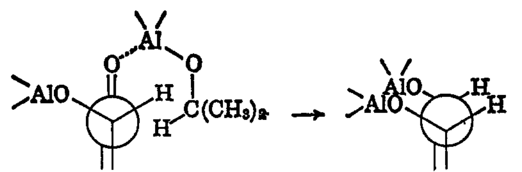


Alternatively, a clearly stepwise reduction, again by a single aluminum alkoxide species, would give the *cis* isomer if Cram's rigid model applies.[28] The steric requirements of the carbinol hydrogen should be considerably less than those of the ring methylenes so that the hydride should approach *cis* to the carbinol hydrogen. Should the system be too complex for application of the rigid-model hypothesis,[29] the steric requirements of the ring, assuming that the large organometallic substituent is equatorial, should again produce *cis* product.





Results obtained in this study are consistent not only with one- and two-aluminum mechanisms, discussed above, but also with purely two-aluminum mechanisms. In this case, reductions at high aluminum stoichiometries would follow the course already described. At low stoichiometries a clearly stepwise route would allow one aluminum alkoxide to effect reduction of one carbonyl, then influence the stereochemistry of the second reduction. Thus, should the reduction require participation of two aluminum-containing species, application of Cram's open-chain model[28] predicts the observed results if the steric requirements of OAl(O-*i*-Pr)$_2$ are greater than those of the carbinol hydro-



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gen.[30] The rigid model should also give the same results as does double reduction by a single aluminum-containing species, if the steric requirements of the organometallic substituent place it above and perpendicular to the plane of the paper.

At present clear differentiation among these proposed routes does not appear possible. Continued work on this reaction is in progress.

Experimental Section

Materials.—Eastman aluminum isopropoxide, Aldrich 1,2-cyclohexanedione, and reagent toluene were distilled before use. Columbia Organic Chemicals *trans*-1,2-cyclohexanediol was recrystallized from toluene. *cis*-1,2-Cyclohexanediol was prepared by permanganate oxidation of cyclohexene,[31] and recrystallized from toluene. The isomeric cyclohexanediols were shown to be homogeneous by gas chromatography. Aldrich 2-hydroxycyclohexanone was distilled immediately before use to ensure existence of the monomer.[32]

Standard Procedure.—In a typical reaction 8.2 g (40 mmoles) of fused aluminum isopropoxide,[33] 1.12 g (10.0 mmoles) of 1,2-cyclohexanedione, and 25 ml of toluene were added, in a dry nitrogen atmosphere, to a dry, 50-ml, one-necked, round-bottomed flask. In all cases the reaction mixture was homogeneous and turned pale yellow immediately. The reaction flask was attached to a 1-m air-cooled condenser which had been flamed dry and capped with a calcium chloride drying tube. Reaction mixtures were heated for 5 hr, either to gentle reflux with a heating mantle, or in a constant temperature bath maintained at 105 ± 0.1°.

Generally, mixtures containing 40 or 20 mmoles of aluminum isopropoxide remained apparently homogeneous and darkened only slightly during the reaction period; those containing 10 mmoles turned somewhat darker and produced a small amount of red-orange solids; with 5 mmoles, mixtures turned quite dark red-orange and appeared to produce large quantities of similarly colored solids.

After 5 hr the typical mixture was cooled, washed with 25 ml of concentrated aqueous potassium sodium tartrate, and allowed to stand overnight. The mixture was filtered and the aqueous phase was separated, continuously extracted for 24 hr with chloroform, then discarded. The volume of the combined toluene and chloroform phases was reduced by distillation at atmospheric pressure and adjusted to 25.0 ml by addition of chloroform.

Qualitative and quantitative analyses were performed with external standards of 0.4 *M* *cis*- and *trans*-1,2-cyclohexanediols and a 3-m column of 5% Carbowax 20M on 60–80 mesh, HMDS-treated Chromasorb W. With a column temperature of 150° and 45–50 psi of helium the *trans* isomer had a retention time 1.2 that of the *cis*.[34]

Product Identification.—Solvent was allowed to evaporate at room temperature from a reaction involving 40 mmoles of aluminum isopropoxide, and the uncrystallizable,[11] residual yellow oil was stored overnight under vacuum and over phosphorus pentoxide. The partly crystalline material thus obtained was diluted to 5.0 ml with 5% absolute ethanol–95% benzene. A 2.0-ml portion was chromatographed, with this solvent system as eluent, on a 350 × 15 mm column of Whatman SG-31 silica gel, activated for 36 hr at 115°. After 125 ml of eluent had been collected, giving only oils on evaporation, three consecutive 10-ml fractions yielded a total of 11 mg of crystalline solids. The next 10-ml fraction gave only a small amount of oil, but a total of 19 mg of crystalline solids was collected from the following five 10-ml fractions. An additional 50 ml of eluent yielded only 5 mg of yellow oil.

Recrystallization from toluene of the more rapidly eluted crystals gave *cis*-1,2-cyclohexanediol, mp 97.8–99.5°; 1:1 mixture with authentic *cis*-1,2-cyclohexanediol, mp 98.0–99.5°; authentic *cis*-1,2-cyclohexanediol, mp 95.5–98.5°. Similar recrystallization of the later fraction gave *trans*-1,2-cyclohexanediol, mp 102.5–104.5°; 1:1 mixture with authentic *trans*-1,2-cyclohexanediol, mp 102.5–104.0°; authentic *trans*-1,2-cyclohexanediol, mp 102.5–103.5°.

Reaction Solids.—These solids were isolated in the filtration step described above. Attempted reaction with aluminum isopropoxide was carried out at gentle reflux by the standard reduction procedure. Attempted hydrolysis with aqueous potassium sodium tartrate was followed by filtration, extraction of the filtrate with chloroform, and analysis as described.

Acknowledgment.—Financial support of this study by a National Science Foundation–University of Miami Institutional Grant is gratefully acknowledged.

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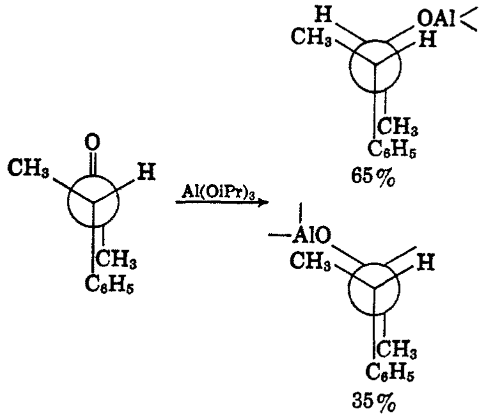
[30] D. J. Cram and F. D. Greene [*J. Am. Chem. Soc.*, **75**, 6005 (1953)] observed that 3-phenyl-2-butanone is reduced by aluminum isopropoxide predominantly to the "wrong" kinetic product, in apparent contraction of Cram's rules. The significance of this anomalous result to the present work is clarified by examining results of MPV reductions of alkylcyclohexanones. Although reduction of 2-methylcyclohexanone with aluminum isopropoxide gives equimolar amounts of the isomeric alcohols[24]—again in apparent contradiction of Cram's rules—a direct relationship does seem to exist between steric requirements of the alkoxide and/or the alkylcyclohexanone and the proportion of cis alcohol in the product. Thus in the present work a concern with stereochemical trends, rather than with absolute ratios themselves, seems justifiable.



[31] K. B. Wiberg and K. A. Saegebarth, *ibid.*, **79**, 2822 (1957).

[32] J. C. Sheehan, R. C. O'Neill, and M. A. White, *ibid.*, **72**, 3376 (1950).

[33] Freshly fused aluminum isopropoxide was used in each run so that the degree of association, while unknown, would presumably remain constant throughout the study; see V. J. Shiner, Jr., D. Whittaker, and V. P. Fernandez, *ibid.*, **85**, 2318 (1963).

[34] R. Nowicki [*Bull. Acad. Polon. Sci., Ser. Sci., Chim.*, **11**, 557 (1963); *Chem. Abstr.*, **60**, 12175*d* (1964)] reports similar results with a poly(ethylene glycol adipate) column and argon.