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# Asymmetric Reactions. VIII. Stereoselectivities in Several Organometallic Reactions with *N*-Benzyl-2,3-*O*-isopropylidene-D-glyceraldimine[1)]

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The present authors have previously reported differences in stereoselectivity between phenyllithium and phenylmagnesium bromide reactions with α-aminonitriles bearing 1,3-dioxolane rings at α-positions,[3)] 2,3-*O*-isopropylidene-D-glyceraldimines,[3,4)] or 2,3-*O*-isopropylidene-D-glyceraldehyde,[5)] *i.e.*, phenyllithium reactions gave *threo* products and Grignard reactions *erythro* products predominantly. The stereoselectivity of the phenyllithium reactions is consistent with Cram's rigid model,[6)] but that of the Grignard reaction cannot be explained by this model. The anomalous stereoselectivity has been explained[3–5)] in terms of the coordination ability of magnesium to $C_3$-oxygen, together with $C_1$-oxygen or $C_1$-nitrogen, and $C_2$-oxygen (Fig. 1). Support for this assumption was obtained[1)] from the fact that no stereoselectivity difference was observed between the tworeactions with substrates having no $C_3$-oxygen.

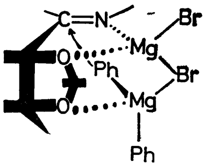


Fig. 1.

It is of interest to investigate other organometallic reactions in connection with the stereoselectivity which might result from the coordination ability of the attacking species. This paper will report on the stereoselectivity exhibited by organometallic compounds of Be, Ca, and Zn.

The phenylcalcium iodide was prepared in ether according to Gilman's method.[7)] The other organometallic reagents were prepared by the addition of the corresponding metal halides into an ether solution of phenyllithium.[7)]

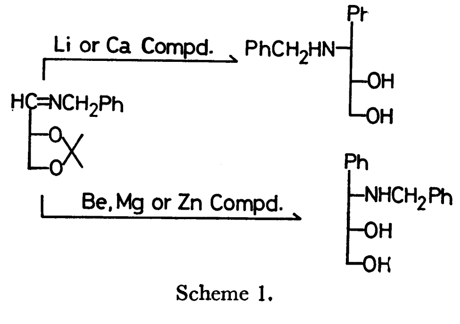
*N*-Benzyl-D-glyceraldimine was treated with 2—3 molar equivalents of the reagents in ether. The reaction mixture was then decomposed with ice water, and the addition products obtained from ether layer were hydrolyzed to give a diastereomeric mixture of 1-benzylamino-1-deoxy-1-*C*-phenyl-*threo*- and -*erythro*-D-glyceritols. The product was confirmed by thin-layer chromatography. The analytical results agreed. In the case of the reaction with phenylcalcium iodide, there appeared in the thin-layer chromatography two spots other than the desired products. Therefore, the sample was purified by preparative thin-layer chromatography. The purified sample gave a single spot and agreeing analytical results.

The diastereomeric ratio was calculated from the optical rotation of the product by reference to that of each sample of the *threo* and *erythro* isomers. The results are shown in Table 1.

TABLE 1. DIASTEREOMER RATIOS PRODUCED BY THE REACTION WITH ORGANOMETALLIC REAGENTS

| Run | Reagent (moles to substrate) | $[\alpha]_D$ | Products<br>*threo* (%) | <br>*erythro* (%) |
|---|---|---|---|---|
| 1 | PhCaI (3) | −31.5 | 67 | 33 |
| 2 | $Ph_2Be+BeCl_2$<br>(3) (0.6) | +15 | 35 | 65 |
| 3 | $Ph_2Zn$ (2) | +17 | 34 | 66 |
| 4 | $Ph_2Zn+ZnCl_2$<br>(1.5) (1.5) | +34 | 23 | 77 |

As is shown in Table 1, the reactions with organometallics of Be and Zn showed a stereoselectivity similar to that of the organomagnesium reaction (giving the *erythro* product predominantly). It is worthy of mention that, in contrast to these reactions, the organocalcium reaction gives *threo* product predominantly, despite the fact that calcium belongs to the alkaline earth group (like Be and Mg) in the periodic table. Investigations[7)] of the relative reactivities of organoalkaline and -alkaline earth metal compounds suggested that organocalcium has a rather ionic character, which could explain the stereoselectivity of the organocalcium reaction. At this stage, however, no clear explanation can be given.



Scheme 1.

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## Experimental

*Reaction of* N-*Benzyl-2,3-*O-*isopropylidene-*D-*glyceraldimine with Phenylcalcium Iodide.* An ethereal solution of *N*-benzyl-2,3-*O*-isopropylidene-D-glyceraldimine (10 g) was added with stirring at 0—5 °C into an ethereal solution of phenylcalcium iodide prepared from calcium (5.5 g) and phenyliodide (28 g). The reaction mixture was refluxed with stirring for 10 hr and then decomposed with ice water. The products were extracted with ether. The ether layer was concentrated *in vacuo* to a syrup. The syrup was hydrolyzed with 6 M hydrochloric acid (30 ml) at 100 °C for 2 hr, thereafter the hydrolysate was decolorized with activated carbon and then extracted four times with 50 ml portions of ethyl acetate after the adjustment of the pH to about 10 with a sodium hydroxide solution. The combined ethyl acetate solution was washed with water, dried over anhydrous sodium sulfate, and concentrated under reduced pressure to give crude products which showed two spots on a tlc besides those of the desired products. The crude products were purified by preparative thin-layer chromatography. The purified sample gave a single spot on a tlc ($R_f$, 0.45; solvent, acetone–benzene (3:5)). Found: C, 74.83; H, 7.20; N, 5.93%. Calcd for $C_{16}H_{19}O_2N$: C, 74.68; H, 7.44; N, 5.44%. The specific rotation of the sample was also measured; the result is shown in Table 1.

*Reaction of* N-*Benzyl-2,3-*O-*isopropylidene-*D-*glyceraldimine with Organoberyllium and Organozinc Compounds.* Organoberyllium and organozinc compounds were prepared from anhydrous beryllium chloride or zinc chloride, and phenyllithium according to the Gilman method.[7] For example, beryllium chloride (9 g) was added, portion by portion,into a stirred solution of phenyllithium prepared from lithium (2.7 g) and phenylbromide (20.1 ml). The mixture was refluxed for 30 min after the addition has been completed. To the resulting solution was added an ethereal solution of *N*-benzyl-2,3-*O*-isopropylidene-D-glyceraldimine with cooling and stirring; subsequently, the same procedure as was used in the phenylcalcium iodide reaction gave a diastereomeric mixture. Each sample gave a single spot on a tlc ($R_f$, 0.45; solvent, acetone–benzene (3:5)). The diastereomeric ratios produced by each reaction were calculated from the optical rotation of the sample and pure D-*threo* and D-*erythro* isomers. The analytical results agreed. Found: [C, 74.64; H, 7.20; N, 5.73% (Run 2)], [C, 74.21; H, 7.64; N, 5.97% (Run 3)], [C, 74.57; H, 7.56; N, 6.24% (Run 4)]. Calcd for $C_{16}H_{19}O_2N$: C, 74.68; H, 7.44; N, 5.44%.