

$$-\frac{dp}{dt} = \{k_{11} + k_{12}K_8[\text{OCH}_3^-]\} \frac{(a - 4x)p}{1 + K_8[\text{OCH}_3^-]}$$

Since phenylhydroxylamine is a strong base and a weak acid, then  $K_8[\text{OCH}_3^-] \ll 1$

$$-\frac{dp}{dt} = \{k_{11} + k_{12}K_8[\text{OCH}_3^-]\}(a - 4x)p$$

or

$$k = k_{11} + k_{12}K_8[\text{OCH}_3^-]$$

If  $K_M = [\text{H}^+][\text{OCH}_3^-]$  is constant in methanol

$$\log(k - k_{11}) = \text{pH} + \log(k_{12}K_8K_M)$$

From this equation the plots of  $\log(k - k_{11})$  vs. pH should give straight lines of unit slope. This was realized as shown in Fig. 3, while no linearity was observed in the plot of  $\log k$  vs. pH.

The order of reactivities of substituted phenylhydroxylamines in the presence of alkali was inconsistent with that in pure methanol, resulting in disagreement with Hammett's equation. These results may be explained by taking into account that the substituent effects of  $k_{12}$  and  $K_8$  are reversed; i.e.,  $k_{12} \times K_8$  corresponds to the rate of the oxidation of  $\text{C}_6\text{H}_5\text{NOH}$ , while the substituent effect in pure methanol contains only

$k_{11}$  which corresponds to free  $\text{C}_6\text{H}_5\text{NHOH}$ . In other words,  $k_{12}$  increases with increasing electron-releasing power of substituent, while  $K_8$  behaves reversely.

The plot of  $\log(k - k_{11})$  vs. pH for unsubstituted phenyl hydroxylamine at 35° gave an equation

$$\log(k - k_{11}) = 1.32\text{pH} - 10.05$$

Hence

$$\log k_{12}K_8 = -\log K_M - 10.05$$

Assuming the ionic product of methanol is  $2 \times 10^{-17}$ <sup>13</sup>

$$k_{12}K_8 \approx 7.5 \times 10^3$$

Since phenylhydroxylamine is a weak acid, the value of  $K_8$  may be much smaller than  $10^6$ , and then  $k_{12} > k_{11}$ .

Hence, the order of reactivity is  $\text{C}_6\text{H}_5\text{NOH} > \text{C}_6\text{H}_5\text{NHOH} \gg \text{C}_6\text{H}_5\text{NH}_2\text{OH}$ . The increase of the oxidation rate with increasing pH coincides with the decrease of the oxidation potential of phenylhydroxylamine with increasing pH.<sup>14</sup> Moreover, the oxidation potential decreases with decreasing  $\sigma$ -value of substituent on phenylhydroxylamine<sup>15</sup> as observed in the present reaction.

(13) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 256.

(14) J. W. Smith and J. G. Wallen, *Trans. Faraday Soc.*, **46**, 290 (1950).

(15) R. E. Lutz and M. R. Lytton, *J. Org. Chem.*, **2**, 68 (1937).

[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY, TOKYO INSTITUTE OF TECHNOLOGY, OHOKAYAMA, MEGUROKU, TOKYO, JAPAN]

## Steric Difference between the Substitution Reaction Products of Lithium Alkyls and Grignard Reagents with $\alpha$ -Aminonitriles.<sup>1</sup> An Asymmetric Reproduction

BY JUJI YOSHIMURA, YOSHIKI OHGO, AND TETSUO SATO

RECEIVED APRIL 3, 1964

Substitution reactions of 3,4-O-isopropylidene N-substituted-D-threosaminonitriles and -D-erythrosaminonitriles with phenylmagnesium bromide and phenyllithium have been investigated. The reaction with phenylmagnesium bromide gave an *erythro* derivative and the reaction with phenyllithium gave *threo* products predominantly, regardless of the configuration of the  $\alpha$ -carbon in the substrate. N-Substituted acetone-D-glyceraldimines also gave the same result. Consideration of the steric difference between the Grignard reaction and the phenyllithium reaction leads to two possible explanations for the asymmetric induction of optically active imine-bearing oxygen-like atoms on the  $\alpha$ - and  $\beta$ -carbon.

In a previous paper,<sup>2</sup> one of the authors reported that the substitution reaction of di-O-isopropylidene-N-phenyl-D-glucosaminonitrile with Grignard reagents gave levorotating compounds and that the reaction with lithium alkyls afforded dextrorotating products predominantly. The results prompted the present study of the steric difference between lithium alkyls and Grignard reagents in the substitution reaction.

### Materials

3,4-O-Isopropylidene-N-phenyl-D-threosamino- and -erythrosaminonitrile (I-T and I-E), the corresponding N-benzyl derivatives (II-T and II-E),<sup>3</sup> and diastereomeric mixtures of N-ethyl and N-dimethyl derivatives (III-T·E and IV-T·E) were prepared by condensing acetone-D-glyceraldehyde with the corresponding amine

(1) This work was presented at the 15th Annual Meeting of the Chemical Society of Japan, Tokyo, April, 1962.

(2) J. Yoshimura, *Bull. Chem. Soc. Japan*, **35**, 536 (1962).

(3) J. Yoshimura, Y. Ohgo, and T. Sato, *ibid.*, **34**, 1197 (1961).

and hydrogen cyanide, followed by fractional crystallization.

The Schiff bases, N-phenyl- and N-benzylacetone-D-glyceraldimine (I-S and II-S), were prepared from acetone-D-glyceraldehyde and the corresponding amines. Properties of the materials used are shown in Table I.

**N-Substituted Acetone-D-glyceraldimines.**—The condensation product of acetone-D-glyceraldehyde and an equivalent amount of benzylamine was distilled at 110° (0.005 mm.). The distillate, however, showed the existence of both the  $-\text{NH}-$ <sup>4</sup> and the  $-\text{C}=\text{N}-$ <sup>5</sup> groups by an infrared absorption spectrum, but no optical activity in spite of the analytical data which were consistent with the theoretical values for II-S. This fact seems to imply that heat promotes isomeri-

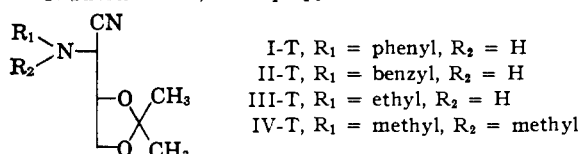
(4) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd Ed., Methuen, London, 1958, p. 2249.

(5) Ref. 4, p. 268.

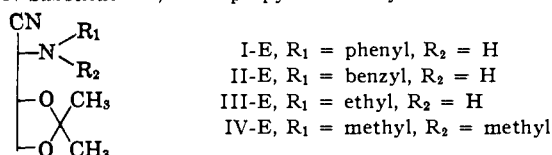
TABLE I

Material	M.p. (b.p., mm.), °C.	$[\alpha]_D^c$ (c, EtOH)
I-T	100-102	-149.4° (0.86)
I-E	124	+184° (0.69)
II-T	86-87	-96° (0.79)
II-E	55-56	+54° (1)
III-T·E	(88, 0.35)	-4.7° (1.1)
IV-T·E	(81, 0.2)	...
I-S	...	+11° (1)
II-S	...	+23° (1)

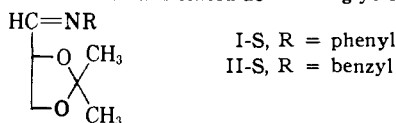
## N-Substituted 3,4-O-isopropylidene-D-threosaminonitriles



## N-Substituted 3,4-O-isopropylidene-D-erythrosaminonitriles



## N-Substituted acetone-D-glyceraldimines



The above phenomenon suggests the occurrence of aldimine-enamine tautomerism, and a paper concerning this phenomenon will be published later.

## Results

Each N-substituted 3,4-O-isopropylidene-D-tetrosaminonitrile or N-substituted acetone-D-glyceraldimine was mixed with 3 or 4 equivalents of phenyllithium or phenylmagnesium bromide in ether and the mixture was refluxed with stirring for about 10 hr. The reaction mixture was decomposed with water and extracted with ether. The sirup obtained by concentrating the ether fraction was subjected to hydrolysis with 6 N hydrochloric acid. The product, after removing neutral by-products such as biphenyl by steam distillation, was neutralized with NaOH solution and then extracted with ethyl acetate. A mixture of acetone-free substituted diastereomers was obtained by concentration of the ethyl acetate fraction, and the mixture was separated into two pure diastereomers by fractional crystallization.

Specific rotations of the crude products and each pure isomer were measured. The data are listed in Table II.

From the optical rotational data listed in Table II are calculated the percentages of each diastereomer in the diastereomeric mixture (Table III).

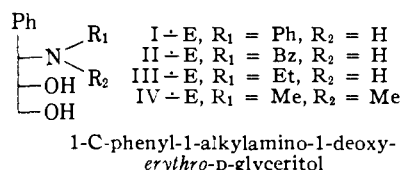
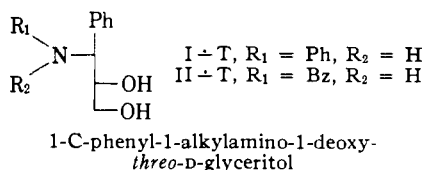
Each diastereomer of these substituted products should have the *D-threo* or *D-erythro* configuration, and

TABLE II

SPECIFIC ROTATIONAL VALUES OF EACH DIASTEREOMERIC MIXTURE OBTAINED BY THE REACTION BETWEEN  $\alpha$ -AMINONITRILES AND ORGANOMETALLIC REAGENTS (MIXTURE  $[\alpha]_D$ ), AND PHYSICAL CONSTANTS OF THEIR PREDOMINANT DIASTEREOMERS

Substrate	Reagent	Mix. $[\alpha]_D$	Sign	$[\alpha]_D^b$	M.p., °C.	Predominant diastereomers						
						Formula	Carbon, %		Hydrogen, %		Nitrogen, %	
						Found	Calcd.	Found	Calcd.	Found	Calcd.	
I-T	PhLi	-11.8°	I-T	-19	112	C <sub>15</sub> H <sub>17</sub> O <sub>2</sub> N	72.92	74.05	6.85	7.04	5.77	5.76
I-T	PhMgBr	+1	I-E	+4	136-137	C <sub>15</sub> H <sub>17</sub> O <sub>2</sub> N	73.58	74.05	7.40	7.04	5.67	5.76
I-E	PhLi	-11	I-T	-17	110-112							
I-E	PhMgBr	0	I-E	+3	136-137							
II-T	PhLi	-33.6	II-T	-81	101-102	C <sub>16</sub> H <sub>19</sub> O <sub>2</sub> N	74.74	74.68	7.69	7.44	5.40	5.44
II-T	PhMgBr	+43	II-E	+68	89-90	C <sub>16</sub> H <sub>19</sub> O <sub>2</sub> N	75.03	74.68	7.07	7.44	5.42	5.44
II-E	PhLi	-32	II-T	-81.3	102							
II-E	PhMgBr	+43.5	II-E	+68	89-90.5							
III-T·E <sup>a</sup>	PhLi	-33.8	III-T									
III-T·E	PhMgBr	+15.9	III-E	+45	83-84	C <sub>11</sub> H <sub>17</sub> O <sub>2</sub> N	68.00	67.66	9.01	8.78	7.09	7.17
IV-T·E <sup>a</sup>	PhMgBr	+14.6	IV-E	+20.5	103-104	C <sub>11</sub> H <sub>17</sub> O <sub>2</sub> N	67.37	67.66	8.91	8.78	7.21	7.17

<sup>a</sup> As N-ethyl and N-dimethyl derivatives did not crystallize, their diastereomeric mixtures were used in the reaction. <sup>b</sup> In every case optical rotation is measured in ethanol (c 1.)



zation during destruction of the asymmetric center. We therefore used the sirups freshly prepared by concentrating the reaction mixture of acetone-D-glyceraldehyde and the corresponding amine (aniline or benzylamine) in ethanol under reduced pressure.

Each structure was confirmed by infrared spectrum, showing the presence of the  $\text{--C=N--}$  group and the absence of the  $\text{--NH--}$  group, and by an optical activity indicating no destruction of the configuration of the asymmetric center. It is of interest that the sirups thus obtained gradually lose their optical activity at room temperature.

It can be presumed from the rotatory power that the levorotating isomer has the former configuration and the dextro isomer the latter.<sup>2,3</sup> This presumption was confirmed by converting the levorotating isomer (II-T) obtained from II-T and phenyllithium to the configurationally known N-acetyl-D-( $-$ )-phenylglycine<sup>6</sup> as follows (Scheme I):

II-T is converted by catalytic debenzoylation, using PdO-BaSO<sub>4</sub> catalyst in dilute hydrochloric acid, into levorotating 1-C-phenyl-1-amino-1-deoxy-D-glyceritol

(6) "Beilstein," Vol. 14, Band II, p. 284; F. Knoop and J. G. Blanco. *Z. physiol. Chem.*, **146**, 274 (1925).

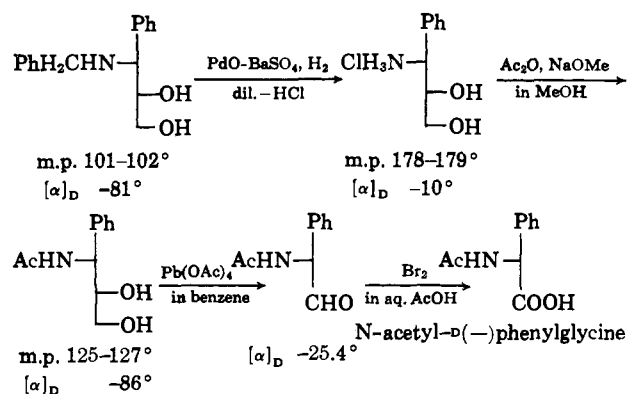
TABLE III

PERCENTAGES OF EACH DIASTEREOMER IN THE DIASTEREOMERIC MIXTURE PRODUCED FROM  $\alpha$ -AMINONITRILES AND ORGANOMETALLIC REAGENTS

$\alpha$ -Aminonitrile	Reagent	Each diastereomer in the mixture, %	
		<i>threo</i>	<i>erythro</i>
I-T	PhLi	69	31
I-T	PhMgBr	13	87
I-E	PhLi	65	35
I-E	PhMgBr	17	83
II-T	PhLi	68	32
II-T	PhMgBr	17	83
II-E	PhLi	67	33
II-E	PhMgBr	16	84

hydrochloride. Acetylation of the product by acetic anhydride in methanol gives 1-C-phenyl-1-acetyl-amino-1-deoxy-D-glyceritol. N-Acetylphenyl-D-glycin-aldehyde obtained by lead tetraacetate oxidation of the acetylated compound was oxidized by bromine to give N-acetyl-D(-)-phenylglycine.

SCHEME I



It follows that the dextrorotating diastereomer II-E must have the D-*erythro* configuration. By comparison of the N-phenyl, N-ethyl, and N-dimethyl derivatives with the N-benzyl derivatives II-T and II-E, it may be concluded that the levorotating isomer pertains to the D-*threo*, and the dextrorotating isomer to the D-*erythro* type in each pair of products.

The results shown in Table III indicate a remarkable interrelation between two organometallic reagents and the configuration of the predominant product; the *threo* product is predominant in the case of the phenyllithium reaction and the *erythro* product in the case of the Grignard reaction, regardless of the configuration of the  $\alpha$ -carbon in the  $\alpha$ -aminonitrile used.

Assuming that a substrate with no asymmetry at the reaction center should also give the same results if steric direction in the substitution reaction is not controlled by the configuration of the  $\alpha$ -carbon in  $\alpha$ -aminonitriles; the reaction of Schiff bases, N-substituted acetone-D-glyceraldimines (I-S and II-S), with organometallic reagents was studied. As anticipated, the Schiff bases reacted with phenyllithium and phenylmagnesium bromide to give 1-C-phenyl-1-alkylamino-1-deoxy-*threo*-D-glyceritol (I-T and II-T) and 1-C-phenyl-1-alkylamino-1-deoxy-*erythro*-D-glyceritol (I-E and II-E, respectively) as the major products. The results are summarized in Table IV.

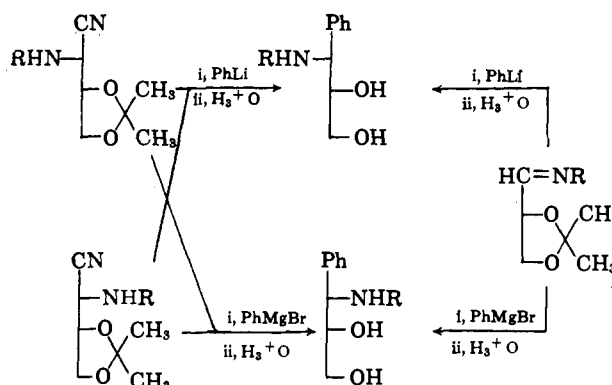
TABLE IV

PERCENTAGES OF EACH DIASTEREOMER IN THE MIXTURES PRODUCED BY REACTION BETWEEN SCHIFF BASES AND ORGANOMETALLIC REAGENTS

Schiff base	Reagent	Mix. $[\alpha]_D$	Each diastereomer in the mixture, %	
			<i>threo</i>	<i>erythro</i>
I-S	PhLi	-13°	74	26
I-S	PhMgBr	+2°	9	91
II-S	PhLi	-24.2°	63	37
II-S	PhMgBr	+35.2°	22	78

The over-all results are summarized in Scheme II.

SCHEME II



### Discussion

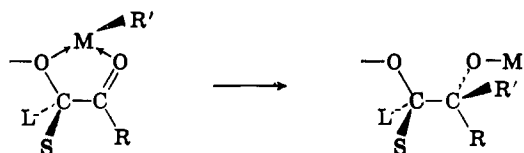
**Dissociation of the C $\alpha$ -CN Bond in  $\alpha$ -Aminonitriles.**—From the fact that steric direction in the substitution reaction is not concerned with the configuration of the  $\alpha$ -carbon but with the organometallic reagent used, it is presumed that dissociation of the C $\alpha$ -CN bond precedes attack of organometallic reagents on the  $\alpha$ -carbon. This assumption is validated by the fact that even aldimine derivatives which have no asymmetry in the reaction center give the same results as  $\alpha$ -aminonitriles.

Consequently, the substitution reaction between  $\alpha$ -aminonitriles and organometallic reagents appears to be an asymmetric reproduction in which the asymmetry at the  $\alpha$ -carbon is destroyed by the dissociation of the C $\alpha$ -CN bond in the first step and is regained by attack of the phenyl group in the second step. Many reactions,<sup>7</sup> known as the substitution of  $\alpha$ -aminonitriles or  $\alpha$ -cyanohydrins with Grignard reagents, can be explained by such a two-stage mechanism.

**Steric Direction.**—Recently, Cram and Kopecky<sup>8</sup> proposed a mechanism for asymmetric induction of  $\alpha$ -alkyloxy carbonyl compounds with Grignard reagents or alkyllithiums from their extensive investigations in stereochemistry. According to their interpretation, Grignard reagents and alkyllithiums form a chelate bridge between two oxygen atoms of  $\alpha$ -alkyloxy carbonyl compounds and then the alkyl portion of these reagents attacks the carbonyl carbon from the less hindered side as presented in the diagram shown.

(7) M. S. Kharasch and O. Reinmuth, "Grignard Reactions of Non-metallic Substances," Prentice-Hall, Inc., New York, N. Y., 1954.

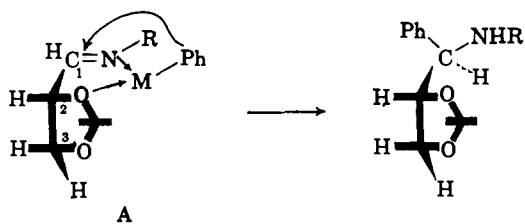
(8) (a) D. J. Cram and K. R. Kopecky, *J. Am. Chem. Soc.*, **81**, 2737 (1959); (b) D. J. Cram and D. R. Wilson, *ibid.*, **85**, 1245 (1963).



Cram's model; L, large group; S, small group; M, metal

Acetone-D-glyceraldimine may be regarded as the same substrate as  $\alpha$ -alkyloxycarbonyl compounds with respect to the addition reaction with organometallic reagents and, therefore, the reaction with acetone-D-glyceraldimine is considered to proceed through the same reaction mechanism.

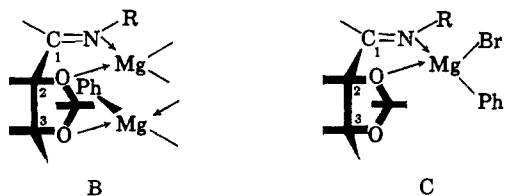
If the above mechanism is applied to acetone-D-glyceraldimine, the *threo* compound must be the predominant product not only in the phenyllithium reaction but also in the Grignard reaction. The results



obtained in the phenyllithium reaction may be interpreted by means of this mechanism. However, the prediction by the mechanism is incompatible with our results in the Grignard reaction. In spite of this inconsistency, the chelate bridge formation between N and O as shown in structure A may be supported by the generally accepted fact that magnesium has a strong affinity for these atoms. Thus, the cause for the inconsistency must be sought in the differences between the substrates studied by Cram and those studied here.

In consequence, attention must be directed to the oxygen atom on C<sub>3</sub>. To give the *erythro* product it is necessary that the phenyl group be located under the plane made by N, C<sub>1</sub>, C<sub>2</sub>, O, and Mg in the transition state.

Two mechanisms can be considered from different kinds of interaction between the C<sub>3</sub>-oxygen atom and the reagent: one is attractive and the other is repulsive. The former is one in which coordination of a magnesium atom other than the bridge magnesium causes the phenyl group to appear under the plane (B). The latter is one in which the halogen atom of the reagent appears over the plane because of repulsion by the C<sub>3</sub>-oxygen atom (C).



Schlenk<sup>9</sup> postulated the Grignard reagent as an equilibrium mixture of R<sub>2</sub>Mg, MgX<sub>2</sub>, and RMgX from the fact that the dioxanate of MgX<sub>2</sub> was precipitated on addition of dioxane to the Grignard solution. Recently, the postulate by Schlenk was strengthened by

(9) W. Schlenk and W. Schlenk, *Ber.*, **63**, 920 (1929).

physicochemical data<sup>10</sup> in the liquid state. On the other hand, the structure of a crystalline Grignard reagent was formulated as RMgX·2Et<sub>2</sub>O by Stucky and Rundle<sup>11</sup> from X-ray diffraction data. It is therefore apparent that the true nature of the Grignard reagent in solution is as yet obscure.

### Experimental

**General Procedure for the Reaction of  $\alpha$ -Aminonitriles or Schiff Bases with Organometallic Reagents.**—To an ether solution of phenyllithium or phenylmagnesium bromide, prepared from 0.06 mole of bromobenzene and 0.12 mole of lithium metal or 0.06 mole of magnesium metal, was added 0.02 mole of aminonitrile or Schiff base with stirring at 0 to 5°. The mixture was refluxed for about 10 hr. with stirring, and then cautiously poured into ice-water covered with 100 ml. of ether. The water layer was separated from the ether layer and twice extracted with 50-ml. portions of ether. The combined ether solution was washed with water, dried, and concentrated *in vacuo* to a sirup. The sirup was subjected to hydrolysis with 6 N hydrochloric acid (20 ml.) at 100° for 2 hr. After removal of the residue insoluble in hydrochloric acid by filtration through activated carbon, the filtrate was decolorized with activated carbon and then extracted four times with 50-ml. portions of ethyl acetate after adjustment of the pH to about 10 with sodium hydroxide solution. The combined ethyl acetate solution was washed twice with 50-ml. portions of water and dried with anhydrous sodium sulfate.

Upon concentration of the ethyl acetate solution to dryness under reduced pressure, a diastereomeric mixture of the crude 1-C-phenyl-1-alkylamino-1-deoxy-D-glyceritol crystallized. The specific rotation of the mixture was measured. The mixture was fractionally crystallized from ethanol or ethanol-acetone to isolate the two pure diastereomers. In general, the predominant diastereomer appears first and a small amount of the other diastereomer is obtained after repeated separation of the predominant diastereomer.

The physical constants and analytical values of 1-C-phenyl-1-alkylamino-1-deoxy-D-glyceritols are listed in Table II. From the specific rotation values of the diastereomeric mixture, the percentage of each diastereomer in the crude mixture was calculated (see Tables III and IV).

**N-Phenylacetone-D-glyceraldimine (I-S).**—To a benzene solution of acetone-D-glyceraldehyde (20 g.) was added aniline (14.3 g.). The solution became turbid after about 10 min. and was allowed to stand for 2 hr. The reaction mixture was concentrated *in vacuo* at 30–40° to give a pale yellow sirup (30.5 g.). The infrared spectrum of the sirup contained an absorption band at 1655 cm.<sup>-1</sup> corresponding to C=N absorption<sup>8</sup> but no marked absorption in the —NH— region; specific rotation of the sirup (in ethanol, *c* 1): [ $\alpha$ ]<sub>D</sub> +11° 3.5 hr. after its preparation, +7° after 48 hr., 0° after 20 days. The optically inactive sirup gave infrared absorption bands at 3380 and 1655 cm.<sup>-1</sup> corresponding to —NH— and C=N absorption, respectively.

Crystals appeared in the sirup on standing. Washing them with isopropyl ether gave fine colorless needles, m.p. 163–164°. The infrared spectrum of the crystals contained an absorption band at 3380 cm.<sup>-1</sup> but no absorption in the 1620–1800 cm.<sup>-1</sup> region, showing the presence of the —NH— group but the absence of the C=N group.

*Anal.* Calcd. for C<sub>12</sub>H<sub>16</sub>NO<sub>2</sub>: C, 70.22; H, 7.37; N, 6.82. Found: C, 69.56; H, 7.03; N, 6.92.

**N-Benzylacetone-D-glyceraldimine (II-S).**—Benzylamine (16.5 g.) was added to a benzene solution of acetone-D-glyceraldehyde (20 g.). The same procedure as that used for I-S gave a pale yellow sirup (30.5 g.). The infrared spectrum contained the absorption band of C=N<sup>8</sup> (at 1670 cm.<sup>-1</sup>) but no marked absorption in the —NH— region (3200–3500 cm.<sup>-1</sup>). The initial specific rotation of the sirup (in ethanol, *c* 1) was [ $\alpha$ ]<sub>D</sub> +23°, which gradually dropped to zero: +23° within 10 hr., +3° in 15 days, and 0° in 40 days. The optically inactive sirup had an absorption at 1680 cm.<sup>-1</sup> and weak absorption (broad) in the 3300–3400 cm.<sup>-1</sup> region, corresponding to a C=N and an —NH— group. When a carbon tetrachloride solution of the sirup was left at room temperature, a small amount of fine colorless needles appeared which had an absorption at 3400 but no absorption at 1680 cm.<sup>-1</sup>.

(10) (a) R. E. Dessy, *J. Org. Chem.*, **25**, 2260 (1960); (b) J. H. Wotiz, C. A. Hollingsworth, and R. E. Dessy, *ibid.*, **21**, 1063 (1956).(11) G. D. Stucky and R. E. Rundle, *J. Am. Chem. Soc.*, **85**, 1002 (1963).

**1-C-Phenyl-1-amino-1-deoxy-threo-D-glyceritol Hydrochloride.**—A suspension of 10 g. of  $\text{PbO-BaSO}_4$  in 50 ml. of water was hydrogenated and then mixed with 50 ml. of 2 *N* hydrochloric acid and 12 g. of compound II-T produced from II-T and phenyllithium, and then hydrogenated with shaking. When the absorption of hydrogen reached 1115 ml. (at 15°), hydrogenation was stopped. The catalyst was removed by filtration through activated carbon and the filtrate was concentrated under reduced pressure at 40–50° to give crystals which were recrystallized from ethanol (m.p. 175–180°). Further recrystallization gave 5.6 g. of colorless needles, m.p. 178–179.5°,  $[\alpha]_D - 10^\circ$  (*c* 1, water).

*Anal.* Calcd. for  $\text{C}_9\text{H}_{14}\text{ClNO}_2$ : C, 53.02; H, 6.93; N, 6.87. Found: C, 53.18; H, 6.65; N, 7.10.

**1-C-phenyl-1-acetylamino-1-deoxy-threo-D-glyceritol.**—To a cold solution of 5.4 g. of 1-C-phenyl-1-amino-1-deoxy-threo-D-glyceritol hydrochloride was added methanolic sodium methylate (prepared from 0.16 g. of sodium and 30 ml. of methanol) and 2.7 g. of acetic anhydride with cooling. The reaction mixture was set aside for 2 days at room temperature. Crystals obtained by concentrating the reaction mixture under reduced pressure were extracted with hot ethyl acetate. From the ethyl acetate solution, after standing at room temperature, 2.5 g. of colorless needles separated (m.p. 125–127°), and another gram of the same substance was obtained from the mother liquor;  $[\alpha]_D - 86^\circ$  (*c* 0.92, ethanol),  $R_f$  0.73 (1-butanol saturated with water).

*Anal.* Calcd. for  $\text{C}_{11}\text{H}_{16}\text{NO}_2$ : C, 63.14; H, 7.23; N, 6.69. Found: C, 62.92; H, 7.41; N, 6.82.

**N-Acetyl-D-phenylglycinaldehyde.**—To a suspension of 1-C-phenyl-1-acetylamino-1-deoxy-threo-D-glyceritol (3.1 g.) in benzene (250 ml.) was added 6.6 g. of lead tetraacetate with stirring. When 10 ml. of acetic acid was added to the mixture, a brown

precipitate appeared whose color disappeared after 2.5 hr. The precipitate was filtered and a sirup was obtained by concentration of the filtrate. The sirup gave only one spot of  $R_f$  0.846, different from that of the raw material ( $R_f$  0.73), on the paper chromatogram developed with 1-butanol saturated with water;  $[\alpha]_D - 25.4^\circ$  (*c* 1.06, benzene).

**N-Acetyl-D-(–)-phenylglycine.**—A mixture of N-acetyl-D-phenylglycinaldehyde (2.62 g.), acetic acid (45 ml.), water (10 ml.), and bromine (0.8 ml.) was stirred at room temperature for 3 hr. After removal of bromine by aeration, the reaction mixture was extracted with a benzene-ethyl acetate mixture. The extract was shown to contain the raw material by its ability to reduce Tollens reagent. The extract (1.5 g.) was reoxidized for 8 hr. by bromine in 60% aqueous acetic acid (120 ml.) in the presence of sodium acetate (3 g.). After aeration, the reaction mixture was extracted with 270 ml. of ethyl acetate, and the ethyl acetate solution was concentrated to a sirup (1.1 g). The hot water extract from the sirup was stirred with 70 ml. of cation exchange resin (IR 120) for 5 min. to remove sodium ion. After removal of the resin, the water solution (300 ml.) was concentrated to give crystals. The crystals were dissolved in hot water and, after standing at room temperature, there appeared a small amount of precipitate which had no optical activity. Colorless needles obtained by concentration of the mother liquor had the following physical constants which agreed with those of N-acetyl-D-(–)-phenylglycine:<sup>6</sup> m.p. 189–191°,  $[\alpha]_D - 140^\circ$  (*c* 0.5, water).

**Acknowledgment.**—The authors are indebted to the members of the Laboratory of Organic Analysis, Tokyo Institute of Technology, for the microanalyses.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, OKLAHOMA STATE UNIVERSITY, STILLWATER, OKLA.]

## The Reactions of Aroyl Halides with Phosphites. Esters of Aroylphosphonic Acids<sup>1,2</sup>

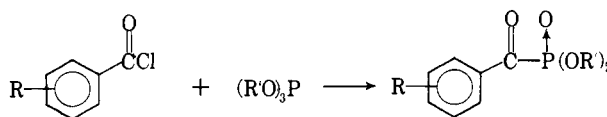
BY K. DARRELL BERLIN AND H. ANNETTE TAYLOR<sup>3</sup>

RECEIVED MARCH 2, 1964

Esters of aroylphosphonic acids were conveniently synthesized by treatment of phosphites with aroyl chlorides *via* a Michaelis-Arbuzov rearrangement. Infrared and proton magnetic resonance spectral analyses were recorded for all esters and support the proposed structures. Dipole moment measurements and n.m.r. data indicate no preferred conformation for dimethyl benzoylphosphonate, dimethyl *p*-anisoylphosphonate, and dimethyl (*p*-chlorobenzoyl)phosphonate. Carbon-phosphorus bond cleavage in the esters is effected by dilute acid or base, although the reaction is much faster with the latter. Mechanisms are presented for the cleavage processes.

The Michaelis-Arbuzov rearrangement as applied to acyl halides has been largely restricted to phosgene,<sup>4,5</sup> chloroformates,<sup>6</sup> acid halides of fatty acids,<sup>7</sup> acid halides of a few dibasic aliphatic acids,<sup>8</sup> carbamoyl chlorides,<sup>9,10</sup> acetyl chloride,<sup>11,12</sup> and benzoyl chloride.<sup>11,12</sup> We

have synthesized a series of disubstituted aroylphosphonates in order to observe the effects of different substituents on the ring and variations in the phosphorus ester groups on the course of the reaction (Table I). The esters obtained (Ia-i) were pale yellow, high-boiling, viscous liquids which were extremely sensitive to moisture and decomposed readily to benzoic acid derivatives and dialkyl hydrogen phosphonates. The reactions are very exothermic and proceed rapidly at room temperature to give homogeneous solutions. Alkyl halides formed *in situ* usually distilled from the reaction flask or were removed by the nitrogen stream used to main-



- Ia, R = H, R' = CH<sub>3</sub>  
 b, R = *p*-OCH<sub>3</sub>, R' = CH<sub>3</sub>  
 c, R = *p*-OCH<sub>3</sub>, R' = C<sub>2</sub>H<sub>5</sub>  
 d, R = *p*-OCH<sub>3</sub>, R' = *i*-C<sub>3</sub>H<sub>7</sub>  
 e, R = *p*-OCH<sub>3</sub>, R' = C<sub>6</sub>H<sub>5</sub>  
 f, R = *p*-OCH<sub>3</sub>, R' = CH<sub>2</sub>CH=CH<sub>2</sub>  
 g, R = *p*-Cl, R' = CH<sub>3</sub>  
 h, R = *o*-Cl, R' = CH<sub>3</sub>  
 i, R = *p*-(CH<sub>3</sub>)<sub>3</sub>C, R' = CH<sub>3</sub>

(1) We gratefully acknowledge support by the National Institutes of Health, GM 10367-01. Partial support by the Research Foundation of the Oklahoma State University is also acknowledged.

(2) Presented in part at the Oklahoma Tetrasectional Meeting of the American Chemical Society, Ponca City, Okla., March, 1964.

(3) Abstracted in part from the thesis of H. A. Taylor submitted in partial fulfillment of the requirements for the Master of Science degree at Oklahoma State University, May, 1964.

(4) M. I. Kabachnik and P. A. Rossiiskaya, *Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk*, 48 (1957); *Chem. Abstr.*, **51**, 10,366 (1957).

(5) A. N. Pudovik and R. N. Platonova, *Zh. Obshch. Khim.*, **29**, 507 (1959); *Chem. Abstr.*, **54**, 254 (1960).

(6) A. E. Arbuzov and A. A. Dunin, *J. Russ. Phys. Chem. Soc.*, **46**, 295 (1914); *Chem. Abstr.*, **8**, 2551 (1914).

(7) B. Ackerman, T. A. Jordan, C. R. Eddy, and D. Swern, *J. Am. Chem. Soc.*, **78**, 4444 (1956).

(8) R. D. Moss, U. S. Patent 3,012,054 (1961); *Chem. Abstr.*, **57**, 4698 (1962).

(9) B. A. Arbuzov and N. I. Rizpolozhenskii, *Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk*, 847 (1952); *Chem. Abstr.*, **47**, 10,457 (1953).

(10) B. A. Arbuzov and N. I. Rizpolozhenskii, *Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk*, 854 (1952); *Chem. Abstr.*, **47**, 9903 (1953).

(11) M. I. Kabachnik and P. A. Rossiiskaya, *Bull. Acad. Sci. U.S.S.R., Classe Sci. Chim.*, 364 (1945); *Chem. Abstr.*, **40**, 4688 (1946).

(12) M. I. Kabachnik and P. A. Rossiiskaya, *ibid.*, 597 (1945); *Chem. Abstr.*, **41**, 88 (1947).