phere before its rotation was determined. A 0.05% solution in 0.01 *N* HNO_3 containing a trace of ceric ammonium nitrate gave α_{5461} + 0.13°, whence $[\alpha]^{15}_{5461}$ + 260° and $[M]^{15}_{5461}$ +2400°. The rotation in the NaD line was slightly dextro. The degree of hydration of the substance was variable owing to the use of a strong desiccant.

Anal. Calcd. for $Fe(C_{10}H_8N_2)_3(ClO_4)_3{\cdot}3H_2O$: Fe, 6.37; N, 9.59. Found: Fe, 6.28; N, 9.50.

l-Tris-2,2′-dipyridyl Iron(III) Perchlorate Trihydrate.—This was obtained in the same manner as the dextro compound, using instead *l*-tris-2,2′-dipyridyl ferrous perchlorate as a microcrystalline powder. A 0.05% solution in the same medium as above gave α_{5461} − 0.13°, whence $[\alpha]^{15}_{5461}$ −260°.

Anal. Calcd. for $Fe(C_{10}H_8N_2)_3{\cdot}(ClO_4)_3{\cdot}3H_2O$: Fe, 6.37; N, 9.59. Found: Fe, 6.40; N, 9.63.

***dl*-Tris-1,10-phenanthroline Osmium(III) Chloride Monohydrate.**—*dl*-Tris-1,10-phenanthroline osmium(II) chloride octahydrate (0.2 g.) in methanol (10 ml.) at 0°, was treated with chlorine gas until the dark brown solution became bluish-red. The osmic complex was immediately precipitated with ether, and the precipitate washed first with 50% methanol ether and then ether.

The dark red micro needles were very soluble in water giving a brilliant bluish-red solution which rapidly turned brown due to reduction. The substance was more stable in the solid state.

Anal. Calcd. for $Os(C_{12}H_8N_2)_3{\cdot}Cl_3{\cdot}H_2O$: Os, 22.24; N, 9.83. Found: Os, 22.1; N, 9.9.

***dl*-Tris-1,10-phenanthroline Osmium(III) Perchlorate Monohydrate.**—*dl*-Tris-1,10-phenanthroline osmium(II) perchlorate dihydrate (0.5 g.) was suspended in 20 ml. of water, cooled to 0° and treated with chlorine until the substance went into solution. The deep reddish-blue solution was warmed to 20°, 10% sodium perchlorate was added until the solution became cloudy and then precipitation was brought about by cooling the mixture on ice and by scratching the sides of the vessel. The precipitate was filtered through a sintered glass filter, washed quickly first with cold absolute alcohol, then with ether and dried in warm air.

The monoclinic prisms were dark red with a grayish-blue reflex. The aqueous solutions rapidly underwent self reduction except in the presence of chlorine or acid.

Anal. Calcd. for $Os(C_{12}H_8N_2)_3(ClO_4)_3{\cdot}H_2O$: Os, 18.17; N, 8.03. Found: Os, 18.3; N, 8.1.

***d*-Tris-1,10-Phenanthroline Osmium(III) Perchlorate Monohydrate.**—*d*-Tris-1,10-phenanthroline osmium(II) perchlorate was treated as the *dl*-perchlorate above. The bluish-red prisms of the active perchlorate were more soluble than the racemate. A 0.01% solution in water containing a trace of chlorine gave α = +0.04°, whence $[\alpha]^{20}_{5461}$ +400°, and $[M]^{20}_{5461}$ +4200°. No rotation was observed in the NaD line.

Anal. Calcd. for $Os(C_{12}H_8N_2)_3(ClO_4)_3{\cdot}H_2O$: Os, 18.17; N, 8.03. Found: Os, 18.3; N, 8.10.

***l*-Tris-1,10-Phenanthroline Osmium(III) Perchlorate Monohydrate.**—The bluish-red prisms of this substance were prepared from *l*-tris-1,10-phenanthroline osmous perchlorate in the same manner as the *dl*-compound. A 0.01% solution in water containing chlorine gave α −0.04°, whence $[\alpha]^{20}_{5461}$ −400°.

Anal. Calcd. for $Os(C_{12}H_8N_2)_3(ClO_4)_3{\cdot}H_2O$: Os, 18.17; N, 8.03. Found: Os, 18.1; N, 8.0.

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NOTES

Preparation of Alkyl Isocyanates Using Alkyl Phosphates

BY THEODORE I. BIEBER[1]

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Isocyanic esters are generally prepared by the phosgenation of primary amines or by the Curtius rearrangement of acyl azides, but the alkylation of an inorganic cyanate constitutes a convenient method in some cases. Ethyl isocyanate may thus be prepared by the reaction of potassium cyanate with potassium ethyl sulfate,[2] ethyl sulfate[3] or ethyl *p*-toluenesulfonate.[3] A satisfactory yield is obtainable only with ethyl sulfate as the ethylating agent. However, the resulting ethyl isocyanate has been observed by us to polymerize very readily, even after several redistillations. It appears likely that this polymerization is catalyzed by sulfur dioxide, a known decomposition product of ethyl sulfate at the alkylation temperature used, and that distillation does not achieve the complete separation of this gas from the low-boiling ethyl isocyanate.

We have found that triethyl phosphate, a readily available substance, is capable of ethylating potassium cyanate at about 200°, affording ethyl isocyanate in good yield. The product so obtained does not polymerize on standing. It should be pointed out that triethyl phosphate is stable at its boiling point (216°), whereas ethyl sulfate boils with considerable decomposition (208°). The reaction of ethyl sulfate with potassium cyanate is rather violent and requires a moderator, like sodium carbonate[3]; the analogous reaction of triethyl phosphate, however, is smooth and unlikely to get out of control. The fact that triethyl phosphate, in contrast to ethyl sulfate, has no corroding action and is safe to handle, also deserves mention.

The ratio of phosphoric ester to potassium cyanate employed in this reaction is considerably greater than one (on a molar basis), so that the principal reaction leading to ethyl isocyanate must be

$$(C_2H_5O)_3PO + KNCO \longrightarrow (C_2H_5O)_2PO_2K + C_2H_5NCO$$

only one ethyl group of triethyl phosphate being utilized. The use of triethyl phosphate in limited amount gives unsatisfactory results.

Butyl isocyanate was similarly prepared, but in smaller yield, by the reaction of potassium cyanate with tributyl phosphate. Butyl isocyanate has previously been obtained by the Curtius rearrangement of valeryl azide but was not separated from

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[1] Address correspondence concerning this paper to the author at 80-40 Lefferts Blvd., Kew Gardens 15, N. Y.

[2] A. Wurtz, *Compt. rend.*, **27**, 241 (1848); *Ann. chim.*, [3] **42**, 43 (1854).

[3] K. H. Slotta and L. Lorenz, *Ber.*, **58**, 1320 (1925).

the toluene used as solvent in the azide decomposition.[4a] The preparation of pure butyl isocyanate by the phosgenation of butylamine has been reported only recently.[5]

Experimental

Ethyl Isocyanate.—In a 500-ml. distilling flask were placed 98 g. of triethyl phosphate and 30 g. of potassium cyanate (along with a few glass beads). Potassium cyanate does not dissolve appreciably in triethyl phosphate, even at higher temperatures. The mixture was strongly heated until distillation occurred. For the next ten minutes heat was applied on and off to maintain distillation at a fairly even rate. The reaction mixture became quite viscous by the end of this time and heating was discontinued when strong white fumes due to the condensation of water vapor started to appear, the water being a result of decomposition within the viscous mass. A parallel experiment had shown that when these fumes were allowed to distil, water droplets appeared in the distillate and caused the evolution of carbon dioxide from the latter (hydrolysis of ethyl isocyanate). The viscous residue in the distilling flask set to a gel on cooling. It consisted chiefly of potassium diethyl phosphate along with some triethyl phosphate.

The distillate, a mixture of ethyl isocyanate and triethyl phosphate, was subjected to distillation, and 16.5 g. of ethyl isocyanate (a 63% yield based on potassium cyanate) was collected at 60–63°. The high-boiling liquid residue from the distillation was triethyl phosphate (16.3 g.).

An experiment employing a smaller relative amount of triethyl phosphate than used above gave a less satisfactory result, since the reaction mixture became viscous and gave rise to water vapor before much product had been collected.

Butyl Isocyanate.—The procedure is very similar to that used for ethyl isocyanate. There were employed 73 g. of tributyl phosphate and 20 g. of potassium cyanate. In this case also, when heating of the reaction mixture was continued after it had become viscous, decomposition with formation of water vapor occurred. The reaction was therefore stopped at this stage. The residue in the distilling flask, consisting chiefly of potassium dibutyl phosphate, solidified on cooling. The distillate contained butyl isocyanate and tributyl phosphate, separable by fractional distillation. After three distillations 7 g. of butyl isocyanate (a 29% yield based on potassium cyanate) boiling at 115–117° was obtained; reported b.p. 113–116°.[5]

Reaction of the butyl isocyanate prepared in this manner with *p*-toluidine in benzene solution yielded 1-butyl-3-(*p*-tolyl)-urea in very good yield, m.p. 118° after recrystallization from an alcohol-water mixture; reported m.p. 119°.[4b]

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(4) (a) J. W. Boehmer, *Rec. trav. chim.*, **55**, 382 (1936); (b) **55**, 386 (1936).

(5) W. Siefken and A. Doser, U. S. Patent 2,326,501 (1943); R. J. Slocombe, E. E. Hardy, J. H. Saunders and R. L. Jenkins, This Journal, **72**, 1890 (1950).

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Optical Enantiomorphs of Isovaline

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A levorotatory isomer ($[\alpha]^{20}\mathrm{D}$ −9.10° in H_2O) was isolated by Ehrlich and Wendel[1] from the yeast fermentation of racemic isovaline (I). Fischer and

$$(C_2H_5)(CH_3)C(NH_2)COOH$$
I

von Grävenitz prepared the dextrorotatory isomer ($[\alpha]^{19}\mathrm{D}$ + 11.0° in water) from the formyl compound with brucine.[1a] They did not prepare the enantiomorph. Because of this lack of concordance, there exists some uncertainty in regard to the rotation value of the isolated isomers and to their optical configuration. For these reasons, racemic isovaline was resolved into its optical enantiomorphs by the general enzymatic procedure developed in this Laboratory.[2–7] This procedure essentially depends upon the asymmetric enzymatic hydrolysis of the N-acylated derivative of the racemic amino acid, followed by the separation of the resulting L-amino acid and acyl-D-amino acid in different solvents.

Two special problems arose in the application of this procedure to the resolution of isovaline. The first of these was whether the N-acylated derivative of an amino acid which lacked a hydrogen atom on the α-carbon atom would be susceptible to the action of hog kidney acylase I.[4] N-Chloroacetyl-DL-isovaline was prepared, and found to be asymmetrically hydrolyzed at the L-isomer at a rate which, although considerably lower than that observed with either chloroacetyl-DL-valine or chloroacetyl-DL-norvaline,[4] was sufficient to serve the present purpose. The second problem was to isolate the extremely soluble L-isovaline from the resolution mixture at the end of the enzymatic reaction. This was solved by the employment of a chromatographic procedure involving a cationic exchange resin.

By these means no difficulty was encountered in preparing L-isovaline ($[\alpha]^{25}\mathrm{D}$ +11.13°) and D-isovaline ($[\alpha]^{25}_{\mathrm{D}}$ −11.28°) in satisfactory yield. It would have been expected that the levorotatory isomer isolated by Ehrlich and Wendel from the fermentation mixture was D-isovaline, and our results are in accord with this assignment of configuration. The fact that our rotation values are higher in magnitude than that reported by Ehrlich and Wendel is not surprising in view of the difficulties which they encountered in their isolation and purification procedures. Our values are in good agreement with that obtained for the dextrorotatory isomer by Fischer and von Grävenitz.[1a]

Experimental Part

N-Chloroacetyl-DL-isovaline.—DL-Isovaline[8] was treated with chloroacetyl chloride and chilled NaOH in the usual manner. On acidification with concd. HCl to *p*H 1.7, N-chloroacetyl-DL-isovaline crystallized in 82% yield. It was recrystallized from water; m.p. 161.5–163.0° (cor.). A m.p. of 162° has been reported for this compound.[9]

Anal.[10] Calcd. for $C_7H_{12}O_3NCl$: C, 43.4; H, 6.3; N, 7.2; Cl, 18.3. Found: C, 43.4; H, 6.4; N, 7.2; Cl, 18.2.

Enzymatic Resolution of Chloroacetyl-DL-isovaline.—Fifty-three grams of N-chloroacetyl-DL-isovaline was dissolved in 2 liters of water and the solution brought to *p*H 7.5 with 2 *N* LiOH. Three grams of acylase I powder[4] was dissolved in the solution, and water added to bring the concentration of the racemic compound to 0.1 *M*. The enzymatic hydrolysis of the substrate could not be followed by the usual manometric ninhydrin procedure, because the

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(1) F. Ehrlich and A. Wendel, *Biochem. Z.*, **8**, 438 (1908).

(1a) E. Fischer and von Grävenitz, *Ann.*, **406**, 5 (1914).

(2) J. P. Greenstein, L. Levintow, C. G. Baker and J. White, *J. Biol. Chem.*, **188**, 647 (1951).

(3) L. Levintow and J. P. Greenstein, *ibid.*, **188**, 643 (1951).

(4) S. M. Birnbaum, L. Levintow, R. B. Kingsley and J. P. Greenstein, *ibid.*, **194**, 455 (1952).

(5) D. Rudman, A. Meister and J. P. Greenstein, This Journal, **74**, 551 (1952).

(6) D. Hamer and J. P. Greenstein, *J. Biol. Chem.*, **193**, 81 (1951).

(7) S. M. Birnbaum and J. P. Greenstein, *Archiv. Biochem. Biophys.*, **39**, 108 (1952).

(8) P. A. Levene and R. Steiger, *J. Biol. Chem.*, **76**, 299 (1928).

(9) K. W. Rosenmund, *Ber.*, **42**, 4473 (1909).

(10) Analyses by R. J. Koegel and staff of this Laboratory.