with standard taper ground glass joints, to which were attached a stirrer, a reflux condenser and Dean–Stark moisture trap. The flask was charged with a mixture consisting of one mole of glyoxal (193 g. of 30% aqueous solution), 2.4 moles of the diol, 1% of *p*-toluenesulfonic acid monohydrate (based on the total weight of diol and monomeric glyoxal) and 160 ml. of redistilled toluene. The heterogeneous mixture was agitated by means of an efficient stirrer and heated to its boiling point, using a Glas-Col heating mantle. For qualitative comparisons of reaction time, the reaction was assumed to start when the first drop of water appeared in the moisture trap and to be concluded when the rate of evolution of water was less than 1–2 ml. per hour. The course of the reaction was checked at intervals by determination of the refractive index of the toluene insoluble phase of the separated distillate, since toward the end of the reaction, this distillate consists essentially of unchanged diol. Further evidence of the progress of the reaction is the gradual increase in reaction temperature from around 87° (a little above the boiling point of the toluene-water azeotrope) to about 120–125° (varying somewhat with the diol used). Disappearance of the second liquid phase is further evidence of completion of the reaction.

The toluene solution was now cooled and washed with dilute sodium bicarbonate solution until free from acid, then with water. The combined washings were extracted with toluene or with chloroform to recover appreciable quantities of acetal which otherwise would be lost. After drying over anhydrous potassium carbonate or calcium chloride, the solvents were removed by distillation and the products, unless polymeric, were purified by vacuum distillation. Final purification involved several crystallizations, in case of solids, and redistillation of liquids.

Reaction times, yield data, properties and analytical data of the products obtained are given in Table II. Of the cyclic acetals prepared during this work, only glyoxal-bis-ethylene acetal has been described previously.

Discussion of Table II

In those cases which are uncomplicated by polymer formation, the relative ease of reaction with glyoxal of the diols studied is in the order: tertiary > secondary > primary. (Compare particularly pinacol, 2,3-butylene glycol and ethylene glycol.) The speed of the reaction increases also with the number of carbon atoms between the two hydroxyl groups (for example, in the cases of ethylene and trimethylene glycols). These relations are obscured when insoluble polymeric acetals are formed.

Boiling points of the cyclic bis-acetals, extrapolated to 760 mm. pressure by means of standard boiling point *vs.* pressure charts,[6] are in general 50–75° higher than that of the parent diol, except in the case of glyoxal-bis-ethylene acetal, where the difference is only about 20°. Solubilities of the bis-acetals are roughly determined by the number of alkyl substituents, and the length of the carbon chain between oxygen atoms. Thus, all those reported in this paper are appreciably soluble in water except those derived from pinacol, 2,5-hexanediol and 11,12-dihydroxytetracosane. On the contrary, they are all readily soluble in *n*-heptane except those derived from ethylene, trimethylene and 1,3-butylene glycols.

Acknowledgment.—We wish to thank Mr. L. B. Bronk and Miss M. Caldwell of this Laboratory for carrying out the carbon and hydrogen analyses and for some of the molecular weight determinations.

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[6] C. Bordenca, *Ind. Eng. Chem., Anal. Ed.*, **18**, 99 (1946).

Action of Sodium Cyanide on β-Hydroxypropionitrile and β-Hydroxypropionic Acid

BY LIU-SHENG TS'AI

In the study of exchange of β-hydroxypropionitrile with cyanide labeled with C^{14}, Ts'ai and Kamen[1] found that under alkaline conditions the cyanide, precipitated as silver cyanide after exchange, showed a drop in activity to such an extent that one could calculate a 9.2% randomization of cyanide and nitrile. The recovery of activity in the separated nitrile, however, was 10-fold too high for the amount of specific activity loss observed by the cyanide. This leads one to suspect that one possible explanation of the discrepancy would be by the reaction of cyanide with nitrile. Further investigation on this matter revealed that this is the case, and the results are reported in the present communication. The final product of the reaction was found to be succinic acid. This result is particularly interesting, since it probably involves a replacement of hydroxy group by a cyanide group which was subsequently hydrolyzed to acid.

It is also possible that β-hydroxypropionitrile under alkaline conditions first hydrolyzes to acid, and the resulting hydroxy acid then reacts with the cyanide. Experiment with β-hydroxypropionic acid and cyanide also gave succinic acid although the yield was not as good as that with β-hydroxypropionitrile. Under the present experimental conditions, it is difficult to decide whether it is the β-hydroxypropionitrile or the β-hydroxypropionic acid that actually reacts with the cyanide.

However the referee of this note has kindly suggested that in his opinion the reaction proceeds step-wise, first by elimination of water to yield acrylonitrile, which is then converted to succinonitrile, which in turn is hydrolyzed to the acid. He supports the first step by the work of Davis and Carpenter[2] who have demonstrated the dehydration of β-hydroxypropionitrile by $Ca(OH)_2$.

Still another possibility is that the sodium cyanide may be hydrolyzed to sodium formate. The formate may then react with the nitrile or the hydrolyzed acid. Separate experiments with sodium formate and β-hydroxypropionitrile and with sodium formate and β-hydroxypropionic acid, however, all gave negative results, thus proving that the formate is not responsible for the replacement reaction.

Experimental

Reaction of β-Hydroxypropionitrile with Sodium Cyanide.—A large test-tube containing 2.66 g. of β-hydroxypropionitrile, 8.82 g. of sodium cyanide and 15 ml. of water was held in a beaker of briskly boiling water for four hours. After cooling, 3 g. of sodium hydroxide was added and the nitrile hydrolyzed.[3] The combined ether extracts (seven extractions) gave a solid product of 0.98 g. (22.2%). This product after two recrystallizations had an acid equivalent of 59.07 g. and melted at 181–182° (m.p. of pure succinic acid simultaneously determined was 182–183°).

Anal. Calcd. for $C_4H_6O_4$: C, 40.68; H, 5.08. Found: C, 40.65; H, 5.14.

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[1] L. S. Ts'ai and M. D. Kamen, *J. Chem. Phys.*, **17**, 585 (1949).

[2] H. S. Davis and E. L. Carpenter, Canadian Patent 435,687; *C. A.*, **40**, 7230 (1946).

[3] "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1947, p. 321.

Reaction of β-Hydroxypropionic Acid and Sodium Cyanide.—The procedure in this experiment was identical with that described above for β-hydroxypropionitrile. β-Hydroxypropionic acid was first prepared by hydrolyzing the corresponding nitrile,[2] and the acid obtained was used without further purification. The amounts of β-hydroxypropionic acid, sodium cyanide and water used were 2.65 g., 8.62 g. and 15 ml., respectively. The succinic acid obtained in this case weighed 0.51 g. (14.9%) and gave m.p. of 181–182°.

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DEPARTMENT OF CHEMISTRY
YENCHING UNIVERSITY
PEKING, CHINA

RECEIVED OCTOBER 9, 1950

NEW COMPOUNDS

p-(2-Ethylhexoxy)-benzoic Acid

A mixture of 42 g. (0.2 mole) of 2-ethylhexyl bromide,[1] 28 g. (0.2 mole) of *p*-hydroxybenzoic acid, 22 g. (0.4 mole) of potassium hydroxide, 150 cc. of alcohol and 50 cc. of water was refluxed for 24 hours (two layers). In order to hydrolyze any ester which may still have been present, some 10% aqueous potassium hydroxide solution was added and the mass refluxed for another 30 minutes. Acidification gave an oily product which was isolated and distilled first under 35 mm. pressure (245°), then under 0.5 mm. (180°). The acid solidified easily and crystallized from a large amount of 80% formic acid in soft, white leaflets, which are converted at 60–61° into "liquid crystals," in analogy to the behavior of *p*-butoxybenzoic acid.[2]

Anal. Calcd. for $C_{15}H_{22}O_3$: C, 72.0; H, 8.8; mol. wt., 250. Found: C, 72.4; H, 9.1; mol. wt., 255 (titration).

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[1] Ch. Weizmann, E. Bergmann and L. Haskelberg, *Chem. and Ind.*, **56**, 1587 (1937).

[2] Bradfield and Jones, *J. Chem. Soc.*, 2660 (1929).

WEIZMANN INSTITUTE OF SCIENCE
REHOVOTH, ISRAEL S. PINCHAS

RECEIVED SEPTEMBER 1, 1950

2-Chlorophenyl-1-naphthylcarbinol[1]

2-Chlorophenyl-1-naphthylcarbinol.—A Grignard reagent was prepared from 11.6 g. of magnesium, 100 ml. of α-bromonaphthalene and 300 ml. of dry ether. When the reaction was complete, a solution of 55.3 g. of *o*-chlorobenzaldehyde in 300 ml. of dry ether was added dropwise with stirring. The mixture was stirred overnight at room temperature and then heated under reflux for one hour, cooled, and finally decomposed with 75 ml. of cold, 20% ammonium chloride solution. The ethereal solution was decanted from the hard residue and the residue was washed twice with ether. The combined ether solutions were washed with water, dried over "Drierite," and finally concentrated. The residue was fractionated under reduced pressure and the fraction distilling at 215–216° (4 mm.) was collected; yield 89.5 g. (85%).

A small portion of the above viscous oil was crystallized three times from dilute ethanol to give soft white needles; m.p. 96–97°.

Anal. Calcd. for $C_{17}H_{13}OCl$: C, 75.98; H, 4.88. Found: C, 76.16; H, 4.91.

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[1] This compound is a previously unisolated intermediate in the synthesis of 1-(*o*-chlorobenzyl)-naphthalene by the method of Bradsher, THIS JOURNAL, **62**, 1077 (1940).

DEPARTMENT OF CHEMISTRY
VIRGINIA POLYTECHNIC INSTITUTE
BLACKSBURG, VIRGINIA FRANK A. VINGIELLO

RECEIVED NOVEMBER 13, 1950

COMMUNICATIONS TO THE EDITOR

THE MOLECULAR WEIGHT DETERMINATION OF POLYPEPTIDES

Sir:

In the course of our attempts to purify and characterize certain of the higher polypeptides by countercurrent distribution it has become apparent that any change affecting a carboxyl or amino group produces a striking effect on the partition ratio of the peptide. Accordingly, the derivatives representing different stages of substitution which result from incomplete reaction can be separated readily. Since with unchanged peptide remaining, the band occurring in the distribution pattern nearest the unchanged substance would be the monosubstituted derivative, a general approach to the problem of molecular weights is suggested. Molecular weight determination by analysis for substituting groups has long been a standard procedure but a decision as to the numbers of groups involved has often been equivocal.

For instance, if a polypeptide with one free $-NH_2$ is treated with sufficient 2,4-dinitrofluorobenzene[1] so that only a fraction of it is converted, distribution of the resulting mixture in a suitable system gives two bands, one of the unchanged polypeptide and a yellow band of the DNP derivative. Determination of the distribution pattern by weight and by absorption at 350 mμ now permits calculation of the molecular weight, provided Beer's law holds. The value ϵ of δ-DNP-ornithine hydrochloride (16,250) can be used as the basis of calculation.

If the peptide contains two amino groups, four bands in the pattern are possible. One band containing the disubstituted product will be furthest removed from that containing the unchanged material. Two possible intermediate mono-substituted products would be expected to have very similar partition ratios and could form overlapping bands unless a very high number of transfers had been applied. Across any one colored band the ratio of weight to absorption should be, and in our experience thus far has been, constant.

With three amino groups in the molecule, two families of overlapping bands and one of the completely substituted peptide could occur. However,

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[1] F. Sanger, *Biochem. J.*, **39**, 507 (1945).