Recently it has been observed that under certain conditions and for some oximino substrates an alkaline medium may be used without disadvantage.[5] It was felt that reduction of compounds of type I in an ammoniacal solution might obviate, the formation of the unwanted diketopiperazines, II, and afford better yields of the desired peptide III. The results were altogether favorable. Also it was found that the dipeptide may be readily isolated by simply volatilizing the solvent, after removal of the catalyst, and drying the product, for the salts readily lose ammonia under these conditions, leaving the substantially pure carboxylic acid derivative.

Experimental

The N-(α-benzyloximinoacyl)-amino acids were prepared substantially after procedures already described.[3,6] A typical hydrogenation experiment was carried out as follows.

To a solution composed of 100 ml. of water and 3 ml. of concentrated ammonia was added 3.5 g. (0.013 mole) of N-(α-benzyloximinopropionyl)-DL-alanine and 3 g. of 10% palladium–charcoal catalyst. The mixture was shaken on a Parr apparatus at about 4 atm. pressure of hydrogen. After an hour, when the calculated hydrogen had been taken up, no further drop in pressure was observed. The catalyst was removed. About 1 ml. of the filtrate was acidified and formed a clear solution, indicating complete reduction. The remainder of the filtrate, in which the odor of toluene was pronounced, was evaporated over a steam-bath and at reduced pressure. The crystalline residue weighed 1.9 g., 90% of theory, gave no test for the ammonium ion and melted 277–278°. Fischer and Kautsch[7] report for alanylalanine the *m.p.* 278°.

Anal. Calcd. for $C_6H_{12}N_2O_3$: N, 17.5. Found: N, 17.0, 17.1.

Other peptides similarly prepared from appropriate intermediates are DL-phenylalanylglycine,[8] m.p. 271–273°; DL-phenylalanyl-L-leucine,[8] m.p. 225–227°; and DL-phenylalanylglycylglycine,[9] m.p. 233–236°.

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(5) W. H. Hartung and Y.-T. Chang, THIS JOURNAL, **74**, 5927 (1952).

(6) K. L. Waters and W. H. Hartung, *J. Org. Chem.*, **12**, 469 (1947).

(7) E. Fischer and K. Kautsch, *Ber.*, **38**, 2376 (1905).

(8) E. Fischer and P. Blank, *Ann.*, **354**, 9 (1907).

(9) F. Sigmund and F. Wesseley, *J. Physiol. Chem.*, **157**, 91 (1926).

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The Preparation of Dialkyl Zinc Compounds

BY ROBERT C. KRUG AND PHILIP J. C. TANG[1]

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During the course of some studies on the reaction of organometallic compounds with monochloromethyl ether considerable difficulty was encountered in the preparation of organozinc compounds. The attempted preparation of dialkyl zinc compounds by the reaction of a mixture of an alkyl iodide and bromide with a zinc–copper couple often resulted in low yield or in failure. Dialkyl zinc compounds may be prepared by several methods the most common being the action of an alkyl iodide on (1) a mixture of zinc dust and copper prepared by the reduction of cupric oxide by hydrogen in the presence of the zinc and (2) an alloy prepared by blending molten zinc and copper. This alloy is usually lathed into turnings and used as such. We have found that an apparently much more reactive zinc–copper couple can be prepared easily from zinc dust and cupric citrate by heating the mixture in an atmosphere of nitrogen to decompose the salt to copper. A comparison of the couples on the basis of simplicity of preparation, length of the induction period of the reaction with the halides, and the yields of the dialkyl zinc compounds obtained indicates the superiority of the new method for small scale laboratory preparations. In the following discussion the zinc–copper couple prepared by method (1) will be referred to as type A, the alloy as type B, and that by the new method as type C.

Type A is somewhat hazardous to prepare as it involves the heating of zinc dust and cupric oxide in an atmosphere of hydrogen just below the point of fusion of the mixture. In this Laboratory the mixture was found to be difficult to reduce completely. A trace of water was often observed in the reaction flask after a prolonged period of reduction. Type B couple involves the operations of melting, casting and latheing and is not practical for a few small scale experiments. Type C couple is made simply by heating with a free flame a mixture of zinc dust and cupric citrate below the point of fusion. The mixture is ready for use in 10–30 minutes depending upon the rate of heating.

The attempted reaction of the alkyl halide with the type A couple usually involved an induction period of one hour or longer while type B couple reacted within about 10 minutes. The reaction with type C couple in some cases was almost instantaneous and less than 10 minutes in all cases studied.

Using the type C couple diethylzinc was prepared in yields of 70%. This figure is below the value of 86–89% crude diethylzinc as given by Noller.[2] Using type A or type B couple dimethylzinc was prepared in this Laboratory in 60% yield. The work has been extended to the preparation of di-*n*-propyl- and di-isopropylzinc with the yields slightly above those obtained using the type B couple. In all cases the reaction was much more vigorous with the type C couple, and this couple gave easily reproducible results. Such was not the case with the type A couple where five runs were successful out of eleven attempts.

Experimental

The zinc dust was used directly as obtained from the J. T. Baker Chemical Co. The type A and type B couples were prepared according to the procedure of Noller.[2] The type C couple was prepared by mixing 130 g. of zinc dust with 25 g. of cupric citrate powder in a 500-ml. three-necked flask. The contents of the flask were heated over a free flame with occasional shaking under a protective current of dry nitrogen until all the cupric citrate had decomposed. This reaction was believed to be complete when moisture and other gases ceased to be evolved. Furthermore, the powder changed in appearance from a green color to a rust color. The mixture was then ready for use.

A 500-ml. three-necked flask containing the couple was equipped with a reflux condenser, a sealed stirrer and a dropping funnel. The apparatus was thoroughly flushed with nitrogen and warmed on a water-bath. Half a mole each of the alkyl bromide and iodide (purified) was placed in the funnel. A few milliliters of the solution were added to the flask and the remainder was added dropwise over a

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(1) Taken in part from the thesis submitted by P. J. C. T. in partial fulfillment of the requirements for the M.S. degree.

(2) C. R. Noller, "Org. Syn." Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, pp. 184–187.

period of 2 to 3 hours in an atmosphere of nitrogen. If during the addition of the halide solution to the couple the reaction became too vigorous a water-bath was used to cool the contents of the flask momentarily. The mixture was then allowed to stand overnight. The flask was connected to a simple vacuum distillation system and any unreacted halides were removed at 100 mm. pressure. The pressure was then reduced to approximately 15 mm. and the dialkyl zinc compound which distilled was collected in a graduated receiver. All connections of the apparatus were of good quality cork generously coated with a very heavy stopcock grease. In the case of dimethylzinc, distillation was effected at atmospheric pressure in a current of nitrogen. The yield of the dialkyl zinc compound was based on this once distilled material.

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v-Triazolo(d)pyrimidines. II. Further Studies in the 2-Aryl Series

BY L. W. HARTZEL AND F. R. BENSON

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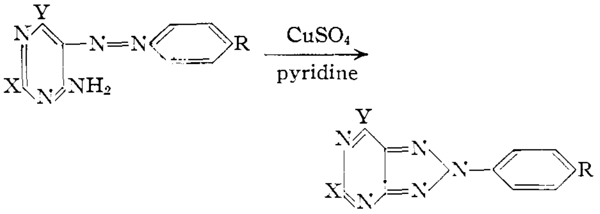
Additional 2-aryl-v-triazolo(d)pyrimidines have been prepared in this Laboratory since those reported previously.[1] These include further examples of 5-amino-7-hydroxy- as well as 5,7-diamino- and 7-amino-5-methylmercapto derivatives. These compounds were prepared by the oxidation of the corresponding 4-amino-5-arylazopyrimidines in the manner originally described.



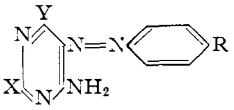
where X = NH_2 or CH_3S and Y = NH_2 or OH

One of the compounds reported in this note, 2-phenyl-5,7-diamino-v-triazolo(d)pyrimidine, has been described elsewhere[2] along with other members of this class.

In Table I there are listed the formulas and analyses of the 4-amino-5-arylazopyrimidines prepared. Some of these compounds contain water of crystallization which it was found impractical to remove. Calculated carbon to nitrogen ratios for these compounds agreed well with the theo-

TABLE I

4-AMINO-5-ARYLAZOPYRIMIDINES[a]

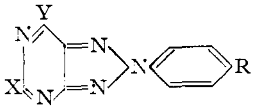


X	Y	R	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found	Carbon/Nitrogen Calcd.	Carbon/Nitrogen Found
NH_2	OH	p-$COOC_4H_9$	$C_{15}H_{18}N_6O_3 \cdot 1^1/_2H_2O$	50.41	50.5	5.92	5.4	23.52	23.8	2.143	2.122
NH_2	OH	p-$CONH_2$	$C_{11}H_{11}N_7O_2$	48.35	47.9	4.06	4.2	35.89	35.7	1.347	1.342
NH_2	OH	p-OH	$C_{10}H_{10}N_6O_2 \cdot 2H_2O^b$	42.55	42.4	5.00	4.54	29.78	29.8	1.429	1.423
NH_2	OH	p-SO_3H	$C_{10}H_{10}N_6O_4S \cdot H_2O$	36.58	36.3	3.69	3.8	25.60	25.5	1.429	1.424
NH_2	NH_2	H	$C_{10}H_{11}N_7^c$	52.39	52.9	4.83	4.8	42.77	43.0	1.225	1.230
NH_2	NH_2	p-COOH	$C_{11}H_{11}N_7O_2 \cdot H_2O$	45.35	45.5	4.50	4.3	33.67	33.4	1.347	1.362
NH_2	NH_2	p-CONHCHCOOH | $(CH_2)_2$COOH	$C_{16}H_{18}N_8O_5 \cdot H_2O^d$	45.71	45.7	4.80	4.7	26.66	26.3	1.715	1.738
CH_3S	OH	H	$C_{11}H_{11}N_5OS^e$	50.56	50.8	4.24	4.2	12.27^f	12.2^f		
CH_3S	OH	p-COOH	$C_{12}H_{11}N_5O_3S$	47.20	47.1	3.63	3.8	10.50^f	10.6^f		

[a] All the compounds decompose above 300° unless otherwise specified. [b] Decomposes 243°. [c] Begins to decompose at 235°. [d] Decomposes 270°. p-Aminobenzoyl-1(+)glutamic acid was used as starting material. [e] Decomposes 260°. [f] Sulfur values.

TABLE II

2-ARYL-V-TRIAZOLO(d)PYRIMIDINES[a]



X	Y	R	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
NH_2	OH	p-$COOC_4H_9$	$C_{15}H_{16}N_6O_3$	54.87	55.2	4.91	4.4	25.60	25.8
NH_2	OH	p-$CONH_2$	$C_{11}H_9N_7O_2$	48.71	48.3	3.34	3.4	36.15	36.1
NH_2	OH	p-OH	$C_{10}H_8N_6O_2$	49.18	49.2	3.30	3.3	34.42	33.9
NH_2	OH	p-SO_3H	$C_{10}H_8N_6O_4S$	38.96	38.8	2.61	2.6	27.27	26.9
NH_2	NH_2	H^b	$C_{10}H_9N_7$	52.85	52.8	3.99	4.2	43.15	43.2
NH_2	NH_2	p-COOH	$C_{11}H_9N_7O_2$	48.71	48.3	3.34	3.5	36.15	36.3
NH_2	NH_2	p-CONHCHCOOH^c | $(CH_2)_2$COOH	$C_{16}H_{16}N_8O_5$	48.00	47.6	4.03	4.5	27.99	27.9
CH_3S	OH	H	$C_{11}H_9N_5OS$	50.95	51.2	3.50	3.8	27.01	27.0
CH_3S	OH	p-COOH	$C_{12}H_9N_5O_3S$	47.52	47.3	2.99	3.1	...	..

[a] All the compounds decompose over 300° unless otherwise specified. [b] Previously described in reference 2. [c] Begins to decompose at 235°.

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[1] F. R. Benson, L. W. Hartzel and W. L. Savell, THIS JOURNAL, **72**, 1816 (1950).

[2] R. P. Parker and J. S. Webb, U. S. Patent 2,543,333, Feb. 27, 1951.