

Ethyl α ,4-Dicyanocinnamate

p-Cyanobenzaldehyde was prepared by the aqueous copper nitrate oxidation of *p*-cyanobenzyl bromide using a method analogous to that of Moses¹ in 47% yield; 32 g. (0.25 mole) of this crude material, m. p. 97–98°, was dissolved in 200 cc. of isobutyl alcohol, together with 28 g. of ethyl cyanoacetate. When 0.5 ml. of piperidine was added, immediate warming took place and precipitation of the product started in about five minutes. After stand-

ing for four hours, the solution was cooled and filtered. The product was crystallized once from a mixture of ethanol and benzene and twice from ethanol alone; 50 g. (88%) of very pale yellow needles, m. p. 168.5–90° (uncor.) was obtained.

Anal. Calcd. for C₁₃H₁₀O₂N₂: C, 69.0; H, 4.46; N, 11.87. Found: C, 69.09, 69.27; H, 4.45, 4.68; N, 11.98.

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(1) Moses, *Ber.*, **33**, 2624 (1900).

COMMUNICATIONS TO THE EDITOR

NIACIN—NIACINAMIDE DIFFERENTIATION IN THE MICROBIOLOGICAL ASSAY PROCEDURE

Sir:

The microbiological niacin assay method of Snell and Wright¹ does not differentiate between niacin and niacinamide. Since these substances have equivalent vitamin activity, the inability to distinguish between them is ordinarily of no concern. In the case of tablets or solutions of niacinamide, designed for therapeutic use, however, the presence of any large proportion of the acid may be of interest. We have found a simple chemical reaction which specifically inactivates niacinamide, but is without action on niacin. It is the reaction usually called Hofmann's reaction,² *i. e.*, the action of bromine and potassium hydroxide upon amides. When applied to niacinamide, β -aminopyridine is formed,³ which is apparently inactive microbiologically. We produce the reaction as follows.

To 1 ml. of a solution containing 1 mg. of niacinamide add 5 ml. of water and 1 ml. of bromine water (satd.), followed by 3 ml. of 30% potassium hydroxide. Allow to stand at room temperature for twenty minutes and then steam for twenty minutes. Cool, add an excess of 10 *N* sulfuric acid (blue to congo red), then remove any excess of bromine by use of a 4% solution of sodium acid sulfite. Use an outside, starch-iodide indicator to determine the end-point. The table indicates the results obtained when niacin, niacinamide and a mixture of the two were treated as

described above. Reaction volume in all cases was 10 ml. The final solutions after neutralization, etc., were assayed by the Snell-Wright procedure.

No.	Vitamin, mg.	Bromine water, ml.	Total assay (niacin activity), mg.
1	1 Niacinamide	0.4	0
2	1 Niacinamide	1.0	0
3	1 Niacin	1.0	1.0
4	1 Niacin plus 1 Niacinamide	1.0	1.0

It is apparent, therefore, that the proportion of niacin to niacinamide in a preparation may be determined by estimation of the vitamin activity before and after treatment with bromine and potassium hydroxide. The possible application of this reaction to a differentiation of the forms of niacin occurring naturally is being investigated.

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β , β -DIMESITYLVINYL ALCOHOL

Sir:

It seemed probable that, in the production of α , α -diarylacetaldehydes by the dehydration of the corresponding hydrobenzoins, β , β -diarylvinyl alcohols were formed as intermediates and that, being unstable, they isomerized to the corresponding aldehydes. Such an isomerization would be expected to become more difficult with increase in the size and complexity of the aryl radicals and it seemed possible that extreme crowding

(1) E. E. Snell and L. D. Wright, *J. Biol. Chem.*, **139**, 675 (1941).

(2) A. W. Hofmann, *Ber.*, **18**, 2734 (1885).

(3) A. Pictet and P. Crépieux, *ibid.*, **28**, 1904 (1895).