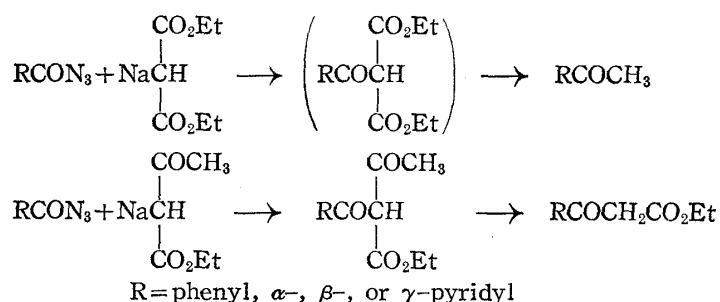


8. Shigehiko Sugasawa and Hiroshi Tomisawa : Acid Azide as an Acylating Agent. I.

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The important role played by acid chloride as an acylating agent is well known. In connection with other works now going on in our hands, we have to use chlorides of various basic acids for such a purpose. The results were, however, not satisfactory because of the difficulty of preparing basic acid chlorides in the state of high purity. That acid azide, readily obtainable from acid hydrazide, can be used to acylate amines by merely standing with them in ethereal solution, has already been shown by Curtius,¹⁾ who has also succeeded in preparing an ester by reacting acid azide with sodium alkoxide.

These facts prompted us to investigate the scope of the reactions of azides of various basic acids as acylating agents and in this paper we are reporting our successful results of acylating malonic ester and acetoacetic ester by means of α -, β -, and γ -pyridine-carboxylic acid azides in the presence of sodium dust in ether solution. Attempts to substitute triethylamine for sodium in the above reaction, so that the condensation can be carried out in homogeneous solution, was unsuccessful, furnishing acylation product only in about 10% yield and recovering most of the starting materials.



Efforts are now being made to prepare the corresponding diazoketone from azide of basic acid and diazomethane.

The authors' thanks are due to the members of the central analysis room of this Institute for analytical data.

Experimental

Acid Azide—For acylating purpose azides of benzoic and α -, β -, and γ -pyridine-carboxylic acids were prepared from the purified hydrazides by the general method. The azides were collected in ether, washed first with cold dilute soda solution free from acid, then with water, and dried over K_2CO_3 .

General Procedure for Acylation of Malonic Ester—Sodium dust (0.5 g.) in ether was added with diethyl malonate (2.6 g.), separating sodium compound of diethyl malonate as white pasty solid. Equimolar portion of acid azide in ether prepared as above was now introduced and the whole was refluxed for 10–15 hrs. with stirring. The cooled reaction mixture was now extracted with soda solution (20 cc. of 10%), filtered through a wet filter, and the filtrate, while being kept under aspirator-vacuum, acidified with HCl (30 cc. of 10%); thus hydrazoic acid generated was removed. Thirty cc. of conc. HCl was then added and the mixture was refluxed for 3–4 hrs. in an oil bath until the cessation of CO_2 -evolution. Most of HCl was now evaporated and the residue was basified with soda solution, separating methyl ketone, which was collected in benzene, washed, dried, and evaporated. The results are summarized in Table I.

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1) Curtius: J. prakt. Chem. [2], 52, 210 (1895).

TABLE I.

Hydrazide of	Product	Yield(%)	Characterized as
Benzoic acid	Acetophenone	68	Oxime, m.p. 56°
α -Picolinic acid	α -Acetylpyridine	45	Picrate, m.p. 133°
Nicotinic acid	β - "	57	" , m.p. 129~131°
Isonicotinic acid	γ - "	45	" , m.p. 127~129°

Acylation of Acetoacetic Ester—The condensation was carried out just as above. In case the product was worked up under 5° with good cooling, acylacetoacetic ester was obtained, but when treated at about 10° fission of acetyl group occurred, giving acylacetic ester as a final product. The results are shown in Table II.

TABLE II.

Hydrazide of	Product	Yield(%)	Derivative
Benzoic acid	Ethyl benzoylacetoacetate	56	Cu salt ²⁾ , m.p. 222~223°(decomp.)
Picolinic acid	Ethyl α -pyridoylacetoacetate	66	Picrate ³⁾ , m.p. 132°(decomp.)
Nicotinic acid	" β - "	64	" ⁴⁾ , m.p. 146~148°
"	Ethyl β -pyridoylacacetate	85	" ⁵⁾ , " 122~124°
Isonicotinic acid	Ethyl γ - "	82	" ⁶⁾ , " 135~137°

2) Identified by direct comparison with an authentic specimen prepared according to Org. Syntheses, Coll. Vol. II, 351 (Japanese Edition). 3) Yellow needles. *Anal.* Calcd. for $C_{12}H_{13}O_4N \cdot C_6H_3O_7N_3$: C, 46.6; H, 3.5; N, 12.2. Found: C, 47.1; H, 3.3; N, 12.4. 4) Yellow pillars. *Anal.* Calcd. for as above. Found: C, 46.9; H, 3.6; N, 12.4. 5) Identified by direct comparison with an authentic specimen prepared according to J. Am. Chem. Soc., 63, 490(1941). 6) Yellow scales. *Anal.* Calcd. for $C_{20}H_{11}O_3N \cdot C_6H_3O_7N_3$: C, 45.2; H, 3.0; N, 13.3. Found: C, 44.9; H, 2.9; N, 13.4.

Summary

Diethyl sodiomalonate and ethyl sodioacetoacetate were treated with azides of α -, β -, and γ -pyridine-carboxylic acids in absolute ether, furnishing the corresponding diethyl pyridoylmalonate and ethyl pyridoylacetoacetate in fair yields. Thus, azide of various basic carboxylic acids can advantageously be used for similar purposes, when acid chloride is hard to obtain in a pure state, which is usually the case in various basic carboxylic acid.

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