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1964

SovietRxiv

Abstract

Full Text

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SYNTHESIS OF 1,2,3-TRIAZOLES WITH ELECTRON-ACCEPTOR SUBSTITUENTS

With the aim of obtaining five-membered heterocycles that readily give a stable organic anion,* we have developed a method for the synthesis of 1,2,3-triazoles containing electron-acceptor groups. These compounds, in the form of sodium salts, were obtained by the reaction of acetylenes activated by electron-acceptor groups with sodium azide in dimethylformamide (DMFA) solution on heating.

Usually, the synthesis of triazoles not containing substituents at the nitrogen atoms is carried out by the reaction of various acetylenes with hydrazoic acid ([1]).

Since work with this acid is extremely unpleasant because of its explosive properties, a method using sodium azide has substantial advantages.

We found that the reaction proceeds most readily in the case of ethynyl ketones, the nitrile and ester of phenylpropiolic acid, whereas the amide of phenylpropiolic acid under the same conditions has time to react only to the extent of 53%, and phenylacetylene is almost completely recovered unchanged.

An analogous synthesis of tetrazoles based on substituted nitriles has been described in the literature; moreover, as in our case, it was noted that the presence of electron-acceptor substituents at the nitrile group accelerates the reaction ([2-4]).

The structure of the ketones of the triazole series obtained was proved by us using 4-butyroyl-1,2,3-triazole as an example, which upon oxidation with potassium permanganate in sulfuric acid gives the known 1,2,3-triazole-4-carboxylic acid. The nitrile of 5-phenyl-1,2,3-triazole-4-carboxylic acid was saponified with acid to the corresponding amide, which proved to be identical with the substance synthesized directly from the amide of phenylpropiolic acid and sodium azide. This amide, by the action of nitrous acid, was converted into the known 5-phenyl-1,2,3-triazole-4-carboxylic acid, which was also isolated upon hydrolysis of the ethyl ester obtained in the present work (No. 3, see Table 1).

The 1,2,3-triazoles described by us are acids, stronger than carbonic acid, since they displace the latter from its salts. The sodium salts of these compounds are stable and can be isolated in analytically pure form, as was shown using

4-butyroyl-1,2,3-triazole as an example. In the IR spectrum of this salt an absorption band of the carbonyl group was found (ν = 1652 cm^{-1}), which is shifted by 30 cm^{-1} toward lower frequencies in comparison with the absorption frequency of the C = O group (ν = 1682 cm^{-1}) of the starting 4-butyroyl-1,2,3-triazole. Such a shift indicates stronger conjugation of the carbonyl group with the ring in the salt than in the starting triazole, which also testifies to the dis-

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* In the scheme, the circle in the five-membered triazole ring denotes the aromaticity of this ring. The negative charge is distributed unevenly among all its atoms.

distribution of the negative charge over the entire ring, and not only over the nitrogen atoms. In addition, the IR spectrum confirms that salt formation is not associated with enolization of the carbonyl group.

On the contrary, the basic properties are manifested extremely weakly. The triazoles obtained by us can be isolated in the free form by treating the sodium salts with dilute mineral acids. Only under the action of concentrated sulfuric acid do these compounds readily go into solution.

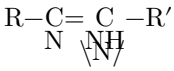
Experimental Part

Synthesis of substituted 1,2,3-triazoles. To 0.02 mol of finely powdered sodium azide in 50 ml of dry DMFA, with stirring and heating to 90° (to 40° in the case of ethynyl ketones), a solution of 0.02 mol of the acetylene compound in 50 ml of DMFA was slowly added. After the entire solution had been added, the mixture was stirred with heating for another 1.5 h and left overnight. The solvent was distilled off in vacuo. The residue of the sodium salt of the triazole was dissolved in water and extracted with ether to remove unreacted starting material. The aqueous layer was acidified with 10% hydrochloric acid and extracted with ether. The ether extracts were washed once with water, dried over sodium sulfate, and the ether was evaporated. The corresponding 1,2,3-triazole was obtained as the residue (yields and constants, see Table 1).

Oxidation of 4-butyroyl-1,2,3-triazole. To a suspension of 1.39 g of 4-butyroyl-1,2,3-triazole in 17 ml of water, 4 ml of conc. sulfuric acid was added, and at 60–70° 5.5 g of finely powdered potassium permanganate was added in portions with stirring. After this, the reaction mass was stirred with heating for another 30 min and left for 48 h at room temperature. The mixture was then filtered while hot, and the precipitate on the filter was washed with a small amount of hot water. On cooling the filtrate with ice, a colorless precipitate of 1,2,3-triazole-4-carboxylic acid separated, m.p. 210–213° (from water). Literature data ([4]), m.p. 213°.

Saponification of the nitrile of 5-phenyl-1,2,3-triazole-4-carboxylic acid. A solution of 1 g of the nitrile of 5-phenyl-1,2,3-triazol-

Table 1



No.	R	R'	Yield, %	M.p., °C, solvent	C, % found	C, % calculated	H, % found	H, % calculated	N, % found	N, % calculated
1	C_3H_7CO	OH*	86	119–121. Water2. Dichloroethane	51.72	51.76	6.52	6.51	30.03	30.19
2	C_6H_5CO	OH	82	123–124. Water2. Cyclohexane – $CHCl_3$	63.40	62.42	4.16	4.06	24.25	24.20
3	COOC	C_2H_5	92	92–93 water	60.79	60.72	5.11	5.10	19.27	19.30
4	CN	C_6H_5	80	166–167 water	63.58	63.52	3.71	3.55	32.95	32.93
5	CONH	C_6H_5	53	273–274 ethyl acetate – DMFA	57.43	57.43	4.31	4.29	29.67	29.77

* The sodium salt of 4-butyroyl-1,2,3-triazole, obtained from the reaction mixture after evaporation of DMFA, was reprecipitated twice from DMFA with ether.
Found, %: C 44.10; H 5.15; N 26.00.
$C_6H_8N_3ONa$. Calculated, %: C 44.19; H 4.94; N 25.76.

** Calculated on the phenylpropiolic acid amide that entered into the reaction, yield 99%.

4-carboxylic acid in 20 ml of conc. sulfuric acid was left in an open dish for three days. The reaction mixture was treated with water; the precipitate was filtered off, washed on the filter with water, and dried. The yield of 5-phenyl-1,2,3-triazole-4-carboxylic acid amide was 72% of theory, mp 274° (from a mixture of DMF and ethyl acetate). A mixed sample with a specimen obtained from phenylpropiolic acid amide and sodium azide gave no depression of the melting point. The amide obtained (0.1 g) was dissolved in 2 ml of conc. sulfuric acid and treated with a solution of sodium nitrite; the precipitated hydrate of 5-phenyl-1,2,3-triazole-4-carboxylic acid was filtered off, mp 204–205°. Literature data [(5)]: mp 205–206°.

Ethyl ether of 5-phenyl-1,2,3-triazole-4-carboxylic acid. A solution of 1 g of the ether and 2.24 g of caustic potash in 50 ml of water was heated for 10 h on a boiling water bath. The cooled solution was treated with 10% hydrochloric acid, and the precipitate of 5-phenyl-1,2,3-triazole-4-carboxylic acid was filtered off, mp of the hydrate 206° (from water).

The authors express their deep gratitude to Yu. N. Sheinker and L. B. Senyavina for recording the IR spectra.

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Received
14 V 1964

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Note: Figure translations are in progress. See original paper for figures.