A NEW TRIFLUOROMETHYL ANALOG OF RIBOFLAVIN

Z. V. Pushkareva and G. A. Vavilov

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In making a systematic study of one of the methods of modifying the molecule of riboflavin in order to obtain biologically-active compounds, we have previously obtained 7-methyl-6-trifluoromethyl-, 6-trifluoromethyl-, and 7-trifluoromethylisoalloxazines with various substituents on N_9 [1]. Substances closest in chemical structure to natural riboflavin are of the most interest. These include 7-methyl-9-(1'-d-ribityl)-6-trifluoromethylisoalloxazine, which exhibited a comparatively high toxicity in preliminary tests (G. N. Platonova). Its synthesis was recently described by L. M. Yagupol'skii et al. [2]. Here we report the synthesis of the isomeric 6-methyl-9-(1'-d-ribityl)-7-trifluoromethylisoalloxazine (**I**), obtained for a comparative study of biological activity and of the influence of the trifluoromethyl group on the redox properties of the isoalloxazines. The starting material was 2-methyl-5-nitrobenzotrifluoride, which was obtained as described by L. M. Yagupol'skii [3] and was reduced to the corresponding amine. The latter was converted with acetic anhydride into 5-acetylamino-2-methylbenzotrifluoride (**II**) and was nitrated with nitrating mixture. After deacylation, the amino group of the 5-amino-2-methyl-4-nitrobenzotrifluoride (**III**) was replaced by chlorine in the usual way via the diazonium compound, and 5-chloro-2-methyl-4-nitrobenzotrifluoride (IV) was obtained; on being boiled in isoamyl alcohol with d-ribitylamine, this gave 2-methyl-4-nitro-5-(1'-d-ribitylamino)benzotrifluoride (V). The latter was hydrogenated using Raney nickel in glacial acetic acid and, after the removal of the catalyst, the o-diamine formed, without isolation from the acetic acid solution, was subjected to condensation with alloxan in the presence of boric acid. Some characteristics of the newly-obtained compounds are given in the table.

Compound I consists of small yellow crystals soluble in acetic acid and sparingly soluble in water and ethanol.

Compound	Mp, °C	Solvent	Empirical formula	Found, %		Calculated, %		Yield, %
				N	F	N	F	
II	103	Aqueous ethanol	$C_{10}H_{10}F_3NO$	6.10	—	6.45	—	83
III	108	"	$C_8H_7F_3N_2O_2$	13.21	—	12.72	—	80
IV	45	"	$C_8H_5ClF_3NO_2$	6.10	23.11	5.85	23.75	81
V	156—7	Water	$C_{13}H_{17}F_3N_2O_5$	8.08	16.09	7.90	16.02	28
I	232—3 (decomp.)	"	$C_{17}H_{17}F_3N_4O_6$	13.30	13.01	13.04	13.12	57

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1 July 1968 Ural Polytechnic Institute, Sverdlovsk

SYNTHESIS OF 2-(5'-NITRO-2'-FURYL)BENZIMIDAZOLES

F. T. Pozharskii, V. Ts. Bukhaeva, A. M. Simonov, and R. A. Savel'eva

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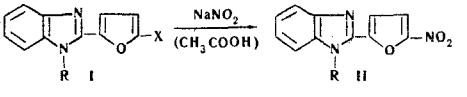
The high bactericidal activity of 2-(5'-nitro-2'-furyl)benzimidazole and its 1-methyl derivative, and also the extremely laborious method of its preparation due to the complexity of the synthesis of the initial hydrochloride of 5-nitrofuran-2-carbimidic ester [1, 2] induced us to search for a simpler route for the preparation of these compounds.

2-(5'-Nitro-2'-furyl)benzimidazoles (II)

Compound	R	Mp, °C (ethanol)	Empirical formula	N, % found	N, % calculated	Yield, %
IIa	H	230—231	$C_{11}H_7N_3O_3$	18.50	18.33	90
II_b	CH_3	212—213	$C_{12}H_9N_3O_3$	17.41	17.28	85
IIc	$CH_2C_6H_5$	160—161	$C_{18}H_{13}N_3O_3$	13.10	13.15	80

We have found that the action of 3 moles of sodium nitrite on solutions of 2-(5'-halo-2'-furyl)benzimidazoles (I) [3] in glacial acetic acid first at room temperature and then at the boil for 2-3 hr gives 2-(5'-nitro-2'-furyl)benzimidazoles (**II**) with a high degree of purity in yields of 80-90%.



R = H, CH_3, $CH_2C_6H_5$ X = Cl, Br

Compounds **IIa** and **IIc** and their methiodides were also obtained from **IIa** in a similar manner to the methods described previously [3].