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ALKYLATION OF 1-METHYL-2-BENZIMID-AZOLYLACETONITRILE

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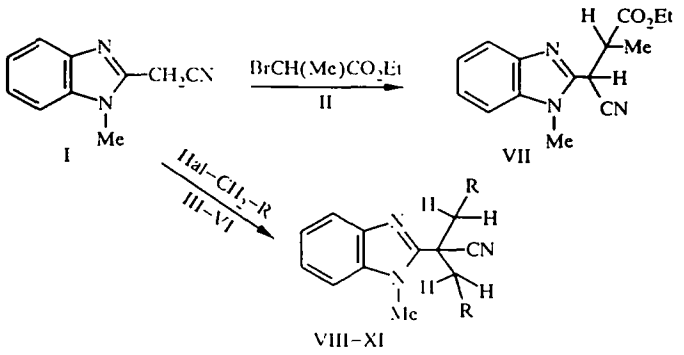
Alkylation of 1-methyl-2-benzimidazolylacetonitrile by esters of α-halogenocarboxylic acids and chloromethylarenes in dimethylformamide in the presence of potassium carbonate proceeds at the carbon atom of the methylene group.

Alkylation of 1-methyl-2-benzimidazolylacetonitrile (I) with α-halogenoketones [1] and methyl p-toluenesulfonate [2] proceeds at the nitrogen atom of the heterocyclic nucleus with the formation of quaternary salts. The alkylation of compound (I) at the methylene group has not been described in the literature.

We studied the alkylation of the nitrile (I) with esters of α-bromopropionic acid (II) and of halogenoacetic acids (III), (IV), as well as benzyl chloride (V) and 6-chloromethylbenzodioxane (VI). When compound (I) was boiled in dimethylformamide with the twofold excess of the alkylating agent in the presence of potassium carbonate, white crystalline products (VII)-(XI) were isolated.



The IR spectra of the compounds obtained contain the medium-intensity absorption band of the nitrile group at 2244 cm^{-1} for the compounds (VIII) and (IX) and 2236 cm^{-1} for the product (VII), or a weak band at 2230 cm^{-1} in the case of the compounds (X) and (XI). The stretching vibrations of the C=O group in the esters (VII)-(IX) occur in the region of 1715-1731 cm^{-1}.

The data of the elemental analysis indicate the presence of two residues of the alkylating agent in the molecules of the compounds (VIII)-(XI), and only one residue in the product (VII) of the alkylation with ethyl α-bromopropionate. These data are also confirmed by the ratio of the integral intensities of the proton signals in the PMR spectra for the benzimidazole and alkyl parts of the molecules of the compounds synthesized.

The direction of the alkylation can be judged on the basis of PMR and IR spectral data. The weak intensity of the band of the nitrile group in the IR spectrum and its position indicate the absence of its conjugation with the benzimidazole part

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TABLE 1. Characteristics of the Compounds (VII)-(XI) Synthesized

Compound	Empirical formula	Found N, % / Calculated N, %	mp, °C	Yield, %
VII	$C_{15}H_{17}N_3O_2$	15.6 / 15.5	99	62
VIII	$C_{16}H_{17}N_3O_4$	13.6 / 13.3	121	51
IX	$C_{18}H_{21}N_3O_4$	12.5 / 12.2	116	35
X	$C_{24}H_{21}N_3$	11.9 / 12.0	120	71
XI	$C_{28}H_{25}N_3O_4$	9.0 / 9.0	158	82

*Compounds (VII)-(X) were recrystallized from propan-2-ol, and compound (XI) was recrystallized from acetonitrile.

TABLE 2. Spectral Data for the Compounds (VII)-(XI) Synthesized

Compound	IR spectrum, ν, cm^{-1}	PMR spectrum, δ, ppm, SSCC (J), Hz
VII	2236 m. (CN), 1715 s (CO)	$CDCl_3$: 1,18 (3H, t, CH_3CH_2); 1,64 (3H, d, J = 7,3, CH_3); 3,68 (1H, m, $CHCH_3$); 3,88 (3H, s, N—CH_3); 4,09 (2H, q, CH_2); 4,51 (1H, d, J = 9, CH—CN); 7,33 (3H, m, H_{arom}); 7,74 (1H, m, H_{arom})
VIII	2244 m. (CN), 1730 s (CO)	$CDCl_3$: 3,28 (2H*, d, J = 17, CH_2); 3,62 (2H*, d, J = 17, CH_2); 3,68 (6H, s, $2CO_2CH_3$); 4,23 (3H, s, N—CH_3); 7,34 (3H, m, H_{arom}); 7,68 (1H, m, H_{arom})
		CF_3CO_2D: 3,71 (2H*, d, J = 17, CH_2); 3,85 (6H, s, $2CO_2CH_3$); 4,02 (2H*, d, J = 17, CH_2); 4,63 (3H, s, N—CH_3); 7,82 (4H, m, H_{arom})
IX	2244 m. (CN), 1731 s (CO)	$CDCl_3$: 1,19 (6H, t, $2CH_3$); 3,26 (2H*, d, J = 17, CH_2); 3,60 (2H*, d, J = 17, CH_2); 4,08 (4H, q, $2CO_2CH_2$); 4,22 (3H, s, N—CH_3); 7,34 (3H, m, H_{arom}); 7,67 (1H, m, H_{arom})
		CF_3CO_2D: 1,30 (6H, t, $2CH_3$); 3,69 (2H*, d, J = 17, CH_2); 3,98 (2H*, d, J = 17, CH_2); 4,29 (4H, q, $2CO_2CH_2$); 4,61 (3H, s, N—CH_3); 7,82 (4H, m, H_{arom})
X	2231 w. (CN)	$CDCl_3$: 3,03 (3H, s, N—CH_3); 3,51 (2H*, d, J = 13, CH_2); 3,78 (2H*, d, J = 13, CH_2); 7,18 (13H, m, $10H_{Ph}$ + $3H_{arom}$); 7,84 (1H, m, H_{arom})
XI	2230 w. (CN)	$CDCl_3$: 3,24 (3H, s, N—CH_3); 3,37 (2H*, d, J = 13, CH_2); 3,63 (2H*, d, J = 13, CH_2); 4,18 (8H, s, 2 O-$(CH_2)_2$-O); 6,5...6,85 (6H, m, H_{arom} benzodioxane); 7,28 (3H, m, H_{arom}); 7,85 (1H, m, H_{arom})

*Protons of two different CH_2 groups.

of the molecule, which is observed in the case of 1,3-dimethyl-2-cyanomethylenebenzimidazoline (ν_{CN} = 2150 cm^{-1}) [2] and its 1,3-diethyl analog (ν_{CN} = 2145 cm^{-1}) [3].

In the initial nitrile (I), the protons of the methylene group are equivalent, and are observed in the PMR spectrum ($CDCl_3$) in the form of a two-proton singlet at 4.05 ppm. In the spectrum of the alkylation product (VII), the proton signal of the CH group of the substituted acetonitrile is present in the form of a doublet at 4.51 ppm (J = 9 Hz) owing to its interaction with the proton of the CH group. The latter, in turn, interacts with the protons of the methyl group (J = 7 Hz), and therefore has the form of a multiplet at 3.68 ppm. Therefore, in the given case, the alkylation proceeds at the carbon atom of the methylene group. It should be noted that, notwithstanding the significant excess of the alkylating reagent and the base, only the monoalkylated product is formed; this is probably due to the steric hindrance produced on the approach of the carbanion with the methyl group of the α-bromopropionic acid residue. Such hindrance is absent for other alkylating agents which we employed. It is known that arylacetonitriles are alkylated by excess of bromoacetic ester forming α,α-diethoxycarbonylmethylarylacetonitriles [4]. We assume that the products (VIII)-(XI) have an analogous structure. A characteristic feature of the PMR spectra of these compounds is the nonequivalence of the protons of the methylene groups at

the carbon atom connected to the benzimidazole part. In spite of the fact that the C atom in the molecules (VIII)-(XI) is connected with two RCH_2 groups, there are no conformations occurring in which the protons of each of the methylene groups indicated were magnetically equivalent, so that these protons have some differing chemical shifts. The spin–spin coupling between them appears as additional splitting into doublets with the geminal constant of 13-17 Hz. In the PMR spectra of the compounds (VIII) and (IX), recorded using deuterotrifluoroacetic acid, the difference in the chemical shifts of the protons under consideration comprises 0.3 ppm. An interesting feature of the PMR spectra of the compounds (VIII)-(XI), recorded in deuterochloroform, is the fact that the difference in the chemical shifts of the given protons is equal to their doubled SSCC and, in this connection, their signals have the form of a four-proton quartet.

An attempt to alkylate the product (I) by an excess of ethyl iodide under analogous conditions, as used in the work [3], led to the formation of a dark yellow residue, having low solubility in organic solvents, which is probably a product of polymerization.

EXPERIMENTAL

The IR spectra were obtained on the Pye Unicam SP 3-300 instrument using tablets of KBr. The PMR spectra were recorded for solutions in $CDCl_3$ or CF_3CO_2D on the Bruker WP-100 SY instrument.

Alkylation of 1-Methyl-2-benzimidazolylacetonitrile. To the solution of 0.85 g (5 mmole) of the nitrile (I) in 5 ml of DMF are added 1 g (7 mmole) of potassium carbonate and 10 mmole of the corresponding alkylating agent (II)-(VI), and the mixture is boiled for 30 min. The solvent is evaporated *in vacuo*, and the residue is treated with water and neutralized with acetic acid. In the case of the products (VII)-(IX) from the precipitated residue, it is mixed with water and washed with ether in the case of (VII), or with propan-2-ol in the case of (VIII) and (IX). The residue is filtered off in the case of the products (X) and (XI). The residues obtained as described above are recrystallized from a suitable solvent. The characteristics of the compounds (VII)-(XI) are presented in Table 1, and their spectral data are presented in Table 2.

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