SYNTHESIS AND REACTIONS OF HETEROCYCLIC AZIDE DERIVATIVES.
6.* REACTIONS OF BENZOTHIAZOLE AZIDES WITH 1,3-DIKETONES AND IOTISCH COMPLEXES

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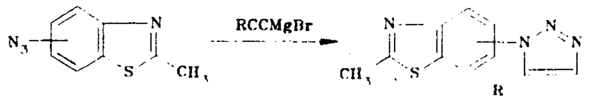
Cycloaddition of 5- and 6-azido-2-methylbenzothiazoles to magnesiumbromoacetylenes and 1,3-diketones leads to the formation of 2-methyl-5(6)-(1,2,3-triazol-1-yl)benzothiazoles. Reaction with benzoylacetone, for instance, results in the formation of two isomeric 4-acyl-1,2,3-triazoles, which differ in the position of the methyl and phenyl substituent radicals.

Dimroth [2, 3] has carried out the synthesis of 1,2,3-triazoles based on the reaction of phenyl azide with acetylene and its derivatives. Our attempts to utilize acetylene and its homologs in reactions with 5- and 6-azido-2-methylbenzothiazoles (I and II) did not produce the desired results, however. In contrast, using more active Iotisch complexes, bromomagnesiummethyl- and bromomagnesiumphenylacetylenes, in place of acetylenic hydrocarbons in reactions with azides I and II, we were able to obtain the desired 1,5-disubstituted 1,2,3-triazoles III-V.

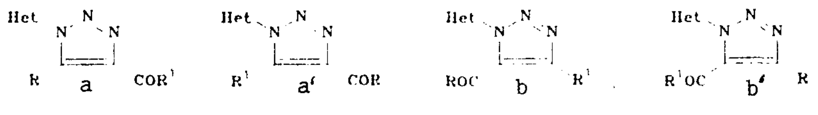


I, II III–V

I, III, V — 5-derivative, II, IV — 6-derivative; III, IV R=Me, V R=Ph

Organic azides are known to form 1,2,3-triazoles upon reaction with active methylene compounds, such as 1,3-diketones and β-keto esters [4, 5]. We have now examined the reactions of azides I and II with a variety of 1,3-diketones, such as acetylacetone, dibenzoylmethane, and benzoylacetone. A series of 2-methyl-5(6)-(1,2,3-triazolyl)benzothiazoles have thus been prepared by treatment of the corresponding azide with a two- or fourfold excess of 1,3-diketone; this was confirmed based on their analytical and spectral data.

In the case of symmetrical 1,3-diketones two possible cycloaddition products can be formed, *a* and b, while in the case of unsymmetrical 1,3-diketones there are four different structures which can be formed, *a*, *a*', b, and b'.



VI–X, XII XI, XIII

VI, VIII, X, XI Het=2-methylbenzothiazolyl-5 5-, VII, IX, XII, XIII Het=2-methylbenzothiazolyl-6; VI, VII R=Me, VIII—XIII R=Ph; VI, VII, X—XIII R^1=Me, VIII, IX R^1=Ph

According to literature data, however, structures b and b', in which the carbonyl group occupies the 5-position in the triazole ring, are not in fact formed [5, 6]; reactions of symmetrical 1,3-diketones, acetylacetone and dibenzoylmethane, with azides I and II should therefore result in cycloaddition to form only one product, and this was observed in the synthesis. The corresponding 1,2,3-triazolylbenzothiazoles VI-IX were obtained in this manner.

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*For Communication 5, see [1].

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TABLE 1. PMR Spectra of Compounds III-VII, X-XIII

Compound	Chemical shift, δ, ppm (in $CDCl_3$)*						
	2-CH	4-H	5-H	6-H	7-H	4-R	5-R
III	2,89	8,09	7,53	—	7,97	7,60	2,40
IV	2,89	8,00	—	7,53	7,89	7,63	2,39
V	2,84	7,90	7,40	—	7,95	7,90	7,31
VI	2,91	8,00	—	7,50	8,05	2,78	2,64
VII	2,91	8,14	7,53	—	7,97	2,77	2,63
X	2,84	7,81	—	7,30	7,85	2,78	7,33
XI	2,90	8,10	—	7,55	8,03	7,59; 8,11	2,72
XII	2,86	7,88	7,25	—	7,85	2,79	7,35
XIII	2,91	8,15	8,00	—	7,60	7,60; 8,29	2,71

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*Benzene ring: 2-CH_3, 4-H, 5-H, 6-H, and 7-H; triazole ring: 4-R and 5-R.

TABLE 2. Physical Characteristics of Compounds III-XIII

Compound	Molecular formula	mp, °C	IR spectrum, cm^{-1}		Yield, %
			Tr*	CO	
III	$C_{11}H_{10}N_4S$	121 ... 122	1076, 1090	—	76
IV	$C_{11}H_{10}N_4S$	107 ... 109	1070, 1080	—	72
V	$C_{16}H_{12}N_4S$	183 ... 184	—	—	54
VI	$C_{13}H_{12}N_4OS$	199 ... 201	1070, 1080	1682	77
VII	$C_{13}H_{12}N_4OS$	150 ... 151	1070, 1090	1670	63
VIII	$C_{23}H_{16}N_4OS$	185 ... 186	—	1650	65
IX	$C_{23}H_{16}N_4OS$	172 ... 173	—	1650	69
X	$C_{18}H_{14}N_4OS$	154 ... 156	1070	1680	30
XI	$C_{18}H_{14}N_4OS$	177 ... 179	1070	1642	27
XII	$C_{18}H_{14}N_4OS$	154 ... 156	1074	1695	30
XIII	$C_{18}H_{14}N_4OS$	119 ... 120	1080	1645	45

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*Tr = triazole.

Upon reaction of azides I and II with benzoylacetone, which is unsymmetrical, the formation of two cycloaddition products is possible in each case. And, in fact, experiments revealed that reaction of benzoylacetone with each of these azides resulted in the formation of two condensation products in each case, X and XI (with azide I), and XII, XIII (with azide II).

In the IR spectra of compounds XI and XIII the carbonyl group stretching vibration bands are shifted toward lower frequency relative to the spectra of compounds X and XII (see Experimental), which leads us to assign 1,2,3-triazole derivatives XI and XIII as 4-benzoyl derivative structures, and compounds X and XII as 4-acetyl derivative structures.

The PMR spectra of compounds III-VII and X-XIII (Table 1) confirm their assigned structures. The spectra contain singlets for the CH_3 groups in the region 2.4-2.9 ppm, and multiplets for the aromatic protons in the 7.2-8.2 ppm region. The 4-H and 7-H protons, depending on the position of the triazole substituent, give rise to doublets with spin-spin coupling constants of 1.5 Hz or 8.4 Hz, while the 5(6)-H protons appear as doublets of doublets with the same coupling constants. The presence of a C_6H_5CO functional group in the 4-position in ketones XI and XIII is adduced based on splitting of the phenyl signal into two groups of signals centered at 8.29 and 7.60 ppm (compound XIII) and 8.11 and 7.59 ppm (compound XI), with an intensity ratio for these two groups equal to 2:3, due to the effect of the magnetically anisotropic CO group on the ortho-phenyl protons closest to it. In the case of isomeric ketones X and XII, the phenyl signal appears in the form of a slightly broadened singlet centered at 7.33-7.35 ppm. The observed form of the phenyl resonance signal in these compounds, as well as in compound V, suggests that the phenyl group is located in the 5-position of the triazole ring, and not in the 4-position, since in the latter event the phenyl signal would be split due to the effect of the neighboring or adjacent $N_{(3)}$ pyridine-type atom (which is known from the literature to have the same influence as a CO group). The $N_{(1)}$ atom in the pyrrole ring would not be expected to exert this type of effect on an adjacent phenyl group in the 5-position of the triazole ring, and indeed the phenyl peak is not split in these compounds.

EXPERIMENTAL

IR spectra were obtained on a UR-20 spectrophotometer using KBr pellets. PMR spectra were recorded on a Bruker WP-100 SY spectrometer using $CDCl_3$ solutions.

The physical and spectral characteristics of the newly synthesized compounds are summarized in Tables 1 and 2. The results of C, H, N elemental analysis agreed with calculations.

2-Methyl-5(6)-(5-methyl-1,2,3-triazol-1-yl)benzothiazoles (III, IV). Over a 6-h period 9.5 ml of an ether solution containing 0.02 moles ethylmagnesium bromide was saturated with methylacetylene (prepared by heating 1,2-dibromopropane with alcoholic base solution. The resulting solution was stirred vigorously as a solution of 0.01 mole 5- or 6-azido-2-methylbenzothiazole (I or II) in a minimum quantity of absolute ether was added over 15 min; the reaction mixture was stirred an additional 30 min and allowed to stand overnight. The next day the reaction mixture was decomposed by the addition of 15% ammonium chloride solution upon cooling. The resulting precipitate was filtered and crystallized from aqueous alcohol. Compounds III and IV exist as colorless crystalline substances.

2-Methyl-5-(5-phenyl-1,2,3-triazol-1-yl)benzothiazole (V). An ether solution (9.5 ml) containing 0.02 moles ethylmagnesium bromide was diluted with 10 ml absolute ether and 2.2 ml phenylacetylene was added; the mixture was refluxed for 30 min. After cooling the mixture was stirred vigorously as 0.01 mole 5-azido-2-methylbenzothiazole (I) was added over 15 min; the latter was dissolved in a minimum amount of absolute ether. The reaction mixture was stirred an additional 30 min, then allowed to stand overnight; the mixture was then decomposed with cooling with 15% ammonium chloride solution. The resulting solid product which formed was filtered and crystallized from alcohol. The product was obtained in the form of yellow crystals, which were soluble in alcohol, acetone, and benzene; yield 54%, mp 183-184°C.

2-Methyl-5(6)-(5-methyl-4-acetyl-1,2,3-triazol-1-yl)benzothiazoles (VI, VII). To a solution of 0.01 mole sodium ethoxide in 40 ml absolute ethanol was added 0.95 g (0.005 moles) azide I or II, respectively, and 2 g (0.02 mole) acetylacetone, and the mixture was refluxed for 4 h, then allowed to stand for 24 h at room temperature. The resulting precipitate was filtered, washed carefully with water, and crystallized twice from aqueous alcohol.

2-Methyl-5(6)-(5-phenyl-4-benzoyl-1,2,3-triazol-1-yl)benzothiazoles (VIII, IX). To a solution of 0.01 mole sodium propoxide in 60 ml propyl alcohol was added 2.24 g (0.01 mole) dibenzoylmethane, and the mixture was heated until it had dissolved completely; 1.25 g (0.005 moles) azide I or II was then added and the mixture was heated on a water bath for another 3 h. The resulting precipitate was filtered and washed with water, alcohol, and ether. After crystallization from alcohol using activated charcoal needle-shaped crystals were obtained.

2-Methyl-5-(5-phenyl-4-acetyl-1,2,3-triazol-1-yl)benzothiazole (X) and 2-Methyl-5-(5-methyl-4-benzoyl-1,2,3-triazol-1-yl)benzothiazole (XI). To a solution of 0.01 mole sodium methoxide in 30 ml absolute methanol was added 0.95 g (0.005 mole) azide I and 1.62 g (0.01 mole) benzoylacetone, and the mixture was refluxed for 3 h. On the next day the precipitate was filtered, washed with alcohol and ether, and allowed to crystallize from alcohol. Long shiny crystals of (XI), mp 177-179°C, are deposited very quickly from the solution, while the filtrate after several days yielded compound (X) in the form of a finely crystalline precipitate, mp 150-152°C. Repeat recrystallization from alcohol gave colorless crystals, mp 154-156°C (X). A mixture of compounds X and XI gave a mixed melting point of 141-142°C. According to TLC, reaction products X and XI constitute pure compounds.

2-Methyl-6-(5-phenyl-4-acetyl-1,2,3-triazol-1-yl)benzothiazole (XII) and 2-Methyl-6-(5-methyl-4-benzoyl-1,2,3-triazol-1-yl)benzothiazole (XIII). The reaction was carried out according to the preceding method. On the second day the resulting precipitate was filtered, washed with water, alcohol, and ether. A second precipitate was deposited from the filtrate after a short time, and it was also removed by filtration. Both reaction products were crystallized from alcohol. In the first case the substance was obtained in the form of very fine needles, mp 119-120°C (XIII). The second reaction product was formed as shiny plates, mp 154-156°C (XII). A mixed melting point determination and TLC analysis verified that the two substances were different.

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