SYNTHESIS OF 2-METHYL-3-(1-ARYL-1*H*-TETRAZOL-5-YL)--1,8-NAPHTHYRIDINES*

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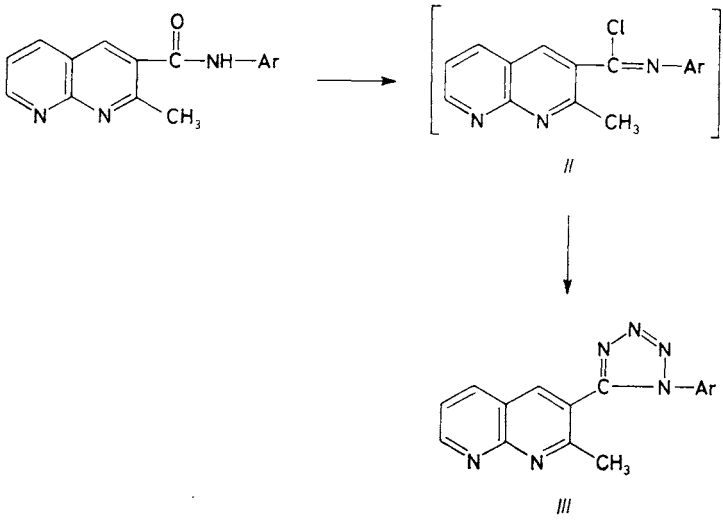
2-Methyl-3-(1-aryl-1*H*-tetrazol-5-yl)-1,8-naphthyridines *III* have been synthesized by the reaction of 2-methyl-N-aryl-1,8-naphthyridine-3-carboxyamides (*I*) with phosphorus pentachloride and azidolysis of the resulting imidoyl chlorides. Structures of these compounds have been established by means of their elemental analyses and spectral data.

A number of 1,8-naphthyridine derivatives is known to be physiologically active and some of them possess antibacterial[1], antimalarial[2] and diuretic[3] properties. Nalidixic acid (1-ethyl-3-carboxy-7-methyl-1,8-naphthyridin-4-one) has been found to be particularly effective against gramnegative bacteria[4] causing chronic urinary tract infections. Based on these observations and in continuation of our earlier work on the synthesis and biological activity of substituted 1,8-naphthyridines[5-9], we report in this communication the synthesis and antibacterial activity of the hitherto unpublished 2-methyl-3-(1-aryl-1*H*-tetrazol-5-yl)-1,8-naphthyridines.

The required 2-methyl-N-aryl-1,8-naphthyridine-3-carboxyamides (*I*) were obtained by condensation of 2-aminonicotinaldehyde with different acetoacetanilides in methanol in the presence of a catalytic amount of piperidine[8]. These N-aryl carboxamides *I* gave the reactive imidoyl chlorides *II* (which were not isolated) when heated with phosphorus pentachloride (see Scheme 1). After the removal of phosphorus oxychloride under reduced pressure, azidolysis of *II* was carried out in aceton medium with sodium azide–aq. sodium acetate[10] to obtain 2-methyl-3--(1-aryl-1*H*-tetrazol-5-yl)-1,8-naphthyridines *IIIa–k* in high yields. Structures of these compounds were confirmed on the basis of their elemental analyses and IR, mass and ^{1}H NMR spectral data. The IR spectra of the products *III* were devoided of bands at 1 670 (amide C=O) and 3 220 (amide—NH) cm^{-1} which were present in the IR spectra of *I*. The ^{1}H NMR spectrum of *IIIa* in hexadeuteriodimethyl sulfoxide showed a three-proton singlet at 3·5 corresponding to the methyl group. Protons at C-4, C-5 and C-7 of the naphthyridine skeleton appeared separately as mul-

* Part IX in the series Substituted 1,8-Naphthyridines; Part VIII: See ref. 9.

tiplets centered at 8·6, 8·8 and 9·2, respectively. The C-6 proton of the naphthyridine moiety appeared along with five aromatic protons as a complex multiplet at 7·2–8·4. Mass spectra of *IIIa* and *IIIg* exhibited strong molecular ion peaks at *m/z* 288 and 302, respectively.



SCHEME 1

All the prepared compounds were screened for their antibacterial activity using the Vincent and Vincent[11] filter paper disc method. The gramnegative and grampositive bacteria employed for the tests were *Escherichia coli*, *Proteus vulgaris* and *Streptococcus albus*, *Sarcina lutea*, respectively. None of the compounds exhibited any promissing activity.

EXPERIMENTAL

Melting points were determined in open capillaries on a Toshniwal melting-point apparatus and are uncorrected. IR spectra (ν_{max}, cm^{-1}) were measured on a Perkin–Elmer 283 Spectrophotometer. The ^1H NMR spectra were recorded on a Varian 60 MHz Spectrometer using tetramethylsilane as an internal standard and chemical shifts are expressed in ppm. Mass spectra were recorded on a Varian MAT CH-7 instrument.

2-Methyl-3-(1-aryl-1*H*-tetrazol-5-yl)-1,8-naphthyridines (*IIIa–k*)

A mixture of *I* (1 mmol) and phosphorus pentachloride (1 mmol) was heated in an oil bath at 120°C for 3 h. After termination of the evolution of hydrogen chloride, traces of phosphorus oxychloride were removed under reduced pressure. The imidoyl chloride thus obtained was treated with an excessive amount of cold solution of sodium azide and sodium acetate in aq. acetone and the reaction mixture was stirred for 24 h. The solid that separated was filtered and crystal-

TABLE I
Analytical data of compounds *III*

Compound[a] (yield, %)	Ar	Formula (mol. wt.)	Calculated/found		
			% C	% H	% N
IIIa	phenyl	$C_{16}H_{12}N$	66·65	4·20	29·15
(65)		(288·3)	66·56	4·26	29·24
IIIb	*o*-methoxyphenyl	$C_{17}H_{14}N_6O$	64·14	4·45	26·40
(70)		(318·3)	64·21	4·40	26·49
IIIc	*m*-methoxyphenyl	$C_{17}H_{14}N_6O$	64·14	4·45	26·40
(67)		(318·3)	64·23	4·40	26·50
IIId	*p*-methoxyphenyl	$C_{17}H_{14}N_6O$	64·14	4·45	26·40
(74)		(318·3)	64·24	4·41	26·49
IIIe	*o*-methylphenyl	$C_{17}H_{14}N_6$	67·53	4·67	27·80
(70)		(302·3)	67·67	4·73	27·90
IIIf	*m*-methylphenyl	$C_{17}H_{14}N_6$	67·53	4·67	27·80
(68)		(302·3)	67·66	4·75	27·91
IIIg	*p*-methylphenyl	$C_{17}H_{14}N_6$	67·53	4·67	27·80
(74)		(302·3)	67·65	4·74	27·92
IIIh	*o*-chlorophenyl	$C_{26}H_{11}ClN_6$	59·54	3·44	26·04
(72)		(322·8)	59·66	3·49	26·16
IIIi	*m*-chlorophenyl	$C_{16}H_{11}ClN_6$	59·54	3·44	26·04
(70)		(322·8)	59·64	3·48	26·18
IIIj	*p*-chlorophenyl	$C_{16}H_{11}ClN_6$	59·54	3·44	26·04
(75)		(322·8)	59·65	3·49	26·15
IIIk	*m*-nitrophenyl	$C_{16}H_{11}N_7O_2$	57·65	3·33	29·42
(60)		(333·3)	57·56	3·38	29·49

[a] M.p. > 300°C.

lized. In some cases, when the solid did not separate the reaction mixture was diluted with water and then, the resulting solid was filtered and crystallized from acetic acid (Table I).

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