1-(3-Pyridyl)-3-arylbenzo[f]quinolines A(a-c) were obtained by the method in [5].

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SYNTHESIS OF N-2-PROPYNYL-ω-AMINOALKYL-8-QUINOLINESULFONAMIDES

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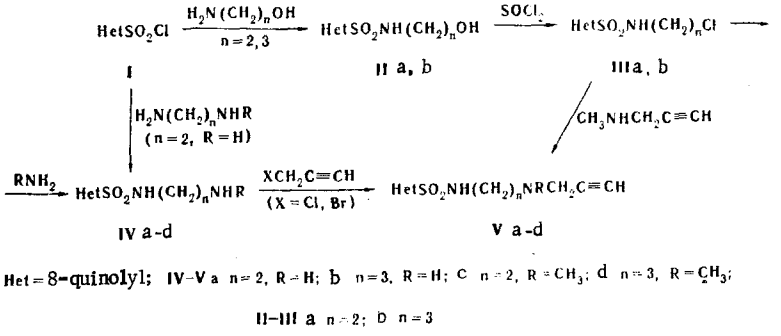
N-2 Propynyl-ω-aminoalkyl-substituted 8-quinolinesulfonamides, which are potential inhibitors of monoaminooxidase, were synthesized by alkylation of ω-aminoalkyl-8-quinolinesulfonamides with propargyl halides or by aminolysis of ω-chloroalkyl-8-quinolinesulfonamides with N-methylpropargylamine.

In connection with the research on the synthesis of inhibitors of monoaminooxidase in the quinoline series – 2-propynylamine derivatives [1, 2] – it seems of interest to obtain quinoline compounds in which heteroatoms (for example, in the form of a sulfonamido group) are also included in the carbon chain to which the 2-propynylamino grouping is attached. We selected quinoline-8-sulfonic acid derivatives for this purpose.

Relatively little study has been devoted to quinoline-8-sulfonamide and its N-substituted derivatives [3-6]. Of the N-(ω-aminoalkyl)quinoline-8-sulfonamides, only the 4-aminobutyl compound has been described [7].

The present communication is devoted to the synthesis of N-2-propynyl-ω-aminoalkyl derivatives of quinoline-8-sulfonamide. The synthesis was accomplished via the scheme:



Het = 8-quinolyl; IV-V a n = 2, R = H; b n = 3, R = H; c n = 2, R = CH_3; d n = 3, R = CH_3;

II-III a n = 2; b n = 3

The reaction of quinoline-8-sulfonyl chloride (I) with the corresponding amino alcohols gave ω-hydroxyalkyl-substituted compounds (IIa, b), which were converted to ω-chloro derivatives (IIIa, b). Ammonolysis or aminolysis of chlorides IIIa, b leads to ω-aminoalkylsulfonamides (IVa-d); the same derivatives (for example,

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TABLE 1. N-Substituted Quinoline-8-sulfonamides

Compound	mp, °C	IR spectrum, cm^{-1}	Found, %				Empirical formula	Calculated, %				Yield, %
			C	H	N	S		C	H	N	S	
IIa	111–112	930, 3540 (OH), 1170, 1330 (SO_2), 1620 (NH)	52,2	4,9	11,2	—	$C_{11}H_{13}N_2O_3S$	52,3	4,8	11,1	—	79
IIb	73–75	930, 3500 (OH), 1170, 1330 (SO_2), 1620 (NH)	54,3	5,2	10,6	—	$C_{12}H_{14}N_2O_3S$	54,1	5,3	10,5	—	50
IIIa	86	—	—	—	10,4	11,6	$C_{11}H_{11}ClN_2O_2S$	—	—	10,3	11,8	47
IIIb	103–105	—	50,7	5,0	9,9	—	$C_{12}H_{13}ClN_2O_2S$	50,0	4,6	9,8	—	41
IVa	113–115	2990, 3320 (NH)	49,9	5,1	15,6	—	$C_{11}H_{13}N_3O_2S \cdot H_2O$	49,7	5,5	15,2	—	52
IVb	170	3240, 3480 (NH)	50,8	6,1	—	—	$C_{12}H_{15}N_3O_2S \cdot H_2O$	50,9	6,0	—	—	48
IVc	185	2700, 3260, 3430 (NH)	49,7	6,8	13,4	—	$C_{12}H_{15}N_3O_2S \cdot 2H_2O$	49,5	7,0	13,3	—	51
IVd	210	2680, 3260, 3380 (NH)	53,1	6,3	14,0	—	$C_{13}H_{17}N_3O_2S \cdot 2H_2O$	53,2	6,7	14,1	—	60
Va	Oil	2120 (C≡C)	56,0	6,0	—	9,8	$C_{14}H_{15}N_3O_2S \cdot 0,5H_2O$	56,0	5,4	—	10,8	30
Vb	Oil	2120 (C≡C)	59,0	5,7	—	10,5	$C_{15}H_{17}N_3O_2S$	59,4	5,6	—	10,6	18
Vc	Oil	2120 (C≡C)	59,0	5,7	—	10,4	$C_{15}H_{17}N_3O_2S$	59,4	5,6	—	10,6	53
Vd	Oil	2120 (C≡C)	60,7	6,1	—	9,9	$C_{16}H_{19}N_3O_2S$	60,6	6,0	—	10,1	59

TABLE 2. PMR Spectra

Compound	Chemical shifts, δ, ppm					
	NH (s)	NCH_3 (s)	C≡CH (t)	$CH_2C\equiv$ (d)	CH_2 (q)	SO_2NH (s)
Va	2,15	—	2,55	3,0	2,20, 2,85	6,75
Vb	1,45	—	2,38	4,70	2,25, 3,24, 3,78	6,80
Vc	—	2,20	2,45	3,35	1,75, 2,75	7,15
Vd	—	2,55	2,75	3,60	1,98, 3,38, 3,48	7,70

IVa) can be obtained by direct sulfonylation of the corresponding diamines with sulfonyl chloride I. The reaction of amino-substituted IVa, b with propargyl bromide leads to Va, b in moderate yields. The analogous alkynylation of N-methylated aminosulfonamides IVc, d proceeds ambiguously and is accompanied by considerable resinification. We were able to obtain derivatives Vc, d only by replacement of the propargyl bromide by propargyl chloride. Compounds Vc, d were synthesized with better results from N-methylpropargylamine and chlorides IIIa, b. The yields and properties of the synthesized compounds are presented in Table 1, and the PMR spectra are presented in Table 2.

It is difficult to form a judgment regarding the presence of a triple bond in Va-d on the basis of the IR absorption at 3300 cm^{-1}, since the frequencies of the NH vibrations of sulfonamido and amino groups are found in the same range. We were able to identify this bond from the weak band of C≡C stretching vibrations at 2100 cm^{-1}: Intramolecular interaction of the π electrons of the triple bond with the unshared pair of electrons of the amine nitrogen atom lowers its intensity [8, 9]. The intensity of this band increases in the spectra of the hydrochlorides of Va-d, and the absorption at 3300 cm^{-1} vanishes or is masked by other absorption bands.

EXPERIMENTAL

The IR spectra of KCl pellets and thin layers of the compounds were recorded with a Unicam SP-1000 spectrometer. The PMR spectra of solutions of the compounds in $CDCl_3$ were recorded with a Hitachi–Perkin-Elmer spectrometer (60 MHz) at 27°C with hexamethyldisiloxane as the internal standard. Silica gel L 40/100μ was used for column chromatography. The following systems were used for thin-layer chromatography (TLC) on Silufol UV-254: carbon tetrachloride–isopropyl alcohol (4:1) (A), acetonitrile–25% ammonia (9:1) (B), and chloroform–methanol (4:1) (C).

N-(2-Hydroxyethyl)- and N-(3-Hydroxypropyl)quinoline-8-sulfonamides (IIa, b). A solution of 8 g (0.04 mole) of quinoline-8-sulfonyl chloride (I) [3] in chloroform was added with stirring in the course of 20 min to a solution of 0.69 mole of 2-aminoethanol or 3-aminopropanol in 30 ml of chloroform, and the mixture was stirred for 1 h. The solvent was then removed by distillation, and the residue was washed with water and crystallized from methanol. The products were homogeneous in system A.

N-(2-Chloroethyl)- and N-(3-Chloropropyl)quinoline-8-sulfonamides (IIIa, b). A 0.02-mole sample of IIa or IIb was added gradually to 7 ml (0.1 mole) of thionyl chloride, and the mixture was heated at 50°C for 1.5 h. It was then poured into ice water, and the aqueous mixture was neutralized with 25% ammonium hydroxide. The resulting precipitate was removed by filtration and crystallized from ethanol. The products were homogeneous in system A.

N-(2-Aminoethyl)- and N-(3-Aminopropyl)quinoline-8-sulfonamides (IVa, b) and Their N-Methyl Derivatives (IVc, d). A) A mixture of 7 mmole of chloride IIIa or IIIb, 18 ml of 25% ammonium hydroxide or 50% aqueous methylamine, and 10 ml of methanol was heated at 100°C for 4 h, after which the solvent was removed by distillation, and the residue was triturated with chloroform. The solid material was removed by filtration and crystallized from 50% ethanol. The products were homogeneous in system B.

B) A solution of 1.95 g (0.01 mole) of quinoline-8-sulfonyl chloride in 20 ml of chloroform was added in the course of 15 min to 3.3 ml (0.05 mole) of anhydrous ethylenediamine, and the mixture was stirred for 30 min. Water (50 ml) was added, and the organic layer was separated and evaporated. The residue was extracted with methanol, the solvent was removed, and the residue was crystallized from methanol. The product was chromatographically homogeneous and was identical to amino compound IVa obtained from chloride IIIa. The yield was 59%.

N-[N-(2-Propynyl)-2-aminoethyl]- and N-[N-(2-Propynyl)-3-aminopropyl]quinoline-8-sulfonamides (Va, b) and Their N-Methyl Derivatives (Vc, d). A) A 0.4-ml (2 mmole) sample of propargyl bromide was added to a suspension of 2 mmole of amine IVa or IVb and 500 mg (3.6 mmole) of potassium carbonate in 5 ml of methanol, and the mixture was refluxed for 6 h. The solvent was then removed by distillation, and the residue was extracted with chloroform. The extract was evaporated to a small volume, and the concentrate was chromatographed with a column filled with 10 g of silica gel; products Va or Vb were eluted with a mixture of chloroform and methanol (50:1). Removal of the solvent gave Va or Vb. The products were homogeneous in systems B and C. The hydrochlorides of these amines, which were obtained with hydrogen chloride in chloroform, were extremely hygroscopic.

A 0.13-ml (1.75 mmole) sample of propargyl chloride was added to a mixture of 1.25 mmole of amine IVc or IVd and 180 mg (1.35 mmole) of potassium carbonate in 3 ml of methanol, and the mixture was refluxed for 11 h. It was then chromatographed as described for Va, b [chloroform – methanol (75:1)]. The products were homogeneous in systems B and C.

B) A mixture of 120 mg (1.15 mmole) of N-methylpropargylamine acid oxalate, 220 mg (1.6 mmole) of potassium carbonate, and 4 ml of methanol was stirred for 10 min, 0.9 mmole of chloride IIIa or IIIb was added, and the mixture was refluxed for 5 h. It was then worked up as in method A. The yields of Va, b were ~60%.

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