162° C (from acetone). Found, %: N 3.30, 3.32. Calculated for $C_{14}H_{25}ClINO$, %: N 3.63.

Allyl bromide derivative of 4-ethynyl-1,2,5-trimethylpiperid-4-ol. A mixture of 2 g of the β-isomer of 4-ethynyl-1,2,5-trimethylpiperid-4-ol [1] and 1.6 g of allyl bromide in 10 ml of absolute benzene was heated at 95–100° C for 7.5 hr. The precipitate was separated off and crystallized from ethanol, giving 2.2 g (61%) of the allyl bromide derivative, mp 204–205° C. Found, %: C 54.42; H 8.38; Br 28.40; N 5.10. Calculated for $C_{13}H_{22}BrNO$, %: C 54.17; H 7.69; Br 27.74; N 4.85.

The allyl bromide derivative of the β-isomer of 1,2,5-trimethyl-4-vinylpiperid-4-ol was obtained in a similar manner to the preceding compound, yield 63%, mp 201–203° C (from ethanol). Found, %: C 54.18; H 8.79; Br 28.32; N 5.03. Calculated for $C_{13}H_{24}BrNO$, %: C 53.80; H 8.34; Br 27.53; N 4.82.

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INVESTIGATIONS IN THE FIELD OF THE CHEMISTRY OF HETEROCYCLES

XLVI. Synthesis and Biological Activity of Some 2-Aminomethyl-3-arylquinazolones*

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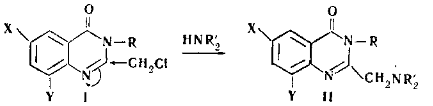
The reaction of 3-aryl-2-chloromethylquinazol-4-ones with secondary amines has given a number of previously unreported 2-aminomethyl-3-arylquinazol-4-ones, and their biological activity has been studied.

Effective preparations with a broad spectrum of pharmacological activity have been found among the 3-aryl-2-methylquinoxazol-4-ones [2–7]. It appeared of interest to synthesize 3-arylquinazol-4-ones with aminomethyl substituents in position 2 and to subject them to pharmacological study.

As the starting compounds we used 3-aryl-2-chloromethylquinazol-4-ones (I) [8] and also 6-chloro-2-chloromethyl-3-(4'-chlorophenyl)quinazol-4-one (Ia) and 6,8-dichloro-2-chloromethyl-3-(4'-ethoxyphenyl) quinazol-4-one (Ib), obtained as described previously [8] from the 4'-chloroanilide of 5-chloroanthranilic acid (III) and the 4'-phenetidide of 3,5-dichloroanthranilic acid (IV), respectively.



a X = Cl, Y = H, R = 4'-ClC$_6$H$_4$; b X = Y = Cl, R = 4'-C$_2$H$_5$OC$_6$H$_4$

The chlorine in the CH_2Cl group of I is activated by the quinazolone ring and, therefore, readily takes part in a nucleophilic substitution reaction. Thus, when compound I was heated with diethylamine, piperidine, and morpholine, the corresponding 2-aminomethyl-3-arylquinazol-4-ones (II) were formed in high yields.

They are colorless crystalline substances which form well-crystalline hydrochlorides and picrates.

The structure of the quinazolone compounds II was confirmed by the UV and IR absorption spectra of Ia, Ib, and V. The UV spectrum of V is characterized by the presence of two maxima at 229 nm (log ε 4.66) and 265 nm (log ε 4.07) (cf. [8]); the IR spectra of Ia, Ib, and V show the following bands: 1690–1688 (CO), 1632–1606, 1595–1565, and 1508–1494 cm^{-1} (these may be assigned provisionally to the vibrations of the quinazolone ring) [9].

The pharmacological tests showed that the quinazolones V–XVIII possesss a tranquillizing and analgesic action; the analgesic activity decreases in the following sequence: VIII > VII > X > XIV > XIII > XVII > XVI*.

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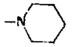
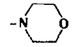
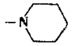
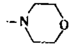
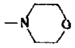
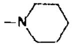
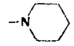
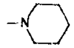
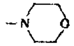
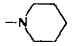
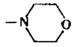
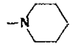
*For part XLV, see [1].

*The investigations were carried out under the direction of Prof. V. M. Grishina, to whom the authors express their deep gratitude.

Table

Constants of the 2-Aminomethyl-3-arylquinazol-4-ones (II)

Compound	R	X	Y	R'$_2$N—	Melting point, °C			Empirical formula	Found, %			Calculated, %			Yield, %
					base*	hydrochloride	picrate		C	H	N	C	H	N	
V	4-ClC$_6$H$_4$	H	H		137—138	236—237	204—205	$C_{20}H_{20}ClN_3O$	67.75	5.60	11.70	67.89	5.69	11.87	85.2
VI	4-ClC$_6$H$_4$	H	H		169—170	212—214	177—178	$C_{19}H_{18}ClN_3O_2$	64.02	5.00	11.67	64.13	5.09	11.80	55.6
VII	C$_6$H$_5$	H	H		121—122	238	193—194	$C_{20}H_{21}N_3O$	75.15	6.60	13.20	75.20	6.62	13.15	50.0
VIII	C$_6$H$_5$	H	H		145—147	248	206—207	$C_{19}H_{19}N_3O_2$	70.79	5.80	12.90	70.99	5.95	13.09	90.3
IX	2-ClC$_6$H$_4$	H	H	—N(C$_2$H$_5$)$_2$	140—141	—	—	$C_{19}H_{20}ClN_3O$	66.52	5.82	12.21	66.76	5.89	12.29	66.1
X	4-BrC$_6$H$_4$	H	H		165—166	—	—	$C_{19}H_{18}BrN_3O_2$	56.91	4.47	10.25	57.00	4.53	10.49	58.8
XI	2-CH$_3$-4-Br-C$_6$H$_3$	H	H		169—170	253—254	180—181	$C_{21}H_{22}BrN_3O$	61.03	5.23	10.01	61.16	5.37	10.19	88.2
XII	C$_6$H$_5$	Br	H		180—181	220—221	225	$C_{20}H_{20}BrN_3O$	60.96	5.01	10.30	60.30	5.06	10.55	68.8
XIII	4-ClC$_6$H$_4$	Cl	H		169—170	224—226	235	$C_{20}H_{19}Cl_2N_3O$	61.66	4.77	10.89	61.85	4.93	10.81	64.3
XIV	4-ClC$_6$H$_4$	Cl	H		126—128	220—222	180—181	$C_{19}H_{17}Cl_2N_3O_2$	58.17	4.33	10.61	58.46	4.39	10.76	54.7
XV	4-C$_2$H$_5$OC$_6$H$_4$	Cl	Cl	—N(C$_2$H$_5$)$_2$	187—189	—	—	$C_{21}H_{23}Cl_2N_3O_2$	59.88	5.29	9.75	60.00	5.51	10.00	71.5
XVI	4-C$_2$H$_5$OC$_6$H$_4$	Cl	Cl		189—190	—	—	$C_{22}H_{23}Cl_2N_3O_2$	61.03	5.27	9.65	61.12	5.36	9.72	65.8
XVII	4-C$_2$H$_5$OC$_6$H$_4$	Cl	Cl		175—177	—	—	$C_{21}H_{21}Cl_2N_3O_3$	57.83	4.65	9.63	58.07	4.87	9.68	65.3
XVIII	C$_6$H$_5$	Br	Br		142—143	—	—	$C_{20}H_{19}Br_2N_3O$	50.07	3.91	8.58	50.33	4.01	8.80	50.0

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*The base VI was recrystallized from methanol, and the others from ethanol.

EXPERIMENTAL

4'-Chloroanilide of 5-chloroanthranilic acid (III). To the ethylmagnesium iodide obtained from 37.5 g (0.24 mole) of ethyl iodide and 5.76 g (0.24 g-at) of magnesium in 90 ml of ether was added 15.3 g (0.12 mole) of 4-chloroaniline, and the mixture was heated for 30 min. A solution of 11.1 g (0.06 mole) of methyl 5-chloroanthranilate in 20 ml of water was added and the mixture was boiled again for 30 min, after which it was decomposed with a solution of ammonium chloride and the ethereal layer was separated off and treated with steam. The residue was crystallized from ethanol. Needles with mp 172–173° C. Yield 10.2 g (60%). Found, %: N 9.68. Calculated for $C_{13}H_{10}Cl_2N_2O$, %: N 9.96.

4'-Phenetidide of 3,5-dichloroanthranilic acid (IV). This was obtained similarly. Yield 85.3%. Needles (from ethanol) with mp 196–197° C. Found, %: N 8.39. Calculated for $C_{15}H_{14}Cl_2N_2O_2$, %: N 8.61.

6-Chloro-2-chloromethyl-3-(4'-chlorophenyl)quinazol-4-one (Ia). This was obtained from III and chloroacetyl chloride in glacial acetic acid solution. Yield 71%. Needles (from ethanol) with mp 182–183° C. IR spectrum: 1690 (CO), 1610, 1590, 1470 cm^{-1} (quinazolone bands). Found, %: C 52.90; H 2.58; N 8.40. Calculated for $C_{15}H_9Cl_3N_2O$, %: C 53.04; H 2.64; N 8.25.

6,8-Dichloro-2-chloromethyl-3-(4'-ethoxyphenyl)quinazol-4-one (Ib). This was obtained similarly from IV. Yield 50%. Needles (from ethanol) with mp 165–166° C. IR spectrum: 1688 (CO), 1632, 1595, 1508 cm^{-1} (quinazolone bands). Found, %: C 53.05; H 3.34; N 7.46. Calculated for $C_{17}H_{13}Cl_3N_2O_2$, %: C 53.24; H 3.44; N 7.30.

3-(4'-Chlorophenyl)-2-piperidinomethylquinazol-4-one (V). A mixture of 3.05 g (0.01 mole) of 2-chloromethyl-3-(4'-chlorophenyl)-quinazol-4-one and 1.7 g (0.02 mole) of piperidine in 20 ml of benzene was boiled for 2 hr, made alkaline with 10% sodium carbonate solution, and treated with steam. The precipitate was crystallized from ethanol. Yield 1.5 g. UV spectrum (in ethanol): λ_{max} (log ε) 229 nm (4.66) and 265 nm (4.07). IR spectrum: 1688 (CO), 1606, 1566, 1494 cm^{-1} (quinazolone bands). Compounds VI–XVIII were obtained similarly (table).

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SYNTHESIS OF 1-ACRYLYL- AND 1-METHACRYLYL-SUBSTITUTED PYRAZOLINES AND PYRAZOLES

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1-Acrylyl- and 1-methacrylyl-substituted 3-methylpyrazolines, 3,5,5-trimethylpyrazolines, 3-methyl-5-phenylpyrazolines, 3-methyl-5-phenylpyrazoles, and 3,5-dimethylpyrazoles have been synthesized.

Until now, only a few N-acrylyl-substituted nitrogen-containing heterocycles were known. In this paper we report the synthesis of several 1-acrylyl-and 1-methacrylylpyrazolines and -pyrazoles by the reaction of acryloyl and methacryloyl chlorides with the corresponding 2-pyrazolines or pyrazoles in the presence of triethylamine. The substances formed are colorless liquids or crystals which readily polymerize.

EXPERIMENTAL

The initial 3,5,5-trimethylpyrazoline, 3-methyl-5-phenylpyrazoline, 3-methyl-5-phenylpyrazole, and 3,5-dimethylpyrazole were obtained by published methods [1-4]. The 3-methylpyrazoline was prepared as described by Matsoyan et al. [5].

Acylation of the pyrazolines and pyrazoles. With vigorous stirring and ice-water cooling, 0.15 mole of acryloyl or methacryloyl chloride was added dropwise to a mixture of 0.1 mole of the appropriate pyrazoline or pyrazole, 75 ml of dry ether, and 0.15 mole of triethylamine in such a way that the temperature of the reaction mixture remained at 5–10° C. Stirring at room temperature was continued for another 3 hr, and the precipitate that had formed (triethylamine hy-