8. J. A. Zoltewicz, T. M. Oestreich, J. K. O'Halloran, and L. S. Helmic, J. Org. Chem., 38, 1949 (1982).
9. M. G. Ponizovskii, O. N. Chupakhin, V. N. Charushin, and G. G. Aleksandrov, Khim. Geterotsikl. Soedin., No. 10, 1410 (1982).
10. E. Buncel, J. W. K. Webb, and J. F. Wiltshire, J. Am. Chem. Soc., 99, 4429 (1977).
11. E. Buncel and J. W. K. Webb, Tetrahedron Lett., 4417 (1976).
12. E. Buncel and W. Eggimann, J. Am. Chem. Soc., 99, 5458 (1977).
13. V. N. Charushin, A. I. Chernyshev, N. N. Sorokin, and O. N. Chupakhin, Org. Magn. Reson., 22, 775 (1984).
14. R. E. Valter, Ring-Chain Isomerism in Organic Chemistry [in Russian], Zinatne, Riga (1978).
15. D. R. Carver and J. F. Wolfe, J. Org. Chem., 47, 1036 (1982).
16. V. N. Charushin, V. G. Baklykov, O. N. Chupakhin, G. M. Petrova, and E. O. Sidorov, Khim. Geterotsikl. Soedin., No. 6, 680 (1984).

PYRIMIDINE DERIVATIVES.

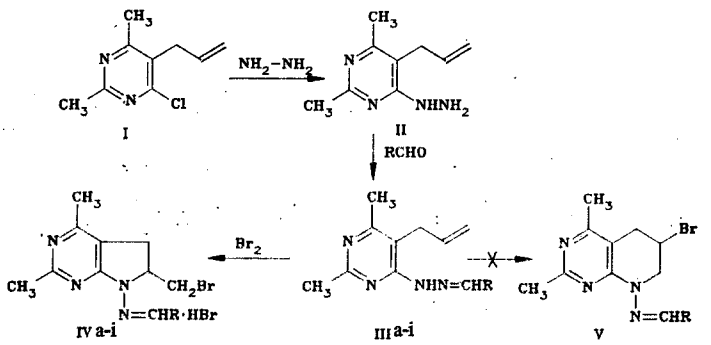
58.* A NEW METHOD FOR SYNTHESIZING 7-AMINOPYRROLO[2,3-d]-PYRIMIDINE DERIVATIVES

R. G. Melik-Ogandzhanyan, A. S. Gapoyan,
V. É. Khachatryan, and V. S. Mirzoyan

UDC 547.853.4.7'75856.07:543.422'51

A number of aldimines of 7-aminopyrrolo[2,3-d]pyrimidine have been synthesized by the action of bromine on hydrazones of 5-allyl-4-hydrazinopyridine. The structures of the compounds obtained were confirmed by IR spectroscopy and mass spectrometry.

Continuing the development of new methods for synthesizing condensed pyrimidine systems [1-3] presenting interest as physiological compounds [4-6], in the present work we have shown the possibility of obtaining 7-aminopyrrolo[2,3-d]pyrimidine derivatives (IVa-i) by the following scheme:



III, IV a R=C_6H_5; b R=4-FC_6H_4; c R=4-$CH_3OC_6H_4$; d R=4-$O_2NC_6H_4$; e R=4-$(CH_3)_2NC_6H_4$; f R=4-$(ClCH_2CH_2)_2NC_6H_4$; g R=2-HOC_6H_4; h R=3-CH_3O, 4-HOC_6H_3; i R=CH=CHC_6H_5

*For Communication 57, see [1].

A. L. Mndzhoyan Institute of Fine Organic Chemistry, Academy of Sciences of the Armenian SSR, Erevan. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 5, pp. 678-681, May, 1985. Original article submitted May 3, 1984.

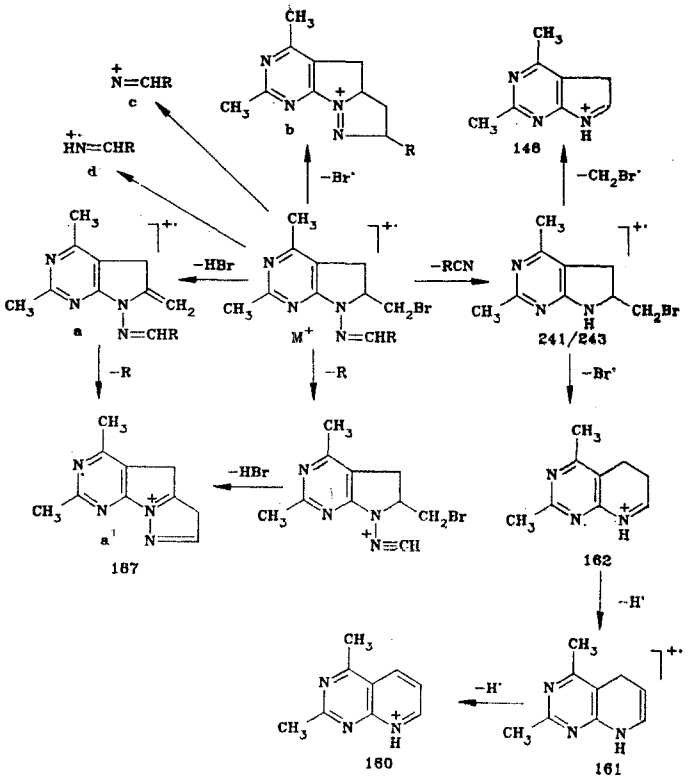
 0009-3122/85/2105-0572$09.50

TABLE 1. Hydrazones Derived from 5-Allyl-4-hydrazino-2,6-dimethylpyrimidine (IIIa-i)

Compound	mp, °C (from ethanol)	R_f	Found, %			Empirical formula	Calculated, %			Yield, %
			C	H	N		C	H	N	
IIIa	148—150	0,63	72,35	6,48	21,12	$C_{16}H_{18}N_4$	72,18	6,81	21,05	81
IIIb	134—135	0,65	67,90	6,26	19,62	$C_{16}H_{17}FN_4$	67,60	5,98	19,71	88
IIIc	150—152	0,62	68,40	7,00	18,90	$C_{17}H_{20}N_4O$	68,91	6,75	18,91	74
IIId	154—156	0,60	62,05	5,52	22,25	$C_{16}H_{17}N_5O_2$	61,73	5,46	22,50	95
IIIe	104—106	0,50	69,80	7,79	22,48	$C_{18}H_{23}N_5$	69,90	7,44	22,65	90
IIIf	135—137	0,73	60,40	6,00	15,30	$C_{20}H_{25}Cl_2N_5$	60,60	6,31	15,15	96
IIIg	118—120	0,67	67,20	6,34	20,07	$C_{16}H_{18}N_4O$	67,61	6,33	19,70	70
IIIh	223—225	0,59	65,30	6,40	18,01	$C_{17}H_{20}N_4O_2$	65,38	6,41	17,95	79
IIIi	124—126	0,65	73,60	7,07	18,84	$C_{18}H_{20}N_4$	73,97	6,84	19,17	71

By heating the 4-chloropyrimidine (I) [2] with hydrazine, we synthesized the 4-hydrazinopyrimidine (II), readily forming the hydrazones (IIIa-i) with the corresponding aldehydes (Table 1). The latter cyclized under the action of bromine to the 7-methyleneamino-6-bromomethyl-2,4-dimethyl-5,6-dihydropyrrolo[2,3-d]pyrimidines (IVa-i) (Table 2) by a scheme analogous to that for the 5-allyl-4-aminopyridines described previously [1]. The structures of the compounds synthesized were confirmed by IR spectroscopy and mass spectrometry. The mass spectra of the hydrazones (IIIa-i) contained fairly strong peaks of the molecular ions (M^+). In each of the spectra the maximum peak was that of the 162 ion,* the formation of which is due to the cleavage of the NH–N bond with the retention of the positive charge on the pyrimidine nucleus. The next in intensity was the peak of the 148 ion formed by the ejection of the NHN=CHR radical. On the whole, the dissociative ionization of compounds (IIIa-i) took place by a scheme analogous to that for the 4-amino derivatives studied previously [1].

The main routes in the fragmentation of M^+ of the free bases (IVa-i) under the action of electron impact can be illustrated by the following scheme:



*In the text and the scheme, the numbers characterizing the ions show the m/z values.

TABLE 2. Hydrobromides of Aldimines Derived from 7-Amino-6-bromomethyl-2,4-dimethyl-5,6-dihydropyrrolo[2,3-d]pyrimidines (IVa-i).

Compound	mp, °C (from ethanol)	R_f	Found, %		Empirical formula	Calculated, %		Yield, %
			Br	N		Br	N	
IVa	240—242	0,60	37,20	13,00	$C_{16}H_{17}BrN_4 \cdot HBr$	37,55	13,14	60
IVb	230—232	0,65	36,01	12,91	$C_{16}H_{16}BrFN_4 \cdot HBr$	36,03	12,61	47
IVc	210—212	0,66	34,82	12,71	$C_{17}H_{19}BrN_4O \cdot HBr$	35,08	12,28	72
IVd	200—202	0,63	34,29	14,76	$C_{16}H_{16}BrN_5O_2 \cdot HBr$	33,97	14,36	87
IVe	215—217	0,15	34,03	14,49	$C_{18}H_{22}BrN_5 \cdot HBr$	34,11	14,92	60
IVf	199—201	0,54	28,06	12,00	$C_{20}H_{24}BrCl_2N_5 \cdot HBr$	28,26	12,36	70
IVg	255—257	0,64	35,81	12,74	$C_{16}H_{17}BrN_4O \cdot HBr$	36,19	12,66	52
IVh	205—207	0,69	35,02	12,96	$C_{18}H_{20}BrN_4 \cdot HBr$	35,32	12,36	40
IVi	203—205	0,45	33,91	12,11	$C_{17}H_{19}BrN_4O_2 \cdot HBr$	33,68	11,80	45

As can be seen from the scheme, the fragmentation process takes place in several directions. The ion *a* formed by the splitting out of hydrogen bromide from M^+ then loses the radical R, which leads to the ion *a'*. The splitting out of HBr and R may also take place in the opposite sequence. The formation of the ion b is connected with the simple elimination of the bromine atom from M^+. The third main fragmentation pathway is the formation of the 241/243 ion, which then breaks down into the 162 and 148 ions. It must be mentioned that the presence of the strong peak of a 148 ion in the spectrum formed as the result of the ejection of the particle CH_2Br is evidence in favor of the ring closure of compound (III) to form the five-membered ring (IV) because if the reaction formed the 8-methyleneamine-6-bromo-2,4-dimethyl-6,7-dihydropyrido[2,3-d]pyrimidine (V), the ejection of the CH_2Br particle from the $[M - RCN]^+$ ion would be impossible. In addition to the directions of fragmentation of M^+ that have been mentioned, simple cleavage of the N—N bond is observed which can also take place with the transfer of a hydrogen atom, forming the ions c and d, respectively.

The IR spectra of compounds (IV) each show absorption bands at 1605 and 1593 cm^{-1} corresponding to aromatic bonds. Absorption in the 1620 cm^{-1} region corresponds to the N=CHR bond. Absorption at 1445 cm^{-1} can be assigned to a methylene group in a ring, and that at 1500 and 760 cm^{-1} to methylene groups present in a side chain [7, 8].

Thus, the spectral characteristics confirm the alternative structure of aminopyrrolopyrimidines (IV) for the compounds synthesized.

EXPERIMENTAL

Mass spectra were taken on an MKh-1303 instrument with direct introduction of the sample into the source at an admission temperature 25-30°C below the melting point of the compound under investigation and with an ionization energy of 30 eV. IR spectra were taken on a UR-20 instrument in KBr tablets. A chromatographic investigation was performed on Silufol UV-254 plates in the butanol—acetic acid—water (2:2:1) system [for (IIIa-i)] and the (4:4:5) system [for (IVa-i)].

TABLE 3. Mass Spectra* of Compounds (IVa-c, e, g, h)

Compound	m/z (relative intensity, %)
IVa	344† (32), 267† (22), 241† (100), 240† (24), 162 (26), 161 (80), 160 (76) 148 (64), 121 (22), 82 (34), 80 (40)
IVb	362† (31), 241† (76), 162 (100), 161 (74), 160 (92), 148 (84), 123 (28), 122 (36), 121 (72), 120 (24), 119 (24)
IVc	374† (100), 295 (16), 294 (20), 293 (40), 279 (13), 162 (22), 161 (64), 160 (50), 148 (60), 120 (12), 94 (22)
IVe	387† (60), 307 (28), 241† (62), 162 (64), 161 (72), 160 (100), 159 (72), 148 (70), 147 (25), 96 (28), 94 (26)
IVg	360† (50), 281 (38), 267 (20), 241† (20), 162 (54), 161 (20), 160 (26), 148 (100), 122 (22), 121 (24), 94 (22)
IVh	390† (24), 310 (42), 241† (16), 231 (20), 229 (28), 162 (20), 160 (100), 159 (60), 148 (20), 144 (28), 118 (28)

*The M^+ peak and the ten strongest peaks are given. The peaks of isotopic ions are not shown.
†Ions containing the ^{79}Br isotope.

5-Allyl-4-hydrazino-3,6-dimethylpyrimidine (II). A mixture of 1.82 g (0.01 mole) of compound (I) and 2 g of hydrazine hydrate in 50 ml of methanol was boiled for 6-8 h. The solvent was distilled off and the residue was treated with 30 ml of water and extracted with 50 ml of chloroform. The chloroform layer was dried with sodium sulfate and, after the solvent had been distilled off, the residue was dissolved in 30 ml of hexane and the solution was left overnight in the refrigerator. The crystals that had deposited were filtered off and dried. Yield 1.47 g (83%), mp 63-65°C. R_f 0.59 (butanol—acetic acid—water (4:4:5)). Found: C 60.40; H 8.11; N 31.25%. $C_9H_{14}N_4$. Calculated: C 60.67; H 8.00; N 31.46%; M^+ 178.

Hydrazones Derived from 5-Allyl-4-hydrazino-2,6-dimethylpyrimidine (IIIa-i). A mixture of 1.78 g (0.01 mole) of compound (II) and 0.01 mole of the appropriate aldehyde in 30 ml of methanol was boiled for 30-40 min, the solvent was distilled off, the residue was treated with ether, and the crystals that deposited were filtered off (Table 1).

Hydrobromides of Aldimine Derivatives of 7-Amino-6-bromomethyl-2,4-dimethyl-5,6-dihydropyrrolo[2,3-d]pyrimidines (IVa-i). A solution of 1.6 g (0.01 mole) of bromine in 15 ml of chloroform was added dropwise over 15 min to a solution of 0.01 mole of the appropriate compound (III) in 30 ml of chloroform. The mixture was left for 30 min, and then the solvent was distilled off and the residue was boiled in 30 ml of ethanol for 8-10 h. The resulting solution was cooled to room temprature, and the crystals that deposited were filtered off and dried (Table 2).

LITERATURE CITED

1. R. G. Melik-Ogandzhanyan, A. S. Gapoyan, V. É. Khachatryan, and V. S. Mirzoyan, Khim. Geterotsikl. Soedin., No. 12, 1686 (1982).
2. R. G. Melik-Ogandzhanyan, A. S. Gapoyan, V. É. Khachatryan, and V. S. Mirzoyan, Khim. Geterotsikl. Soedin., No. 1, 118 (1982).
3. R. G. Melik-Ogandzhanyan, A. S. Gapoyan, V. É. Khachatryan, V. S. Mirzoyan, Zh. S. Manukyan, and S. A. Papoyan, Arm. Khim. Zhurn., 33, 1020 (1980).
4. R. V. Rao, J. Med. Chem., 11, 1686 (1968).
5. D. H. Kim and A. A. Santilli, US Patent No. 3,775,412; Chem. Abstr., 80, 70826 (1974).
6. F. Troxler and G. Bormann, British Patent No. 1,936,791; Chem. Abstr., 72, 111499 (1970).
7. K. Nakanishi, Infrared Absorption Spectroscopy. Practical, Holden-Day, San Francisco (1962).
8. L. J. Bellamy, Infrared Spectra of Complex Molecules (2nd ed.), Wiley, New York (1958).