Chemistry of Natural Compounds, Vol. 34, No. 3, 1998

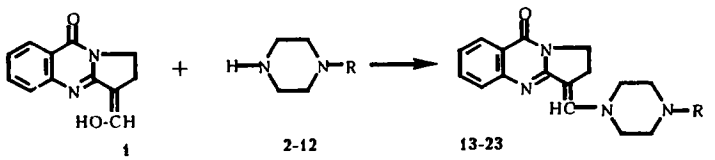
TRANSFORMATION OF NATURAL COMPOUNDS. VII. SYNTHESIS OF α-PIPERAZINYLMETHYLENEDEOXYVASICIN-4-ONES

B. Zh. Élmuradov and Kh. M. Shakhidoyatov

UDC 547.944/945+547.856

α-Piperazinylmethylenedeoxyvasicinones have been synthesized by the interaction of α-hydroxymethylenedeoxyvasicinones with various N-substituted piperazines.

We have previously synthesized α-hydroxy- and α-dimethyl(dialkyl, hetaryl)aminomethylenedeoxyvasicin-4-ones [1-4] and have shown that the hydroxy groups and dimethylamino groups in them react with amines, add hydrocyanic acid [1, 3], undergo transamination [4-6], etc. In the present paper, we report results that we have obtained on the interaction of α-hydroxymethylenedeoxyvasicin-4-one (**1**) with various substituted piperazines (**2**−**12**). As the latter, we used 4-methyl- (**2**), 4-phenyl- (**3**), 4-*m*-tolyl- (**4**), 4-*o*-anisyl- (**5**), 4-*p*-chloro- (**6**), 4-*p*-fluoro- (**7**), 4-*p*-nitro- (**8**), 4-*m*-trifluoromethylphenylpiperazines (**9**), and 4-(2,3-dimethylphenyl)- (**10**), 4-diphenylmethyl- (**11**), and 4-diphenylhydroxymethylpiperazines (**12**).



1 **2-12** **13-23**

2, 13 R = CH_3; **3, 14** R=C_6H_5; **4, 15** R= *m*-C_6H_4-CH_3;
5, 16 R =*o*-$C_6H_4OCH_3$; **6, 17** R=*p*-C_6H_4-Cl; **7, 18** R= *p*-C_6H_4-F;
8,19 R =*p*-C_6H_4-NO_2; **9,20** R=*m*-C_6H_4-CF_3; **10, 21** R=$C_6H_3(CH_3)_2$ w 2,3;
11,22 R = $(C_6H_5)_2CH$; **12,23** R=$(C_6H_5)_2C(OH)$

The reaction was conducted by heating equimolar amounts of the reactants in chloroform solution (method A), or at room temperature for 24 h (method B).

The yields and some physicochemical characteristics of the compounds obtained are given in Table 1. The yields of products by method A were high (85-98%), the nature of the substituent at the nitrogen atom in position 4 of the piperazine ring having no fundamental influence on the yield of reaction products. Such behavior might have been expected and is explained by the fact that the substituents are remote from the piperazine reaction center.

The structures of the compounds synthesized were confirmed by their IR and mass spectra. In the IR spectra there were absorption bands in the 1685-1695 cm^{-1} (ν_{CO}) region and no absorption bands at 3350-3600 cm^{-1} (ν_{OH}). The mass spectra of the compounds synthesized had only weak peaks of the molecular ions or, in some cases, they were even absent. The main fragments were represented by the peaks of ions formed by the splitting out of the substituted piperazine residue and the peaks of ions with *m/z* 186 and 185 corresponding to the deoxyvasicinone ion.

Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, Tashkent, fax (3712) 62 70 71. Translated from Khimiya Prirodnykh Soedinenii, No. 3, pp. 331-333, May-June, 1998. Original article submitted January 26, 1998.

 0009-3130/98/3403-0298$20.00

TABLE 1. Yields and Some Physicochemical Characteristics of the α-Substituted Piperazinylmethylenedeoxyvasicinones

Initial piperazine	R	Reaction product	Yield, %		mp, °C	R_f
			method A	method B		
2	CH_3	13	94	43	165–67	0.41
3	C_6H_5	14	98	47	208–10	0.64
4	m-$C_6H_4CH_3$	15	84	35	217–19	0.70
5	o-$C_6H_4OCH_3$	16	86	54	209–11	0.54
6	p-C_6H_4-Cl	17	89	60	246–48	0.66
7	p-C_6H_4-F	18	98	65	223–25	0.66
8	p-$C_6H_4NO_2$	19	89	40	347–49	0.79
9	m-C_6H_4-CF_3	20	94	68	233–35	0.70
10	2,3-$C_6H_3(CH_3)_2$	21	98	34	241–43	0.60
11	$(C_6H_5)_2CH$	22	90	38	243–45	0.64
12	$(C_6H_5)_2(OH)C$	23	87	30	340–42	0.51

EXPERIMENTAL

IR spectra were taken on a UR-20 spectrometer in KBr tablets, and mass spectra on an MKh-1303 instrument. TLC was conducted on Silufol UV-254 plates with the eluent chloroform–methanol (10:1).

Interaction of α-Hydroxymethylenedeoxyvasicinone (1) with Piperazines.

Method A. α-4-Methylpiperazinylmethylenedeoxyvasicinone (13). A solution of 100 mg (0.46 mmole) of (**1**) in 10 ml of anhydrous chloroform was treated with 50 mg (0.5 mmole) of (**2**), and the mixture was heated on the water bath at 60-65°C for 4 h. The chloroform was distilled off and the residue was crystallized from acetone. This gave 130 mg of (**13**), with mp 165-167°C.

Compounds (**14**, **17-20**, **22**, and **23**) were obtained analogously.

α-4-*m*-Tolylpiperazinylmethylenedeoxyvasicinone (15). A suspension of 364 mg (1.7 mmole) of (**1**), 406 mg (1.95 mmole) of 4-*m*-tolylpiperazine (**4**) and 161 mg (1.95 mmole) of sodium bicarbonate in 30 ml of chloroform was boiled for 3 h. Then the reaction mixture was cooled, and the inorganic precipitate that deposited was filtered off and washed with chloroform. The solvent was distilled off from the combined chloroform solutions, and the residue was crystallized from acetone. This gave 540 mg of (**15**) with mp 217-219°C.

Compounds (**16** and **21**) were obtained analogously.

Method B. A solution of 3 mmole of (**1**) in 50 ml of chloroform was treated with 3.1 mmole of *p*-chlorophenylpiperazine (**6**). The reaction mixture was left at room temperature for 24 h and the chloroform was distilled off. After the residue had been purified by recrystallization from acetone, 700 mg (60%) of (**17**) with mp 246-248°C was obtained.

An increase in the reaction time did not lead to a rise in the yield of compound (**17**).

The synthesis of compounds (**13-16**) and (**17-23**) by method B was conducted similarly (see Table 1).

REFERENCES

1. Kh. M. Shakhidoyatov, Quinazol-4-ones and Their Biological Activity [in Russian], Tashkent (1988), p. 58.
2. Kh. M. Shakhidoyatov, É. O. Oripov, and Ch. Sh. Kadyrov, in: Abstracts of Lectures at the IInd All-Union Symposium on Organic Synthesis [in Russian], Moscow (1976).
3. Kh. M. Shakhidoyatov, É. O. Oripov, L. M. Yun, and Ch. Sh. Kadyrov, in: Abstracts of Lectures at an All-Union Conference on the Reactivity of Azines [in Russian], Novosibirsk (1979).
4. Kh. M. Shakhidoyatov, É. O. Oripov, A. Prisbaev, and Ch. Sh. Kadyrov, Khim. Prir. Soedin., 825 (1976).
5. É. Oripov, Kh. M. Shakhidoyatov, Ch. Sh. Kadyrov, and N. D. Abdullaev, Khim. Prir. Soedin., 684 (1979).
6. É. Oripov, L. M. Yun, Kh. M. Shakhidoyatov, and Ch. Sh. Kadyrov, Khim. Prir. Soedin., 603 (1978).