QUINAZOLINES

XII. 4-THIO ANALOGS OF DEOXYVASICINONE, ITS DERIVATIVES AND HOMOLOGS

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6-Methoxy-2-phenyl- and 1,3-dimethyldihydroquinazoline-4-thiones and 2,4-dimercaptoquinazolines s have been obtained from the corresponding dihydroquinazolin-4-ones [2-6]. Analysis of the information in the literature shows that thioamides possess a broad spectrum of biological action. Thus, 2,6-dichlorothiobenzamide is used under the name of "Prefix" as a herbicide [7, 8], and the thioanilides of acetic and propionic acids and N-propylthioacetanilides are defoliants for the cotton plant, the soybean plant, and tomatoes [9, 10].

It is known that on passing from amides to thioamides the reactivity of the compounds in nucleophilic substitution reaction rises [5] , and therefore it was of interest of obtain thio analogs of deoxyvasicinone and its derivatives and homologs and to compare their chemical and biological properties with those of the initial dihydroquinazolinones [1]. With this aim we have studied the reaction of deoxyvasicinone (Ia) and its substituted derivatives (Ib-d) and homologs (Ie-g) with phosphorus pentasulfide. The reaction took place smoothly when 1 mole of a dihydroquinazolin-4-one (I) was boiled with 1 mole of P_2S_5 in xylene for 2-3 h,

I II

a) x=H, n=1; b) x=6-NO_2, n=1; c) x=7-NO_2, n=1; d) x=6-NH_2, n=1; e) x=H, n=3; f) x=6-Cl, n=3; g) x=6-I, n=3,

while when compound (Id) was heated with phosphorus pentasulfide at 150-160°C in the absence of xylene no reaction took place:

Initial compound	Reaction products	Yield, %	mp, °C (solvent from recrystallization)	R_f	mol. wt.	Empirical formula
Ia	IIa	60	142—143 (hexane)	0,52	202	$C_{11}H_{10}N_2S$
Ib	IIb	34	165—168 (ethanol)	—	—	$C_{11}H_9N_3O_2S$
Ic	IIc	62	173—175 (aqueous methanol)	0,42	—	$C_{11}H_9N_3O_2S$
Id	IId	46	165—168 (ethanol)	—	—	$C_{11}H_{11}N_2S$
Ie	IIe	67	103—104 (ethanol)	—	230	$C_{13}H_{14}N_2S$
If	IIf	44	117—118 (hexane)	—	—	$C_{13}H_{13}N_2SCl$
Ig	IIg	48	111—114 (ethanol)	—	—	$C_{13}H_{13}N_2SJ$

[The R_f values were determined on the diethyl ether—petroleum ether (1 : 1) system on alumina].

The structures of the compounds synthesized were shown by the results of elementary analysis and their IR, PMR, and mass spectra, and their individuality was checked by thin-layer chromatography on alumina. Their IR spectra lacked the absorption bands of the carbonyl groups of the initial compounds in the 1600-1700 cm^{-1} region and showed new absorption bands at 1400-1200 cm^{-1}. In the mass spectra of (IIa and e), as for deoxyvasicinone itself and its derivatives [12], the strongest peaks are those of the molecular ions, and the intensities of the M − 1 ion are 84% for (IIa) and 60% for (IIe). In the mass spectrum of (IIa) there is a fragmentary ion with m/e 169 corresponding to the splitting off of the SH group (M − 33) from the molecular ion (M^+ = 202 → 169), determined by the isomeric composition of the isotopes of the ions with m/e 169 and of the molecular peak.

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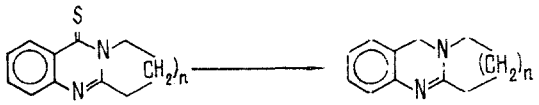
The PMR spectrum of (IIa) shows the signals of the protons of three methylene groups at 2.24 ppm (2 H, C-10, multiplet), 3.2 ppm (2 H, C-9, triplet), 4.41 ppm (2 H, C-11, triplet), and 8.6 ppm (1 H, C-5, doublet).

It must be mentioned that the reduction of the thio analogs of deoxyvasicinone (II) with zinc in hydrochloric acid leads, as in the case of deoxyvasicinone itself [12], to deoxypeganine and its homologs (IIIa, e).



II a, e III a, e

EXPERIMENTAL

The IR spectra were taken on a UR-20 spectrometer, the mass spectra on an MKh-1303 instrument, and the PMR spectra on a JNM-100 instrument (solvent $CDCl_3$; standard TMS). The results of elementary analysis corresponded to the calculated figures. Deoxyvasicinone and its derivatives and homologs were synthesized by a known method [13].

Reaction of Deoxyvasicinone (Ia) with Phosphorus Pentasulfide. Synthesis of (IIa). A suspending of 1 g (0.005 mole) of deoxyvasicinone and 1.3 g (0.005 mole) of phosphorus pentasulfite in 5 ml of absolute m-xylene was boiled for 2 h. Then the reaction mixture was filtered, the residue on the filter was washed with xylene, and the filtrate was treated with 7 ml of 10% caustic soda. The crystals that deposited were filtered off, carefully washed with water, and dried. This gave 0.95 g of crude product with mp 135-140°C. Recrystallization from hexane yielded 0.63 g (60%) of the 4-thio analog of deoxyvasicinone (IIa) with mp 142-143°C; mol. wt. 202 (mass-spectrometrically); R_f 0.52. PMR spectrum ($CDCl_3$), ppm: 2.24 (m, 2 H, CH_2), 2.20 (t, 2 H, CH_2), 4.41 (t, 2 H, CH_2), 7.54 (m, 3 H, arom. protons), 8.60 (d, 1 H, arom. proton). The hydrochloride had mp 234-235°C (ethanol). Yield 97%.

Compounds (IIb-g) were obtained similarly to (IIa).

Reaction of 6-Aminodeoxyvasicinone with Phosphorus Pentasulfide in the Absence of a Solvent. A mixture of 0.5 g (0.0025 mole) of 6-aminodeoxyvasicinone and 0.6 g of phosphorus pentasulfide was heated in an oil bath at 155-160°C for 2 h. Then the mixture was treated with 5 ml of 10% caustic soda and the crystals that deposited were filtered off, washed several times with water, and dried. Recrystallization from aqueous ethanol gave 0.26 g of the initial (Id) with mp 245-246°C. A mixture with an authentic sample showed no depression of the melting point.

Reduction of the Thio Analog of Deoxyvasicinone (IIa). A reaction mixture consisting of a solution of 0.17 g of (IIa) in 6 ml of 10% hydrochloric acid with the addition of 0.6 g of zinc dust was stirred for 4 h and was left overnight, after which the excess of zinc was filtered off and was washed several times with hydrochloric acid solution and with water. The filtrate was made alkaline with 25% ammonia solution and extracted with chloroform, and the organic layer was dried with anhydrous sodium sulfate. The residue from the evaporation of the solvent was recrystallized from hexane, giving 0.07 g (49%) of deoxypeganine (IIIa) with mp 85-86°C, which corresponds to the figure given in the literature [11, 13]. A mixed point with an authentic sample showed no depression.

Compound (IIIe) was reduced similarly.

SUMMARY

4-Thio analogs of deoxyvasicinone have been synthesized by the reaction of deoxyvasicinone and its derivatives and homologs with phosphorus pentasulfide. The reduction of these thio analogs has given deoxypeganine and its homologs.

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