

REACTIONS OF AMIDINOYL ISOTHIOCYANATES WITH ENAMINES

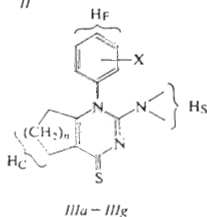
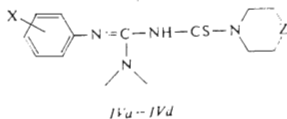
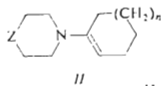
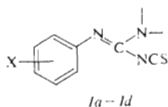
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Amidinoyl isothiocyanates react with simple enamines *II* to give derivatives of 1,4-dihydropyrimidine *III* and amidinoylthioureas *IV*. Spectral data (IR, UV, ^1H NMR) of compounds synthesized are presented.

Amidinoyl isothiocyanates *I*, which are relatively readily accessible, are reactive compounds well entering the cycloaddition reactions by their heterodiene grouping. Some (2 + 2) cycloadditions taking place at the C=N grouping¹, or at the C=S double bond of the isothiocyanate group have already been reported². The diene grouping enabling the (4 + 2) cycloaddition to proceed was utilized for preparation of dimers of these isothiocyanates³ and for reaction with HSCN (ref.⁴). This paper reports the preparation of sixmembered heterocycles by reaction of some simple enamines with the easily polarizable grouping of amidinoyl isothiocyanates.



Amidinoyl isothiocyanates *Ia-d* were found to react almost immediately with N-(1-cyclohexenyl- or pentenyl)morpholine or piperidine (*II*) in a 2 : 1 molar ratio affording two compounds; both were safely identified (cf. Table I). The first was the

expected corresponding, 1,2-disubstituted hexahydroquinazoline-4-thione when using cyclohexenylmorpholine or piperidine, or 1,2-disubstituted tetrahydro-1*H*-cyclopenta-[*d*]-pyrimidine-4-thione when starting from cyclopentenylmorpholine or piperidine. The second product was a derivative of amidinoylthiourea. Formation of both types of substances can be rationalized as follows: Isothiocyanate *I* reacts through its 1,4-dipole with the C=C bond of the enamine *II* via cycloaddition to furnish the unstable and not isolated intermediate; cleavage of a molecule of secondary amine resulted in its stabilization ("aromatization"). The latter reacts with another

TABLE I

Data characterizing pyrimidines *IIIa*—*IIIg*

Compound	X Z	N ^{<} _n ^a	Mol. formula <i>M_r</i>	Calculated/Found			M.p., °C yield, %
				% C	% H	% N	
<i>IIIa</i>	4-Br —	Mo 1	C ₁₇ H ₁₈ BrN ₃ OS (392.6)	52.04 52.17	4.62 4.49	10.70 10.51	228—231 61
<i>IIIb</i>	4-Cl —	Mo 1	C ₁₇ H ₁₈ ClN ₃ OS (347.8)	58.69 58.51	5.21 5.13	9.22 9.34	231—234 69
<i>IIIc</i>	H —	DP 1	C ₂₅ H ₂₁ N ₃ S (395.5)	75.91 75.83	10.62 5.27	10.62 10.71	169—172 71
<i>III_d</i>	H —	PPA 1	C ₂₃ H ₂₄ N ₄ S (388.5)	71.09 71.23	6.23 6.17	14.42 14.53	226—227 65
<i>IIIe</i>	4-Br —	Mo 2	C ₁₈ H ₂₀ BrN ₃ OS (406.4)	53.20 53.11	4.96 4.76	10.34 10.46	176—178 65
<i>III_f</i>	4-Cl —	Mo 2	C ₁₈ H ₂₀ ClN ₃ OS (361.9)	59.74 59.57	5.37 5.45	11.71 11.47	238—241 68
<i>III_g</i>	H —	Mo 2	C ₁₈ H ₂₁ N ₃ OS (327.4)	66.02 66.13	6.47 6.23	12.81 12.63	240—245 74
<i>IVa</i>	4-Br CH ₂	Mo —	C ₁₇ H ₂₃ BrNaOS (411.4)	49.63 49.80	5.63 5.37	13.62 13.51	139—140 72
<i>IVb</i>	4-Cl CH ₂	Mo —	C ₁₇ H ₂₃ ClNaOS (366.9)	55.65 55.71	6.32 6.40	15.27 15.42	142—145 67
<i>IVc</i>	H O	DP —	C ₂₄ H ₂₄ N ₄ OS (416.5)	69.20 69.31	5.81 5.70	13.45 13.57	140—142 69
<i>IVd</i>	H O	PPA —	C ₂₂ H ₂₇ N ₃ OS (409.5)	64.52 64.47	6.65 6.70	17.10 17.35	158—159 61

^a Mo morpholine, DP diphenylamine, PPA phenylpiperazine.

molecule of *I* to the corresponding amidinoylthiourea *IV*. This reaction course is in line with those indicative of reactions of aroyl isothiocyanates with enamines⁵ or some fluorinated benzimidoyl isothiocyanates; the cycloaddition intermediate was in some cases isolated⁶. Like systems, as ketene diacetals react by the same cycloaddition-elimination mechanism with benzimidoyl isothiocyanates⁷.

The structure of final pyrimidines *IIIa–IIIg* was unambiguously inferred from spectral data (Tables II and III). The vibrations in IR spectra are indicative of a pyrimidine ring (1 600 cm^{-1}), and a saturated cyclohexane or cyclopentane ring (2 900 cm^{-1}). The UV spectra reveal a band at 340 nm very characteristic of all 1,2-di-

TABLE II
Spectral data of pyrimidines *IIIa–IIIg*

Compound	IR, cm^{-1}			UV, nm			
	$\nu(\text{C}=\text{C})$	$\nu(\text{C}=\text{N})$	$\nu(\text{CH})$	λ_{max}	$\log \epsilon$	λ_{max}	$\log \epsilon$
<i>IIIa</i>	1 585	1 620	2 845, 2 950	225	4.25	344	4.48
<i>IIIb</i>	1 590	1 615	2 840, 2 950	221	4.25	345	4.49
<i>IIIc</i>	1 590	1 620	2 845, 2 950	282	4.25	343	4.28
<i>III d</i>	1 595	1 630	2 830, 2 940	250	4.26	340	4.36
<i>IIIe</i>	1 585	1 610	2 850, 2 930	227	4.25	342	4.39
<i>III f</i>	1 590	1 610	2 850, 2 930	222	4.24	340	4.45
<i>III g</i>	1 590	1 610	2 845, 2 930	229	4.20	340	4.39

TABLE III
¹H NMR Data (δ , ppm) of pyrimidines *IIIa–IIIg*

Compound	H_C^a			H_S^b	H_F^c	
<i>IIIa</i>	—	2.05	2.55	2.89	3.37	7.51
<i>IIIb</i>	—	2.03	2.60	2.91	3.37	7.45
<i>IIIc</i>	—	2.05	2.43	3.00	—	6.96
<i>III d</i>	—	2.00	2.57	2.98	3.47	7.10
<i>IIIe</i>	1.67	2.07	2.53	2.75	3.36	7.42
<i>III f</i>	1.67	—	2.51	2.75	3.35	7.42
<i>III g</i>	1.69	2.10	2.42	2.75	3.31	7.45

^a Protons of the cycloalkane moiety, ^b protons at amine component ^c protons of the aromatic substituent.

substituted pyrimidines⁵. The ¹H NMR spectra display clearly distinguishable signals of protons of the original secondary amine and the newly appearing ones of the cyclohexane or cyclopentane ring. The absence of the enamine proton ($\text{—}\overset{|}{\text{N}}\text{—}\overset{|}{\text{C}}=\overset{|}{\text{C}}\text{—H}$) provides an evidence for elimination of the secondary amine. Identity of amidinoylthioureas *Iva—IVd* was corroborated by an independent synthesis from the corresponding isothiocyanate and secondary amine. The equimolar benzene solutions of *Ia—Id* and secondary amines gave upon standing the respective thioureas *IV*; their physical constants and spectral data were in a good agreement with those of the thioureas isolated.

EXPERIMENTAL

Infrared spectra of saturated chloroform solutions were measured with a Specord, model 71 (Zeiss, Jena) spectrophotometer in KBr cells ($l = 0.24$ mm). The electron absorption spectra were taken with a Specord UV-VIS (Zeiss, Jena) apparatus in the 200—800 nm range in 10 mm quartz cells; concentration of methanolic solutions of compounds *IIIa—IIIg* was $3 \cdot 10^{-5}$ mol l^{-1} . The ¹H NMR spectra of pyrimidines *IIIa—IIIg* dissolved in deuteriochloroform were recorded with a Tesla BS 487 C instrument operating at 80 MHz; tetramethylsilane was the internal reference.

Amidinoyl isothiocyanates were prepared according to⁵, N(1-cyclohexenyl- and pentenyl)-morpholine according to⁸.

A solution of *I* (20 mmol) and *II* (10 mmol) in acetone (25 ml) was boiled for 15 min, the red solution was left to stand at the room temperature overnight and the separated yellow precipitate of the dihydropyrimidine derivative was suction-filtered, washed with a little amount of ether and crystallized from ethanol. The mother liquor was concentrated to a minimal volume, the separated amidinoylthiourea was filtered off, washed with a little amount of ether and crystallized from ethanol. Yields and physical constants of pyrimidines *IIIa—IIIg* and thioureas *Iva—IVd* are listed in Table I, spectral data of *IIIa—IIIg* in Tables II and III.

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