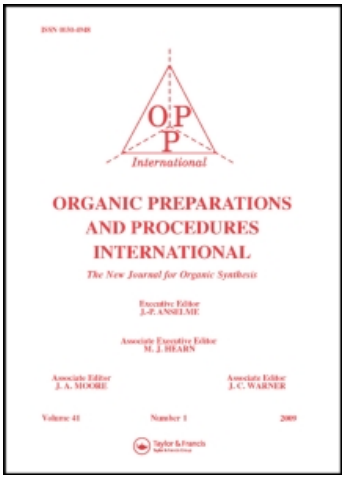

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REACTIONS OF SOME AROMATIC AMINES WITH CINNAMOYL ISOTHIOCYANATE

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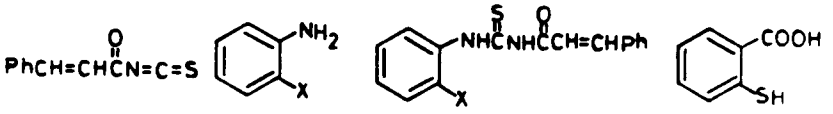
An earlier study[1] showed that cinnamoyl isothiocyanate (1) reacted readily with aromatic and heteroaromatic amines to afford the corresponding thioureas which could be isomerized in high yield to hexahydropyrimidine derivatives. These results prompted the study of the reaction of 1 with a wider range of amines. The o-substituted anilines (2), 2-aminopyridine (10) and 3-amino-5-phenyl-(2H)-pyrazole (11) seemed to be good candidates for the synthesis of thioureas useful as precursors of condensed heterocyles.

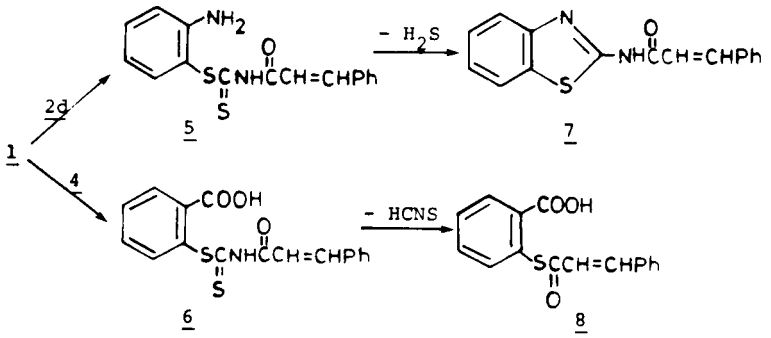
Thus, it was found that anilines containing o-amino, o-hydroxy or o-carboxy groups were attacked by 1 at the amino group to afford 1:1 adducts (3a-c). The ^{1}H-NMR spectra of compounds 3a-c exhibit two doublets of trans-ethylenic protons (J_{AB}= 16 Hz), thus establishing that C=C bonds had been presereved, in cont-



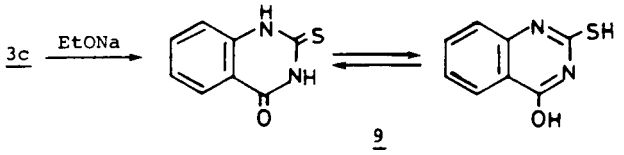
1 2 3 4

a) X = NH_2 b) X = OH
c) X = CO_2H d) X = SH

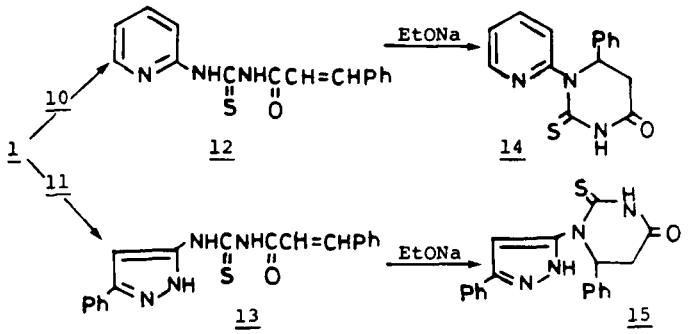
rast, 2-aminothiophenol (2d) and 2-mercaptobenzoic acid (4) were attacked by 1 at the thiol function. The reactivity of the substituents appears to decrease in the order SH > NH_2 > OH, in agreement with previous results.[2] Treatment of 5 with ethanolic hydrochloric acid resulted in the loss of H_2S to afford 2-cinnamoylaminobenzothiazole (7); the structure 7 was established by independent synthesis via the reaction of 2-aminobenzothiazole and cinnamoyl chloride in pyridine. In contrast, 6 lost HCNS when treated with the same reagent, to yield the acyl derivatives 8.



In contrast to the behaviour of compounds 5 and 6 towards the action of ethanolic hydrochloric acid, 3c gave 4-hydroxy-2-mercaptoquinazoline (9) when treated with ethanolic sodium ethoxide.



As expected, the reaction of 1 with 2-aminopyridine (10) and 5-amino-3-phenylpyrazole (11) resulted in exclusive attack on the amino group, as we previously observed for other isothiocyanates,[3-5] giving 12 and 13 respectively. Their IR and ^{1}H-NMR



10 = 2-Aminopyridine 11 = 5-Amino-3-phenylpyrazole

spectra are in accord with the proposed structures. Compounds **12** and **13** could be readily isomerized to the interesting hexahydropyrimidine derivatives **14** and **15** on treatment with ethanolic sodium ethoxide. Analytical and spectral data are in good agreement with the presumed structures. Their ^{1}H-NMR spectra displayed heterocyclic protons $-CH_2CH-$ in pyrimidine with an ABX spin system, and the signals characteristic of the trans-ethylenic protons disappeared.

EXPERIMENTAL SECTION

All melting points are uncorrected. IR spectra were recorded (KBr) on a Pye-Unicam SP-1100 Spectrophotometer. ^{1}H-NMR spectra were recorded on a Varian EM-390 (90 MHz) Spectrometer and chemical shifts are expressed in ppm downfield from TMS as the internal standard. Analytical data were obtained from the Microanalytical Unit at Cairo University.

Reaction of 2a-d, 4, 10 and 11 with 1. General Procedure.- solutions of **2a-d**, **4**, **10**, and **11** (0.01 mol) in dry acetone (50 ml) was added during 10 minutes to stirred and cooled solutions of cinnamoyl isothiocyanate **1**, (0.012 mol) in the same solvent (75 ml). The reaction mixture was left to stand overnight. The precipitate formed was collected, washed with 10 ml methanol, dried and crystallized from a suitable solvent. Compounds **12** and **13** were obtained by the above procedure except that the reaction

TABLE 1. List of Newly Prepared Compounds

Compound No.	Yield (%)	mp.°C (Solvent)	Elemental Analysis (%) Found (Calcd.)			
			C	H	N	S
3a	65	199	64.54	4.70	13.93	10.90
		(Ethanol)	64.64	5.05	14.14	10.77
3b	80	277	64.73	4.50	9.03	10.62
		(DMF)	64.42	4.69	9.39	10.73
3c	77	196	62.81	3.92	8.53	9.64
		(Dioxane)	62.57	4.29	8.58	9.81
5	85	170	61.48	4.24	8.50	20.04
		(Acetone)	61.14	4.45	8.91	20.38
6	72	265	59.51	3.92	4.24	18.54
		(Acetone)	59.47	3.79	4.08	18.65
7	78	244	68.58	4.01	9.70	11.32
		(Ethanol)	68.57	4.28	10.00	11.42
8	83	174	67.44	4.13		10.92
		(Ethanol)	67.60	4.22		11.26
9	67	300	53.63	3.52	15.44	18.13
		(Methanol)	53.93	3.37	15.73	17.97
12	83	168	63.51	4.72	14.54	11.13
		(1-Propanol)	63.60	4.59	14.84	11.30
13	70	246	65.30	4.61	15.72	8.82
		(Dioxane)	65.51	4.59	16.09	9.19
14	62	227	63.24	4.33	14.90	10.91
		(Ethanol)	63.60	4.59	14.84	11.30
15	93	203	65.14	4.33	16.32	9.34
		(Ethanol)	65.51	4.59	16.09	9.19

mixture was refluxed for 1 hr. before being allowed to stand overnight.

Reaction of Ethanolic HCl with 5 and 6.- A solution of 5 (2 g) in ethanol (50 ml) containing conc. hydrochloric acid (3 ml) was refluxed for 1 hr. The reaction mixture was poured on ice and the colourless precipitate was collected, and crystallized from the proper solvent (cf. Table 1).

TABLE 2. Spectral Data of the Newly Prepared Compounds

Compd.	IR(KBr) cm^{-1}	^1H-NMR, ppm ($CDCl_3$)
3a	3400, 3330-3100 (NH and NH_2); 1680 (CO) and 1625 (C=C)	6.5-7.2 (m, 2H); 7.25-8.0 (m, 9H); 11.45 (brs, NH); 12.0 (brs, NH).
3b	3500 (OH); 3300-3100 (NH); 1680 (CO) and 1625 (C=C).	6.75-7.3 (m, 4H); 7.3-8.0 (m, 6H); 8.6 (d, 1H);11.3 (brs, NH); 13.0 (brs,NH).
3c	3320-2750 (NH and OH dimer); 1710-1660 (CO) and 1630(C=C).	6.95-8.35 (m, 11H); 11.5 (brs, NH); 13.3 (brs, NH).
5	3310, 3200 (NH_2); 1675 (CO); 1650 (NH_2) and 1625 (C=C).	(DMSO-d_6), 7.0-8.1 (m, 11H) and 8.5 (br, 2H).
6	3600-2500 (NH and OH dimer); 1670, 1660 (CO), and 1630 (C=C).	(DMSO-d_6), 6.65 (m, 11H).
7	3180 (NH); 1690 (CO), and 1630 (C=C).	(DMSO-d_6), 6.95-8.15 (m, 11H).
8	3300-2400 (OH dimer); 1710-1675 (CO and C=C).	(DMSO-d_6), 7.0-8.0 (m, 11H).
9	3500 (OH); 3100 (NH); 1710 (CO), and 1630 (C=C).	(DMSO-d_6), 7.05-7.9 (m, 4H).
12	3250, 3060 (NH); 1680 (CO); 1630 (C=C).	7.05-8.85 (m, 11H); 9.5 and 13.2 (brs, 2H, lost after D_2O exchange).
13	3450, 3240, 3180 (NH); 1675 (CO), and 1630 (C=C).	(DMSO-d_6), 6.6 (s, 1H); 7.1 (d, 1H); 7.4-7.7 (m, 10H); 7.85 (d, 1H); 13.3 (br, d, 2H).
14	3300-3050 (NH), and 1720 (CO).	2.9 (dd, 2H); 4.85 (m, 1H); 4.7-7.85 (m, 9H); and 10.1 (brs, 1H).
15	3600-3100 (NH); and 1680 (CO).	2.85 (dd, 2H); 4.8 (m, 1H); 6.7-7.6 (m, 11H); 9.3 (brs, 1H), and 11.1 brs, 1H).

Reaction of 2-aminobenzothiazole and cinnamoyl chloride .- To a solution of 2-aminobenzothiazole (0.01 mol) in pyridine (30 ml) was added cinnamoyl chloride (0.012 mol). The reaction mixture was heated for 10 minutes, left to cool and poured over ice. The

resulting solid product was collected and crystallized. It proved to be (mp., mixed mp. and IR) identical with compound 7.

Action of sodium ethoxide on 3c, 12 and 13 .- A suspension of 3c, 12, or 13 (0.01 mol) in sodium ethoxide (0.015 mol in 30 ml ethanol) was refluxed for 1 hr., cooled, poured over ice, neutralized with conc. hydrochloric acid, and left to stand for 2 hrs. The resulting solid product (9, 14, or 15) was collected by filtration, washed with water and crystallized from the appropriate solvent (cf. Table 1).

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