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Synthesis of Some New Arylazo Derivatives of Thio Pyrimidines

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A number of 2-thio analogues of 5-arylazo-pyrimidines have been synthesised by the condensation of 6-methyl-2-thio uracil, 2-methylthio-4-hydroxy-6-methyl pyrimidine and 2-ethylthio-4-hydroxyl-6-methyl pyrimidine with diazotised anilines. The structure of these compounds was further confirmed by I.R. Spectra.

STUDIES have shown that arylazogroups are active in promoting antineoplastic activity.[1,2] Recently, the synthesis of a number of pyrimidine derivatives bearing the arylazo group has been reported from these laboratories.[3] In further quest for novel anticancer drugs, an attempt has been made to synthesise some thio analogues of pyrimidines bearing the arylazo group at position 5.

The compounds described in this communication have been synthesised, by reacting aryl diazonium chlorides with properly substituted pyrimidines. The structure of the compounds have been established by I. R. spectra (all compounds gave a characteristic peak of $-N=N-$ bond, at position 5, enolic-OH gp. at position 4 and thiol gp. at position 2). The arylazo group at position 5 was further confirmed by reducing the arylazo derivative with Sn + HCl. In case of 2-methylthio-4-hydroxy-6-methyl-5-phenylazo-pyrimidine, 5-amino-2-methylthio-4-hydroxy - 6 - methyl pyrimidine was obtained.

The reaction of aryl diazonium chloride with pyrimidine was smooth and the coupled products were obtained in good yields. The reactivity followed the expected course, diazonium chlorides with electron with drawing groups in position 2 and 4 gave better yields.

Experimental

6-methyl--2--thiouracil, 2-methylthio--4-hydroxy-6-methyl pyrimidine and 2-ethylthio-4-hydroxy-6 methyl pyrimidine, which were required as a starting material for synthesis, were prepared by the method reported in literature.[4]

Aniline (0.93 g, 0.01 mol.) was dissolved in dilute hydrochloric acid (10 ml.) and cooled to 0° in an ice bath. Sodium nitrite (0.69 g., 0.01 mol.) was then gradually added. The diazonium salt solution so obtained was filtered into a cold, stirred solution of 6-methyl-2-thio-uracil (1.42 g., 0.01 mol.) in 10 ml. of 10% sodium hydroxide containing 2-3 gms. of sodium acetate. The reaction mixture was held at 0° for 4 hrs. and then left at room temp. for 2 days when a reddish brown solid was separated out. It was filtered, washed well with water and crystallised from ethanol-pyridine mixture and had a m. pt. of 70°.

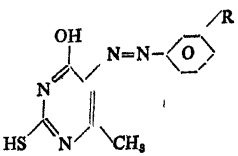
Analysis: Found : N, 21.8%, calculated for $C_{11}H_9N_4OS$: N, 22.8%.

Other substituted arylazo thio uracils were prepared by the above method starting with substituted anilines. The characteristics of these compounds have been entered in Tables 1-3.

Infra red spectra of these compounds show a band in 1640 – 1590 cm^{-1} region corresponding to N=N stretching (Tables 1-3) which confirms the presence of azo bonding. The spectra also show absorption bands in the regions, 2600-2500 cm^{-1} (S-H stretching), 2970-2950 cm^{-1} (C-H stretching due to CH_3), 3600-3500 cm^{-1} and 1400-1300 cm^{-1} (OH group).

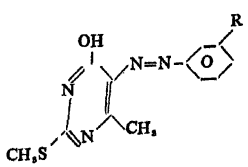
* For correspondence.

TABLE 1—CHARACTERISTICS OF 6-METHYL-2-THIO-5-ARYLAZOURACILS



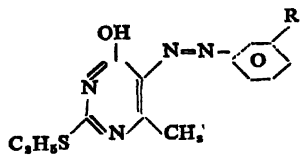
No.	R	M.P. °C	Colour	Formula	I. R. Frequency -N=N-cm
1.	H	70	B	$C_{10}H_{10}SON_4$	1590
2.	2-CH_3	182	B	$C_{12}H_{12}SON_4$	1600
3.	3-CH_3	80	B	$C_{12}H_{12}SON_4$	1590
4.	4-CH_3	168	YB	$C_{12}H_{12}SON_4$	1620
5.	2-OCH_3	155	B	$C_{12}H_{12}SO_2N_4$	1600
6.	3-OCH_3	280	YB	$C_{12}H_{12}SO_2N_4$	1600
7.	4-OCH_3	225	B	$C_{12}H_{12}SO_2N_4$	1640
8.	4-Br	71	Y	$C_{11}H_9SON_4Br$	1630
9.	4-I	220 d	OY	$C_{11}H_9SON_4I$	1630
10.	2-NO_2	224	Y	$C_{11}H_9SO_3N_5$	1590
11.	3-NO_2	215	Y	$C_{11}H_9SO_3N_5$	1600
12.	4-NO_2	225	O	$C_{11}H_9SO_3N_5$	1630
13.	2-Cl	285	Y	$C_{11}H_9SO_2N_4Cl$	1600
14.	3-Cl	95	Y	$C_{11}H_9SO_2N_4Cl$	1595
15.	4-Cl	164	B	$C_{11}H_9SO_2N_4Cl$	1610

TABLE 2—CHARACTERISTICS OF 2-METHYLTHIO-4-HYDROXY-6-METHYL-5-ARYLAZOPYRIMIDINES



No.	R	M.P. °C	Colour	Formula	I. R. frequency cm^{-1}
1.	R	82	YG	$C_{12}H_{12}SON_4$	1600
2.	2-CH_3	105	R	$C_{12}H_{14}SON_4$	1600
3.	3-CH_3	73	B	$C_{12}H_{14}SON_4$	1610
4.	4-CH_3	108	B	$C_{12}H_{14}SON_4$	1630
5.	2-OCH_3	250	O	$C_{12}H_{14}SO_2N_4$	1590
6.	3-OCH_3	75	B	$C_{12}H_{14}SO_2N_4$	1620
7.	4-OCH_3	75	B	$C_{12}H_{14}SO_2N_4$	1600
8.	2-Cl	265	B	$C_{12}H_{11}SON_4Cl$	1620
9.	3-Cl	270	Y	$C_{12}H_{11}SON_4Cl$	1630
10.	4-Cl	160	B	$C_{12}H_{11}SON_4Cl$	1640
11.	4-Br	210	B	$C_{12}H_{11}SON_4Br$	1630
12.	4-F	78	B	$C_{12}H_{11}SON_4F$	1630
13.	2 . 6 Dichloro	105	B	$C_{12}H_{10}SON_4Cl_2$	1600

TABLE 3—CHARACTERISTICS OF 2-ETHYLTHIO-4-HYDROXY-6-METHYL 5-ARYLAZOPYRIMIDINLS



No.	R	M.P. °C	Colour	Formula	I. R. Frequency
1.	H	98	B	$C_{12}H_{12}ON_4$	1600
2.	2-CH_3	100	B	$C_{13}H_{14}ON_4$	1600
3.	3-CH_3	95	B	$C_{13}H_{14}ON_4$	1610
4.	4-CH_3	91	B	$C_{13}H_{14}ON_4$	1640
5.	2-OCH_3	75	B	$C_{13}H_{14}O_2N_4$	1610
6.	3-OCH_3	110	B	$C_{13}H_{14}O_2N_4$	1600
7.	4-OCH_3	230	Y	$C_{13}H_{14}O_2N_4$	1630
8.	2-Cl	110	B	$C_{12}H_{11}ON_4Cl$	1610
9.	3-Cl	112	Y	$C_{12}H_{11}ON_4Cl$	1620
10.	4-Cl	102	Y	$C_{12}H_{11}ON_4Cl$	1640
11.	4-I	158	Y	$C_{12}H_{11}ON_4I$	1630
12.	4-F	114	B	$C_{12}H_{11}ON_4F$	1630
13.	2-NO_2	125	Y	$C_{12}H_{11}O_3N_5$	1590
14.	3-NO_2	220	Y	$C_{12}H_{11}O_3N_5$	1600
15.	4-NO_2	210	Y	$C_{12}H_{11}O_3N_5$	1620
16.	2 : 6 Dichloro	225	Y	$C_{12}H_{10}ON_4Cl_2$	1610

B=Brown, Y=Yellow, O=Orange, G=Green.

All melting points are uncorrected and were determined by using a Kofler hot stage apparatus.

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