Synthesis of 2-Aryl[1,2,4]triazolo[1,5-*a*]pyrimidines

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Synopsis. 2-(Aroylamino)pyrimidines (**4**) have been converted into 1-(2-pyrimidyl)-5-aryl-1*H*-tetrazoles (**6**) by treatment with PCl_5 followed by azidolysis in aqueous acetone solution. Pyrolysis of **6** in decalin gave 2-aryl[1,2,4]triazolo[1,5-*a*]pyrimidines (**8**). A reasonable pathway for the formation of **8** from **6** is suggested. Structures of all the compounds have been established by elemental analysis and spectral data.

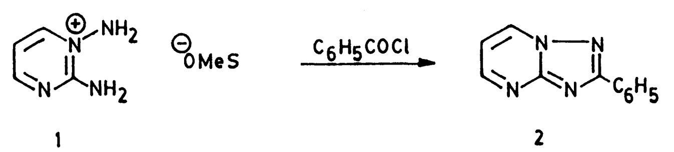
1-Aminopyrimidinium salt (**1**), obtained from 2-aminopyrimidine and *O*-(mesitylsulfonyl)hydroxylamine, on reaction with benzoyl chloride is known to give 2-phenyl[1,2,4]triazolo[1,5-*a*]pyrimidine[1] (**2**, mp 185—0.5 °C) in a very low yield (8%). In view of the synthetic utility of 1,5-disubstituted tetrazoles[2] and in continuation of our studies on thermal decomposition of 1-heteroaryl-5-aryl-1*H*-tetrazoles,[3-6] we report a convenient synthesis of 2-aryl[1,2,4]triazolo[1,5-*a*]pyrimidines by the pyrolysis of 1-(2-pyrimidyl)-5-aryl-1*H*-tetrazoles.

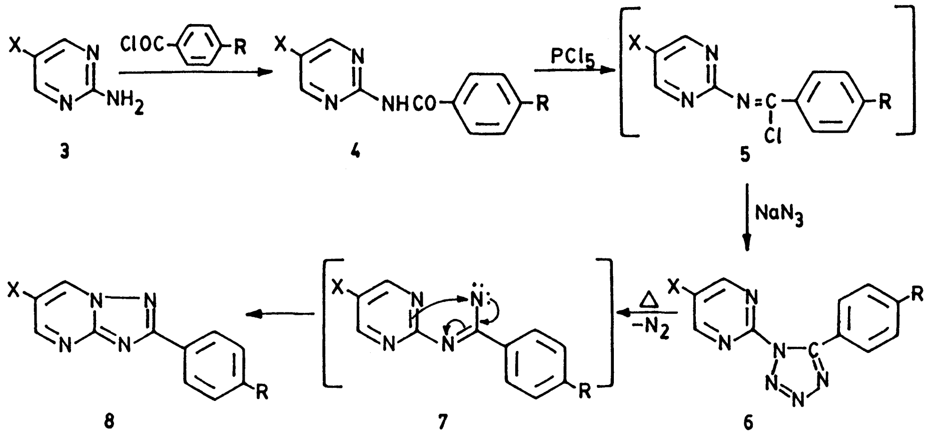
Results and Discussion

Benzoylation of 2-aminopyrimidine (**3**, X=H) in the presence of pyridine gave 2-benzamidopyrimidine[7] (**4a**). Treatment of **4a** with PCl_5, followed by reaction with NaN_3 of the resulting *N*-(2-pyrimidyl)arenecarboximidoyl chloride (**5a**) without isolation, led to the formation of a colorless compound, **6a**, mp 95 °C. The compound was analyzed for $C_{11}H_8N_6$. In its mass spectrum the molecular ion was observed at *m/z* 224. Its IR spectrum revealed the absence of amide and azide functions. The presence of >C=N– in the compound was indicated by the appearance of a band at 1600 cm^{-1}. Its ^1H NMR spectrum ($CDCl_3$) revealed two peaks—a multiplet at δ 7.1—7.5 and a doublet at δ 8.6 in 3 : 1 ratio. The doublet is assignable to protons in 4 and 6 positions of the pyrimidine ring. On the basis of these data the compound **6a** has been assigned as 1-(2-pyrimidyl)-5-phenyl-1*H*-tetrazole (**6a**) structure.

A number of 2-(aroylamino)pyrimidines (**4b—l**, Table 1) obtained by the reaction of 2-amino-, 2-amino-5-chloro-, and 2-amino-5-bromopyrimidines[8] with benzoyl, *p*-toluoyl, *p*-anisoyl, *p*-chlorobenzoyl chlorides in the presence of pyridine were converted into 1-(2-pyrimidyl)-5-aryl-1*H*-tetrazoles (**6b—l**) on treatment with PCl_5 followed by azidolysis.

Heating a mixture of **6a** and finely ground pure sand at 180—190 °C and column chromatography of the reaction mixture gave a colorless crystalline compound, **8a**, mp 186 °C. On the basis of the elemental analysis and spectral data [IR(KBr): 1600 cm^{-1} (>C=N), no absorptions due to >C=O, >NH, and N_3 functions. ^1H NMR ($CDCl_3$) δ 7.3—7.75 (m, phenyl protons), δ 8.2—9.0 (m, pyrimidine protons) in 5 : 3 ratio and MS: M^+ at *m/z* 196], the compound **8a** has been assigned as 2-phenyl[1,2,4]triazolo[1,5-*a*]pyrimidine





a: X=R=H; b: X=H, R=Me; c: X=H, R=OMe; d: X=H, R=Cl; e: X=Cl, R=H; f: X=Cl, R=Me; g: X=Cl, R=OMe; h: X=R=Cl; i: X=Br, R=H; j: X=Br, R=Me; k: X=Br, R=OMe; l: X=Br, R=Cl.

Table 1. Characterization Data of 2-(Aroylamino)pyrimidines (**4**), 1-(2-Pyrimidyl)-5-aryl-1*H*-tetrazoles (**6**) and 2-Aryl[1,2,4]triazolo[1,5-*a*]pyrimidines (**8**)

Compd.	Mp θ_m/°C	Yield %	IR cm^{-1} NH	C=O	C=N	Mol. formula	Calcd (%) C	H	N	Found (%) C	H	N
4a	142—143[7]	90	3300	1650	—	—	—	—	—	—	—	—
4b	148—149	85	3250	1660	—	$C_{12}H_{11}N_3O$	67.60	5.16	19.72	67.57	5.12	19.65
4c	181—182	78	3200	1650	—	$C_{12}H_{11}N_3O_2$	62.88	4.80	18.34	62.85	4.62	18.28
4d	109—111	95	3320	1670	—	$C_{11}H_8N_3OCl$	56.53	3.43	17.99	56.52	3.40	17.82
4e	139—140	85	3310	1650	—	$C_{11}H_8N_3OCl$	56.53	3.43	17.99	56.51	3.41	17.85
4f	129—130	82	3200	1665	—	$C_{12}H_{10}N_3OCl$	58.18	4.04	16.97	58.08	4.01	16.93
4g	184—185	87	3280	1660	—	$C_{12}H_{10}N_3O_2Cl$	54.65	3.79	15.94	54.62	3.75	15.88
4h	165—166	84	3310	1680	—	$C_{11}H_7N_3OCl_2$	49.25	2.61	15.67	49.20	2.58	15.62
4i	178—179	78	3320	1670	—	$C_{11}H_8N_3OBr$	47.48	2.88	15.11	47.38	2.65	15.08
4j	129—130	80	3250	1665	—	$C_{12}H_{10}N_3OBr$	49.32	3.42	14.38	49.29	3.31	14.28
4k	169—170	74	3330	1660	—	$C_{12}H_{10}N_3O_2Br$	46.75	3.25	13.64	46.72	3.18	13.60
4l	154—155	84	3300	1685	—	$C_{11}H_7N_3OBrCl$	42.24	2.24	13.44	42.22	2.20	13.42
6a	94—95	65	—	—	1600	$C_{11}H_8N_6$	58.93	3.57	37.50	58.91	3.52	37.42
6b	138—139	58	—	—	1600	$C_{12}H_{10}N_6$	60.50	4.20	35.29	60.40	4.16	35.22
6c	191—192	49	—	—	1600	$C_{12}H_{10}N_6O$	56.69	3.94	33.07	56.58	3.88	33.00
6d	185—186	68	—	—	1600	$C_{11}H_7N_6Cl$	51.06	2.71	32.50	51.00	2.60	32.39
6e	194—195	64	—	—	1600	$C_{11}H_7N_6Cl$	51.06	2.71	32.50	51.02	2.73	32.52
6f	146—147	55	—	—	1610	$C_{12}H_9N_6Cl$	52.84	3.30	30.83	52.86	3.33	30.80
6g	169—170	52	—	—	1600	$C_{12}H_9N_6OCl$	49.91	3.12	29.12	49.85	3.14	29.10
6h	151—152	60	—	—	1610	$C_{11}H_6N_6Cl_2$	45.05	2.05	28.67	45.00	2.00	28.62
6i	205—206	55	—	—	1605	$C_{11}H_7N_6Br$	43.56	2.31	27.73	43.50	2.30	27.78
6j	140—141	60	—	—	1590	$C_{12}H_9N_6Br$	45.43	2.84	26.50	45.60	2.71	26.45
6k	161—162	65	—	—	1610	$C_{12}H_9N_6OBr$	43.24	2.70	25.23	43.47	2.65	24.98
6l	148—149	62	—	—	1620	$C_{11}H_6N_6BrCl$	39.11	1.78	24.89	39.20	1.75	24.82
8a	186[1]	50	—	—	1600	$C_{11}H_8N_4$	67.35	4.08	28.57	67.30	4.01	28.50
8b**	200—201	42	—	—	1610	$C_{12}H_{10}N_4$	68.57	4.76	26.67	68.52	4.70	26.65
8c	280—281	40	—	—	1600	$C_{12}H_{10}N_4O$	63.72	4.42	24.78	63.69	4.38	24.70
8d	142—143	52	—	—	1580	$C_{11}H_7N_4Cl$	57.27	3.04	24.30	57.36	3.00	24.28
8e	230—231	55	—	—	1590	$C_{11}H_7N_4Cl$	57.27	3.04	24.30	57.30	3.02	24.20
8f	115—116	53	—	—	1605	$C_{12}H_9N_4Cl$	58.89	3.68	22.90	58.90	3.60	22.85
8g	218—219	45	—	—	1610	$C_{12}H_9N_4OCl$	55.28	3.45	21.50	55.26	3.40	21.38
8h	160—161	58	—	—	1605	$C_{11}H_6N_4Cl_2$	49.81	2.26	21.13	49.80	2.20	20.92
8i	144—145	50	—	—	1580	$C_{11}H_7N_4Br$	48.00	2.55	20.36	48.32	2.50	20.28
8j	203—204	52	—	—	1600	$C_{12}H_9N_4Br$	49.83	3.11	19.38	49.80	3.00	19.46
8k	165—166	53	—	—	1610	$C_{12}H_9N_4OBr$	47.21	2.95	18.36	47.19	2.86	18.38
8l	150—151	62	—	—	1610	$C_{11}H_6N_4BrCl$	42.65	1.94	18.09	42.60	1.90	18.06

6b* ^{1}H NMR ($CDCl_3$): δ 2.48 (s, 3H), 7.2—7.75 (m, 5H), 8.1 (d, 2H), M^+ at m/z 238.
8b** ^{1}H NMR ($CDCl_3$): δ 2.42 (s, 3H), 7.25—7.6 (m, 5H), 8.2 (d, 2H), M^+ at m/z 210.

(**8a**) structure. The yield of **8a** in this reaction was 25%. Pyrolysis of 1-(2-pyrimidyl)-5-phenyl-1*H*-tetrazole was also carried out in toluene, xylene, tetralin, and decalin. The tetrazole was recovered unchanged even after prolonged refluxing in toluene (bp 110 °C) or xylene (bp 140 °C). Refluxing the tetrazole in tetralin (bp 210 °C) for 3 h yielded **8a** in 35% yield. Decomposition of the tetrazole was complete by refluxing in decalin (bp 180 °C) for 3 h to give **8a** in 50% yield. Decomposition of other 1-(2-pyrimidyl)-5-aryl-1*H*-tetrazoles (**6b—l**) in decalin resulted in the formation of the corresponding **8b—l** (Table 1). The formation of **8**, in the pyrolysis of **6**, can be reasonably explained through stepwise elimination of a molecule of nitrogen from **6** and the cyclization of the resulting nitrene intermediate **7** in singlet state.[9]

Experimental

2-(Aroylamino)pyrimidines (4). General Procedure: To a solution of 2-aminopyrimidine in pyridine was added an equimolar amount of aroyl chloride with shaking. After the addition was complete, the reaction mixture was allowed to stand at room temperature for 2 h. The crude product that separated on dilution was filtered, washed with 10% sodium hydrogencarbonate solution, then several times with water. The dry solid was recrystallized from benzene-methanol to give pure **4** as summarized in Table 1.

1-(2-Pyrimidyl)-5-aryl-1*H*-tetrazoles (6). General Procedure: A mixture of **4** (5.00 mmol) and PCl_5 (1.3 g, 5.00 mmol) was heated at 100 °C for 1 h, when the evolution of fumes of HCl ceased. Excess of $POCl_3$ was removed under reduced pressure and the residual imidoyl chloride was treated with ice-cold sodium azide (0.37 g, 5.00 mmol) and excess of sodium acetate trihydrate in water (25 cm^3) and acetone (30 cm^3) with stirring. The stirring was continued overnight, acetone was removed under reduced pressure, and the remaining aqueous portion was extracted with chloroform. The dried chloroform extract was chromatographed over a column of neutral alumina, eluting with benzene to give pure **6** (Table 1).

Thermal Decomposition of 6. General Procedure: A solution of 1-(2-pyrimidyl)-5-aryl-1*H*-tetrazole (**6**, 2.50 mmol) in decalin (25 cm^3) was refluxed for 3 h. The decalin was removed by distillation under reduced pressure. The residue was extracted with chloroform, the extract was concentrated and the residue was subjected to chromatography over a neutral alumina column, eluting with benzene-ethyl acetate (10 : 1) mixture to give pure **8** (Table 1).

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