

Chaitanya G. Dave* and Rina D. Shah

Organic Syntheses Laboratory, M. G. Science Institute, Navrangpura, Ahmedabad 300 009, India

Received May 22, 1998

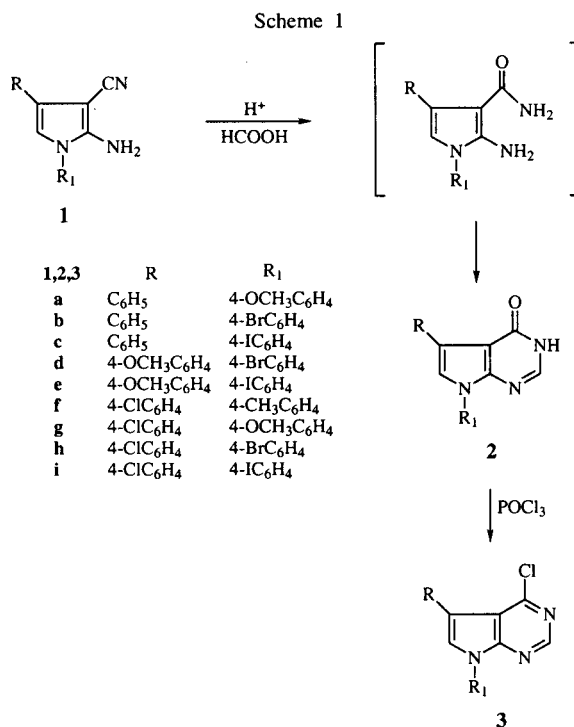
Some new 7,9-disubstituted 7*H*-1,2,3,4-tetrazolo[1,5-*c*]pyrrolo[3,2-*e*]pyrimidines **5** have been synthesized either by diazotization of 4-hydrazino-5,7-disubstituted-7*H*-pyrrolo[2,3-*d*]pyrimidines **4** obtained by hydrazinolysis of 4-chloro-5,7-disubstituted-7*H*-pyrrolo[2,3-*d*]pyrimidines **3** or via a substitution reaction between **3** and sodium azide. 5,7-Disubstituted-7*H*-pyrrolo[2,3-*d*]pyrimidin-4(3*H*)-ones **2** were obtained by cyclocondensation of 2-amino-3-cyano-1,4-disubstituted pyrroles **1** with formic acid which on chlorination using phosphorus oxychloride afforded **3**. A novel route for the synthesis of 4-amino-5,7-disubstituted-7*H*-pyrrolo[2,3-*d*]pyrimidines **6** by the reductive ring cleavage of **5** has been reported.

J. Heterocyclic Chem., **35**, 1295 (1998).

The investigation of fused tetrazolopyrimidines as a potent antagonist contributed to a wide range of biological activities such as analgesic [1], antiinflammatory [1], anti-convulsant [2], antiulcer [3], anticancer [4,5], antifolate [6], antiallergic [3], antihypertensive [7], antimalarial [8] and antitumour [9] activities. Moreover, the capability of fused tetrazolopyrimidines to undergo reductive ring cleavage to form fused aminopyrimidines [6,10], known for their valuable pharmacological properties and as intermediates in the construction of a variety of triheterocycles was also studied [11]. Therefore, it was thought to undertake the synthesis of novel 7*H*-1,2,3,4-tetrazolo[1,5-*c*]pyrrolo[3,2-*e*]pyrimidines and to study their transformations to 4-amino-5,7-disubstituted-7*H*-pyrrolo[2,3-*d*]pyrimidines via reductive ring opening of tetrazolopyrrolopyrimidines.

The target triheterocyclic 7,9-disubstituted 7*H*-1,2,3,4-tetrazolo[1,5-*c*]pyrrolo[3,2-*e*]pyrimidines **5** were constructed by the annellation of the tetrazole ring onto the existing 4-chloro-5,7-disubstituted-7*H*-pyrrolo[2,3-*d*]pyrimidines **3** and 4-hydrazino-5,7-disubstituted-7*H*-pyrrolo[2,3-*d*]pyrimidines **4**. 2-Amino-3-cyanopyrroles **1** were refluxed in boiling formic acid to obtain 5,7-disubstituted-7*H*-pyrrolo[2,3-*d*]pyrimidin-4(3*H*)-ones **2**. The reaction is believed to proceed through the formation of the corresponding 2-amino-3-carboxamidopyrroles followed by cyclization. Compounds **2** were refluxed in phosphorus oxychloride in order to obtain 4-chloro-5,7-disubstituted-7*H*-pyrrolo[2,3-*d*]pyrimidines **3** (Scheme 1).

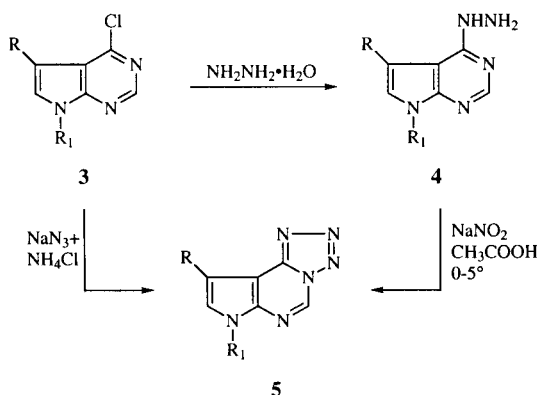
The chloro group present at position-4 in the pyrrolo[2,3-*d*]pyrimidine ring of **4** was found to be highly reactive towards nucleophilic substitution reactions with sodium azide and hydrazine hydrate. The desired tetrazolopyrrolopyrimidines **5** have been prepared by two different routes. In the first route, 4-chloro-5,7-disubstituted-7*H*-pyrrolo[2,3-*d*]pyrimidines **3** were converted to 4-hydrazino-5,7-disubstituted-7*H*-pyrrolo[2,3-*d*]pyrimidines **4** by the substitution reaction with hydrazine hydrate (99%) in refluxing ethanol, which in turn was dia-



zotized with sodium nitrite in glacial acetic acid to obtain tetrazolopyrrolopyrimidines **5** (Method A). In the second route, 4-chloropyrrolo[2,3-*d*]pyrimidines **3** were reacted with sodium azide in the presence of ammonium chloride in which *in situ* generation of ammonium azide facilitated the reaction in dimethyl sulfoxide with stirring at 90° (Method B) (Scheme 2).

Since the reductive ring cleavage of the tetrazole moiety constituted a synthetically important process for the preparation of amines, 4-amino-5,7-disubstituted-7*H*-pyrrolo[2,3-*d*]pyrimidines **6** have been synthesized for the first time from tetrazolopyrrolopyrimidines **5** employing zinc in acetic acid as the reducing agent under boiling conditions and it was found that the compounds thus

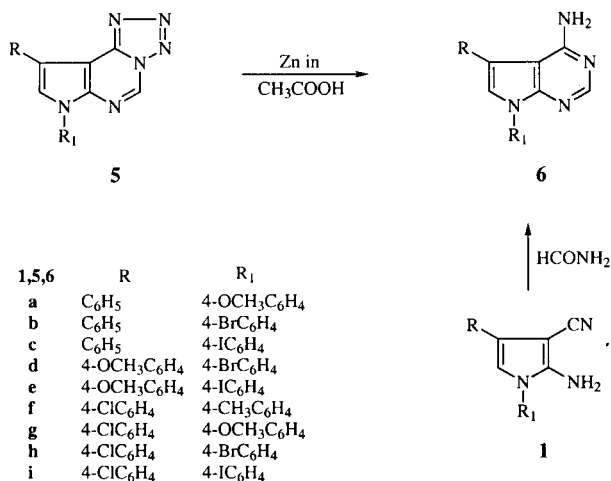
Scheme 2



3,4,5	R	R ₁
a	C ₆ H ₅	4-OCH ₃ C ₆ H ₄
b	C ₆ H ₅	4-BrC ₆ H ₄
c	C ₆ H ₅	4-IC ₆ H ₄
d	4-OCH ₃ C ₆ H ₄	4-BrC ₆ H ₄
e	4-OCH ₃ C ₆ H ₄	4-IC ₆ H ₄
f	4-ClC ₆ H ₄	4-CH ₃ C ₆ H ₄
g	4-ClC ₆ H ₄	4-OCH ₃ C ₆ H ₄
h	4-ClC ₆ H ₄	4-BrC ₆ H ₄
i	4-ClC ₆ H ₄	4-IC ₆ H ₄

obtained were identical with those reported by Dave *et al.* [12] by cyclocondensation of 2-amino-3-cyanopyrroles **1** with formamide at reflux temperature (Scheme 3). The attempted ring cleavage of **6** using reducing agents such as sodium borohydride [13] and zinc-nickel chloride hexahydrate [14] was unsuccessful and in all the cases the starting compounds **5** were recovered.

Scheme 3

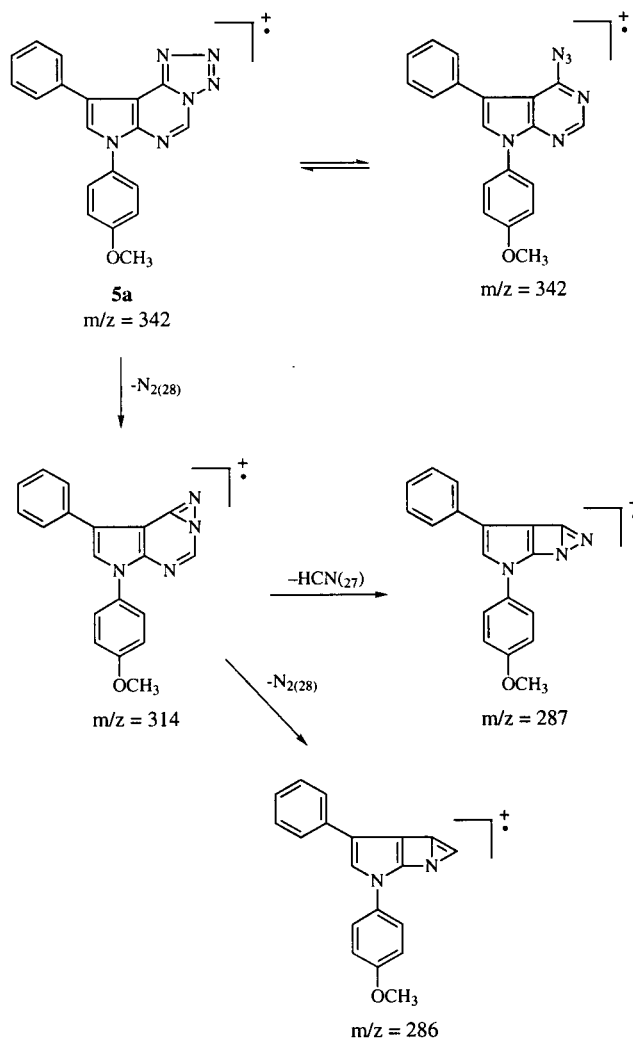


1,5,6	R	R ₁
a	C ₆ H ₅	4-OCH ₃ C ₆ H ₄
b	C ₆ H ₅	4-BrC ₆ H ₄
c	C ₆ H ₅	4-IC ₆ H ₄
d	4-OCH ₃ C ₆ H ₄	4-BrC ₆ H ₄
e	4-OCH ₃ C ₆ H ₄	4-IC ₆ H ₄
f	4-ClC ₆ H ₄	4-CH ₃ C ₆ H ₄
g	4-ClC ₆ H ₄	4-OCH ₃ C ₆ H ₄
h	4-ClC ₆ H ₄	4-BrC ₆ H ₄
i	4-ClC ₆ H ₄	4-IC ₆ H ₄

The ir (potassium bromide) spectra of **2** exhibited absorption bands near 3300-3260 cm⁻¹ and 1684-1672 cm⁻¹ due to the ring -NHCO- functionality. The ¹H nmr (deuterio-dimethyl sulfoxide) spectra of **2** displayed a multiplet in the region δ 6.95-7.90 corresponding to aromatic protons, while a broad singlet was found to be present due to ring

NH proton at δ 10.50-11.10. Three absorption bands assigned to NH stretching vibrations were obtained in the region 3460-3210 cm⁻¹ where as the bending vibration due to the amino functional group appeared in the region 1652-1624 cm⁻¹ in compounds **4**, which were found to be absent in the case of compounds **5**. Further, the absence of a band near 2100 cm⁻¹ excluded the possibility of azido formation and proved the construction of the tetrazole ring onto the pyrrolo[2,3-*d*]pyrimidines **3** and **4**. The aromatic protons resonated at δ 7.00-8.50 producing a multiplet in the ¹H nmr (deuteriochloroform) spectra of **3** and **4**, while in the case of **4**, the hydrazino protons appeared in the form of a singlet in the region δ 4.10-4.20 and δ 6.10-6.20 integrating for two and one protons respectively. The ¹H nmr (deuteriochloroform) spectra of **5** gave satisfactory results in which aromatic protons resonated at δ 7.10-8.20 in the form of a multiplet. The transformation of **5** to **6** was supported by the presence of two bands responsible for NH stretching vibrations near 3480-3110 cm⁻¹ together with a

Scheme 4



bending vibrations 1645-1630 cm⁻¹ in their ir spectra. A broad singlet in the area δ 5.20-5.30 was due to amino

group integrating for two protons along with a multiplet in the region δ 7.00-8.40 because aromatic protons were pre-

Table I
Physical and Analytical Data for Compounds 2a-i, 3a-i and 4a-i

Compound No.	Reaction time (hours)	Yield %	mp°C crystallization solvent	Molecular formula	Analysis %		
					C	H	N
2a	10	79	208-210	C ₁₉ H ₁₅ N ₃ O ₂	71.91	4.77	13.24
			[a]		71.60	4.46	13.50
2b	10	59	229-230	C ₁₈ H ₁₂ BrN ₃ O	59.03	3.30	11.47
			[a]		59.41	3.49	11.76
2c	14	50	227-229	C ₁₈ H ₁₂ IN ₃ O	52.32	2.93	10.17
			[a]		52.69	2.64	10.39
2d	11	80	277-279	C ₁₉ H ₁₄ BrN ₃ O ₂	57.59	3.56	10.61
			[a]		57.80	3.75	10.83
2e	10	76	235-237	C ₁₉ H ₁₄ IN ₃ O ₂	51.49	3.18	9.48
			[a]		51.56	3.49	9.80
2f	13	80	223-225	C ₁₉ H ₁₄ ClN ₃ O	67.96	4.20	12.51
			[a]		67.76	4.41	12.15
2g	12	79	254-256	C ₁₉ H ₁₄ ClN ₃ O ₂	64.87	4.01	11.95
			[a]		64.75	4.19	12.03
2h	10	76	323-325	C ₁₈ H ₁₁ BrClN ₃ O	53.96	2.77	10.49
			[a]		53.57	2.97	10.41
2i	11	81	286-288	C ₁₈ H ₁₁ ClIN ₃ O	48.29	2.48	9.39
			[a]		48.43	2.87	9.61
3a	17	87	132-133	C ₁₉ H ₁₂ ClN ₃ O	68.37	3.63	12.59
			[b]		68.70	3.12	12.30
3b	18	89	123-124	C ₁₈ H ₁₁ BrClN ₃	56.20	2.88	10.92
			[b]		56.43	3.09	10.49
3c	17	50	101-102	C ₁₈ H ₁₁ ClIN ₃	50.08	2.57	9.73
			[b]		50.38	2.87	10.01
3d	16	85	162-163	C ₁₉ H ₁₃ BrClN ₃ O	55.03	3.16	10.13
			[b]		54.81	2.95	10.28
3e	19	56	100-101	C ₁₉ H ₁₃ ClIN ₃ O	49.43	2.84	9.10
			[b]		49.71	2.71	8.89
3f	17	80	182-184	C ₁₉ H ₁₃ Cl ₂ N ₃	64.42	3.70	11.86
			[b]		64.02	3.49	11.46
3g	16	89	165-167	C ₁₉ H ₁₃ Cl ₂ N ₃ O	61.64	3.54	11.35
			[b]		61.55	3.81	11.67
3h	17	86	136-137	C ₁₈ H ₁₀ BrCl ₂ N ₃	51.58	2.41	10.03
			[b]		51.31	2.29	9.81
3i	17	56	99-100	C ₁₈ H ₁₀ Cl ₂ IN ₃	46.38	2.16	9.02
			[b]		46.01	2.36	9.31
4a	18	80	218-220	C ₁₉ H ₁₇ N ₅ O	68.86	5.17	21.14
			[b]		68.53	5.38	21.40
4b	2.5	76	179-181	C ₁₈ H ₁₄ BrN ₅	56.85	3.71	18.42
			[b]		56.49	3.48	18.03
4c	2	65	101-102	C ₁₈ H ₁₄ IN ₅	50.60	3.30	16.39
			[b]		50.43	3.23	16.16
4d	3.5	65	165-166	C ₁₉ H ₁₆ BrN ₅ O	55.62	3.93	17.07
			[b]		55.42	3.84	16.91
4e	4	61	166-167	C ₁₉ H ₁₆ IN ₅ O	49.90	3.53	15.32
			[b]		49.79	3.43	15.03
4f	3	80	155-156	C ₁₉ H ₁₆ ClN ₅	65.23	4.61	20.02
			[b]		65.02	4.39	19.88
4g	3.5	69	165-166	C ₁₉ H ₁₆ ClN ₅ O	62.38	4.41	19.15
			[b]		62.21	4.23	19.13
4h	4	69	191-192	C ₁₈ H ₁₃ BrCl ₂ N ₅	52.13	3.16	16.89
			[b]		52.51	3.02	16.70
4i	4.5	65	167-168	C ₁₈ H ₁₃ ClIN ₅	46.83	2.84	15.17
			[b]		47.07	2.65	15.01

[a] = *N,N*-dimethylformamide:ethanol (6:4 v/v) and [b] = ethanol:chloroform (8:2 v/v).

Table 2
Physical and Analytical Data for Compounds 5a-i

Compound No.	Reaction time (hours)		Yield %		mp °C crystallization solvent	Molecular formula	Analysis %		
	Method		Method				C	H	N
	A	B	A	B					
5a	2	3	62	61	216-218 [a]	C ₁₉ H ₁₄ N ₆ O	66.65 66.46	4.12 4.27	24.55 24.78
5b	2	3	63	60	225-227 [a]	C ₁₈ H ₁₁ BrN ₆	55.26 55.50	2.84 2.99	21.49 21.56
5c	2	3	52	50	227-229 [a]	C ₁₈ H ₁₁ IN ₆	49.33 49.09	2.53 2.43	19.18 18.98
5d	2	3	55	54	221-223 [b]	C ₁₉ H ₁₃ BrN ₆ O	54.17 54.34	3.11 3.25	19.95 19.74
5e	2	3	59	58	209-211 [a]	C ₁₉ H ₁₃ IN ₆ O	48.73 48.81	2.80 2.75	17.95 17.88
5f	2	3	64	64	223-225 [a]	C ₁₉ H ₁₃ ClN ₆	63.25 63.02	3.63 3.41	23.30 23.51
5g	2	3	60	54	214-216 [b]	C ₁₉ H ₁₃ ClN ₆ O	60.56 60.44	3.48 3.35	22.30 22.40
5h	2	3	67	70	213-215 [b]	C ₁₈ H ₁₀ BrClN ₆	50.79 51.01	2.37 2.51	19.75 19.56
5i	2	3	57	55	238-240 [b]	C ₁₈ H ₁₀ ClIN ₆	45.74 45.99	2.13 2.29	17.78 18.01

[a] = chloroform and [b] = 1,4-dioxane.

Table 3
Physical Data of Compounds 6a-i

Compound No.	Reaction time (hours)	Yield %	mp °C	
			Found	Reported [12]
6a	1.0	66	184-185	185-186
6b	0.5	64	187-188	187-188
6c	1.5	63	189-190	190-192
6d	1.0	66	240-241	237-239
6e	0.75	63	225-226	225-226
6f	1.0	71	199-200	200-201
6g	0.5	64	223-225	224-226
6h	1.5	65	248-250	248-249
6i	1.0	61	231-232	231-232

Table 4
IR and ¹H NMR Spectral Data for Compounds 2a-i, 3a-i, 4a-i, 5a-i and 6a-i

Compound No.	ir (potassium bromide) cm ⁻¹	¹ H nmr (δ ppm)
2a	3270, 1680, 1604, 1520	3.90 (s, 3H, OCH ₃), 6.95-7.80 (m, 11H, Ar-H), 10.95 (s, 1H, NH)
2b	3280, 1684, 1600, 1516	7.20-7.90 (m, 11H, Ar-H), 10.75 (s, 1H, NH)
2c	3300, 1684, 1596, 1512	7.10-7.90 (m, 11H, Ar-H), 10.50 (s, 1H, NH)
2d	3280, 1672, 1596, 1508	3.85 (s, 3H, OCH ₃), 7.10-7.90 (m, 10H, Ar-H), 10.55 (s, 1H, NH)
2e	3260, 1680, 1600, 1508	3.90 (s, 3H, OCH ₃), 7.00-7.90 (m, 10H, Ar-H), 10.60 (s, 1H, NH)
2f	3210, 1672, 1600, 1504	2.90 (s, 3H, CH ₃), 7.10-7.90 (m, 10H, Ar-H), 10.75 (s, 1H, NH)
2g	3270, 1680, 1596, 1508	3.93 (s, 3H, OCH ₃), 7.20-7.90 (m, 10H, Ar-H), 10.70 (s, 1H, NH)
2h	3260, 1684, 1600, 1504	7.20-7.90 (m, 10H, Ar-H), 10.65 (s, 1H, NH)

Table 4 (continued)
 IR and ¹H NMR Spectral Data for Compounds 2a-i, 3a-i, 4a-i, 5a-i and 6a-i

Compound No.	ir (potassium bromide) cm ⁻¹	¹ H nmr (δ ppm)
2i	3270, 1672, 1592, 1508	7.10-7.80 (m, 10H, Ar-H), 11.10 (s, 1H, NH)
3a	3060, 1604, 1520	7.20-7.80 (m, 11H, Ar-H)
3b	3050, 1600, 1500	7.10-7.90 (m, 11H, Ar-H)
3c	3060, 1604, 1500	7.00-7.90 (m, 11H, Ar-H)
3d	3050, 2960, 2850, 1600, 1500	3.85 (s, 3H, OCH ₃), 7.15-7.85 (m, 10H, Ar-H)
3e	3060, 2960, 2850, 1604, 1504	3.92 (s, 3H, OCH ₃), 7.10-7.90 (m, 10H, Ar-H)
3f	3050, 2950, 2840, 1604, 1504	2.90 (s, 3H, CH ₃), 7.20-8.05 (m, 10H, Ar-H)
3g	3050, 2950, 2850, 1608, 1500	3.90 (s, 3H, OCH ₃), 7.10-8.05 (m, 10H, Ar-H)
3h	3050, 2960, 2850, 1600, 1500	7.25-8.10 (m, 10H, Ar-H)
3i	3060, 2950, 2840, 1592, 1504	7.20-8.05 (m, 10H, Ar-H)
4a	3410, 3340, 3240, 1652, 1584, 1516	3.85 (s, 3H, OCH ₃), 4.15 (s, 2H, NH ₂), 6.10 (s, 1H, NH), 7.10-8.10 (m, 11H, Ar-H)
4b	3450, 3320, 3230, 1624, 1592, 1508	4.12 (s, 2H, NH ₂), 6.15 (s, 1H, NH), 7.30-8.30 (m, 11H, Ar-H)
4c	3440, 3330, 3210, 1628, 1604, 1500	4.10 (s, 2H, NH ₂), 6.10 (s, 1H, NH), 7.20-8.30 (m, 11H, Ar-H)
4d	3450, 3330, 3220, 1632, 1600, 1500	3.85 (s, 3H, OCH ₃), 4.14 (s, 2H, NH ₂), 6.16 (s, 1H, NH), 7.10-8.30 (m, 10H, Ar-H)
4e	3440, 3340, 3240, 1636, 1604, 1504	3.86 (s, 3H, OCH ₃), 4.13 (s, 2H, NH ₂), 6.10 (s, 1H, NH), 7.25-7.40 (m, 10H, Ar-H)
4f	3440, 3320, 3220, 1652, 1604, 1500	2.90 (s, 3H, CH ₃), 4.14 (s, 2H, NH ₂), 6.10 (s, 1H, NH), 7.30-8.30 (m, 10H, Ar-H)
4g	3450, 3320, 3210, 1656, 1608, 1500	3.90 (s, 3H, OCH ₃), 4.15 (s, 2H, NH ₂), 6.10 (s, 1H, NH), 7.30-8.40 (m, 10H, Ar-H)
4h	3460, 3330, 3220, 1632, 1604, 1500	4.19 (s, 2H, NH ₂), 6.20 (s, 1H, NH), 7.30-8.50 (m, 10H, Ar-H)
4i	3450, 3320, 3210, 1636, 1600, 1504	4.15 (s, 2H, NH ₂), 6.18 (s, 1H, NH), 7.20-8.50 (m, 10H, Ar-H)
5a	1604, 1508	3.92 (s, 3H, OCH ₃), 7.20-8.20 (m, 11H, Ar-H)
5b	1600, 1500	7.30-8.20 (m, 11H, Ar-H)
5c	1608, 1496	7.20-8.20 (m, 11H, Ar-H)
5d	1612, 1492	3.90 (s, 3H, OCH ₃), 7.30-8.20 (m, 10H, Ar-H)
5e	1604, 1500	3.92 (s, 3H, OCH ₃), 7.30-8.25 (m, 10H, Ar-H)
5f	1604, 1508	2.80 (s, 3H, CH ₃), 7.10-8.00 (m, 10H, Ar-H)
5g	1608, 1500	3.90 (s, 3H, OCH ₃), 7.10-8.10 (m, 10H, Ar-H)
5h	1604, 1504	7.30-8.20 (m, 10H, Ar-H)
5i	1600, 1504	7.20-8.20 (m, 10H, Ar-H)
6a	3470, 3296, 1650, 1584, 1516	3.90 (s, 3H, OCH ₃), 5.25 (s, 2H, NH ₂), 7.10-8.30 (m, 11H, Ar-H)
6b	3470, 3290, 1650, 1570, 1500	5.25 (s, 2H, NH ₂), 7.10-8.40 (m, 11H, Ar-H)
6c	3460, 3290, 1630, 1585, 1500	5.25 (s, 2H, NH ₂), 7.00-8.20 (m, 11H, Ar-H)
6d	3460, 3270, 1630, 1585, 1495	3.88 (s, 3H, OCH ₃), 5.30 (s, 2H, NH ₂), 7.00-8.40 (m, 10H, Ar-H)
6e	3460, 3270, 1630, 1580, 500	3.89 (s, 3H, OCH ₃), 5.20 (s, 2H, NH ₂), 7.10-8.40 (m, 10H, Ar-H)
6f	3470, 3290, 1630, 1580, 1510	2.80 (s, 3H, CH ₃), 5.20 (s, 2H, NH ₂), 7.10-8.40 (m, 10H, Ar-H)
6g	3480, 3300, 1640, 1580, 1510	3.80 (s, 3H, OCH ₃), 5.20 (s, 2H, NH ₂), 7.20-8.30 (m, 10H, Ar-H)
6h	3465, 3280, 1636, 1580, 1485	5.30 (s, 2H, NH ₂), 7.20-8.40 (m, 10H, Ar-H)
6i	3480, 3240, 1640, 1585, 1500	5.25 (s, 2H, NH ₂), 7.10-8.40 (m, 10H, Ar-H)

sent in the ^1H nmr (deuteriochloroform) spectra of compounds **6**. The mass fragmentation of compound **5a** was in agreement with the pattern of fused tetrazolopyrimidine systems [1,15] giving the molecular ion peak at 342. The fragments at 314, 287 and 286 were the results of subsequent elimination of nitrogen and hydrogen cyanide or for successive removal of two nitrogen molecules. The mass fragmentation pattern is depicted in the Scheme 4.

EXPERIMENTAL

Melting points were determined by the electrothermal method in an open capillary tube and are uncorrected. The ir spectra are recorded in cm^{-1} in potassium bromide pellets on Buck scientific spectrophotometer. The ^1H nmr spectra were recorded on Varian 300 and 400 MHz spectrometer in deuteriodimethyl sulfoxide or deuteriochloroform using tetramethylsilane as the internal standard and the chemical shifts are expressed in δ ppm. The mass spectra were recorded on LKB 9000 mass spectrometer. The purity of the compounds was routinely checked by tlc using silica gel G and the spots were exposed to iodine vapor.

General Procedure for the Synthesis of 5,7-Disubstituted-7H-pyrrolo[2,3-d]pyrimidin-4(3H)-ones **2a-i**.

A mixture of 2-amino-3-cyano-1,4-disubstituted pyrroles [12,16] (**1**, 0.01 mole) and formic acid (30 ml) was stirred at reflux temperature for 10-13 hours. The reaction mixture was then allowed to cool, poured onto crushed ice (50 g), neutralized with sodium hydroxide solution (5 N), filtered, dried and crystallized (Table 1).

General Procedure for the Synthesis of 4-Chloro-5,7-disubstituted-7H-pyrrolo[2,3-d]pyrimidines **3a-i**.

5,7-Disubstituted-7H-pyrrolo[2,3-d]pyrimidin-4(3H)-ones **2**, (0.01 mole) were refluxed with phosphorus oxychloride (25 ml) for a period of 17-20 hours (tlc). After the completion of reaction, the excess of phosphorus oxychloride was removed *in vacuo*. The cooled reaction mixture was then slowly added onto the crushed ice (25 g). The resulting solid was filtered, washed with sodium bicarbonate (5% w/v) followed by cold water, dried and crystallized (Table 1).

General Procedure for the Synthesis of 4-Hydrazino-5,7-disubstituted-7H-pyrrolo[2,3-d]pyrimidines **4a-i**.

4-Chloro-5,7-disubstituted-7H-pyrrolo[2,3-d]pyrimidines **3** (0.01 mole) were reacted with hydrazine hydrate (99%, 15 ml) in boiling ethanol (25 ml) for the period of 2.0-4.5 hours (tlc). The cooled reaction mixture was then added to ice cold water (50 ml) and neutralized with aqueous acetic acid (5 N). The solid thus obtained was filtered, washed with water, dried and crystallized (Table 1).

General Procedure for the Synthesis of 7,9-Disubstituted 7H-1,2,3,4-tetrazolo[1,5-c]pyrrolo[3,2-e]pyrimidines **5a-i**.

Method A.

4-Hydrazino-5,7-disubstituted-7H-pyrrolo[2,3-d]pyrimidines **4** (0.01 mole) were dissolved in glacial acetic acid (40 ml) and the aqueous solution of sodium nitrite (20% w/v, 4.2 ml) was added in small portions with cooling (0-5°) with constant stirring. The reaction mixture was stirred for 2 hours at this temper-

ature and poured onto the crushed ice (25 g). The solid obtained was filtered, washed with water, sodium bicarbonate (20% w/v) followed by water, dried and crystallized (Table 2).

Method B.

To the well stirred solution of ammonium chloride (0.011 mole, 0.059 g) and sodium azide (0.011 mole, 0.072 g) in dimethyl sulfoxide (25 ml) was added 4-chloro-5,7-disubstituted-7H-pyrrolo[2,3-d]pyrimidines **3** (0.01 mole) in portions with constant stirring. The reaction mixture was stirred for 2 hours at 90° and for one hour at room temperature. The cold solution was poured onto the crushed ice (25 g) and the solid obtained was filtered, washed with water, dried and crystallized (Table 2).

General Procedure for the Synthesis of 4-Amino-5,7-disubstituted-7H-pyrrolo[2,3-d]pyrimidines **6a-i**.

To the mixture of 7,9-disubstituted 7H-1,2,3,4-tetrazolo[1,5-c]-pyrrolo[3,2-e]pyrimidines **5** (0.002 mole) in glacial acetic acid (10 ml) was added the powdered zinc (0.5 g) cautiously over a period of 0.5 hour (an exothermic reaction was observed). The reaction mixture was then refluxed for 0.5-1.5 hours, cooled and poured onto the crushed ice (25 g). The resulting mixture was neutralized to pH 7 with ammonia solution (6 N) and extracted with chloroform (2 x 30 ml). The total chloroform layer was dried over anhydrous magnesium sulfate, concentrated *in vacuo* and crystallized from a mixture of ethanol:chloroform (8:2 v/v) (Table 3).

Acknowledgment.

We wish to thank the Regional Sophisticated Instrumental Center, Central Drug Research Institute, Lucknow and Chandigarh, India for nmr and mass spectra.

REFERENCES AND NOTES

- [1] C. J. Shishoo, M. B. Devani, M. D. Karverkar, G. V. Ullas, S. Ananthan, V. S. Bhadi, R. B. Patel and T. P. Gandhi, *Indian J. Chem.*, **21B**, 666 (1982).
- [2] W. J. Haulihan and M. K. Eberle, US Patent 3 642,814 (1972); *Chem. Abstr.*, **76**, 140839 (1972).
- [3] J. S. Bindra, US Patent 4 085,213 (1978); *Chem. Abstr.*, **89**, 1975824 (1978).
- [4] K. Hiedo and M. Yasuo, Japan Patent 5577 (1959); *Chem. Abstr.*, **54**, 14280 (1960).
- [5] K. Hiedo and M. Yasuo, Japan Patent 17,236 (1960); *Chem. Abstr.*, **55**, 17664 (1961).
- [6] C. J. Shishoo and K. S. Jain, *J. Heterocyclic Chem.*, **29**, 883 (1992).
- [7] L. K. Chain, H. S. Wei and H. M. Kuhn, *Tai-wan yao Hsueh Tsa Chih*, **38**, 2428 (1986); *Chem. Abstr.*, **108**, 94490 (1988).
- [8] G. Franco, L. Maria and P. Giueseppe, *J. Heterocyclic Chem.*, **26**, 613 (1989).
- [9] E. S. Hand and D. C. Backer, *Can. J. Chem.*, **62**, 2570 (1984).
- [10] E. L. Brady and R. M. Herbst, *J. Org. Chem.*, **24**, 922 (1959).
- [11] C. G. Dave and M. C. Shukla, *J. Heterocyclic Chem.*, **34**, 1805 (1997).
- [12] C. G. Dave, P. R. Shah and S. P. Upadhyaya, *J. Indian Chem. Soc.*, **114**, 713 (1987).
- [13] F. Rolla, *J. Org. Chem.*, **47**, 4327 (1997).
- [14] A. Boruah, M. Boruah, D. Prajapati and S. S. Jagir, *Synlett*, 1253 (1997).
- [15] C. Wentrup, *Tetrahedron*, **26**, 4969 (1970).
- [16] K. Gewald and M. Henschel, *J. Prakt. Chem.*, **318**, 663 (1976).