

Synthesis of Novel 1-Aryl[1]benzoxepino[5,4-*c*]pyrazole and [1]Benzoxepino[5,4-*d*]pyrimidine Derivatives

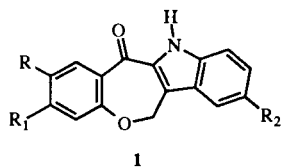
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Several 1-aryl[1]benzoxepinopyrazoles were prepared by reaction of 4-hydroxymethylene[1]benzoxepinones with appropriate phenylhydrazine hydrochlorides. The direct condensation of hydroxymethylenebenzoxepinones with variously substituted amidines failed to give benzoxepinopyrimidines. These compounds were obtained *via* the key intermediates morpholine enamino benzoxepinones.

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In connection with our program of preparing new polyheterocyclic compounds which might exhibit potential biological activity, we have recently described the synthesis of some 5*H*,12*H*-[1]benzoxepino[4,3-*b*]indol-6-ones **1**, which are analogues of natural indole alkaloids and contain a new heterocyclic ring system [1].

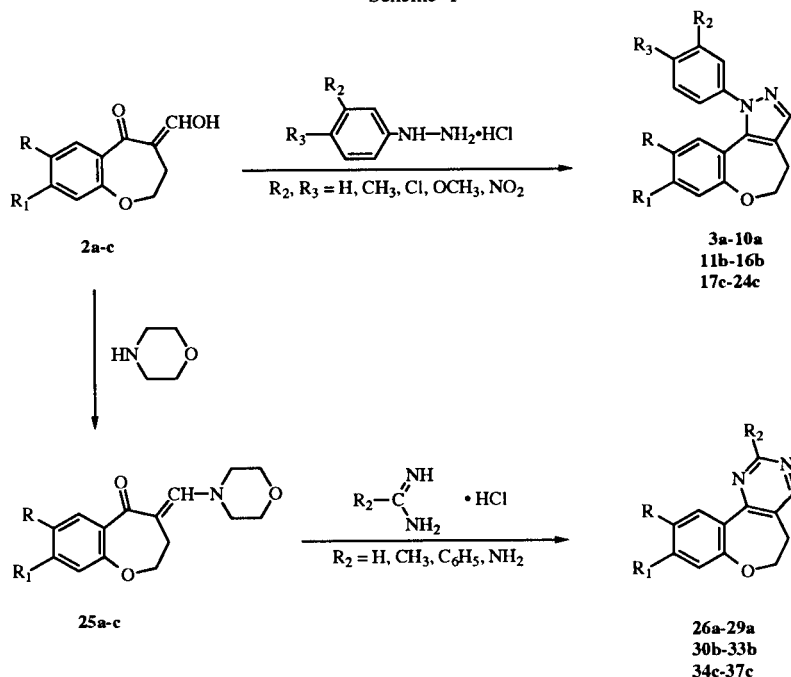


R, R₁ = H, CH₃
R₂ = H, Cl, F, OCH₃

In pursuing our study on heterobenzoxepin compounds, in this paper we report the synthesis and the structure elucidation of some novel pyrazole and pyrimidine derivatives, such as 1-aryl-4,5-dihydro-1*H*[1]benzoxepino[5,4-*c*]pyrazoles **3a-10a**, **11b-16b**, **17c-24c**, and 2-substituted 5,6-dihydro[1]benzoxepino[5,4-*d*]pyrimidines **26a-29a**, **30b-33b**, **34c-37c**, wherein the pyrazole and the pyrimidine moieties are fused to a benzoxepin nucleus.

Several benzoxepinopyrazole derivatives were previously described [2] and some of them were submitted to biological evaluation [2a]. Among these, only a few derivatives have a phenyl group on the pyrazole nucleus and none have this group in the 1 position as in **3a-24c**. The synthetic sequence utilized in the preparation of compounds **3a-24c** is illustrated in Scheme 1. The preparation of the

Scheme 1



Series a: R = R₁ = H
Series b: R = CH₃; R₁ = H
Series c: R = R₁ = CH₃

Table 1
Physical Data of Compounds 3a-10a

Compound No.	R	R ₁	R ₂	R ₃	Yield (%)	Mp (°C) (recrystallization solvent)	Molecular Formula	Analysis (%)		
								C	Calcd./Found H	N
3a	H	H	H	H	34	118-120 (petroleum ether 60-80°)	C ₁₇ H ₁₄ N ₂ O	77.86 78.01	5.34 5.43	10.69 10.59
4a	H	H	H	CH ₃	39	123-124 (petroleum ether 100-140°)	C ₁₈ H ₁₆ N ₂ O	78.26 78.05	5.80 5.90	10.14 10.03
5a	H	H	CH ₃	H	37	116-117 (petroleum ether 60-80°)	C ₁₈ H ₁₆ N ₂ O	78.26 78.10	5.80 5.95	10.14 9.98
6a	H	H	H	Cl	35	139-141 (petroleum ether 60-80°)	C ₁₇ H ₁₃ N ₂ OCl	68.80 68.95	4.38 4.50	9.44 9.30
7a	H	H	Cl	H	57	112-114 (petroleum ether 60-80°)	C ₁₇ H ₁₃ N ₂ OCl	68.80 68.66	4.38 4.53	9.44 9.30
8a	H	H	H	OCH ₃	32	121-122 (petroleum ether 60-80°)	C ₁₈ H ₁₆ N ₂ O ₂	73.97 73.90	5.48 5.58	9.59 9.45
9a	H	H	H	NO ₂	36	113-114 (petroleum ether 100-140°)	C ₁₇ H ₁₃ N ₃ O ₃	66.45 66.34	4.23 4.33	13.68 13.60
10a	H	H	NO ₂	H	32	119-120 (petroleum ether 100-140°)	C ₁₇ H ₁₃ N ₃ O ₃	66.45 66.40	4.23 4.31	13.68 13.65

Table 2
IR, NMR and Mass Spectral Data of Compounds 3a-10a

Compound No.	IR (cm ⁻¹)	¹ H-NMR (δ ppm) [a]	MS m/z (R.I.%)
3a	1600, 1580, 1210, 970, 860, 760	3.03 (t, 2H, 4-CH ₂), 4.44 (t, 2H, 5-CH ₂), 6.82-7.68 (m, 10H, Ar-H)	M ⁺ 262 (100)
4a	1510, 1200, 1050, 970, 810, 760	2.32 (s, 3H, Ph-CH ₃), 3.02 (t, 2H, 4-CH ₂), 4.38 (t, 2H, 5-CH ₂), 6.81-7.62 (m, 9H, Ar-H)	M ⁺ 276 (100)
5a	1600, 1580, 1230, 1200, 780, 760	2.35 (s, 3H, Ph-CH ₃), 3.05 (t, 2H, 4-CH ₂), 4.44 (t, 2H, 5-CH ₂), 6.88-7.67 (m, 9H, Ar-H)	M ⁺ 276 (100)
6a	1490, 1200, 1090, 970, 840, 760	3.03 (t, 2H, 4-CH ₂), 4.44 (t, 2H, 5-CH ₂), 6.83-7.68 (m, 9H, Ar-H)	M ⁺ 296 (100)
7a	1590, 1210, 1020, 970, 790, 760	3.02 (t, 2H, 4-CH ₂), 4.44 (t, 2H, 5-CH ₂), 6.80-7.70 (m, 9H, Ar-H)	M ⁺ 296 (100)
8a	1510, 1240, 1200, 1020, 840, 760	3.02 (t, 2H, 4-CH ₂), 3.82 (s, 3H, Ph-OCH ₃), 4.40 (t, 2H, 5-CH ₂), 6.83-7.63 (m, 9H, Ar-H)	M ⁺ 292 (100)
9a	1600, 1500, 1340, 1220, 860, 780	2.95 (t, 2H, 4-CH ₂), 4.43 (t, 2H, 5-CH ₂), 6.90-8.33 (m, 9H, Ar-H)	M ⁺ 307 (100)
10a	1520, 1340, 1210, 1020, 800, 760	3.05 (t, 2H, 4-CH ₂), 4.45 (t, 2H, 5-CH ₂), 6.87-8.37 (m, 9H, Ar-H)	M ⁺ 307 (100)

[a] Recorded in deuteriochloroform.

Table 3
Physical Data of Compounds 11b-16b

Compound No.	R	R ₁	R ₂	R ₃	Yield (%)	Mp (°C) (recrystallization solvent)	Molecular Formula	Analysis (%)		
								C	Calcd./Found H	N
11b	CH ₃	H	H	H	35	95-96 (petroleum ether 40-60°)	C ₁₈ H ₁₆ N ₂ O	78.26 78.35	5.80 5.90	10.14 10.24
12b	CH ₃	H	CH ₃	H	56	108-109 (petroleum ether 60-80°)	C ₁₉ H ₁₈ N ₂ O	78.62 78.72	6.21 6.24	9.66 9.63
13b	CH ₃	H	H	Cl	38	78-79 (petroleum ether 60-80°)	C ₁₈ H ₁₅ N ₂ OCl	69.57 69.61	4.83 4.95	9.02 9.00
14b	CH ₃	H	H	OCH ₃	33	81-82 (petroleum ether 40-60°)	C ₁₉ H ₁₈ N ₂ O ₂	74.51 74.70	5.88 5.95	9.15 9.08
15b	CH ₃	H	H	NO ₂	36	149-150 (petroleum ether 60-80°)	C ₁₈ H ₁₅ N ₃ O ₃	67.29 67.36	4.67 4.76	13.08 13.07
16b	CH ₃	H	NO ₂	H	38	150-151 (petroleum ether 60-80°)	C ₁₈ H ₁₅ N ₃ O ₃	67.29 67.40	4.67 4.87	13.08 13.09

Table 4
IR, NMR and Mass Spectral Data of Compounds 11b-16b

Compound No.	IR (cm ⁻¹)	¹ H-NMR (δ ppm) [a]	MS m/z (R.I.%)
11b	1600, 1520, 1220 970, 820, 760	2.03 (s, 3H, 9-CH ₃), 3.03 (t, 2H, 4-CH ₂), 4.41 (t, 2H, 5-CH ₂), 6.65-7.66 (m, 9H, Ar-H)	M ⁺ 276 (100)
12b	1610, 1590, 1240, 1200, 860, 780	2.03 (s, 3H, 9-CH ₃), 2.37 (s, 3H, Ph-CH ₃), 3.03 (t, 2H, 4-CH ₂), 4.41 (t, 2H, 5-CH ₂), 6.70-7.68 (m, 8H, Ar-H)	M ⁺ 290 (96), 39 (100)
13b	1490, 1220, 1090, 1040, 970, 830	2.05 (s, 3H, 9-CH ₃), 2.97 (t, 2H, 4-CH ₂), 4.40 (t, 2H, 5-CH ₂), 6.63-7.67 (m, 8H, Ar-H)	M ⁺ 310 (100)
14b	1510, 1300, 1260, 1030, 970, 830	2.07 (s, 3H, 9-CH ₃), 3.03 (t, 2H, 4-CH ₂), 3.87 (s, 3H, Ph-OCH ₃), 4.42 (t, 2H, 5-CH ₂), 6.72-7.70 (m, 8H, Ar-H)	M ⁺ 306 (100)
15b	1600, 1500, 1220, 1030, 850, 830	2.10 (s, 3H, 9-CH ₃), 2.96 (t, 2H, 4-CH ₂), 4.45 (t, 2H, 5-CH ₂), 6.67-8.37 (m, 8H, Ar-H)	M ⁺ 321 (100)
16b	1530, 1230, 1210, 1030, 830, 740	2.05 (s, 3H, 9-CH ₃), 3.00 (t, 2H, 4-CH ₂), 4.41 (t, 2H, 5-CH ₂), 6.57-8.40 (m, 8H, Ar-H)	M ⁺ 321 (100)

[a] Recorded in deuteriochloroform.

Table 5
Physical Data of Compounds 17c-24c

Compound No.	R	R ₁	R ₂	R ₃	Yield (%)	Mp (°C) (recrystallization solvent)	Molecular Formula	Analysis (%)		
								C	H	N
17c	CH ₃	CH ₃	H	H	34	121-122 (petroleum ether 40-60°)	C ₁₉ H ₁₈ N ₂ O	78.62 78.71	6.21 6.31	9.66 9.59
18c	CH ₃	CH ₃	H	CH ₃	33	137-138 (petroleum ether 60-80°)	C ₂₀ H ₂₀ N ₂ O	78.95 79.05	6.58 6.68	9.21 9.21
19c	CH ₃	CH ₃	CH ₃	H	52	115-116 (petroleum ether 60-80°)	C ₂₀ H ₂₀ N ₂ O	78.95 79.10	6.58 6.70	9.21 9.25
20c	CH ₃	CH ₃	H	Cl	35	118-120 (petroleum ether 60-80°)	C ₁₉ H ₁₇ N ₂ OCl	70.26 70.20	5.24 5.35	8.63 8.60
21c	CH ₃	CH ₃	Cl	H	37	81-83 (petroleum ether 60-80°)	C ₁₉ H ₁₇ N ₂ OCl	70.26 70.13	5.24 5.27	8.63 8.66
22c	CH ₃	CH ₃	H	OCH ₃	33	143-144 (petroleum ether 60-80°)	C ₂₀ H ₂₀ N ₂ O ₂	75.00 74.94	6.25 6.33	8.75 8.70
23c	CH ₃	CH ₃	H	NO ₂	35	176-177 (petroleum ether 60-80°)	C ₁₉ H ₁₇ N ₃ O ₃	68.06 67.99	5.07 5.01	12.54 12.60
24c	CH ₃	CH ₃	NO ₂	H	32	156-157 (petroleum ether 60-80°)	C ₁₉ H ₁₇ N ₃ O ₃	68.06 68.20	5.07 5.15	12.54 12.59

Table 6
IR, NMR and Mass Spectral Data of Compounds 17c-24c

Compound No.	IR (cm ⁻¹)	¹ H-NMR (δ ppm) [a]	MS m/z (R.I.%)
17c	1590, 1180, 1040, 950, 760, 690	1.90 (s, 3H, 9-CH ₃), 2.20 (s, 3H, 8-CH ₃), 3.03 (t, 2H, 4-CH ₂), 4.39 (t, 2H, 5-CH ₂), 6.58-7.67 (m, 8H, Ar-H)	M ⁺ 290 (100)
18c	1500, 1250, 1170, 1080, 1020, 820	1.92 (s, 3H, 9-CH ₃), 2.20 (s, 3H, 8-CH ₃), 2.40 (s, 3H, Ph-CH ₃), 3.02 (t, 2H, 4-CH ₂), 4.39 (t, 2H, 5-CH ₂), 6.63-7.65 (m, 7H, Ar-H)	M ⁺ 304 (100)
19c	1600, 1580, 1240, 1040, 850, 780	1.92 (s, 3H, 9-CH ₃), 2.20 (s, 3H, 8-CH ₃), 2.37 (s, 3H, Ph-CH ₃), 3.04 (t, 2H, 4-CH ₂), 4.40 (t, 2H, 5-CH ₂), 6.65-7.67 (m, 7H, Ar-H)	M ⁺ 304 (100)
20c	1490, 1190, 1090, 1050, 890, 860	1.96 (s, 3H, 9-CH ₃), 2.21 (s, 3H, 8-CH ₃), 2.99 (t, 2H, 4-CH ₂), 4.36 (t, 2H, 5-CH ₂), 6.55-7.61 (m, 7H, Ar-H)	M ⁺ 324 (100)
21c	1580, 1190, 1040, 880, 790, 680	1.98 (s, 3H, 9-CH ₃), 2.23 (s, 3H, 8-CH ₃), 3.01 (t, 2H, 4-CH ₂), 4.41 (t, 2H, 5-CH ₂), 6.83-7.85 (m, 7H, Ar-H)	M ⁺ 324 (100)
22c	1510, 1300, 1250, 1170, 1130, 840	1.92 (s, 3H, 9-CH ₃), 2.18 (s, 3H, 8-CH ₃), 3.03 (t, 2H, 4-CH ₂), 3.85 (s, 3H, Ph-OCH ₃), 4.37 (t, 2H, 5-CH ₂), 6.62-7.63 (m, 7H, Ar-H)	M ⁺ 320 (100)
23c	1600, 1520, 1340, 1250, 1040, 860	2.00 (s, 3H, 9-CH ₃), 2.23 (s, 3H, 8-CH ₃), 2.93 (t, 2H, 4-CH ₂), 4.43 (t, 2H, 5-CH ₂), 6.63-8.53 (m, 7H, Ar-H)	M ⁺ 335 (100)
24c	1530, 1340, 1240, 1040, 860, 740	1.90 (s, 3H, 9-CH ₃), 2.20 (s, 3H, 8-CH ₃), 2.97 (t, 2H, 4-CH ₂), 4.37 (t, 2H, 5-CH ₂), 6.53-8.37 (m, 7H, Ar-H)	M ⁺ 335 (100)

[a] Recorded in deuteriochloroform.

Table 7
Physical Data of Compounds 26a-29a, 30b-33b, 34c-37c

Compound No.	R	R ₁	R ₂	Yield (%)	Mp (°C) (recrystallization solvent)	Molecular Formula	Analysis (%)		
							C	Calcd./Found II	N
26a	H	H	H	30	49-50 (petroleum ether 60-80°)	C ₁₂ H ₁₀ N ₂ O	72.73 72.63	5.05 5.10	14.14 14.21
27a	H	H	CH ₃	37	63-64 (petroleum ether 60-80°)	C ₁₃ H ₁₂ N ₂ O	73.58 73.70	5.66 5.79	13.21 13.15
28a	H	H	C ₆ H ₅	31	81-83 (petroleum ether 60-80°)	C ₁₈ H ₁₄ N ₂ O	78.83 78.69	5.11 5.07	10.22 10.20
29a	H	H	NH ₂	32	137-138 (petroleum ether 100-140°)	C ₁₂ H ₁₁ N ₃ O	67.61 67.75	5.16 5.24	19.72 19.83
30b	CH ₃	H	H	30	55-57 (petroleum ether 40-60°)	C ₁₃ H ₁₂ N ₂ O	73.58 73.57	5.66 5.74	13.21 13.10
31b	CH ₃	H	CH ₃	56	116-117 (petroleum ether 60-80°)	C ₁₄ H ₁₄ N ₂ O	74.34 74.50	6.19 6.30	12.39 12.45
32b	CH ₃	H	C ₆ H ₅	35	123-125 (petroleum ether 60-80°)	C ₁₉ H ₁₆ N ₂ O	79.17 79.28	5.56 5.63	9.72 9.75
33b	CH ₃	H	NH ₂	38	208-209 (benzene)	C ₁₃ H ₁₃ N ₃ O	68.72 68.56	5.73 5.80	18.50 18.43
34c	CH ₃	CH ₃	H	51	93-94 (petroleum ether 40-60°)	C ₁₄ H ₁₄ N ₂ O	74.34 74.42	6.19 6.23	12.39 12.32
35c	CH ₃	CH ₃	CH ₃	31	84-85 (petroleum ether 60-80°)	C ₁₅ H ₁₆ N ₂ O	75.00 74.94	6.67 6.53	11.67 11.55
36c	CH ₃	CH ₃	C ₆ H ₅	42	120-122 (petroleum ether 60-80°)	C ₂₀ H ₁₈ N ₂ O	79.47 79.59	5.96 6.11	9.27 9.41
37c	CH ₃	CH ₃	NH ₂	31	204-205 (petroleum ether 100-140°)	C ₁₄ H ₁₅ N ₃ O	69.71 69.84	6.22 6.30	17.43 17.40

Table 8
IR, NMR and Mass Spectral Data of Compounds 26a-29a, 30b-33b, 34c-37c

Compound No.	IR (cm ⁻¹)	¹ H-NMR (δ ppm)	MS m/z (R.I.%)
26a	1600, 1580, 1530, 1200, 1040, 760	2.93 (t, 2H, 5-CH ₂), 4.59 (t, 2H, 6-CH ₂), 7.07-9.21 (m, 6H, Ar-H) [a]	M ⁺ 198 (100)
27a	1600, 1570, 1540, 1220, 1030, 800	2.80 (s, 3H, 2-CH ₃), 2.88 (t, 2H, 5-CH ₂), 4.60 (t, 2H, 6-CH ₂), 7.10-8.53 (m, 5H, Ar-H) [a]	M ⁺ 212 (100)
28a	1600, 1580, 1530, 1200, 1030, 740	2.97 (t, 2H, 5-CH ₂), 4.59 (t, 2H, 6-CH ₂), 7.18-8.65 (m, 10H, Ar-H) [a]	M ⁺ 274 (90), 39 (100)
29a	3350, 3200, 1640, 1590, 1540, 1040	2.70 (t, 2H, 5-CH ₂), 4.46 (t, 2H, 6-CH ₂), 6.60 (s, 2H, 2-NH ₂), 7.10-8.23 (m, 5H, Ar-H) [b]	M ⁺ 213(58), 28 (100)
30b	1580, 1540, 1210, 1060, 1040, 830	2.40 (s, 3H, 10-CH ₃), 2.90 (t, 2H, 5-CH ₂), 4.55 (t, 2H, 6-CH ₂), 7.07-9.20 (m, 5H, Ar-H) [a]	M ⁺ 212 (66), 27 (100)
31b	1580, 1540, 1210, 1080, 1040, 820	2.42 (s, 3H, 10-CH ₃), 2.82 (s, 3H, 2-CH ₃), 2.83 (t, 2H, 5-CH ₂), 4.75 (t, 2H, 6-CH ₂), 7.00-8.52 (m, 4H, Ar-H) [a]	M ⁺ 226 (39), 42 (100)
32b	1580, 1540, 1510, 1040, 770, 690	2.43 (s, 3H, 10-CH ₃), 2.90 (t, 2H, 5-CH ₂), 4.57 (t, 2H, 6-CH ₂), 7.00-8.70 (m, 9H, Ar-H) [a]	M ⁺ 288 (89), 27 (100)
33b	3350, 3175, 1620, 1580, 1540, 840	2.33 (s, 3H, 10-CH ₃), 2.65 (t, 2H, 5-CH ₂), 4.41 (t, 2H, 6-CH ₂), 6.53 (s, 2H, 2-NH ₂), 6.97-8.93 (m, 4H, Ar-H) [b]	M ⁺ 227 (31), 28 (100)
34c	1620, 1580, 1310, 1140, 1060, 790	2.30 (s, 6H, 9- and 10-CH ₃), 2.93 (t, 2H, 5-CH ₂), 4.57 (t, 2H, 6-CH ₂), 7.00, 7.97, 8.60 and 9.25 (four s, 4H, for 2-, 4-, 8- and 11-Cl) [a]	M ⁺ 226 (33), 27 (100)
35c	1620, 1580, 1200, 1140, 1080, 860	2.28 (s, 3H, 9- and 10-CH ₃), 2.82 (s, 3H, 2-CH ₃), 2.91 (t, 2H, 5-CH ₂), 4.50 (t, 2H, 6-CH ₂), 6.93, 7.87 and 8.45 (three s, 3H, for 4-, 8- and 11-Cl) [a]	M ⁺ 240 (43), 42 (100)
36c	1620, 1560, 1520, 1140, 780, 700	2.33 (s, 6H, 9- and 10-CH ₃), 2.95 (t, 2H, 5-CH ₂), 4.53 (t, 2H, 6-CH ₂), 6.92-8.58 (m, 8H, Ar-H) [a]	M ⁺ 302 (100)
37c	3350, 3200, 1660, 1580, 1540, 1180	2.27 (s, 2H, 9- and 10-CH ₃), 2.68 (t, 2H, 5-CH ₂), 4.40 (t, 2H, 6-CH ₂), 6.50 (s, 2H, 2-NH ₂), 6.93, 7.73 and 8.20 (three s, 3H, for 4-, 8- and 11-Cl) [b]	M ⁺ 241 (37), 28 (100)

[a] Recorded in deuteriochloroform. [b] Recorded in dimethyl sulfoxide-d₆.

starting 4-hydroxymethylene-3,4-dihydro[1]benzoxepin-5(2*H*)-ones **2a-c**, has already been described [1,3]. The condensation of these compounds with hydrazine to give the benzoxepinopyrazoles or with secondary amines to give the corresponding enamines, analogues of the 4-morpholinomethylene-3,4-dihydro[1]benzoxepin-5(2*H*)-ones **25a-c**, has already been reported [2a,2c,3], while, to the best of our knowledge, the reaction of compounds **2a-c** with phenylhydrazines was never investigated.

In our research, the target benzoxepinopyrazoles **3a-24c** were directly obtained by reflux in methanol of compounds **2a-c** with phenylhydrazine hydrochlorides. The physical properties are given in Tables 1, 3, and 5, respectively.

The structures of all compounds **3a-10a**, **11b-16b** and **17c-24c** were assigned on the basis of literature data, spectral data and chemical evidence.

The ir, mass and ¹H nmr spectra were in agreement with the proposed structures and are reported in Tables 2, 4, and 6. All the compounds showed uv spectra analogous among them, with two principal maxima in the 262-268 and 200-204 nm ranges. In addition, the 2-phenyl-4,5-dihydro-2*H*-[1]benzoxepino[5,4-*c*]pyrazole, already described in the literature [2e], presents physical and spectral properties quite different from those of the isomer 1-phenyl-4,5-dihydro-1*H*-[1]benzoxepino[5,4-*c*]pyrazole **3a**.

Only a few 5,6-dihydro[1]benzoxepino[5,4-*d*]pyrimidine derivatives are described in literature [4].

The preparation of the 2-substituted 5,6-dihydro[1]benzoxepino[5,4-*d*]pyrimidines **26a-29a**, **30b-33b** and **34c-37c** was envisioned as resulting from the condensation of an appropriately substituted amidine with the enaminoketone derivatives **25a-c**. Indeed, the compounds **2a-c** failed to give the desired benzoxepinopyrimidines **26a-37c** upon direct reaction with substituted amidines under a variety of conditions. This unreactivity of **2a-c** was circumvented by converting the **2a-c** to the morpholine enaminoketones **25a-c** that have been used to activate similar systems for condensation reactions [5]. Compound **25a** was previously described [3]. Treatment of **25a-c** with substituted amidines in the presence of sodium ethoxide gave the pyrimidine derivatives **26a-37c** in moderate to good yields. The physical and spectral data of the various prepared benzoxepinopyrimidines are reported in Tables 7 and 8.

EXPERIMENTAL

Melting points were determined using a Reichert Köfler hot-stage apparatus and are uncorrected. Infrared spectra were obtained on a PVE/UNICAM Model PU 9561 spectrophotometer in Nujol mulls. Nuclear magnetic resonance spectra were recorded on a Varian EM 360 A spectrometer using tetramethylsilane (TMS) as an internal standard. Mass spectra were obtained on a

Hewlett-Packard 5988 A spectrometer using a direct injection probe and an electron beam energy of 70eV. The uv spectra were measured in 95% ethanol on a Perkin-Elmer Model Lambda 15 spectrophotometer. Magnesium sulfate was always used as the drying agent. Evaporation was made *in vacuo* (rotating evaporator). Analytical tlc was carried out on Merck 0.25 mm precoated silica gel glass plates (60 F-254). Elemental analyses were performed by our Analytical Laboratory and agreed with theoretical values to within ±0.4%.

General Procedure for the Preparation of 1-Aryl-4,5-dihydro-1*H*-[1]benzoxepino[5,4-*c*]pyrazoles **3a-24c**.

The required phenylhydrazine hydrochloride (2.1 mmoles) was added to a solution of 2 mmoles of **1a-c** in 10 ml of methanol and the reaction mixture was refluxed for 5 hours. After cooling the yellow solid, if present, was collected and the solution was evaporated under reduced pressure. The solid and the residue were washed with an aqueous potassium carbonate solution and extracted with chloroform. The organic layer was dried and concentrated *in vacuo* to give crude **3a-24c**. The recrystallization solvents, yields, melting points, analytical, and spectral data are given in Tables 1, 2, 3, 4, 5, and 6.

General Procedure for the Preparation of Enaminoketones **25b-c**.

A solution of 4.3 mmoles of **2b-c** and 5 mmoles of morpholine in 12 ml of dry benzene was stirred at room temperature for 20 hours and then at reflux for 4 hours. After cooling, the precipitate solid was collected: yield of 77% and 87% for **25b** and **25c**, respectively. They can be directly used in the subsequent reaction with various amidines.

7-Methyl-4-morpholinomethylene-3,4-dihydro[1]benzoxepin-5(2*H*)-one **25b**.

This compound was obtained as yellow crystals (petroleum ether 100-140°), mp 123-124°; ir: 1640 (C=O), 1520 (C=C) cm⁻¹; ¹H nmr (deuteriochloroform): 2.33 (s, 3H, 7-CH₃), 2.69 (t, 2H, 3-CH₂), 3.48 (mc, 4H, 2 CH₂N), 3.77 (mc, 4H, 2 CH₂O), 4.20 (t, 2H, 2-CH₂), 6.94-7.61 (m, 4H, Ar-H and 4-CH) ppm; ms: m/z (relative intensity) 287 (M⁺ 16), 270 (100).

Anal. Calcd. for C₁₆H₁₉NO₃: C, 70.33; H, 6.96; N, 5.13. Found: C, 70.23; H, 7.05; N, 4.99.

7,8-Dimethyl-4-morpholinomethylene-3,4-dihydro[1]benzoxepin-5(2*H*)-one **25c**.

This compound was obtained as white crystals (methanol), mp 166-167°; ir: 1640 (C=O), 1520 (C=C) cm⁻¹; ¹H nmr (deuteriochloroform): 2.23 (s, 6H, 7- and 8-CH₃), 2.70 (t, 2H, 3-CH₂), 3.47 (mc, 4H, 2 CH₂N), 3.70 (mc, 4H, 2 CH₂O), 4.17 (t, 2H, 2-CH₂), 6.80, 7.56 and 7.58 (three s, 3H, for 4-CH, 6-CH and 9-CH) ppm; ms: m/z (relative intensity) 273 (M⁺ 19), 256 (100).

Anal. Calcd. for C₁₇H₂₁NO₃: C, 71.08; H, 7.32; N, 4.88. Found: C, 70.97; H, 7.40; N, 4.82.

General Procedure for the Preparation of 5,6-Dihydro[1]benzoxepino[5,4-*d*]pyrimidines **26a-37c**.

The morpholine enaminoketone **25a-c** (1.7 mmoles) and the required amidine hydrochloride (3.4 mmoles) were added to a solution of 0.078 g (3.4 mmoles) of sodium in 25 ml of ethanol. The mixture was heated to reflux for 2-3 hours, until tlc analysis showed disappearance of the starting morpholine enamino-

ketone. After cooling the resulting precipitate was collected, washed with water and dried to give the crude compounds **26a-37c**. The recrystallization solvents, yields, melting points, analytical, and spectral data are given in Tables 7 and 8.

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