Substituted γ-Lactones [1,2]: On the Structural Elucidation of the Reaction Products from 4-Aroyl-3-hydroxy-2(5*H*)-furanones and 1,2-Diamines

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The reaction pathway of 4-aroyl-3-hydroxy-2(5*H*)-furanones **1** with diamines depends on the nature of the amine as well as on the applied reaction conditions. Thus, the reaction of **1a-d** with 5,6-diamino-1,3-dimethyluracil **5** led to the formation of two isomeric Schiff bases **7a-d** and **8a-d**. Conversely type **1** compounds reacted with 4,5-diaminopyrimidine **9** or 2,3-diaminopyridine **10** to form the mono acid-base adducts **11a** and **11b** respectively. When type **1** compounds were reacted with aliphatic diamines **13a-d** or *p*-phenylenediamine and *p*-xylenediamine, respectively also an immediate formation of acid-base adducts **15a-f** was observed. The reaction of a number of *O*-methylated type **1** compounds with 1,2-ethylenediamine afforded the novel seven-membered ring compounds **18a-d** in good yields. The analogous reaction of **O**-alkylated **1a** with *o*-phenylenediamine **2** or 2,3-diaminonaphthalene gave the expected tricyclic ring systems **19** or **20**.

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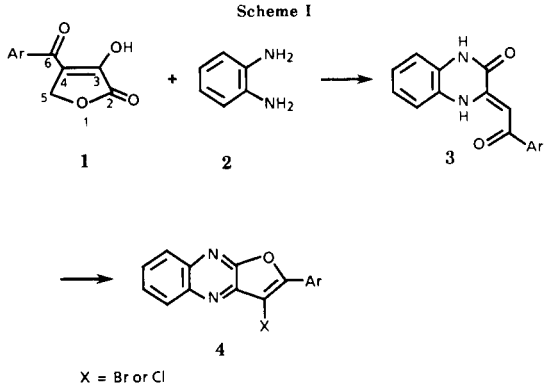
In our efforts to use easily accessible starting materials as entries into heterocyclic ring systems, we investigated a number of bi- and tricarbonyl compounds and their reaction with mono- and binucleophiles such as diamines and hydrazines [5-9]. Of special interest to us was to investigate whether such reactions could lead to the formation of seven-membered ring systems. The tricarbonyl compounds **1** have kept our interest for quite some time as a readily available class of compounds for the synthesis of heterocycles including the desired seven-membered ring systems. The latter are of special interest in view of the clinical and commercial importance of tranquilizers incorporating a diazepine ring system [10]. Instead of the sought after seven-membered ring system, earlier and preliminary results by us showed that **1** yielded with **2**, a 2(1*H*)-quinoxalinone **3** [6], in which the binucleophilic attack of **2** occurred on C-3 followed by attack on C-2 of **1**, with opening of the lactone ring followed by a retro-aldol condensation with loss of formaldehyde. The resulting quinoxalines after halogenation with *N*-halosuccinimide followed by treatment with concentrated sulfuric acid yielded the furoquinoxalines **4** [11] (Scheme I).

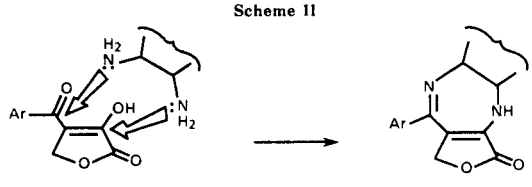
Scheme I



1 2 3 4

However, reconsideration of the electrophilicity of the C-3, C-2, and C-6 carbon atoms of **1** towards binucleophilic reagents convinced us that these compounds offer many possibilities for the construction of various heterocyclic systems including the desired 1,4-diazepine with a fused γ-lactone ring (Scheme II).

Scheme II

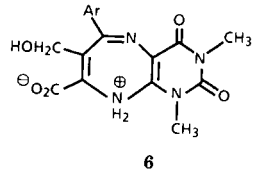


It must be borne in mind that the reactivity and the selectivity of the binucleophilic reagent (*e.g.* 1,2-diamine) and the carbonyl carbon atoms of **1** will depend on factors emanating from the substrate and the medium of the reaction which influence the structure of the products(s). Thus, in the present paper we wish to report our findings toward this target.

Reaction of Aromatic Heterocyclic Diamines with Type **1** Compounds.

Reactions of compounds of type **1** with 5,6-diamino-1,3-dimethyluracil **5** were straightforward. It simply involved the mixing of methanolic solutions of both reactants.

On the basic of elemental analysis and ^{1}H-nmr data of the formed product its structure originally thought to be the zwitterionic structure **6**. However, a careful examina-



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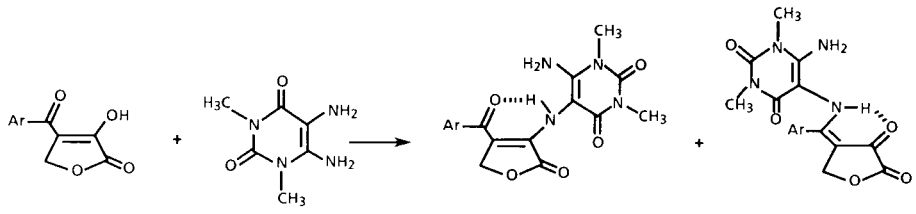
Scheme III



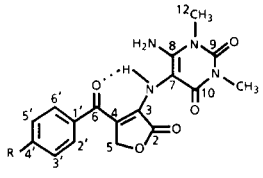
1 5 7a-d 8a-d

a) Ar = C_6H_5
b) Ar = p-$CH_3C_6H_4$
c) Ar = p-$H_3COC_6H_4$
d) Ar = p-BrC_6H_4

tion of this reaction revealed, after tedious recrystallization, that the product consisted of two structurally very similar isomers **7** and **8** which proved to be two different Schiff bases (Scheme III). A structure assignment based solely on ^1H- and ^{13}C-nmr data (Tables I and II) proved to be ambiguous. The ^1H-nmr spectra of the reaction mixtures provided two different methylene singlets at δ 5.02 to 5.04 and 4.83 to 4.93 ppm respectively which were used to calculate the ratio of **7** and **8**. Eventually, an X-ray analysis was done which permitted us to assign unambiguously the correct structures to **7** and **8**. Compounds **7c** and **8b** gave suitable crystals for such an analysis (Tables III-VI).

TABLE I

^{13}C NMR Chemical Shift Assignments For Schiff bases 7a-d

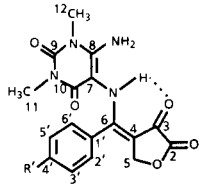


Carbon #	Chemical Shift in DMSO-d_6 (ppm)			
	7a	7b	7c	7d
	R=H	p-CH_3	p-OCH_3	p-Br
2	171.06(s)	170.41(s)	170[b]	170.48(s)
3	---[a]	---[a]	---[a]	---[a]
4	113.81(s)	114.08(s)	114.50(s)	113.35(s)
5	69.70(t)	69.55(t)	69.55(t)	69.50(t)
6	189.87(s)	189.39(s)	188.63(s)	188.78(s)
1′	139.50(s)	136.95(s)	132.28(s)	138.60(s)
2′	127.35(d)	127.51(d)	129.82(d)	129.20(d)
3′	127.35(d)	127.51(d)	112.39(d)	130.07(d)
4′	131.28(d)	141.90(s)	162.09(s)	125.37(s)
5′	127.35(d)	127.51(d)	112.39(d)	130.07(d)
6′	127.35(d)	127.51(d)	129.82(d)	129.20(d)
R[c]	---	21.09(q)	55.31(q)	---
7	90.72(s)	90.71(s)	90.77(s)	90.76(s)
8	---[a]	---[a]	149.59(s)	149.36(s)
9	149.52(s)	149.51(s)	149.94(s)	149.70(s)
10	157.71(s)	157.55(s)	157.68(s)	157.29(s)
11	29.73(q)	29.63(q)	29.84(q)	28.79(q)
12	27.33(q)	27.24(q)	27.25(q)	27.26(q)

[a] No definitely identifiable carbon signal observed.
[b] Broad Signal observed.
[c] C-atom of phenyl group substituent

TABLE II

^{13}C NMR Chemical Shift Assignments For Schiff bases 8a-d



Carbon #	Chemical Shift in DMSO-d_6 (ppm)			
	8a	8b	8c	8d
	R′=H	p-CH_3	p-OCH_3	p-Br
2	167.62(s)	167.89(s)	167.19(s)	166.64(s)
3	172.27(s)	172.05(s)	171.70(s)	172.48(s)
4	105.04(s)	105.20(s)	104.90(s)	104.94(s)
5	66.00(t)	66.06(t)	65.77(t)	65.91(t)
6	166.84(s)	166.94(s)	166.51(s)	166.18(s)
1′	130.95(s)	128.11(s)	122.79(s)	130.16(s)
2′	128.32(d)	126.64(d)	128.27(d)	128.83(d)
3′	126.58(d)	128.95(d)	113.55(d)	131.50(d)
4′	130.53(d)	140.42(s)	160.61(s)	124.17(s)
5′	126.58(d)	128.95(d)	113.55(d)	131.50(d)
6′	128.32(d)	126.64(d)	128.27(d)	128.83(d)
R[a]	---	20.96(q)	54.92(q)	---
7	88.77(s)	88.78(s)	86.85(s)	88.52(s)
8	150.09(s)	150.15(s)	149.91(s)	150.09(s)
9	152.10(s)	152.06(s)	151.74(s)	152.15(s)
10	158.32(s)	158.27(s)	158.07(s)	158.25(s)
11	30.03(q)	30.04(q)	29.68(q)	30.01(q)
12	27.58(q)	27.60(q)	27.18(q)	27.56(q)

[a] C-atom of phenyl group substituent

Perspective views of these compounds are presented in Figures 1 and 2. The more basic NH_2 group of **3** was involved in forming the Schiff base linkage of both **7** and **8**. In the case of **7** the C-3 carbon atom of **1** was involved while **8** was formed by attack on the C-6 carbonyl group.

Attempted cyclization of the Schiff bases **7** to a furopteridine, the heterocyclic system of a pigment occurring in the rings of certain butterflies [12], failed. Also a cyclization of **7** or **8** to a diazepine ring involving the 6-amino group of **3** and the side-chain carbonyl group of type **1** compounds was without success.

The reaction of **1** with 4,5-diaminopyrimidine **9** and 2,3-

TABLE III
Crystal Data and Intensity Collections for **7c** and **8b**

Crystal data	**7c**	**8b**
Empirical formula	$C_{18}H_{18}N_4O_6$	$C_{19}H_{22}N_4O_6$
Formula weight	386.36	402.40
Color and habit	yellow needles	red prisms
Size (mm)	0.08 x 0.18 x 0.42	0.30 x 0.30 x 0.50
Crystal system	monoclinic	orthorhombic
Space group	$P2_{1/c}$	Pb_{ca}
Unit-cell dimensions (a, b, c Å)	a 15.293(3) b 8.702(1) c 15.110(3)	a 27.954(7) b 16.849(4) c 8.424(3)
(angles °)	β 115.16(1)	
Volume (Å3)	1820.1(5)	3968(2)
Z (formulae/cell)	4	8
F (000) (e^-)	808	1696
Data Collection		
Diffractometer	Nicolet R3m	Nicolet R3m
Radiation	Mo-K_a (λ 0.71073 Å)	Mo-K_a (λ 0.71073 Å)
Monochromator	highly oriented graphite crystal	highly oriented graphite crystal
Temperature (K)	294	294
2 θ range (°)	3.0 - 45.0	3.0 - 55.0
h, k, l limits	18, 11, 18	30, 19, 11
Scan type	θ/2θ	θ/2θ
Scan speed (° min^{-1})	variable; 2.0 - 29.3	variable; 1.5 - 8.0
Scan range (°)	$0.8 > K_{\alpha1} - 0.8 < K_{\alpha2}$	± 1.0
Standard reflections	3 measured every 37	3 measured every 37
Reflections collected	2696 total; 2389 independent	4853 total; 4282 independent
Reflections observed	1125; F > 6σ (F)	1148; F > 6σ (F)
Solution and Refinement		
System used	Nicolet SHELXTL PLUS (MicroVAX II)	Nicolet SHELXTL PLUS (MicroVAX II)
Solution	direct methods (SX:TREF)	direct methods (SX:TREF)
Final residuals	R(F) 0.0382 wR(F) 0.0349	R(F) 0.0655 wR(F) 0.0692
Goodness-of-Fit	S 1.22	S 2.31
Largest | shift/ESD |	0.001	0.002
Number of variables	326	276
Data-to-parameter ratio	3.5:1	4.2:1
Max/Min excursions	0.15 and -0.14 $e^-Å^{-3}$	0.28 $e^-Å^{-3}$

diaminopyridine **10** gave contrasting results from the analogous reaction between **1** with **5**, if reacted under identical reaction conditions. These reactions did not give Schiff bases but, according to their ^{13}C-nmr spectra,

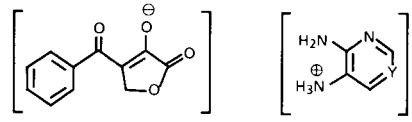
TABLE IV.
Atomic Coordinates (x 10^4) and Equivalent Isotropic Displacement Parameters ($Å^2$ x 10^3) for **7c** and **8b** (with Standard Deviations in Parentheses)

Compound 7c

ATOM	X	Y	Z	U(eq)
C(1)	8441(4)	1312(7)	8385(4)	44(3)
C(2)	9223(4)	353(7)	8713(4)	53(3)
C(3)	9204(3)	-961(7)	8209(4)	49(3)
C(4)	8386(4)	-1355(7)	7379(4)	47(3)
C(5)	7592(3)	-409(6)	7075(4)	37(2)
C(6)	7599(3)	933(6)	7565(3)	35(2)
O(7)	10019(3)	-1853(6)	8582(3)	81(2)
C(8)	10081(7)	-3165(14)	8062(9)	107(6)
C(9)	6785(4)	2013(6)	7200(4)	42(3)
O(10)	6930(3)	3386(4)	7402(3)	72(2)
C(11)	5805(3)	1535(5)	6518(3)	35(2)
C(12)	5246(4)	2596(7)	5677(4)	45(3)
O(13)	4321(2)	1844(4)	5154(2)	47(2)
C(14)	4286(4)	542(7)	5630(3)	41(3)
C(15)	5221(3)	363(6)	6503(3)	32(2)
O(16)	3598(2)	-290(4)	5357(2)	52(2)
N(17)	5273(3)	-862(5)	7084(3)	35(2)
C(18)	6066(3)	-1105(6)	8010(3)	31(2)
C(19)	6295(3)	-2(6)	8748(4)	37(2)
N(20)	7153(3)	-251(5)	9581(3)	39(2)
C(21)	7731(3)	-1522(6)	9726(4)	42(2)
N(22)	7437(3)	-2606(5)	8990(3)	39(2)
C(23)	6609(3)	-2405(7)	8139(4)	36(2)
O(24)	5806(2)	1169(4)	8696(2)	49(2)
C(25)	7476(5)	920(10)	10362(6)	65(3)
O(26)	8470(2)	-1695(4)	10474(3)	58(2)
C(27)	8065(5)	-3962(9)	9152(7)	60(4)
N(28)	6382(4)	-3511(6)	7455(4)	50(2)
H(1)	8483(29)	2222(54)	8737(32)	48(16)
H(2)	9860(32)	608(48)	9283(31)	50(14)
H(4)	8384(29)	-2261(52)	7066(30)	39(15)
H(5)	7011(28)	-643(45)	6480(29)	33(13)
H(8a)	10787(50)	-3650(77)	8490(50)	142(27)
H(8b)	10185(47)	-2607(81)	7537(47)	109(34)
H(8c)	9607(40)	-4045(64)	7975(44)	87(25)
H(12a)	5564(32)	2668(58)	5240(34)	60(18)
H(12b)	5117(33)	3618(55)	5873(32)	54(16)
H(17)	4758(40)	-1438(66)	6922(44)	101(25)
H(25a)	8142(42)	1021(66)	10554(41)	97(24)
H(25b)	7155(38)	1938(65)	10061(38)	87(23)
H(25c)	7253(48)	508(82)	10873(52)	146(34)
H(27a)	8309(46)	-3975(76)	8660(48)	121(33)
H(27b)	8677(47)	-3589(66)	9676(44)	105(24)
H(27c)	7770(39)	-4766(68)	9175(42)	82(27)
H(28a)	6719(41)	-4425(72)	7629(43)	102(25)
H(28b)	5778(33)	-3470(53)	6978(36)	54(17)

Compound 8b

ATOM	X	Y	Z	U(eq)
C(1)	3924(3)	4277(6)	4258(11)	37(4)
C(2)	4287(4)	4281(6)	5362(13)	51(4)
C(3)	4679(4)	3780(7)	5214(13)	49(4)
C(4)	4694(4)	3267(7)	3929(14)	54(4)
C(5)	4332(3)	3255(6)	2822(12)	46(4)
C(6)	3932(3)	3757(6)	2990(11)	35(3)
C(7)	5086(4)	3798(7)	6412(13)	82(6)
C(8)	3533(3)	3728(6)	1877(10)	31(3)
C(9)	3302(4)	3021(6)	1463(11)	40(4)
C(10)	3451(4)	2190(5)	1910(13)	53(4)
O(11)	3062(3)	1680(4)	1256(9)	60(3)
C(12)	2748(4)	2119(7)	473(13)	52(5)
C(13)	2878(4)	2978(6)	611(12)	43(4)
O(14)	2403(3)	1829(4)	-210(10)	69(3)
O(15)	2628(2)	3506(4)	-11(9)	59(3)
N(16)	3342(3)	4417(5)	1318(9)	39(3)
C(17)	3597(3)	5145(6)	1270(11)	30(3)
C(18)	3420(4)	5789(6)	2051(12)	37(4)
N(19)	3644(3)	6515(5)	1901(9)	37(3)
C(20)	4059(4)	6612(7)	931(13)	46(4)
N(21)	4206(3)	5954(6)	180(10)	46(3)
C(22)	4011(3)	5195(7)	282(12)	43(4)
N(23)	3031(3)	5755(6)	2985(12)	50(4)
C(24)	3462(4)	7221(6)	2755(14)	64(5)
O(25)	4231(2)	7265(4)	815(9)	60(3)
C(26)	4633(4)	6045(8)	-851(14)	80(5)
O(27)	4175(3)	4629(5)	-443(9)	65(3)
O(28)	2274(3)	306(4)	-1329(11)	66(4)
C(29)	1926(4)	360(7)	-2566(15)	78(6)
H(1)	3661	4640	4371	57(10)
H(2)	4269	4637	6250	57(10)
H(4)	4961	2914	3809	57(10)
H(5)	4352	2901	1931	57(10)
H(7a)	5017	4184	7217	194(22)
H(7b)	5378	3936	5882	194(22)
H(7c)	5119	3284	6892	194(22)
H(10a)	3473	2134	3042	57(10)
H(10b)	3754	2057	1438	57(10)
H(16)	2987(34)	4308(52)	718(102)	57(10)
H(23a)	2869(31)	5202(57)	3063(111)	57(10)
H(23b)	2925(36)	6174(57)	3249(129)	57(10)
H(24a)	3673	7661	2578	194(22)
H(24b)	3446	7109	3871	194(22)
H(24c)	3148	7351	2369	194(22)
H(26a)	4710	5545	-1332	194(22)
H(26b)	4900	6222	-223	194(22)
H(26c)	4568	6429	-1665	194(22)
H(28)	2319(35)	759(57)	-969(127)	57(10)
H(29a)	1868	-157	-3000	194(22)
H(29b)	2042	706	-3386	194(22)
H(29c)	1633	570	-2141	194(22)



11 a Y = N
11 b Y = C

rather yielded simply the salts **11a** and **11b**. The C-3 of the lactone ring undergoes a considerable downfield shift (δ 156.74-157.86 ppm) as compared to that of **1** and, as expected, the chemical shift of C-2 is little affected by the salt formation.

The conditions which are applied for bringing about the reaction of **1** with diamines also plays a role as to the structure of the reaction product. Thus, when instead of alco-

hol, glacial acetic acid was used as solvent, **1a** reacted with **9** by a retro-aldol condensation with elimination of formaldehyde to yield compound **12** [6].

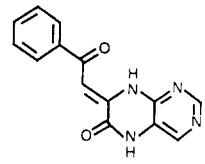


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TABLE V.
Bond Angles (°) for 7c and 8b

Compound 7c

C(6)-C(1)-C(2)	120.8(6)
C(3)-C(2)-C(1)	120.0(5)
C(4)-C(3)-C(2)	120.6(5)
O(7)-C(3)-C(2)	116.4(5)
O(7)-C(3)-C(4)	123.0(6)
C(5)-C(4)-C(3)	118.9(6)
C(6)-C(5)-C(4)	121.5(5)
C(5)-C(6)-C(1)	118.1(5)
C(9)-C(6)-C(1)	119.8(5)
C(9)-C(6)-C(5)	121.9(4)
C(8)-O(7)-C(3)	119.6(5)
O(10)-C(9)-C(6)	119.6(5)
C(11)-C(9)-C(6)	122.1(5)
C(11)-C(9)-O(10)	118.1(5)
C(12)-C(11)-C(9)	117.4(5)
C(15)-C(11)-C(9)	134.0(5)
C(15)-C(11)-C(12)	108.3(4)
O(13)-C(12)-C(11)	104.8(4)
C(14)-O(13)-C(12)	109.7(4)
C(15)-C(14)-O(13)	108.6(5)
O(16)-C(14)-O(13)	123.3(5)
O(16)-C(14)-C(15)	128.0(5)
C(14)-C(15)-C(11)	108.4(5)
N(17)-C(15)-C(11)	136.4(5)
N(17)-C(15)-C(14)	115.1(5)
C(18)-N(17)-C(15)	122.8(4)
C(19)-C(18)-N(17)	120.1(4)
C(23)-C(18)-N(17)	118.3(5)
C(23)-C(18)-C(19)	121.5(5)
N(20)-C(19)-C(18)	115.7(5)
O(24)-C(19)-C(18)	124.8(5)
O(24)-C(19)-N(20)	119.5(5)
C(21)-N(20)-C(19)	124.3(5)
C(25)-N(20)-C(19)	118.7(5)
C(25)-N(20)-C(21)	117.0(5)
N(22)-C(21)-N(20)	117.0(4)
O(26)-C(21)-N(20)	121.8(5)
O(26)-C(21)-N(22)	121.2(5)
C(23)-N(22)-C(21)	121.3(4)
C(27)-N(22)-C(21)	116.6(5)
C(27)-N(22)-C(23)	122.1(5)
N(22)-C(23)-C(18)	119.9(5)
N(28)-C(23)-C(18)	122.6(5)
N(28)-C(23)-N(22)	117.4(5)

Compound 8b

C(6)-C(1)-C(2)	120.9(9)
C(3)-C(2)-C(1)	121.2(10)
C(4)-C(3)-C(2)	118.2(9)
C(7)-C(3)-C(2)	121.2(11)
C(7)-C(3)-C(4)	120.6(10)
C(5)-C(4)-C(3)	121.2(10)
C(6)-C(5)-C(4)	120.4(10)
C(5)C(6)-C(1)	118.2(9)
C(8)-C(6)-C(1)	120.4(8)
C(8)-C(6)-C(5)	121.5(9)
C(9)-C(8)-C(6)	122.8(9)
N(16)-C(8)-C(6)	119.6(9)
N(16)-C(8)-C(9)	117.3(8)
C(10)-C(9)-C(8)	126.9(9)
C(13)-C(9)-C(8)	124.6(9)
C(13)-C(9)-C(10)	108.4(9)
O(11)-C(10)-C(9)	103.9(8)
C(12)-O(11)-C(10)	110.3(8)
C(13)-C(12)-O(11)	109.9(11)
O(14)-C(12)-O(11)	122.2(10)
O(14)-C(12)-C(13)	127.9(12)
C(12)-C(13)-C(9)	107.4(10)
O(15)-C(13)-C(9)	131.2(9)
O(15)-C(13)-C(12)	121.4(10)
C(17)-N(16)-C(8)	123.4(8)
C(18)-C(17)-N(16)	119.6(9)
C(22)-C(17)-N(16)	118.3(9)
C(22)-C(17)-C(18)	121.9(10)
N(19)-C(18)-C(17)	119.8(10)
N(23)-C(18)-C(17)	122.9(10)
N(23)-C(18)-N(19)	117.3(10)
C(20)-N(19)-C(18)	121.5(9)

TABLE V. (continued)

C(24)-N(19)-C(18)	120.8(8)
C(24)-N(19)-C(20)	117.8(9)
N(21)-C(20)-N(19)	115.1(9)
O(25)-C(20)-N(19)	118.4(11)
O(25)-C(20)-N(21)	126.4(10)
C(22)-N(21)-C(20)	127.6(9)
C(26)-N(21)-C(20)	115.9(9)
C(26)-N(21)-C(22)	116.5(9)
N(21)-C(22)-C(17)	114.0(10)
O(27)-C(22)-C(17)	123.3(10)
O(27)-C(22)-N(21)	122.7(10)

TABLE VI.
Bond Distances (Å) for 7c ad 8b

Compound 7c		Compound 8b	
Bond	Length	Bond	Length
C(1)-C(2)	1.368(7)	C(1)-C(2)	1.377(13)
C(1)-C(6)	1.395(6)	C(1)-C(6)	1.381(11)
C(2)-C(3)	1.367(7)	C(2)-C(3)	1.389(14)
C(3)-C(4)	1.385(7)	C(3)-C(4)	1.386(14)
C(3)-O(7)	1.370(6)	C(3)-C(7)	1.520(13)
C(4)-C(5)	1.375(7)	C(4)-C(5)	1.376(13)
C(5)-C(6)	1.381(6)	C(5)-C(6)	1.408(12)
C(6)-C(9)	1.467(6)	C(6)-C(8)	1.458(12)
O(7)-C(8)	1.411(9)	C(8)-C(9)	1.400(12)
C(9)-O(10)	1.230(5)	C(8)-N(16)	1.360(11)
C(9)-C(11)	1.472(6)	C(9)-C(10)	1.509(12)
C(11)-C(12)	1.508(6)	C(9)-C(13)	1.387(14)
C(11)-C(15)	1.349(6)	C(10)-O(11)	1.491(11)
C(12)-O(13)	1.450(6)	O(11)-C(12)	1.324(12)
O(13)-C(14)	1.355(6)	C(12)-C(13)	1.495(13)
C(14)-C(15)	1.485(6)	C(12)-O(14)	1.226(12)
C(14)-O(16)	1.197(6)	C(13)-O(15)	1.247(11)
C(15)-N(17)	1.362(6)	N(16)-C(17)	1.418(11)
N(17)-C(18)	1.425(5)	C(17)-C(18)	1.362(12)
C(18)-C(19)	1.399(6)	C(17)-C(22)	1.429(12)
C(18)-C(23)	1.368(6)	C(18)-N(19)	1.380(11)
C(19)-N(20)	1.395(5)	C(18)-N(23)	1.344(12)
C(19)-O(24)	1.246(5)	N(19)-C(20)	1.427(12)
N(20)-C(21)	1.374(6)	N(19)-C(24)	1.481(11)
N(20)-C(25)	1.477(7)	C(20)-N(21)	1.341(12)
C(21)-N(22)	1.380(6)	C(20)-O(25)	1.206(11)
C(21)-O(26)	1.222(5)	N(21)-C(22)	1.392(12)
N(22)-C(23)	1.380(5)	N(21)-C(26)	1.486(12)
N(22)-C(27)	1.474(7)	C(22)-O(27)	1.221(11)
C(23)-N(28)	1.346(6)	O(28)-C(29)	1.429(13)
N(17)-H(17)	0.876(55)	N(16)-H(16)	1.130(92)
N(28)-H(28a)	0.923(61)	N(23)-H(23a)	1.039(92)
N(28)-H(28b)	0.899(45)	N(23)-H(23b)	0.797(94)
		O(28)-H(28)	0.830(93)

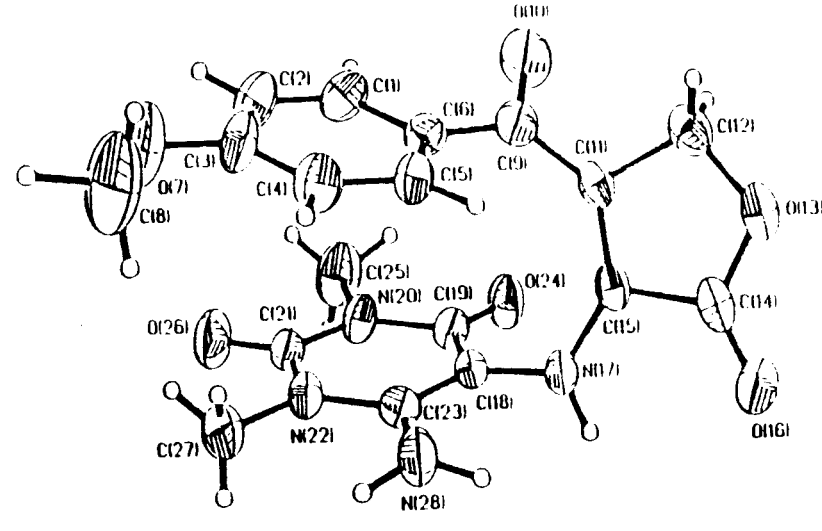


Figure 1

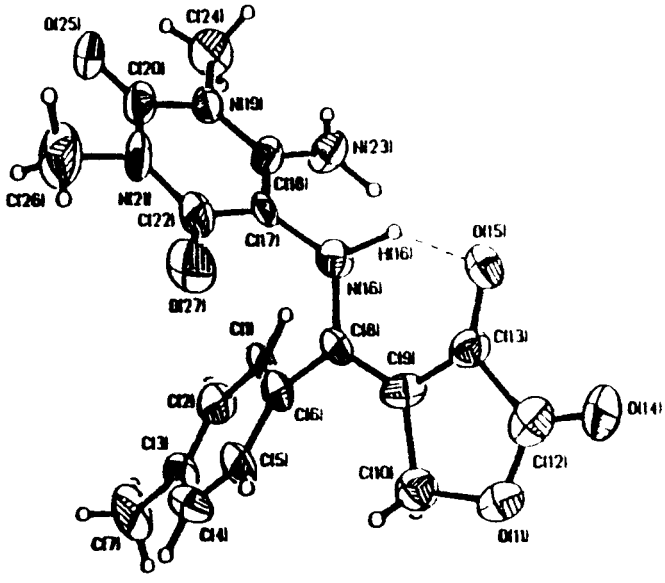


Figure 2

Reaction of Type **1** Compounds with Aliphatic Diamines **13a-d** and *p*-Phenylendiamine **13e**.

These reactions were carried out similarly to the previously described ones. Solutions of the appropriate lactone and diamine in chloroform were combined (see Experimental section), whereupon a colorless product quickly precipitated. The elemental analyses of these products showed that they contained the same number of atoms as the starting materials. However, again according to ir and ^{13}C-nmr evidence, the lactone moiety was still intact and, taking into consideration that the products were colorless, the originally assigned structures as Schiff bases **14** or (in their enamino form) **16** became untenable, and our previously assigned zwitterionic structures **16** had to be corrected [6]. The only possible structures that agree with all the evidence are the salts **15** (Scheme IV). They originated simply by an acid-base reaction between the amine and the enolic protons of type **1** compounds. A comparison of the ir spectra of the salts, **15**, with the one of **1a** further confirmed the new assignment. The lactone carbonyl absorption of **1a** appeared at 1750 cm^{-1}, its enol stretch absorption at 1685 cm^{-1}, and the benzoyl carbonyl stretch at 1630 cm^{-1}. All type **15** compounds exhibited a strong ir absorption in the 1750 cm^{-1} region. In addition, the enolic OH stretch was no longer present indicating that the site of reaction was at this position. Changing the enol into enolate also increased the electron density on the oxygen, resulting in a significant downfield shift in the ^{13}C-nmr spectra of the peak due to the enolic carbon atom, along with a lesser shift of the lactone carbonyl carbon. This indeed was observed. The peak for the enolic carbon was shifted 11 ppm downfield, and the peak of the lactone carbonyl atom was shifted 5 ppm from 169 to 174 ppm (see Experimental section).

TABLE VII
Crystal Data and Intensity Collections for 18a

Crystal Data	
Empirical formula	$C_{13}H_{12}N_2O_2$
Formula weight	228.27
Color and habit	Colorless plates
Size (mm)	0.20 x 0.45 x 0.55
Crystal system	Monoclinic
Space group	P21/c (No. 14)
Unit cell dimensions	a 11.425(1)
(a, b, c Å)	b 9.749(1)
(angles °)	c 21.074(2)
	β 103.768(8)
Volume (Å3)	2281.9(4)
Z (formulae/cell)	8
Absorption coeff. (cm-1)	0.86
F (000) (e$^-$)	960
Data Collection	
Diffractometer	Siemens R3m/V
Radiation	MoK$_a$ (λ 0.71073 Å)
Monochromator	Highly oriented graphite crystal
Temperature (K)	294
2θ Range (deg)	3.0 to 55.0
h, k, l Limits	−14 → 14, 0 → 12, 0 → 27
Scan type	2θ–θ
Scan speed (deg/min)	Variable; 2.0 to 8.0
Scan range (deg)	0.8 on either side of K$_{\alpha 2}$
Standard reflections	3 measured every 37
Reflections collected	5733 total; 5277 independent; R(int) = 0.0163
Reflections observed	2686; F > 6σ(F)
Solution and Refinement	
System used	Siemens SHELXTL PLUS (MicroVAX II)
Solution	Direct methods (XS:TREF)
Refinement method	Full-matrix Least-squares (XLS)
Final residuals	R(F) 0.0544 wR(F) 0.0590
Goodness-of-fit	S 2.14
Max and Mean | Shift/ESD |	0.001 and 0.000
Number of variables	314
Data-to-parameter ratio	8.6:1
Max/Min Excursions	0.56 and −0.33 e$^-$Å^{-3}

TABLE VIII
Atomic Coordinates (x 10^4) and Equivalent Isotropic Displacement Parameters (Å^2 x 10^3) for 18a

ATOM	X	Y	Z	U(eq)
N(1)	5682(2)	4987(3)	1923(1)	44(1)
C(2)	6826(3)	4829(3)	2388(2)	49(1)
C(3)	7546(3)	6172(4)	2517(1)	53(1)
N(4)	8275(2)	6500(3)	2052(1)	45(1)
C(5)	7779(2)	6547(3)	1437(1)	36(1)
C(5A)	6517(2)	6252(3)	1121(1)	35(1)
C(6)	5945(3)	6736(3)	441(1)	48(1)
O(7)	4687(2)	6389(2)	333(1)	50(1)
C(8)	4490(3)	5742(3)	862(2)	45(1)
O(8)	3516(2)	5326(3)	889(1)	66(1)
C(8A)	5644(2)	5646(3)	1361(1)	36(1)
C(9)	8574(2)	7032(3)	1011(1)	38(1)
C(10)	9212(3)	8242(3)	1174(2)	46(1)
C(11)	9985(3)	8706(4)	807(2)	57(1)
C(12)	10130(3)	7969(4)	278(2)	58(1)
C(13)	9492(3)	6768(4)	105(2)	54(1)
C(14)	8713(3)	6295(3)	470(2)	46(1)
N(1#)	10963(2)	6483(3)	2464(1)	61(1)
C(2#)	11537(3)	5986(4)	1955(2)	67(1)
C(3#)	12262(3)	4732(4)	2135(2)	61(1)
N(4#)	13498(2)	4923(3)	2525(1)	51(1)
C(5#)	13668(2)	5568(3)	3073(1)	39(1)
C(5A#)	12773(2)	6255(3)	3350(1)	41(1)
C(6#)	13031(3)	6694(5)	4054(2)	76(2)
O(7#)	11904(2)	7236(3)	4145(1)	86(1)
C(8#)	11054(3)	7177(4)	3577(2)	58(1)
O(8#)	10049(2)	7572(3)	3534(1)	82(1)
C(8A#)	11612(3)	6576(3)	3073(1)	40(1)
C(9#)	14922(2)	5545(3)	3498(1)	36(1)
C(10#)	15428(3)	4316(3)	3750(2)	49(1)
C(11#)	16568(3)	4275(4)	4161(2)	55(1)
C(12#)	17207(3)	5473(4)	4321(2)	50(1)
C(13#)	16732(3)	6696(4)	4057(2)	47(1)
C(14#)	15588(3)	6735(3)	3655(2)	45(1)

TABLE IX.
Bond Angles (°) for 18a

Molecule A		Molecule B	
C(2)-N(1)-C(8A)	119.0(3)	C(2#)-N(1#)-C(8A#)	119.1(3)
N(1)-C(2)-C(3)	112.9(3)	N(1#)-C(2#)-C(3#)	114.1(3)
C(2)-C(3)-N(4)	115.6(3)	C(2#)-C(3#)-N(4#)	116.4(3)
C(3)-N(4)-C(5)	119.9(2)	C(3#)-N(4#)-C(5#)	119.0(3)
N(4)-C(5)-C(5A)	126.9(3)	N(4#)-C(5#)-C(5A#)	127.8(2)
N(4)-C(5)-C(9)	115.5(2)	N(4#)-C(5#)-C(9#)	116.5(3)
C(5A)-C(5)-C(9)	117.5(2)	C(5A#)-C(5#)-C(9#)	115.5(2)
C(5)-C(5A)-C(6)	121.9(3)	C(5#)-C(5A#)-C(6#)	122.3(2)
C(5)-C(5A)-C(8A)	130.3(3)	C(5#)-C(5A#)-C(8A#)	130.1(3)
C(6)-C(5A)-C(8A)	107.5(2)	C(6#)-C(5A#)-C(8A#)	107.5(3)
C(5A)-C(6)-O(7)	105.5(2)	C(5A#)-C(6#)-O(7#)	105.2(2)
C(6)-O(7)-C(8)	109.7(2)	C(6#)-O(7#)-C(8#)	110.0(3)
O(7)-C(8)-O(8)	122.5(3)	O(7#)-C(8#)-O(8#)	121.9(3)
O(7)-C(8)-C(8A)	108.8(3)	O(7#)-C(8#)-C(8A#)	108.1(3)
O(8)-C(8)-C(8A)	128.7(3)	O(8#)-C(8#)-C(8A#)	130.0(3)
N(1)-C(8A)-C(5A)	131.8(2)	N(1#)-C(8A#)-C(5A#)	131.9(3)
N(1)-C(8A)-C(8)	119.6(3)	N(1#)-C(8A#)-C(8#)	119.0(3)
C(5A)-C(8A)-C(8)	108.5(3)	C(5A#)-C(8A#)-C(8#)	109.1(2)
C(5)-C(9)C(10)	118.6(3)	C(5#)-C(9#)-C(10#)	119.7(3)
C(5)-C(9)-C(14)	122.2(3)	C(5#)-C(9#)-C(14#)	121.5(3)
C(10)-C(9)-C(14)	119.2(3)	C(10#)-C(9#)-C(14#)	118.7(2)
C(9)-C(10)-C(11)	120.6(3)	C(9#)-C(10#)-C(11#)	120.7(3)
C(10)-C(11)-C(12)	120.0(3)	C(10#)-C(11#)-C(12#)	119.7(3)
C(11)-C(12)-C(13)	120.1(3)	C(11#)-C(12#)-C(13#)	120.2(3)
C(12)-C(13)-C(14)	120.3(3)	C(12#)-C(13#)-C(14#)	119.9(3)
C(9)-C(14)-C(13)	119.8(3)	C(9#)-C(14#)-C(13#)	120.7(3)

TABLE X.
Bond Distances (Å) for 18a

Molecule A		Molecule B	
N(1)-C(2)	1.443(4)	N(1#)-C(2#)	1.466(5)
N(1)-C(8A)	1.338(4)	N(1#)-C(8A#)	1.323(4)
C(2)-C(3)	1.537(5)	C(2#)-C(3#)	1.476(5)
C(3)-N(4)	1.465(4)	C(3#)-N(4#)	1.467(4)
N(4)-C(5)	1.285(4)	N(4#)-C(5#)	1.289(4)
C(5)-C(5A)	1.465(3)	C(5#)-C(5A#)	1.455(4)
C(5)-C(9)	1.497(4)	C(5#)-C(9#)	1.498(3)
C(5A)-C(6)	1.503(4)	C(5A#)-C(6#)	1.505(4)
C(5A)-C(8A)	1.357(4)	C(5A#)-C(8A#)	1.353(4)
C(6)-O(7)	1.441(3)	C(6#)-O(7#)	1.446(4)
O(7)-C(8)	1.346(4)	O(7#)-C(8#)	1.350(4)
C(8)-O(8)	1.199(4)	C(8#)-O(8#)	1.194(4)
C(8)-C(8A)	1.480(4)	C(8#)-C(8A#)	1.485(5)
C(9)-C(10)	1.387(4)	C(9#)-C(10#)	1.382(4)
C(9)-C(14)	1.389(4)	C(9#)-C(14#)	1.385(4)
C(10)-C(11)	1.382(5)	C(10#)-C(11#)	1.382(4)
C(11)-C(12)	1.371(5)	C(11#)-C(12#)	1.377(5)
C(12)-C(13)	1.382(5)	C(12#)-C(13#)	1.373(5)
C(13)-C(14)	1.386(5)	C(13#)-C(14#)	1.379(4)

Formation of the 1,4-Diazepine Ring System.

Taking these facts into account it seemed to us that the first step toward building the 1,4-diazepine ring should be to mask the acidic proton of the enolic group. This was accomplished by treatment of the furanones **1** with diazomethane to give the enol ethers **17a-d**. Once the enolic proton was no longer available for an acid-base reaction, both C-3 and C-6 became reactive towards nucleophilic attack. Thus, the reaction of 1,2-ethylenediamine with type **17** compounds gave the 1,4-diazepines **18** in good yields.

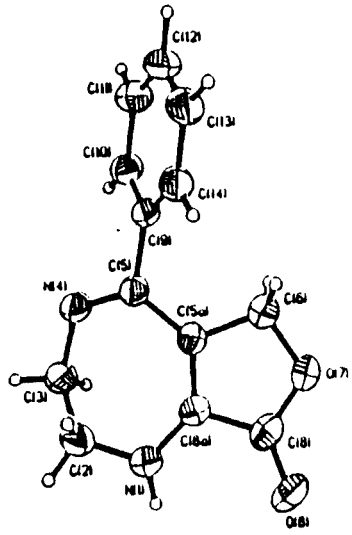
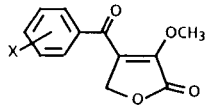


Figure 3

TABLE XI

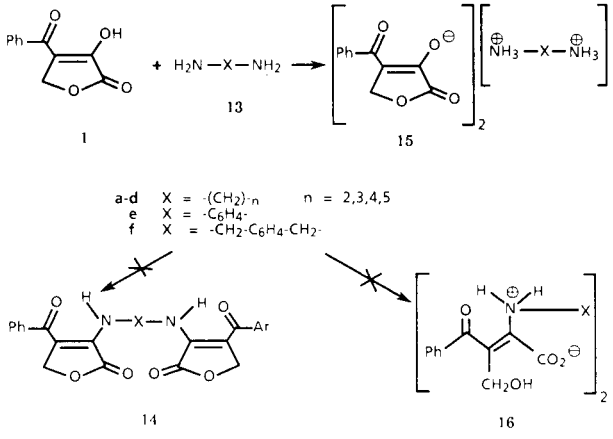
Spectroscopic Data for 4-Aroyl-3-methoxy-2(5H)-furanones 17a-d



Compound	Exact ms m/e Calcd. for (Molecular Formula)	Found	^{1}H-nmr ($CDCl_3$)
*17a (X = H)	218.0579 ($C_{12}H_{10}O_4$)	218.0568	3.90 (s, 3H, OCH_3), 5.00 (s, 2H, OCH_2), 7.30-8.00 (m, 5H, ArH)
17b (X = 4-OCH_3)	248.0685 ($C_{13}H_{12}O_5$)	248.0695	3.91, 3.92 (2s, 6H, 2OCH_3), 4.99 (s, 2H, OCH_2), 6.97, 7.89 (2d, 4H, ArH)
17c (X = 4-Cl)	252.0189 ($C_{12}H_9ClO_4$)	252.0168	4.03 (s, 3H, OCH_3), 5.02 (s, 2H, OCH_2), 7.47, 7.81 (2d, 4H, ArH)
17d (X = 3Cl)	252.0189 ($C_{12}H_9ClO_4$)	252.0171	4.00 (s, 3H, OCH_3), 5.02 (s, 2H, OCH_2) 7.55 (m, 4H, ArH)

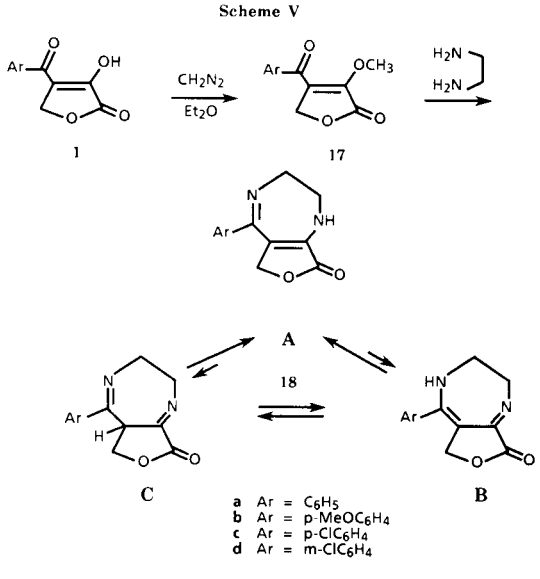
*^{13}C-nmr (DMSO-d_6): δ 59.23, 67.81, 128.31, 128.70, 129.23, 134.04, 136.59, 144.34, 167.55, 189.76

Scheme IV

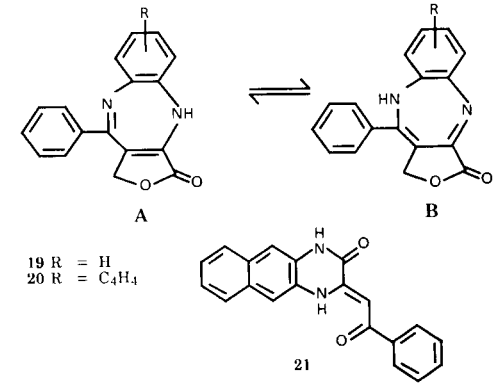


A careful analysis of the ^{1}H-nmr, ^{13}C-nmr, ir spectra and ms data of **18a** (see Experimental) agrees well with the assigned structure. The ^{1}H-nmr data also reveal that the diazepines **18** occur as tautomers with tautomer **C** as a minor contributor. Definite proof for the structures of type **18** compounds was secured by an X-ray analysis (Tables VII-X) (Figure 3). Similarly, compounds **18b-d** were prepared; their spectral data agreed well with those of **18a** and therefore we are confident of our structure assignments for the novel diazepine species (Scheme V).

Scheme V



Though the reaction of **17a** with two aromatic 1,2-diamines, *o*-phenylenediamine and 2,3-diaminonaphthalene in boiling methanol for long periods of time (over three days) also led to the formation of the expected 1,4-diazepines **19** and **20** respectively, they were formed only in disappointingly low yields. The ^{1}H-nmr spectra (DMSO-d_6) of **19** and **20** revealed that they exist in two tautomeric forms **A** and **B**.



In an attempt to improve the yield of **20** the reaction was run at a higher temperature by using isopropanol as a solvent. However, under these conditions only **21** was isolated. Its formation can be explained by an analogous reaction sequence involving a retro aldol condensation as given in Scheme I.

Conclusion.

Inspecting the p*K*a values for each of the conjugate acids of the employed amines [13], it became clear that the basicity of the amine was a factor in the type of reaction observed. For the straight chain alkyl diamines, most of the amino groups are in the same basicity range as ammonia. It was therefore not surprising to observe that these diamines exclusively undergo an acid-base reaction with the enolic protons of the furanones rather than a nucleophilic addition reaction. The mode of reaction of **9** and **10** also can be explained by the difference of the p*K*'s of their respective amino groups. The basicities of the 5-amino group of **9** and the 3-amino group of **10** are strong enough to undergo salt formation with type **1** compounds whereas the amino group in the 4- or 2-position respectively are neither basic enough to form a salt nor under these conditions nucleophilic enough to give a Schiff base. However both the amino groups in **2** are nucleophilic enough to undergo Schiff base formation. The result with **5** also can be explained by the difference in nucleophilicity of its two amino groups.

By cancelling the acidity of **1** *via* alkylation led to binucleophilic attack by the diamine on C-3 and C-6 and the formation of the diazepine ring system. The geometric constraints on the 1,4-diazepine system, imposed by the *ortho*-diaminoaryl species employed in the reaction with **1a**, also seemed to play a role in determining the structure of the product formed. The relative positions of the amino groups in **2** are fixed by the planarity of the benzene or naphthalene ring. Thus, the formation of a seven-membered ring is not favored in comparison to six-membered ring formation. Therefore, the reaction occurred on C-3 and C-2 of type **1** compounds to give a six-membered ring

with opening of the lactone ring and loss of formaldehyde (Scheme I). An analogous course of reaction was observed when **1a** was refluxed in glacial acetic acid with **9** leading to formation of **12** [6]. A similar conclusion, which agrees with our findings, was reached earlier by others in interpreting the results of a reaction of certain 1,3-diketones with *ortho*-diaminoaryls in which the desired diazepine system was formed also in only low yields [14,15].

EXPERIMENTAL

Melting points were determined on a Mel-Temp melting point apparatus and are uncorrected. Analytical tlc was performed using ascending technique with EM silica gel 60 F_{254} precoated on plastic sheets. The ir spectra were obtained on a Perkin-Elmer model 599 spectrometer and were calibrated against the 1601 cm^{-1} band of polystyrene. The nmr spectra were recorded on IBM NR-80 or Nicolet NT 300 MHz spectrometers. Chemical shifts are expressed in δ scale in parts per million downfield from internal tetramethylsilane (Me_4Si) and apparent coupling constants (J) are given in Hertz (Hz). A Hewlett-Packard 5995 Gas Chromatograph/Mass Spectrometer was used to record ms data at 70 eV. The X-ray data were recorded on a Nicolet R3m diffractometer and analyzed on a Micro VAX II using the SHELXTL PLUS series of crystallographic programs. Elemental analyses were performed by M-H-W Laboratories, Phoenix, Arizona.

Reaction of the Type **1** Compounds with 5,6-Diamino-1,3-dimethyluracil **5** to Form 4-Aroyl-3-[*N*-(6-amino-3,5-dimethyluracil)amino]-2(5*H*)-furanone (**7**) and 4-{1-[*N*-(6-Amino-3,5-dimethyluracil)-amino]aral}-2,3(5*H*)furandione (**8**). General Procedure.

To a solution of **5** (0.50 g, 2.94 mmoles) in methanol (75 ml) was added a solution of the appropriately substituted furanone **1** (3.68 mmole) in methanol (75 ml) and the mixture stirred at room temperature, under argon, overnight (at least 18 hours). During this time a yellow to orange powdery precipitate formed. The solid was filtered off to yield Schiff base **8**. The filtrate was evaporated to dryness, and the remaining residue triturated with a small amount of hot chloroform. The yellow solid was filtered off and proved to be Schiff base **7**.

4-Benzoyl-3-[*N*-(6-amino-3,5-dimethyluracil)amino]-2(5*H*)-furanone (**7a**).

This compound was obtained in 1.5% yield (0.016 g) as a fine yellow crystalline solid, mp 262-264° with dec; ^{1}H-nmr (300 MHz, DMSO-d_6): δ 2.87 (s, 3H), 3.02 (s, 3H), 5.04 (s, 2H), 6.73 (bs, 2H deuterium oxide exchangeable), 7.27 and 7.39 (2 bs, 6H, 1H deuterium oxide exchangeable); ms: m/e 356 (M^+), 256, 180 (base peak), 105, 95, 77, 68; ir (potassium bromide): cm^{-1} 3380, 3280, 3180, 1770, 1710, 1605.

Anal. Calcd. for $C_{17}H_{16}N_4O_5$: C, 57.30; H, 4.49; N, 15.73. Found: C, 56.94; H, 4.70; N, 15.61.

4-{1-[*N*-(6-Amino-3,5-dimethyluracil)amino]benzal}-2,3(5*H*)-furandione (**8a**).

This compound was obtained in 69% yield (0.72 g) as a bright orange powdery solid; mp 246-247° with dec; ^{1}H-nmr (300 MHz, DMSO-d_6): δ 2.35 (s, 3H), 3.22 (s, 3H), 4.83 (s, 2H), 7.36 (s, 2H, deuterium oxide exchangeable), 7.41 (m, 7H), 11.08 (bs, 1H, deuterium oxide exchangeable), ms: m/e 339 (M^+-H_2O), 268, 256 (base peak), 170, 143, 115, 104, 77, 68; ir (potassium bromide): cm^{-1} 3340, 3200, 1775, 1700, 1645, 1620, 1605.

Anal. Calcd. for $C_{17}H_{16}N_4O_5 \cdot H_2O$: C, 54.54; H, 4.81; N, 14.97. Found: C, 54.66; H, 4.50; N, 15.17.

4-(4-Methylbenzoyl)-3-[*N*-(6-amino-3,5-dimethyluracil)amino]-2-(5*H*)-furanone (**7b**).

This compound was obtained in 2.3% yield (0.025 g) as a fine bright yellow, needle-like, crystalline solid, mp 252-253° dec; ^{1}H-nmr (300 MHz, DMSO-d_6): δ 2.29 (s, 3H), 2.89 (s, 3H), 3.04 (s, 3H), 5.04 (s, 2H), 6.71 (bs, 2H, deuterium oxide exchangeable), 7.09 (m, 2H), 7.32 (m, 2H), 7.5 (bs, 1H, deuterium oxide exchangeable); ms: m/e 370 (M^+), 270, 180, 119 (base peak), 95, 91, 68. Exact Mass Calculated for $C_{18}H_{18}N_4O_5$ 370.1358. Found: 370.1322; ir (potassium bromide): cm^{-1} 3410, 3300, 3220, 1770, 1705, 1640, 1610.

Anal. Calcd. for $C_{18}H_{18}N_4O_5$: C, 58.38; H, 4.86; N, 15.14. Found: C, 57.97; H, 4.80; N, 14.85.

4-{1-[*N*-(6-Amino-3,5-dimethyluracil)amino]-4-methylbenzal}-2,3-(5*H*)-furandione (**8b**).

This compound was obtained in 26% yield (0.283 g) of fine, bright orange crystals, mp 222-223° dec; ^{1}H-nmr (300 MHz, DMSO-d_6): δ 2.31 (s, 3H), 2.97 (s, 3H), 3.24 (s, 3H), 4.85 (s, 2H), 7.23, 7.29 (d, 4H, J = 8.10 Hz), 7.34 (s, 2H, deuterium oxide exchangeable), 11.11 (bs, 1H, deuterium oxide exchangeable); ms: m/e 354 (M^+-NH_2), 298, 282 (base peak), 270, 184, 157, 118, 117, 115, 102, 91, 77, 68, 65; ir (potassium bromide): cm^{-1} 3400, 3320, 3220, 1750, 1700, 1650, 1620.

Anal. Calcd. for $C_{18}H_{18}N_4O_5$: C, 58.38; H, 4.86; N, 15.14. Found: C, 58.09; H, 4.90; N, 15.18.

4-(4-Methoxybenzoyl)-3-[*N*-(6-amino-3,5-dimethyluracil)amino]-2-(5*H*)-furanone (**7c**).

This compound was obtained in 2.3% yield (0.017 g) as a bright orange crystalline solid, mp 247-248° dec; ^{1}H-nmr (300 MHz, DMSO-d_6): δ 2.89 (s, 3H), 3.04 (s, 3H), 3.78 (s, 3H), 5.03 (s, 2H), 6.70 (s, 2H), 6.81 (m, 2H), 7.40 (m, 2H); ms: m/e 386 (M^+), 286, 180, 162, 135 (base peak), 107, 95, 77, 68.

Anal. Calcd. for $C_{18}H_{18}N_4O_6$: C, 55.96; H, 4.66; N, 14.51. Found: C, 55.96; H, 4.79; N, 14.50.

4-{1-[*N*-6-Amino-3,5-dimethyluracil)amino]-4-methoxybenzal}-2,3-(5*H*)-furandione (**8c**).

This compound was obtained in 33% yield (0.23 g) as a bright orange, crystalline solid; mp 262-264° dec; ^{1}H-nmr (300 MHz, DMSO-d_6): δ 2.97 (s, 3H), 3.25 (s, 3H), 3.77 (s, 3H), 4.93 (bs, 2H), 6.96, 7.33 (d, 4H, J = 8.40 Hz), 7.34 (s, 2H, showed partial deuterium oxide exchangeable), 11.18 (bs, 1H, deuterium oxide exchangeable); ms: m/e 368 (M^+-H_2O), 352, 314, 298 (base peak), 286, 216, 212, 200, 173, 134, 133, 103, 77, 68.

Anal. Calcd. for $C_{18}H_{18}N_4O_6 \cdot CH_3OH$: C, 54.55; H, 4.31; N, 13.93. Found: C, 54.71; H, 4.80; N, 14.20.

4-(4-Bromobenzoyl)-3-[*N*-(6-amino-3,5-dimethyluracil)amino]-2-(5*H*)-furanone (**7d**).

This compound was obtained in 13% yield (0.17 g) as a bright yellow, powdery solid (dec at 218-226°); ^{1}H-nmr (300 MHz, DMSO-d_6): δ 2.91 (s, 3H), 3.09 (s, 3H), 5.02 (s, 2H), 6.79 (s, 2H, deuterium oxide exchangeable), 7.29, 7.45, and 7.6 (3 bs, 5H, with the one at 7.6 deuterium oxide exchangeable); ms: m/e (M^+ of 437 was only seen using chemical ionization), 336, 334, 212, 210, 185,

183, 180, 157, 155, 95, 76, 75, 68; ir (potassium bromide): cm^{-1} 3420, 3350, 3310, 3240, 1775, 1710, 1650, 1605.

Anal. Calcd. for $C_{17}H_{15}N_4O_5Br$: C, 46.90; H, 3.45; N, 12.87; Br, 18.39. Found: C, 46.48; H, 3.84; N, 12.46; Br, 18.08.

4-{1-[*N*-(6-Amino-3,5-dimethyluracil)amino]-4-bromobenzal}-2,3-(5*H*)-furandione (**8d**).

This compound was obtained in 57% yield (0.725 g) as a bright yellow powdery solid (dec at 254-260°); ^{1}H-nmr (300 MHz, DMSO-d_6): δ 2.97 (s, 3H), 3.23 (s, 3H), 4.84 (s, 2H), 7.35 (s, 2H, deuterium oxide exchangeable), 7.34, 7.63 (d, 4H, J = 10.2 Hz), 11.01 (s, 1H, deuterium oxide exchangeable); ms: m/e 418, 416 (M^++2-H_2O, M^+-H_2O), 364, 362, 348, 346, 336, 334, 279, 277, 262, 260, 250, 248, 223, 221, 195, 193, 184, 183, 182, 181, 180, 169, 168, 167, 142, 140, 115, 102, 68.

Anal. Calcd. for $C_{17}H_{15}N_4O_5Br$: C, 46.90; H, 3.45; N, 12.87. Found: C, 46.86; H, 3.72; N, 12.96.

4-Aminopyrimidino-5-ammonium 4-Benzoyl-2(5*H*)-furanone-3-oxide (**11a**).

To a solution of furanone **1a** (5.0 mmoles) in methanol (45 ml) was slowly added a solution of 4,5-diaminopyrimidine **9** (5.0 mmoles) in ethanol (40 ml) and stirred at room temperature overnight (at least 18 hours), during which time a pale yellow precipitate formed. The solid was collected and dried, 58% yield of a light yellow powdery solid, mp 154-155°; ^{1}H-nmr (300 MHz, DMSO-d_6): δ 4.93 (s, 2H), 7.4 (m, 5H), 7.75 (bs, 2H, deuterium oxide exchangeable), 7.96 (m, 2H), 8.14 (s, 1H); ^{13}C-nmr (75.5 MHz, DMSO-d_6) δ 68.34 (t), 111.19 (s), 122.59 (d), 127.53 (d), 128.08 (s), 128.67 (d), 130.87 (d), 139.47 (s), 142.32 (d), 155.68 (s), 156.74 (s), 173.85 (s), 187.20 (s); ir (potassium bromide): cm^{-1} 3450, 3380, 3300, 3200, 1750, 1675.

Anal. Calcd. for $C_{15}H_{14}N_4O_4$: C, 57.32; H, 4.46; N, 17.83. Found: C, 56.97; H, 4.64; N, 17.60.

2-Aminopyridino-3-ammonium 4-Benzoyl-2(5*H*)-furanone-3-oxide (**11b**).

To a solution of furanone **1a** (1.5 mmoles) in chloroform (35 ml) was slowly added a solution of 2,3-diaminopyridine **10** (3.0 mmoles) in chloroform (40 ml). A precipitate formed almost immediately upon addition of the diamine. Stirring was continued at room temperature overnight (at least 18 hours), after which time the solid was collected and dried, yield ~100%, mp 151-151.5°; ^{1}H-nmr (300 MHz, DMSO-d_6): δ 4.93 (s, 2H), 6.66 (d, d, 1H, J = 7.80 Hz, J = 6.00 Hz), 6.99 (d, 1H, J = 7.80 Hz, J = 1.20 Hz), 7.23 (d, d, 1H, J = 6.30 Hz, J = 1.20 Hz), 7.4 (m, 3H), 7.9 (d, 2H, J = 6.90 Hz), 6.6-8.2 (broad, 5H, 2H deuterium oxide exchangeable); ^{13}C-nmr (75.5 MHz, DMSO-d_6) δ 68.60 (t), 110.74 (s), 113.37 (d), 119.60 (d), 122.72 (d), 127.45 (d), 128.59 (d), 130.75 (d), 133.40 (s), 139.79 (s), 145.29 (s), 157.86 (s), 174.91 (s), 187.69 (s); ir (potassium bromide): cm^{-1} 3390, 3300, 3220, 1745, 1635.

Reaction of type **1** compound with straight-chain alkyl terminal diamines **13a-f**. General Procedure.

A solution of the appropriately substituted furanone **1** (1.5 mmole) in chloroform (75 ml) was treated with the diamine **13** (3.0 mmole). A colorless precipitate formed almost immediately upon addition of diamine. The mixture was stirred at room temperature overnight (at least 18 hours), after which time the solid was collected and dried.

Ethylenediammonium Bis(4-benzoyl-2(5*H*)-furanone-3-oxide) (**15a**).

This compound was obtained in ~100% yield, mp 147-147.5°; ^{1}H-nmr (300 MHz, DMSO-d_6): δ 3.03 (s, 4H), 4.91 (s, 4H), 7.33-7.45 (m, 6H), 7.97 (d, 4H, J = 8.10 Hz), 8.19, (bs, 6H, deuterium oxide exchangeable); ^{13}C-nmr (75.5 MHz, DMSO-d_6) δ 36.84 (t), 68.51 (t), 109.28 (s), 127.40 (d), 128.50 (d), 130.55 (s), 139.82 (s), 158.59 (s), 174.73 (s), 186.72 (s); ir (potassium bromide): cm^{-1} 3000, 1775, 1750, 1645, 1630.

Anal. Calcd. for $C_{24}H_{24}N_2O_8$: C, 61.54; H, 5.13; N, 5.98. Found: C, 61.22; H, 5.25; N, 6.06.

Propylene-1,3-diammonium Bis(4-benzoyl-2(5*H*)-furanone-3-oxide) (**15b**).

This compound was obtained in ~96% yield, mp 119-121°; ^{1}H-nmr (300 MHz, DMSO-d_6): δ 1.82 (q, 2H, J = 7.50 Hz), 2.85 (t, 4H, J = 7.50 Hz), 4.89 (s, 4H), 7.35 and 7.99 (2 m, 16H, 6H, deuterium oxide exchangeable); ^{13}C-nmr (75.5 MHz, DMSO-d_6) δ 25.49 (t), 36.39 (t), 68.56 (t), 108.81 (s), 127.36 (d), 128.59 (d), 130.43 (d), 139.95 (s), 159.07 (s), 174.81 (s), 186.53 (s); ir (potassium bromide): cm^{-1} 3000, 1775, 1755, 1645.

Butylene-1,4-diammonium Bis(4-benzoyl-2(5*H*)-furanone-3-oxide) (**15c**).

This compound was obtained in 95% yield, mp 161-162°; ^{1}H-nmr (300 MHz, DMSO-d_6): δ 1.55 (bs, 4H), 2.76 (bs, 4H), 4.90 (s, 4H), 7.35 and 7.99 (2 m, 16H, 6H, deuterium oxide exchangeable); ^{13}C-nmr (75.5 MHz, DMSO-d_6) δ 24.56 (t), 38.46 (t), 68.59 (t), 108.94 (s), 127.41 (d), 128.64 (d), 130.51 (d), 139.99 (s), 159.13 (s), 174.82 (s), 186.65 (s); ir (potassium bromide): cm^{-1} 3000, 1775, 1765, 1650, 1610.

Anal. Calcd. for $C_{26}H_{28}N_2O_8$: C, 62.89; H, 5.68; N, 5.64. Found: C, 62.83; H, 5.82; N, 5.82.

Pentylene-1,5-diammonium Bis(4-benzoyl-2(5*H*)-furanone-3-oxide) (**15d**).

This compound was obtained in 89% yield, mp 160-160.5°; ^{1}H-nmr (300 MHz, DMSO-d_6): δ 1.32 (q, 2H, J = 6.90 Hz), 1.50 (q, 4H, J = 6.90 Hz), 2.73 (t, 4H, J = 7.50 Hz), 4.89 (s, 4H), 7.35 (m, 6H), 7.91 (bs, 6H, deuterium oxide exchangeable), 8.01 (m, 4H); ^{13}C-nmr (75.5 MHz, DMSO-d_6) δ 22.87 (t), 26.56 (t), 38.69 (t), 68.54 (t), 108.84 (s), 127.36 (d), 128.61 (d), 130.47 (d), 139.96 (s), 159.07 (s), 174.78 (s), 186.54 (s); ir (potassium bromide): cm^{-1} 3000, 1760, 1665, 1645, 1600.

Anal. Calcd. for $C_{27}H_{30}N_2O8$: C, 63.53; H, 5.88; N, 5.49. Found: C, 63.77; H, 6.16; N, 5.65.

p-Phenylenediammonium Bis(4-benzoyl-2(5*H*)-furanone-3-oxide) (**15e**).

This compound was obtained in 43% yield, mp 145-145.5; ^{1}H-nmr (300 MHz, DMSO-d_6): δ 4.98 (s, 4H), 6.79 (s, 4H), 7.43 (t, 4H, J = 6.90 Hz), 7.53 (t, 2H, J = 7.20 Hz), 7.92 (d, 4H, J = 7.20 Hz), 6.0-8.4 (broad, 6H, deuterium oxide exchangeable); ^{13}C-nmr (75.5 MHz, DMSO-d_6): δ 68.21 (t), 115.16 (s), 118.89 (d), 127.77 (d), 128.76 (d), 131.71 (d), 134.16 (s), 138.54 (s), 151.81 (s), 172.15 (s), 187.96 (s); ir (potassium bromide): cm^{-1} 3040, 2950, 2880, 2560, 1760, 1640.

Anal. Calcd. for $C_{28}H_{24}N_2O_8$: C, 65.11; H, 4.65; N, 5.43. Found: C, 64.92; H, 4.80; N, 5.33.

p-Xylenediammonium Bis(4-benzoyl-2(5*H*)-furanone-3-oxide) (**15f**).

This compound was obtained in 83% yield, mp 168-170°; ^{1}H-nmr (300 MHz, DMSO-d_6): δ 3.99 (s, 4H), 4.90 (s, 4H), 7.38 (m, 10H), 8.00 (d, 4H, J = 6.60 Hz), 6.8-9.0 (braod, deuterium oxide

exchangeable); ^{13}C-nmr (75.5 MHz, DMSO-d_6): δ 42.22 (t), 68.49 (t), 108.68 (s), 127.32 (d), 128.61 (d), 128.93 (d), 130.37 (d), 134.69 (s), 139.93 (s), 158.96 (s), 174.75 (s), 186.36 (s); ir (potassium bromide): cm^{-1} 3450, 3000, 1750, 1645, 1600.

Preparation of 4-Aroyl-3-methoxy-2(5*H*)-furanones **17a-d**. General Procedure.

A solution of a type **1** compound (5 mmoles) in ether was treated with an etheral solution of diazomethane until the nitrogen bubbling ceased. After evaporation of the solvent type **17** compounds were isolated as oils and were used without further purification for the preparation of type **18** compounds. Pertinent ms and ^{1}H-nmr data are given in Table XI.

Preparation of 7-Aryl-4,5-dihydro-2-oxo-3*H*,8*H*-furo[3,4-*b*][1,4]diazepines (**18**). General Procedure.

A solution of **17** (5 mmoles) in chloroform (75 ml) was treated with 1,2-ethylenediamine (6 mmoles) and stirred at room temperature overnight. The solvent was then evaporated, and the resulting residue recrystallized from methanol.

7-Phenyl-4,5-dihydro-2-oxo-3*H*,8*H*-furo[3,4-*b*][1,4]diazepine (**18a**).

This compound was obtained in 61% yield (0.69 g), mp 191-192°; ^{1}H-nmr (250 MHz, deuteriochloroform): δ 3.55 (bs, 2H), 4.18 (bs, 2H), 4.76 (s, 2H), 5.72 (bs, 1H), 7.39-7.46 (m, 5H); ^{13}C-nmr (75.5 MHz, DMSO-d_6) δ 47.99 (t), 55.77 (t), 69.11 (t), 110.19 (s), 128.08 (d), 129.01 (d), 137.42 (s), 139.79 (s), 163.78 (s), 169.27 (s); ir: (potassium bromide): cm^{-1} 3400, 3148, 2885, 1759, 1651; ms: m/e 228 (M^+, base peak) (potassium bromide): cm^{-1} 3400, 3148, 2885, 1759, 1651; ms: m/e 228 (M^+, base peak) 227, 183, 171, 156, 143, 140, 128, 115, 105, 91, 77.

Anal. Calcd. for $C_{13}H_{12}N_2O_2$: C, 68.12; H, 5.26; N, 12.28. Found: C, 68.16; H, 5.31; N, 12.30.

7-(4-Methoxyphenyl)-4,5-dihydro-2-oxo-3*H*,8*H*-furo[3,4-*b*][1,4]diazepine (**18b**).

This compound was obtained in 91% yield (1.2 g), mp 188°; ^{1}H-nmr (80 MHz, deuteriochloroform): δ 3.61 (bs, 2H), 3.83 (s, 3H), 4.17 (m, 2H), 4.78 (s, 2H), 4.45 (bs, 1H), 6.90, 7.40 (2d, 4H); ms: m/e 258 (M^+, base peak), 257, 213, 199, 186, 172, 158, 145, 134, 115, 102.

Anal. Calcd. for $C_{14}H_{14}N_2O_2$: C, 65.10; H, 5.46; N, 10.85. Found: C, 65.06; H, 5.59; N, 10.66.

7-(4-Chlorophenyl)-4,5-dihydro-2-oxo-3*H*,8*H*-furo[3,4-*b*][1,4]diazepine (**18c**).

This compound was obtained in 42% yield (0.55 g), mp 178-180°; ^{1}H-nmr (80 MHz, deuteriochloroform): δ 3.56 (bs, 2H), 4.17 (m, 2H), 4.74 (s, 2H), 5.45 (bs, 1H), 7.38 (s, 4H); ms: m/e 264, 262 (M^++2, M^+ [base peak]), 263, 261, 219, 217, 207, 205, 181, 155, 151, 149, 142, 140, 129, 127, 115, 111.

Anal. Calcd. for $C_{13}H_{11}ClN_2O_2$: C, 59.43; H, 4.22; N, 10.67. Found: C, 59.50; H, 4.46; N, 10.48.

7-(3-Chlorophenyl)-4,5-dihydro-2-oxo-3*H*,8*H*-furo[3,4-*b*][1,4]diazepine (**18d**).

This compound was obtained in 65% yield (0.86 g), mp 104-107°; ^{1}H-nmr (80 MHz, deuteriochloroform): δ 3.57 (m, 2H), 4.20 (m, 2H), 4.75 (s, 2H), 7.43 (m, 4H); ms: m/e 264, 262 (M^++2, M^+ [base peak]), 263, 261, 219, 217, 207, 205, 192, 190, 182, 156, 154, 151, 149, 129, 127, 111.

Anal. Calcd. for $C_{13}H_{11}ClN_2O_2$: C, 59.43; H, 4.22. Found: C, 59.62; H, 4.36.

2-Oxo-9-phenyl-3*H*,10*H*-furo[3,4-*f*]benzo[*b*][1,4]diazepine (**19**).

A solution of **17** (5 mmoles) and **2** (5 mmoles) in methanol (50 ml) was heated under reflux for 3 days. The reaction mixture was concentrated and left to cool. The precipitated product was filtered off and recrystallized from methanol, yield 7% of bright orange crystals, mp 187°; ^{1}H-nmr (250 MHz, DMSO-d_6): δ 5.71, 5.93 (2s, 6:1, 2H), 7.39 (m, 9H), 11.76, 12.59 (2s, 6:1, 1H); ms: m/e 276 (M^+, 87), 248 (24), 247 (65), 171 (15), 105 (100), 102 (11), 90 (16), 77 (80).

Anal. Calcd. for $C_{17}H_{12}N_2O_2$: C, 73.90; H, 4.38. Found: C, 73.75; H, 4.50.

2-Oxo-11-phenyl-3*H*,12*H*-furo[3,4-*f*]naphtho[2,3-*b*][1,4]diazepine (**20**).

It was obtained analogously from 2,3-diaminonaphthalene instead of **2**, yield 4% of dark brownish crystals, mp 210-212°; ^{1}H-nmr (250 MHz, DMSO-d_6): δ 4.62, 5.71 (2s, 3:1, 2H), 7.41 (m, 11H), 11.75, 13.7 (2s, 3:1, 1H); ms: m/e 326 (M^+, 52), 283 (26), 281 (100), 244 (12), 140 (13).

Anal. Calcd. for $C_{21}H_{14}N_2O_2$: C, 77.28; H, 4.32. Found: C, 77.35; H, 4.22.

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REFERENCES AND NOTES

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