Reaction of 4,5-Diamino-1,6-dihydropyrimidin-6-ones with Two Equivalents of Chalcones

Braulio Insuasty*, Monica Ramos and Rodolfo Moreno

Department of Chemistry, Universidad del Valle, A. A. 25360, Cali, Colombia

Jairo Quiroga

Department of Chemistry, Universidad de los Andes, A. A. 4976, Santafé de Bogotá, Colombia

Adolfo Sánchez and Manuel Nogueras

Department of Organic Chemistry, Universidad de Jaén, 23071 Jaén, Spain

Norbert Hanold and Herbert Meier*

Institute of Organic Chemistry, University of Mainz, 55099 Mainz, Germany

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The reaction of 4,5-diamino-1,6-dihydropyrimidin-6-ones **1** with two equivalents of the chalcones **2** leads in an acidic medium to the formation of the 2,3,6,7-tetrahydro-1*H*-pyrimido[4,5-*b*][1,4]diazepin-6-one derivatives **3a-d**. The structure elucidation of the products is based on nmr measurements and an X-ray diffraction.

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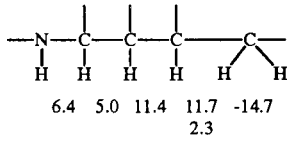
The reaction of 1,3-diaryl-2-propenones (chalcones) with 1,2-diamines is a versatile method for the synthesis of condensed 1,4-diazepine systems [1-6]. Recently we reported on the generation of 1*H*-pyrimido[4,5-*b*]-[1,4]diazepin-6-ones by 1:1 additions of 4,5-diamino-1,6-dihydropyrimidin-6-ones and chalcones [6]. Alternatively, two equivalents of acetophenone derivatives can react with the diamine in such a cyclization reaction [7]. Actually, we found that 4,5-diamino-1,6-dihydropyrimidin-6-ones **1** can also react with two equivalents of chalcones **2**.

The nmr studies revealed the formation of 1:2 adducts with a building block which could be easily characterized by vicinal and geminal couplings in a $^1H,^1H$ COSY measurement.



coupling constants in Hz (±0.3 Hz), DMSO-d_6

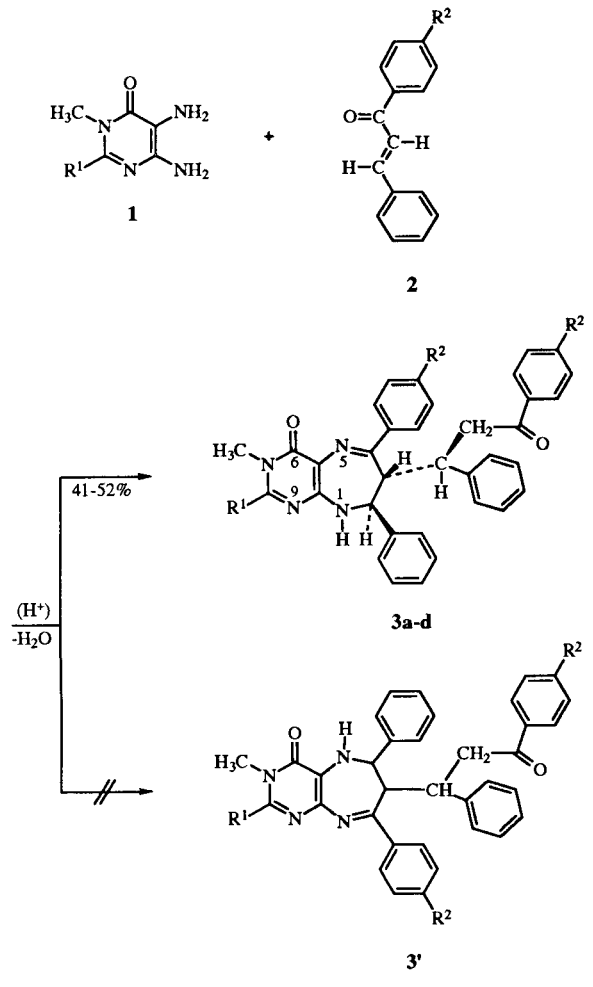
Principally, such a chain can be fully or partly incorporated in a heterocyclic ring, for example, in a 1,4-diazonine, a 1,4-diazocine or a 1,4-diazepine. Moreover, different regioisomeric cyclization products can be conceived - due to reaction of **2** with an unsymmetrical diamine **1**. An unambiguous structural proof was achieved by the crystal structure analysis discussed below.

We assume for the initial step a condensation reaction between the carbonyl groups of **2** and the 5-amino group of **1** which should have a higher nucleophilicity [8-11]. In the second step a Michael type addition of the 4-amino group to the C=C double bond can take place. Thus, a 1*H*-pyrimido[4,5-*b*][1,4]diazepine ring system is formed, which adds again in a Michael addition to another equivalent chalcone **2**. The reactive CH_2 group in the 3-position thereby attacks on the β-C atom of the α,β-unsaturated ketone **2**. Thus, the products **3a-d** are generated. There is no evidence for the regioisomers **3'** (Scheme 1).

Altogether three chiral centers are formed in structure **3** and therefore one could principally expect four diastereomeric pairs of enantiomers; however, only one pair is observed [12]. The vicinal coupling constant ^3J = 5.0 Hz between 2-H and 3-H would correspond to a *trans* configuration with two pseudoequatorial hydrogen atoms or to a *cis* configuration based on pseudoaxial/pseudoequatorial H positions. By steric reasons it is most likely that the second chalcone molecule attacks on C-3 from the side opposite to the aryl group on C-2. The *trans* configuration predicted by this argument is proven by the X-ray analysis. Finally, C-α of the side chain is the third chiral center. Obviously, the direct proximity to the chiral ring system with two bulky substituents induces a further stereodifferentiation in favor of the arrangement (2*S*,3*R*,α*R*) and its enantiomer (2*R*,3*S*,α*S*). Both enantiomers are present in the elementary cell of the investigated crystal. The stereochemistry established by X-ray crystallography (Figure 1) corresponds to a CC bond formation by a selective Si side attack of C-3 on the β-C atom of the α,β-unsaturated ketone.

Tables 1 and 2 summarize the ^1H- and ^{13}C chemical shifts of **3a-d**. The assignment of the signals is supported

Scheme 1



3	R^1	R^2	Yield (%)
a	OCH_3	H	43
b	OCH_3	OCH_3	41
c	SCH_3	H	52
d	SCH_3	OCH_3	50

by a $^1H,^1H$ COSY technique and a $^1H,^{13}C$ shift correlation.

The predominant fragmentation in the EI-MS spectra of **3a-d** leads to a cleavage of the side chains on C-3. The eliminated chalcone is registered as a radical cation as well as a neutral fragment.

Compound **3c** was selected for a crystal structure analysis. The molecular structure shown in Figure 1 demonstrates the *trans* position of the substituents at C-2 and C-3. The non-planar diazepine ring is deflected in such a way that the 3-oxo-1,3-diphenylpropyl side chain is located below the bicyclic system. The bond lengths in the 7-membered ring, especially the lengths of the CN bonds prove structure **3** and rule out the regioisomeric constitution **3'**. Details are listed in the Experimental.

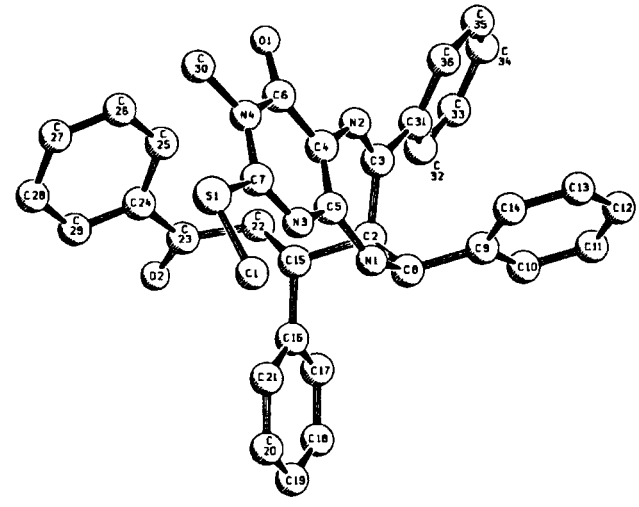


Figure 1. Molecular structure of **3c**, drawing of the enantiomer (2*S*,3*R*,α*R*)-2,3,6,7-tetrahydro-7-methyl-8-methylthio-3-(3-oxo-1,3-diphenylpropyl)-2,4-diphenyl-1*H*-pyrimido[4,5-*b*][1,4]diazepin-6-one **3c** (The numbering corresponds to the Tables in the Experimental but not to the nomenclature).

Table 1

^1H NMR Data of **3a-d** (δ Values in DMSO-d_6)

3		a	b	c	d
1-H	d	7.86	7.77	7.93	7.87
2-H	t	4.25	4.21	4.28	4.23
3-H	dd	4.44	4.40	4.47	4.43
α-CH	td	3.55	3.52	3.56	3.51
β-CH_2	dd	3.36	3.26	3.36	3.27
		2.90	2.83	2.91	2.83
7-CH_3	s	3.36	3.35	3.49	3.47
8-R^1	s	3.98	3.97	2.58	2.57
Aryl-H	AA'BB'C	6.91 (2H)	6.78 (2H)	6.91 (2H)	6.78 (2H)
	or	7.00 (1H)	6.87 (2H)	7.00 (1H)	6.87 (2H)
	AA'BB'	7.09 (2H)	6.90 (2H)	7.09 (2H)	6.90 (2H)
		7.23 (4H)	7.00 (1H)	7.23 (4H)	7.00 (1H)
		7.34 (4H)	7.09 (2H)	7.33 (4H)	7.09 (2H)
		7.42 (2H)	7.22 (1H)	7.42 (2H)	7.22 (1H)
		7.51 (3H)	7.33 (2H)	7.51 (3H)	7.33 (2H)
		7.75 (2H)	7.40 (2H)	7.76 (2H)	7.40 (2H)
			7.52 (2H)		7.51 (2H)
			7.74 (2H)		7.75 (2H)
Aryl-OCH_3	s	—	3.72	—	3.73
	s		3.77		3.77

Table 2

^{13}C NMR Data of **3a-d** (δ Values in DMSO-d_6)

3	a	b	c	d
CH_2	43.9	43.7	43.9	43.7
3-CH	40.2	40.2	40.2	40.3
HC-3	54.8	54.6	55.2	54.9
HC-2	57.6	57.5	57.5	57.6
OCH_3	55.2	55.0	—	55.0
		55.2	—	55.4
		55.3		
SCH_3	—	—	14.2	14.2

Table 2 (continued)

3	a	b	c	d
N-CH_3	27.6	27.5	29.9	29.9
CH (arom.)	125.4	113.0	125.4	113.0
	126.5	113.6	126.6	113.6
	126.6	125.4	126.8	125.4
	126.7	126.5	127.7	126.6
	127.7	126.6	127.7	126.7
	127.7	127.8	127.7	127.8
	127.7	128.0	127.7	128.2
	127.8	128.3	127.9	128.3
	128.1	128.3	128.3	128.3
	128.3	130.0	128.4	130.0
	128.4		128.4	
	133.0		133.0	
Cq	105.5	105.3	106.7	106.7
	136.0	128.9	135.9	128.8
	140.8	135.2	140.7	135.0
	142.3	140.9	142.1	140.8
	143.5	143.5	143.5	143.5
	151.2	151.0	150.7	150.6
	152.9	152.7	157.5	156.9
	157.1	156.9	158.8	158.5
	160.9	159.4	160.3	159.6
		160.7		160.3
		162.9		162.9
CO (ketone)	197.9	196.1	197.9	196.1

Table 3

Fractional Coordinates of Non-hydrogen Atoms and Isotropic Temperature Factors with Estimated Deviation in Parentheses

Atom	X/a	Y/b	Z/c	B_{iso}
S1	0.6784(2)	0.0019(2)	0.1100(1)	4.51(8)
N1	0.5555(5)	-0.0968(4)	0.3685(4)	3.3(2)
N2	0.7564(5)	-0.2244(4)	0.3916(4)	3.0(2)
N3	0.6242(5)	-0.0577(4)	0.2515(4)	3.0(2)
N4	0.7867(5)	-0.1179(4)	0.2001(4)	5.6(3)
O1	0.8912(4)	-0.2228(4)	0.2660(3)	4.8(2)
O2	0.4247(5)	-0.4776(5)	0.2639(4)	7.2(3)
C1	0.5667(7)	0.0762(5)	0.1354(5)	4.6(3)
C2	0.5590(5)	-0.2470(5)	0.4326(4)	2.9(3)
C3	0.6877(6)	-0.2564(5)	0.4393(4)	2.8(3)
C4	0.7272(5)	-0.1705(5)	0.3263(4)	2.9(3)
C5	0.6385(6)	-0.1112(5)	0.3167(4)	2.6(3)
C6	0.8089(7)	-0.1741(5)	0.2673(5)	3.4(3)
C7	0.6937(6)	-0.0620(5)	0.1956(5)	3.3(3)
C8	0.5294(6)	-0.1460(5)	0.4385(4)	3.1(3)
C9	0.5816(4)	-0.1091(4)	0.5165(3)	3.3(3)
C10	0.5445(4)	-0.1431(4)	0.5875(3)	4.6(3)
C11	0.5911(4)	-0.1123(4)	0.6603(3)	6.2(5)
C12	0.6747(4)	-0.0474(4)	0.6620(3)	6.7(5)
C13	0.7118(4)	-0.0134(4)	0.5910(3)	6.4(4)
C14	0.6653(4)	-0.0442(4)	0.5183(3)	4.4(3)
C15	0.5033(6)	-0.2889(5)	0.3569(4)	3.3(3)
C16	0.3747(3)	-0.2789(4)	0.3567(3)	3.4(3)
C17	0.3139(3)	-0.3233(4)	0.4130(3)	3.6(3)
C18	0.1973(3)	-0.3113(4)	0.4146(3)	5.8(4)
C19	0.1415(3)	-0.2549(4)	0.3599(3)	5.9(4)
C20	0.2023(3)	-0.2105(4)	0.3036(3)	6.3(4)
C21	0.3189(3)	-0.2225(4)	0.3020(3)	4.9(4)
C22	0.5387(7)	-0.3877(5)	0.3514(5)	4.1(3)
C23	0.5028(6)	-0.4268(5)	0.2730(5)	4.0(3)
C24	0.5650(5)	-0.4018(4)	0.2008(3)	3.8(3)
C25	0.6750(5)	-0.3690(4)	0.2092(3)	5.1(4)

Table 3 (continued)

Atom	X/a	Y/b	Z/c	B_{iso}
C26	0.7334(5)	-0.3486(4)	0.1419(3)	6.7(4)
C27	0.6819(5)	-0.3611(4)	0.0662(3)	7.2(5)
C28	0.5719(5)	-0.3940(4)	0.0577(3)	8.6(6)
C29	0.5134(5)	-0.4144(4)	0.1250(3)	7.7(5)
C30	0.8657(7)	-0.1231(6)	0.1361(5)	4.9(3)
C31	0.7414(4)	-0.3071(3)	0.5078(3)	3.1(3)
C32	0.6837(4)	-0.3728(3)	0.5471(3)	4.7(3)
C33	0.7390(4)	-0.4207(3)	0.6085(3)	6.0(4)
C34	0.8519(4)	-0.4028(3)	0.6306(3)	6.2(4)
C35	0.9096(4)	-0.3371(3)	0.5914(3)	5.5(4)
C36	0.8544(4)	-0.2893(3)	0.5300(3)	4.2(3)

Table 4

Interatomic Distances (Å) with Estimated Standard Deviations in Parentheses

S1	-	C1	1.807(9)	C10	-	C14	2.416(7)
S1	-	C7	1.737(8)	C11	-	C12	1.395(8)
N1	-	N3	2.252(9)	C11	-	C13	2.416(7)
N1	-	C4	2.460(9)	C12	-	C13	1.395(7)
N1	-	C5	1.37(1)	C12	-	C14	2.415(7)
N1	-	C8	1.44(1)	C13	-	C14	1.394(7)
N1	-	C9	2.499(8)	C15	-	C16	1.531(8)
N2	-	C2	2.499(9)	C15	-	C22	1.56(1)
N2	-	C3	1.271(9)	C16	-	C17	1.395(7)
N2	-	C4	1.40(1)	C16	-	C18	2.416(6)
N2	-	C6	2.34(1)	C16	-	C20	2.416(6)
N2	-	C31	2.338(8)	C16	-	C21	1.395(7)
N3	-	N4	2.340(8)	C17	-	C18	1.395(5)
N3	-	C4	2.413(9)	C17	-	C19	2.416(6)
N3	-	C5	1.367(9)	C17	-	C21	2.416(8)
N3	-	C7	1.29(1)	C18	-	C19	1.395(7)
N4	-	O1	2.266(8)	C18	-	C20	2.416(8)
N4	-	C4	2.411(9)	C19	-	C20	1.395(7)
N4	-	C6	1.43(1)	C19	-	C21	2.416(6)
N4	-	C7	1.39(1)	C20	-	C21	1.395(5)
N4	-	C30	1.47(1)	C22	-	C23	1.49(1)
O1	-	C4	2.378(9)	C23	-	C24	1.50(1)
O1	-	C6	1.22(1)	C24	-	C25	1.394(8)
O2	-	C22	2.37(1)	C24	-	C26	2.416(8)
O2	-	C23	1.21(1)	C24	-	C28	2.417(8)
O2	-	C24	2.326(9)	C24	-	C29	1.396(8)
C2	-	C3	1.53(1)	C25	-	C26	1.395(8)
C2	-	C8	1.57(1)	C25	-	C27	2.416(8)
C2	-	C15	1.54(1)	C25	-	C29	2.417(8)
C3	-	C4	2.37(1)	C26	-	C27	1.394(8)
C3	-	C31	1.497(9)	C26	-	C28	2.416(8)
C3	-	C36	2.478(9)	C27	-	C28	1.395(8)
C4	-	C5	1.39(1)	C27	-	C29	2.416(8)
C4	-	C6	1.43(1)	C28	-	C29	1.395(8)
C5	-	C6	2.42(1)	C31	-	C32	1.395(7)
C5	-	C7	2.30(1)	C31	-	C33	2.417(7)
C6	-	C7	2.45(1)	C31	-	C35	2.417(7)
C6	-	C30	2.47(1)	C31	-	C36	1.396(7)
C7	-	C30	2.50(1)	C32	-	C33	1.395(7)
C8	-	C9	1.525(9)	C32	-	C34	2.416(7)
C9	-	C10	1.395(7)	C32	-	C36	2.416(7)
C9	-	C11	2.417(7)	C33	-	C34	1.395(7)
C9	-	C13	2.416(7)	C33	-	C35	2.416(7)
C9	-	C14	1.396(8)	C34	-	C35	1.394(7)
C10	-	C11	1.395(7)	C34	-	C36	2.415(7)
C10	-	C12	2.416(7)	C35	-	C36	1.394(7)

Table 5

Bond Angles (Degrees) with Estimated Standard Deviations in Parentheses

C1	-	S1	-	C7	101.2(4)
C5	-	N1	-	C8	129.3(6)
C3	-	N2	-	C4	125.5(6)
C5	-	N3	-	C7	120.1(6)
C6	-	N4	-	C7	121.1(6)
C6	-	N4	-	C30	116.9(6)
C7	-	N4	-	C30	122.0(6)
C3	-	C2	-	C8	108.1(6)
C3	-	C2	-	C15	113.7(6)
C8	-	C2	-	C15	111.5(6)
N2	-	C3	-	C2	126.1(6)
N2	-	C3	-	C31	115.0(6)
C2	-	C3	-	C31	118.9(6)
N2	-	C4	-	C5	128.6(7)
N2	-	C4	-	C6	112.2(6)
C5	-	C4	-	C6	118.9(7)
N1	-	C5	-	N3	110.8(6)
N1	-	C5	-	C4	126.7(7)
N3	-	C5	-	C4	122.5(6)
N4	-	C6	-	O1	117.2(7)
N4	-	C6	-	C4	115.3(7)
O1	-	C6	-	C4	127.4(7)
S1	-	C7	-	N3	122.5(6)
S1	-	C7	-	N4	115.5(6)
N3	-	C7	-	N4	122.0(7)
N1	-	C8	-	C2	113.1(6)
N1	-	C8	-	C9	114.7(6)
C2	-	C8	-	C9	109.2(5)
C8	-	C9	-	C10	118.0(5)
C8	-	C9	-	C14	122.0(5)
C10	-	C9	-	C14	120.0(5)
C9	-	C10	-	C11	120.0(5)
C10	-	C11	-	C12	119.9(5)
C11	-	C12	-	C13	120.0(5)
C12	-	C13	-	C14	120.0(5)
C9	-	C14	-	C13	120.0(5)
C2	-	C15	-	C16	110.0(5)
C2	-	C15	-	C22	110.0(6)
C16	-	C15	-	C22	111.5(6)
C15	-	C16	-	C17	120.2(5)
C15	-	C16	-	C21	119.8(5)
C17	-	C16	-	C21	120.0(5)
C16	-	C17	-	C18	120.0(5)
C17	-	C18	-	C19	120.0(5)
C18	-	C19	-	C20	120.0(5)
C19	-	C20	-	C21	120.0(5)
C16	-	C21	-	C20	120.0(5)
C15	-	C22	-	C23	111.8(6)
O2	-	C23	-	C22	123.1(7)
O2	-	C23	-	C24	117.7(7)
C22	-	C23	-	C24	119.2(6)
C23	-	C24	-	C25	120.4(6)
C23	-	C24	-	C29	119.6(6)
C25	-	C24	-	C29	120.0(5)
C24	-	C25	-	C26	120.0(5)
C25	-	C26	-	C27	120.0(5)
C26	-	C27	-	C28	120.0(5)
C27	-	C28	-	C29	120.0(5)
C24	-	C29	-	C28	120.0(5)
C3	-	C31	-	C32	122.2(5)
C3	-	C31	-	C36	117.8(5)
C32	-	C31	-	C36	119.9(4)
C31	-	C32	-	C33	120.0(4)
C32	-	C33	-	C34	120.0(4)
C33	-	C34	-	C35	120.1(4)
C34	-	C35	-	C36	120.0(4)
C31	-	C36	-	C35	120.0(4)

Table 6

Anisotropic Thermal Parameters (Å^2)

Atom	U(1,1)	U(2,2)	U(3,3)	U(2,3)	U(1,3)	U(1,2)
S1	0.061(1)	0.055(2)	0.055(1)	0.022(1)	0.002(1)	-0.007(1)
N1	0.040(4)	0.033(4)	0.055(5)	0.010(3)	0.013(4)	0.012(3)
N2	0.036(4)	0.031(4)	0.045(4)	0.005(3)	-0.003(3)	0.007(3)
N3	0.031(4)	0.028(4)	0.054(4)	0.005(3)	-0.003(3)	0.001(3)
N4	0.073(4)	0.065(5)	0.077(5)	-0.005(4)	0.015(3)	-0.006(4)
O1	0.042(3)	0.053(4)	0.087(5)	0.014(3)	0.014(3)	0.018(3)
O2	0.073(4)	0.091(6)	0.111(6)	-0.016(4)	0.013(4)	-0.042(4)
C1	0.054(5)	0.041(5)	0.077(6)	0.022(5)	-0.004(5)	0.008(4)
C2	0.032(4)	0.030(5)	0.049(5)	-0.004(4)	0.000(3)	0.008(3)
C3	0.040(5)	0.026(4)	0.040(5)	0.001(4)	0.007(4)	0.003(4)
C4	0.027(4)	0.042(5)	0.043(5)	0.011(4)	0.002(4)	-0.001(4)
C5	0.037(4)	0.022(4)	0.040(5)	0.011(4)	-0.001(4)	-0.005(4)
C6	0.048(5)	0.033(5)	0.048(5)	0.011(4)	-0.004(4)	-0.015(4)
C7	0.030(4)	0.029(5)	0.067(6)	0.002(4)	0.004(4)	0.000(4)
C8	0.046(5)	0.030(5)	0.043(5)	0.002(4)	0.001(4)	0.003(4)
C9	0.033(5)	0.031(5)	0.060(6)	0.005(4)	0.005(4)	0.016(4)
C10	0.074(6)	0.045(6)	0.057(6)	0.007(5)	0.013(5)	0.008(5)
C11	0.098(9)	0.089(9)	0.047(7)	-0.009(6)	-0.009(6)	0.043(7)
C12	0.075(8)	0.094(9)	0.083(9)	-0.045(7)	-0.018(6)	0.032(7)
C13	0.054(6)	0.075(8)	0.112(9)	-0.028(8)	-0.009(6)	0.005(6)
C14	0.049(5)	0.054(6)	0.065(6)	-0.006(5)	-0.003(5)	-0.002(5)
C15	0.038(4)	0.044(5)	0.044(5)	0.008(4)	0.006(4)	-0.003(4)
C16	0.042(4)	0.035(5)	0.050(5)	-0.006(4)	-0.009(4)	-0.001(4)
C17	0.044(5)	0.049(5)	0.046(5)	0.008(4)	0.003(4)	-0.011(4)
C18	0.042(6)	0.091(8)	0.085(7)	0.000(6)	-0.010(5)	-0.019(5)
C19	0.042(5)	0.077(7)	0.103(8)	-0.017(6)	-0.017(6)	-0.004(5)
C20	0.067(7)	0.076(8)	0.094(8)	0.013(6)	-0.028(6)	0.002(6)
C21	0.058(6)	0.059(6)	0.066(6)	0.019(5)	-0.010(5)	-0.003(5)
C22	0.054(5)	0.047(6)	0.053(5)	-0.008(5)	0.004(4)	0.002(4)
C23	0.046(5)	0.033(5)	0.074(6)	-0.002(5)	0.005(4)	0.006(4)
C24	0.056(5)	0.037(5)	0.050(6)	-0.013(4)	0.005(4)	0.006(4)
C25	0.067(7)	0.059(6)	0.070(7)	-0.005(5)	0.007(5)	-0.007(5)
C26	0.104(8)	0.068(8)	0.085(8)	0.003(7)	0.022(7)	-0.017(6)
C27	0.11(1)	0.063(7)	0.10(1)	-0.002(7)	0.042(8)	0.013(7)
C28	0.12(1)	0.14(1)	0.068(8)	-0.008(8)	0.010(7)	0.017(9)
C29	0.083(7)	0.13(1)	0.079(8)	-0.042(8)	-0.002(7)	-0.015(7)
C30	0.069(6)	0.061(6)	0.060(6)	0.012(5)	0.034(5)	0.010(5)
C31	0.047(5)	0.034(5)	0.035(4)	0.000(4)	0.003(4)	0.009(4)
C32	0.072(6)	0.050(6)	0.058(6)	0.012(5)	0.020(5)	0.007(5)
C33	0.115(9)	0.049(6)	0.061(6)	0.019(5)	-0.010(6)	0.010(6)
C34	0.112(9)	0.069(7)	0.054(6)	0.012(6)	-0.005(6)	0.044(7)
C35	0.070(6)	0.092(8)	0.047(6)	0.011(6)	-0.010(5)	0.034(6)
C36	0.063(6)	0.055(6)	0.042(5)	0.003(4)	-0.004(4)	0.013(5)

EXPERIMENTAL

Melting points are uncorrected. The ^{1}H- and ^{13}C nmr spectra were recorded on a Bruker AM 400 in DMSO-d_6. The mass spectra were obtained on a Finnigan M 95 spectrometer operating at 70 eV.

General Procedure for the Preparation of the Substituted 1*H*-Pyrimido[4,5-*b*][1,4]diazepin-6-ones **3a-d**.

A solution of 0.40 g (2.35 mmoles) of 4,5-diamino-1,6-dihydro-2-methoxy-1-methylpyrimidin-6-one **1** (R^1 = OCH_3) or 0.44 g (2.35 mmoles) of 4,5-diamino-1,6-dihydro-1-methyl-2-methylthiopyrimidin-6-one **1** (R^1 = SCH_3) and 4.70 mmoles of 1,3-diaryl-2-propenone [0.98 g **2** (R^2 = H) or 1.12 g **2** (R^2 =

OCH_3)] in 15 ml of dry ethanol and 1 ml of acetic acid was refluxed for 8 hours. The reaction mixture was cooled to 0° and stored at that temperature. The yellow precipitate which formed overnight was filtered off and recrystallized from methanol. The yields amount to 41-52% (Scheme 1) [13].

2,3,6,7-Tetrahydro-8-methoxy-7-methyl-3-(3-oxo-1,3-diphenylpropyl)-2,4-diphenyl-1*H*-pyrimido[4,5-*b*][1,4]diazepin-6-one **3a**.

The pale yellow compound melted at 224° and had ms: (70 eV) m/z (%) = 568 (31, $M^{+\bullet}$), 360 (32), 359 (100), 256 (16), 105 (29), 77 (23).

Anal. Calcd. for $C_{36}H_{32}N_4O_3$: C, 76.03; H, 5.67; N, 9.85. Found: C, 75.94; H, 5.83; N, 9.62.

2,3,6,7-Tetrahydro-8-methoxy-4-(4-methoxyphenyl)-3-(3-methoxyphenyl-3-oxo-1-phenylpropyl)-7-methyl-2-phenyl-1*H*-pyrimido[4,5-*b*][1,4]diazepin-6-one **3b**.

The yellow compound melted at 142° and had ms: (70 eV) m/z (%) = 628 (11, $M^{+\bullet}$), 390 (53), 389 (45), 286 (17), 238 (100), 237 (63), 135 (78), 77 (49).

Anal. Calcd. for $C_{38}H_{36}N_4O_5$: C, 72.59; H, 5.77; N, 8.91. Found: C, 72.14; H, 5.93; N, 8.72.

2,3,6,7-Tetrahydro-7-methyl-8-methylthio-3-(3-oxo-1,3-diphenylpropyl)-2,4-diphenyl-1*H*-pyrimido[4,5-*b*][1,4]diazepin-6-one **3c**.

The pale yellow compound melted at 247° and had ms: (70 eV) m/z (%) = 584 (37, $M^{+\bullet}$), 376 (35), 375 (100), 272 (13), 105 (36), 77 (25).

Anal. Calcd. for $C_{36}H_{32}N_4O_2S$: C, 73.95; H, 5.52; N, 9.58. Found: C, 73.99; H, 5.41; N, 9.41.

2,3,6,7-Tetrahydro-4-(4-methoxyphenyl)-3-(3-methoxyphenyl-3-oxo-1-phenylpropyl)-7-methyl-8-methylthio-2-phenyl-1*H*-pyrimido[4,5-*b*][1,4]diazepin-6-one **3d**.

The yellow compound melted at 146° and had ms: (70 eV) m/z (%) = 644 (20), 406 (16), 405 (16), 238 (95), 237 (63), 135 (100), 77 (50).

Anal. Calcd. for $C_{38}H_{36}N_4O_4S$: C, 70.79; H, 5.63; N, 8.69. Found: C, 70.44; H, 5.93; N, 8.52.

Crystallographic information: $C_{36}H_{32}N_4O_2S$, FW = 584.74, monoclinic, space group $P2_1/n$ with a = 11.8470 (10), b = 15.1530 (10), c = 16.8290 (10) Å, β = 93.230 (10)°, V = 3016.1 (2) $Å^3$, Z = 4, Dx = 1.29 g cm^{-3}. Data collection was performed on a Nonius CAD-4 diffractometer, $\omega/2\theta$ scans, θ_{max} = 49.3°. No absorption correction was made, 5488 measured reflections, 5301 unique reflections. Refinement on F^2, R(F) = 0.058, wR = 0.066, S = 1.796, $(\Delta/\sigma)_{max}$ <0.0001. Mo K_α radiation was used, λ = 0.71073 Å. The cell parameters were determined from 23 reflections, θ = 10.0 -18.0, μ = 0.14 mm^{-1}, T = 296 (1) K. The used crystal needle had the dimensions 0.10 x 0.08 x 0.05 mm. R_{int} = 0.0375; h = o → 8, k = o → 15, l = -17 → o, three standard reflections, intensity variation of 2%, $\Delta\rho_{max}$ = 0.205 e $Å^3$, $\Delta\rho_{min}$ = -209 e $Å^3$, extinction correction: SHELXL 93, extinction coefficient 0.065 (8).

The structural parameters are listed in the Tables 3-6.

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[12] The limit of detection in the ^{13}C nmr-spectra of the crude materials amounts to approximately 5%.

[13] The reactions carried out with 1:1 mixtures of **1** and **2** yielded the same products **3**.