# The Reaction of Aromatic α,β-Unsaturated Ketones with 4,5-Diamino-1,6-dihydropyrimidin-6-ones



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Received June 23, 1993

The reaction of 4,5-diamino-1,6-dihydropyrimidin-6-ones **1** with one equivalent of the chalcones **2** leads in an acidic medium to the formation of the 2,4-diaryl-2,3,6,7-tetrahydro-1*H*-pyrimido[4,5-*b*][1,4]diazepin-6-ones **3a-m**. The structure elucidation of the products is based on detailed nmr investigations including selective $^{13}C\{^1H\}$ decoupling experiments.

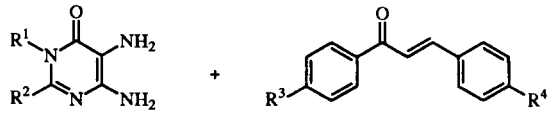
*J. Heterocyclic Chem.*, **31**, 61 (1994).

The reaction of 1,3-diaryl-2-propenones (chalcones) with *ortho*-diamines represents a convenient synthesis of condensed 1,4-diazepine systems [1-5]. Alternatively two equivalents of acetophenone derivatives can enter with the diamine such a cyclization reaction [6].

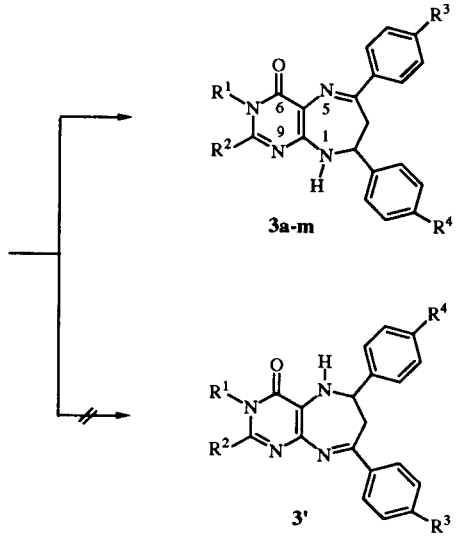
The objective of the present work is the synthesis and characterization of 2,4-diaryl-2,3,6,7-tetrahydro-1*H*-pyrimido[4,5-*b*][1,4]diazepin-6-ones, compounds for which interesting biological and pharmacological properties can be assumed [7,8]. Heating of 4,5-diamino-1,6-dihydro-2-methoxypyrimidin-6-one or 4,5-diamino-1,6-dihydro-2-methylthiopyrimidin-6-one or the 1-methyl derivatives of both with molar quantities of 1,3-diaryl-2-propenones in ethanol in the presence of catalytic amounts of acetic acid generates the desired structures **3a-m** in yields between 89 and 35%. Electron withdrawing substituents $R^3$ like the nitro group enhance the reactivity, electron releasing groups like the methoxy group lower it.

The diamines **1** contain non-equivalent amino groups and could therefore lead to regioisomeric cyclization products **3** and **3'**; however, the formation of a single product

Scheme 1



**1** **2**



**3a-m** **3'**

| Compound 3 | $R^1$ | $R^2$ | $R^3$ | $R^4$ | Yield (%) | Mp (°C) |
|---|---|---|---|---|---|---|
| **a** | H | $OCH_3$ | H | H | 70 | 226 |
| **b** | H | $OCH_3$ | Cl | H | 51 | 224 |
| **c** | H | $OCH_3$ | $OCH_3$ | H | 35 | 204-206 |
| **d** | H | $OCH_3$ | $NO_2$ | H | 89 | 242-243 |
| **e** | H | $OCH_3$ | $NO_2$ | $CH_3$ | 87 | 208-210 |
| **f** | H | $SCH_3$ | H | H | 71 | 220-221 |
| **g** | H | $SCH_3$ | Cl | H | 76 | 242 |
| **h** | H | $SCH_3$ | $OCH_3$ | H | 37 | 198-200 |
| **i** | H | $SCH_3$ | $NO_2$ | H | 74 | 238 |
| **j** | $CH_3$ | $OCH_3$ | Cl | H | 54 | 204-206 |
| **k** | $CH_3$ | $OCH_3$ | $NO_2$ | $CH_3$ | 51 | 212 |
| **l** | $CH_3$ | $SCH_3$ | Cl | H | 70 | 200-202 |
| **m** | $CH_3$ | $SCH_3$ | $NO_2$ | H | 75 | 218 |

was observed in every case. We assume for the initial step a condensation reaction between the carbonyl group of **2** and the 5-amino group of **1** which should have the higher nucleophilicity in comparison to the 4-amino group, due to the electron withdrawing effect of the amide function [9-12]. In the second step a Michael type addition of the 4-amino group to the CC double bond can take place.

The uv/visible spectra of **3a-m** in methanol contain three to four bands; most characteristic is an absorption maximum in the range of 230-280 nm and a second one shifted towards longer wavelengths ($360 \leq \lambda \text{ max} \leq 420$ nm). The ir spectra show typical bands at 3380-3420 $cm^{-1}$ and 1620-1635 $cm^{-1}$ for the N-H and C=N stretching vibrations. A superposition of other coupled C=C vibrations of the ring system is observed for the region of 1600 $cm^{-1}$.

The direct structure proof of **3a-m** is based on the nmr investigation. The $^1H$ nmr data are summarized in Table 1. The proton on N-1 gives rise to a doublet ($^3J = 5.6 \pm 0.1$ Hz) indicating the vicinal position of the proton on C-2. The geminal protons on C-3 have a coupling constant $^2J = -14.1 \pm 0.2$ Hz and vicinal couplings of $^3J_{trans} = 6.0 \pm 0.2$ Hz and $^3J_{cis} = 1.4 \pm 0.2$ Hz to 2-H. That generates two doublets of doublets and a hardly resolved triplet in the ABMX spin pattern at 400 MHz in DMSO. The comparison with the measurement for **3j** in deuteriochloroform shows the great influence of the solvent. The coupling between 1-H and 2-H disappears in chloroform; 1-H gener-

Table 1

$^1H$ NMR Data of **3a-m** (δ Values, TMS as the Internal Standard, 400 MHz)

| Compound 3 | Solvent | 1-NH d (s) | 2-H t (d) | 3-H dd | dd | 7-$R^1$ s | 8-$R^2$ s | 2-Ar | 4-Ar | |
|---|---|---|---|---|---|---|---|---|---|---|
| **a** | $(CD_3)_2SO$ | 7.68 | 5.15 | 2.80 | 3.71 | 11.66 | 3.85 | 7.05-7.20 | 7.12-7.51 | |
| **b** | $(CD_3)_2SO$ | 7.77 | 5.16 | 2.75 | 3.75 | 11.63 | 3.85 | 7.05-7.17 | 7.23 7.53 | |
| **c** | $(CD_3)_2SO$ | 7.56 | 5.12 | 2.78 | 3.66 | 11.66 | 3.84 | 7.06-7.19 | 6.73 7.50 | 3.70 ($OCH_3$) |
| **d** | $(CD_3)_2SO$ | 8.04 | 5.20 | 2.77 | 3.89 | 11.81 | 3.87 | 7.04-7.17 | 7.77 8.03 | |
| **e** | $(CD_3)_2SO$ | 8.04 | 5.13 | 2.76 | 3.87 | 11.80 | 3.87 | 6.97 6.98 | 7.80 8.05 | 2.13 ($CH_3$) |
| **f** | $(CD_3)_2SO$ | 7.78 | 5.18 | 2.84 | 3.71 | 11.70 | 2.49 | 7.04-7.25 | 7.04-7.55 | |
| **g** | $(CD_3)_2SO$ | 7.85 | 5.18 | 2.80 | 3.74 | 11.70 | 2.49 | 7.06-7.19 | 7.24 7.60 | |
| **h** | $(CD_3)_2SO$ | 7.67 | 5.16 | 2.84 | 3.67 | 11.65 | 2.50 | 7.08-7.21 | 6.76 7.55 | 3.71 ($OCH_3$) |
| **i** | $(CD_3)_2SO$ | 8.09 | 5.21 | 2.82 | 3.87 | 12.19 | 2.49 | 7.04-7.17 | 7.77 8.03 | |
| **j** | $(CD_3)_2SO$ | 7.72 | 5.17 | 2.76 | 3.73 | 3.34 | 3.95 | 7.05-7.18 | 7.23 7.53 | |
| | $CDCl_3$ | 5.24 | 4.85 | 3.32 | 3.08 | 3.40 | 3.92 | 7.25-7.35 | 7.21 7.67 | |
| **k** | $CDCl_3$ | 5.39 | 4.85 | 3.34 | 3.16 | 3.41 | 3.93 | 7.14 7.14 | 7.86 8.07 | 2.30 ($CH_3$) |
| **l** | $(CD_3)_2SO$ | 7.78 | 5.18 | 2.82 | 3.71 | 3.38 | 2.56 | 7.07-7.19 | 7.24 7.54 | |
| **m** | $(CD_3)_2SO$ | 8.04 | 5.22 | 2.85 | 3.85 | 3.99 | 2.57 | 7.05-7.19 | 7.76 8.03 | |

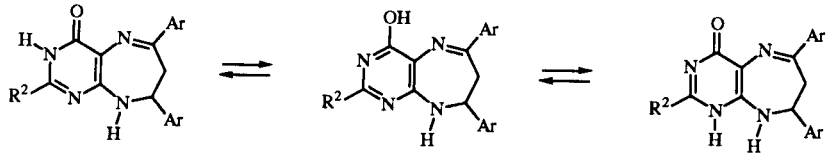
Table 2

$^{13}C$ NMR Data of **3a-m** (δ Values, in DMSO-$d_6$, TMS as the Internal Standard, 100 MHz)

| Compound 3 | | **a** | **b** | **c** | **d** | **e** | **f** | **g** | **h** | **i** | **j** | **j [a]** | **k [a]** | **l** | **m** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | C-2 | 59.2 | 59.0 | 59.4 | 58.6 | 58.1 | 59.6 | 59.3 | 59.7 | 58.9 | 59.1 | 61.2 | 60.2 | 59.5 | 59.0 |
| | C-3 | 38.8 | 38.6 | 38.5 | 38.7 | 38.7 | 39.1 | 38.8 | 38.7 | 38.9 | 38.6 | 40.5 | 40.8 | 38.8 | 38.9 |
| | C-4 | 157.5 | 156.0 | 157.4 | 154.2 | 154.4 | 159.2 | 157.7 | 159.0 | 155.9 | 156.3 | 159.0 | 156.7 | 157.9 | 158.1 |
| | C-5a | 106.4 | 106.3 | 106.4 | 106.7 | 106.5 | 107.8 | 107.7 | 107.8 | 108.0 | 106.1 | 107.4 | 107.4 | 107.5 | 107.7 |
| | C-6 | 162.4 | 162.3 | 162.5 | 162.2 | 162.1 | 162.0 | 161.8 | 162.1 | 161.9 | 161.0 | 162.3 | 162.2 | 160.3 | 160.3 |
| | C-8 | 154.0 | 154.1 | 154.1 | 154.3 | 154.0 | 157.3 | 156.4 | 158.0 | 157.9 | 152.9 | 153.4 | 153.8 | 157.2 | 156.3 |
| | C-9a | 152.8 | 152.9 | 152.8 | 153.3 | 153.3 | 152.4 | 152.5 | 152.4 | 152.6 | 151.1 | 150.0 | 150.5 | 150.6 | 150.8 |
| Ar | $C_i$ | 140.7 | 139.5 | 133.4 | 143.3 | 140.4 | 140.4 | 139.2 | 133.0 | 143.3 | 143.4 | 142.8 | 146.1* | 143.5 | 143.3 |
| | | 143.6 | 143.4 | 143.1 | 146.5 | 146.6 | 143.7 | 143.4 | 143.5 | 146.2* | 139.5 | 138.6 | 139.6 | 139.2 | 146.8* |
| | $C_{o,m}$ | 125.9 | 125.8 | 112.9 | 122.9 | 122.9 | 126.0 | 125.9 | 113.0 | 122.9 | 125.9 | 126.1 | 123.3 | 125.9 | 122.9 |
| | | 126.1 | 127.5 | 126.0 | 125.7 | 125.7 | 126.3 | 127.6 | 126.0 | 125.8 | 127.6 | 128.1 | 126.0 | 127.6 | 125.8 |
| | | 127.5 | 127.9 | 127.7 | 126.9 | 127.0 | 127.6 | 127.9 | 127.9 | 127.1 | 127.8 | 128.2 | 127.3 | 127.9 | 127.1 |
| | | 127.9 | 127.9 | 127.9 | 127.9 | 128.5 | 127.9 | 128.0 | 128.0 | 128.0 | 127.8 | 129.0 | 129.7 | 127.9 | 128.0 |
| | $C_p$ | 126.7 | 126.7 | 126.7 | 126.8 | 135.8 | 126.8 | 126.8 | 126.8 | 126.9 | 126.7 | 128.3 | 138.3 | 126.8 | 126.9 |
| | | 128.1 | 132.9 | 157.4 | 146.5 | 146.6 | 128.4 | 133.2 | 159.8 | 146.7* | 132.9 | 135.1 | 147.7* | 133.2 | 146.2* |
| | | | | 55.0 ($OCH_3$) | | 20.4 ($CH_3$) | | | 55.0 ($OCH_3$) | | | | 21.0 ($CH_3$) | | |
| | 7-R | ----- | ----- | ----- | ----- | ----- | ----- | ----- | ----- | ----- | 27.4 | 28.0 | 28.1 | 29.8 | 29.8 |
| | 8-R | 54.1 | 54.1 | 54.1 | 54.3 | 54.2 | 12.6 | 12.6 | 12.6 | 12.6 | 55.1 | 55.3 | 55.4 | 14.0 | 14.1 |

[a] Measurements in $CDCl_3$.

Scheme 2



**3a-i**

ates a singlet that is shifted by 2.48 ppm to higher field. 2-H and the proton of C-3 in the *trans* position to 2-H show upfield shifts of 0.32 and 0.65 ppm, respectively. The proton 3-H in the *cis* position to 2-H (first column of 3-H in Table 1) is shifted downfield by 0.56 ppm. We assume that the exceptional change in the $^1$H nmr spectrum is due to a particular interaction of the relatively acidic 1-NH protons and the basic solvent DMSO.

The $^{13}$C nmr data of **3a-m** are summarized in Table 2. The great difference in the chemical shifts of the quaternary carbon atoms C-5a and C-9a can be taken as a hint for a push-pull substituted CC double bond in structure **3**; however, in order to rule out the isomeric structure **3'** we had to perform selective low-power $^{13}$C, $^1$H-decoupling experiments. Both carbon signals are doublets with $^3J_{CH}$ = 5.4 Hz in the coupled $^{13}$C nmr spectra. Irradiation into the proton signal of 2-H leads to a singlet for the signal of C-9a; additionally, the signal of C-5a becomes a singlet by irradiation into the doublet of 1N-H. The carbonyl group (C-6) provokes in the fully coupled $^{13}$C nmr spectrum a singlet which is not affected by the decoupling experiments. (The exchanging proton 7-H in **3a-i** at $\delta$ = 11.8 ±0.4 doesn't lead to any coupling in the $^{13}$C nmr). Thus the single frequency decoupling experiments are only consistent with structure **3**.

Furthermore, another point concerning the constitution of the heterocycles **3** should be mentioned. The $^{13}$C nmr signals for C-6 and C-8 of the compounds **3a-i** are unusually broad and can only be detected in the case of a high signal-noise ratio. This effect cannot be observed for the *N*-methyl compounds **3j-m**.

We assume that the intermolecular exchange of the proton on N-7 can include further tautomeric structures. Nevertheless, the lactam form on the left side of Scheme 2 should be the most important one; otherwise greater shift differences for C-6 should be expected for the NH and the $NCH_3$ compounds **3a-i** and **3j-m**, respectively.

## EXPERIMENTAL

Melting points are uncorrected. The ir spectra were obtained in potassium bromide pellets with a Perkin-Elmer 599B spectrometer. The uv spectra were recorded on a Shimadzu UV-160A in methanol. The $^1$H and $^{13}$C nmr spectra were run on a Bruker AM 400 in DMSO-$d_6$ or deuteriochloroform. The mass spectra were obtained on a Finnigan M95 spectrograph operating at 70 eV.

2,4-Diaryl-2,3,6,7-tetrahydro-1*H*-pyrimido[4,5-*b*][1,4]diazepin-6-ones **3a-m**.

General Procedure.

A solution of 3.2 mmoles of **1** (4,5-diamino-1,6-dihydro-2-methoxypyrimidin-6-one or 4,5-diamino-1,6-dihydro-2-methoxy-1-methylpyrimidin-6-one or 4,5-diamino-1,6-dihydro-2-methylthiopyrimidin-6-one or 4,5-diamino-1,6-dihydro-1-methyl-2-methylthiopyrimidin-6-one) and 3.2 mmoles of 1,3-diaryl-2-propenone (chalcone) **2** was refluxed in 15 ml absolute ethanol and 1 ml acetic acid for 8 hours. The reaction mixture was cooled down to 0° and the precipitate formed overnight was filtered off. The obtained solid was recrystallized from methanol. The yields and the melting points are summarized in Scheme 1.

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

This compound had ms: (70 eV) m/z (%) = 346 (100, $M^{+\cdot}$), 331 (31, $M^{+\cdot}$-$CH_3$), 269 (22, $M^{+\cdot}$-$C_6H_5$), 242 (49, $M^{+\cdot}$-$C_6H_5CNH$), 140 (23, $C_5H_6N_3O_2^+$), 104 (42, $C_6H_5CNH^+$).

*Anal.* Calcd. for $C_{20}H_{18}N_4O_2$: C, 69.35; H, 5.24; N, 16.17. Found: C, 69.59; H, 5.44; N, 15.85.

4-(4-Chlorophenyl)-2,3,6,7-tetrahydro-8-methoxy-2-phenyl-1*H*-pyrimido[4,5-*b*][1,4]diazepin-6-one (**3b**).

This compound had ms: (70 eV) m/z (%) = 382/380 (35/100, $M^{+\cdot}$, Cl isotope pattern), 367/365 (15/42, $M^{+\cdot}$-$CH_3$, Cl isotope pattern), 278/276 (14/38, $M^{+\cdot}$-$C_6H_5CNH$), 269 (24, $M^{+\cdot}$-$C_6H_4Cl$), 242 (30, $M^{+\cdot}$-$ClC_6H_4CNH$), 167 (29), 140 (52, $C_5H_6N_3O_2^+$), 104 (21, $C_6H_5CNH^+$).

*Anal.* Calcd. for $C_{20}H_{17}ClN_4O_2$: C, 63.08; H, 4.50; N, 14.71. Found: C, 62.88; H, 4.69; N, 14.40.

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

This compound had ms: (70 eV) m/z (%) = 376 (100, $M^{+\cdot}$), 361 (30, $M^{+\cdot}$-$CH_3$), 272 (29, $M^{+\cdot}$-$C_6H_5CNH$), 238 (68), 140 (25, $C_5H_6N_3O_2^+$), 135 (58), 103 (24, $C_6H_5CN^{+\cdot}$).

*Anal.* Calcd. for $C_{21}H_{20}N_4O_3$: C, 67.01; H, 5.36; N, 14.88. Found: C, 66.79; H, 5.30; N, 14.59.

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

This compound had ms: (70 eV) m/z (%) = 391 (100, $M^{+\cdot}$), 376 (42, $M^{+\cdot}$-$CH_3$), 287 (28, $M^{+\cdot}$-$C_6H_5CNH$), 269 (23, $M^{+\cdot}$-$C_6H_4NO_2$), 242 (23, $M^{+\cdot}$-$NO_2C_6H_4CNH$), 167 (25), 140 (29, $C_5H_6N_3O_2^+$), 104 (24, $C_6H_5CNH^+$).

*Anal.* Calcd. for $C_{20}H_{17}N_5O_4$: C, 61.38; H, 4.38; N, 17.89. Found: C, 61.11; H, 4.30; N, 17.69.

2,3,6,7-Tetrahydro-8-methoxy-2-(4-methylphenyl)-4-(4-nitrophenyl)-1*H*-pyrimido[4,5-*b*][1,4]diazepin-6-one (**3e**).

This compound had ms: (70 eV) m/z (%) = 405 (100, $M^{+\cdot}$), 390 (28, $M^{+\cdot}$-$CH_3$), 301 (28, $M^{+\cdot}$-$C_6H_5CNH$), 287 (46), 278 (43), 257 (27, $M^{+\cdot}$-$NO_2C_6H_4CN$), 242 (23), 155 (28), 141 (30), 118 (99, $H_3C$-$C_6H_4CNH^+$), 103 (31, $C_6H_5CN^{+\cdot}$).

*Anal.* Calcd. for $C_{21}H_{19}N_5O_4$: C, 62.22; H, 4.72; N, 17.27. Found: C, 62.50; H, 5.01; N, 17.02.

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

This compound had ms: (70 eV) m/z (%) = 362 (100, $M^{+\cdot}$), 347 (32, $M^{+\cdot}$-$CH_3$), 258 (52, $M^{+\cdot}$-$C_6H_5CNH$), 156 (28, $C_5H_6N_3OS^+$), 104 (81, $C_6H_5CNH^+$).

*Anal.* Calcd. for $C_{20}H_{18}N_4OS$: C, 66.28; H, 5.01; N, 15.46. Found: C, 65.98; H, 5.30; N, 15.17.

4-(4-Chlorophenyl)-2,3,6,7-tetrahydro-8-methylthio-2-phenyl-1*H*-pyrimido[4,5-*b*][1,4]diazepin-6-one (**3g**).

This compound had ms: (70 eV) m/z (%) = 398/396 (40/100, $M^{+\cdot}$, Cl isotope pattern), 383/381 (10/29, $M^{+\cdot}$-$CH_3$, Cl isotope pattern), 294/292 (12/30, $M^{+\cdot}$-$C_6H_5CNH$), 156 (27, $C_5H_6N_3OS^+$), 138 (27), 104 (26, $C_6H_5CNH^+$).

*Anal.* Calcd. for $C_{20}H_{17}ClN_4OS$: C, 60.52; H, 4.32; N, 14.12. Found: C, 60.38; H, 4.33; N, 14.02.

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

This compound had ms: (70 eV) m/z (%) = 392 (100, $M^{+\cdot}$), 377 (20, $M^{+\cdot}$-$CH_3$), 288 (21, $M^{+\cdot}$-$C_6H_5CNH$), 238 (55), 156 (20, $C_5H_6N_3OS^+$), 135 (60), 103 (24, $C_6H_5CN^{+\cdot}$).

*Anal.* Calcd. for $C_{21}H_{20}N_4O_2S$: C, 64.27; H, 5.14; N, 14.28. Found: C, 63.95; H, 5.20; N, 13.98.

2,3,6,7-Tetrahydro-8-methylthio-4-(4-nitrophenyl)-2-phenyl-1*H*-pyrimido[4,5-*b*][1,4]diazepin-6-one (**3i**).

This compound had ms: (70 eV) m/z (%) = 407 (27, $M^{+\cdot}$), 252 (95), 206 (21), 178 (25), 131 (63), 103 (100, $C_6H_5CN^{+\cdot}$).

*Anal.* Calcd. for $C_{20}H_{17}N_5O_3S$: C, 58.96; H, 4.21; N, 17.19. Found: C, 58.89; H, 4.40; N, 16.89.

4-(4-Chlorophenyl)-2,3,6,7-tetrahydro-8-methoxy-7-methyl-2-phenyl-1*H*-pyrimido[4,5-*b*][1,4]diazepin-6-one (**3j**).

This compound had ms: (70 eV) m/z (%) = 396/394 (27/100, $M^{+\cdot}$, Cl isotope pattern), 381/379 (12/35, $M^{+\cdot}$-$CH_3$, Cl isotope pattern), 292/290 (2/5, $M^{+\cdot}$-$C_6H_5CNH$, Cl isotope pattern).

*Anal.* Calcd. for $C_{21}H_{19}ClN_4O_2$: C, 63.88; H, 4.85; N, 14.19. Found: C, 63.81; H, 4.70; N, 13.95.

2,3,6,7-Tetrahydro-8-methoxy-7-methyl-2-(4-methylphenyl)-4-(4-nitrophenyl)-1*H*-pyrimido[4,5-*b*][1,4]diazepin-6-one (**3k**).

This compound had ms: (70 eV) m/z (%) = 419 (37, $M^{+\cdot}$), 404 (20, $M^{+\cdot}$-$CH_3$), 301 (33, $M^{+\cdot}$-$C_6H_5CNH$), 155 (30), 118 (100).

*Anal.* Calcd. for $C_{22}H_{21}N_5O_4$: C, 63.00; H, 5.05; N, 16.70. Found: C, 63.02; H, 4.95; N, 16.51.

4-(4-Chlorophenyl)-2,3,6,7-tetrahydro-7-methyl-8-methylthio-2-phenyl-1*H*-pyrimido[4,5-*b*][1,4]diazepin-6-one (**31**).

This compound had ms: (70 eV) m/z (%) = 412/410 (34/91, $M^{+\cdot}$, Cl isotope pattern), 397/395 (11/29, $M^{+\cdot}$-$CH_3$, Cl isotope pattern), 299 (36, $M^{+\cdot}$-$C_6H_4Cl$), 242/240 (21/57), 171 (50), 88 (100).

*Anal.* Calcd. for $C_{21}H_{19}ClN_4OS$: C, 61.38; H, 4.66; N, 13.63. Found: C, 61.51; H, 4.60; N, 13.35.

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

This compound had ms: (70 eV) m/z (%) = 421 (100, $M^{+\cdot}$), 405 (26, $M^{+\cdot}$-$CH_3$), 299 (26, $M^{+\cdot}$-$C_6H_4NO_2$), 171 (42), 88 (60).

*Anal.* Calcd. for $C_{21}H_{19}N_5O_3S$: C, 59.84; H, 4.54; N, 16.62. Found: C, 59.64; H, 4.41; N, 16.80.

Acknowledgment.

We are grateful to COLCIENCIAS for financial support.

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