Pergamon

Tetrahedron 54 (1998) 9903–9910

TETRAHEDRON

A Novel Fused Heterocyclic System - Synthesis of Substituted 9,10-Dihydro-1,3,4,6,7,10-hexaazacyclohepta[*de*]naphthalen-8(7*H*)-ones

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Received 13 May 1998; revised 12 June 1998; accepted 15 June 1998

Abstract: 4-Amino-5-chloro-2,7-bis(dimethylamino)pyrimido[4,5-*d*]pyrimidine (**5**) was prepared starting from 1,1-diamino-2,2-dicyanoethylene (**1**) and dichloromethylenedimethylimmonium chloride (**2**). After reacting with α–aminoacidic esters, **5** was converted into a series of new pyrimido[4,5-*d*]pyrimidines (**7**), which underwent cyclization to yield substituted 9,10-dihydro-1,3,4,6,7,10-hexaazacyclohepta[*de*]naphthalen-8(7*H*)-ones (**8**). © 1998 Published by Elsevier Science Ltd. All rights reserved.

Dedicated on the 70th birthday of A. R. Katritzky, Department of Chemistry, University of Florida, Gainesville

INTRODUCTION

The bicyclic pyrimido[4,5-*d*]pyrimidine system has been very little investigated. Since the first synthesis by S. H. Chatterji and N. Anand in 1958[1], this system has been studied by several laboratories[2-8]. Shortly ago, we reported another approach to this system from *o*-aminocyanopyrimidine and N-(dichloromethylene)dialkyliminium chlorides[9]. The present paper describes the preparation of a series of new pyrimido[4,5-*d*]pyrimidine derivatives (**5** and **7a-f**) starting from 1,1-diamino-2,2-dicyanoethylene (**1**) and dichloromethylenedimethylimmonium chloride (**2**).

The synthesis of the earliest known diazepine was reported by Fischer in 1883[10]. From then on, numerous research papers have been published focussed on the diazepine chemistry. The discovery that fusion of a third ring to diazepine skeleton maintains or enhances anxiolytic activity led to extensive investigations of tricyclic heterocyclic ring-fused diazepine derivatives. Most of them are *ortho*-fused systems. Only a few of them are *ortho*- and *peri*-fused systems, such as pyrido[1,2,3-*ef*][1,5]benzodiazepines, pyrido[3,2,1-*jk*][1,4]benzodiazepines, naphtho[1,2-*ef*][1,4]diazepines and naphtho[1,8-*ef*][1,4]diazepines[11]. In the present paper, the formation of a hitherto unknown tricyclic heterocyclic ring-fused system via cylization of **7** is reported. In this system, a [1,4]diazepine ring is *ortho*- and *peri*-fused to pyrimido[4,5-*d*]pyrimidine skeleton.

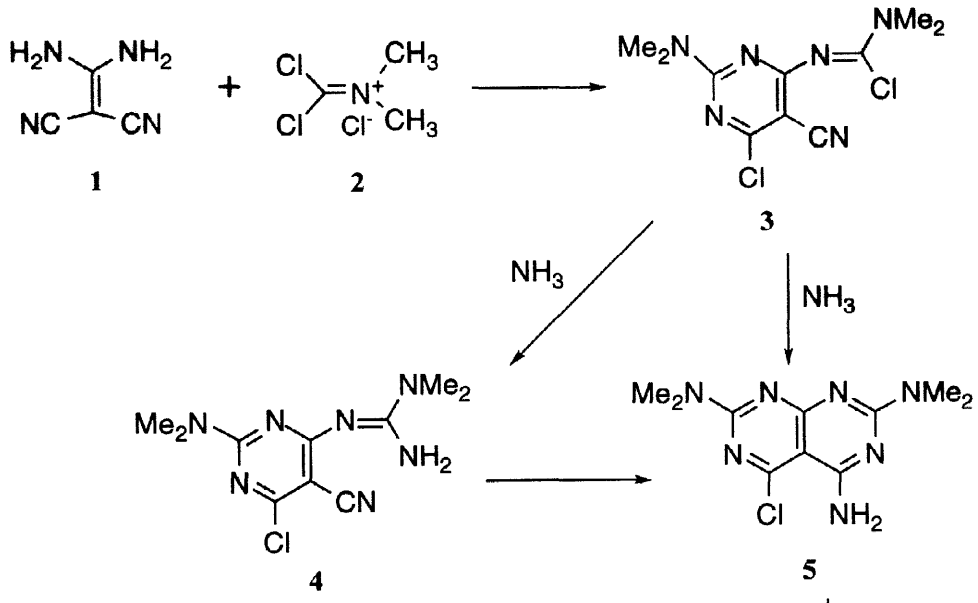
RESULTS AND DISCUSSION

Previously, we reported the preparation of 4-chloro-5-cyano-2-dimethylamino-6-(dimethylamino-chloro)azomethinopyrimidine (**3**) by the reaction of **1** with two moles of **2** in good yield[12]. The treatment of

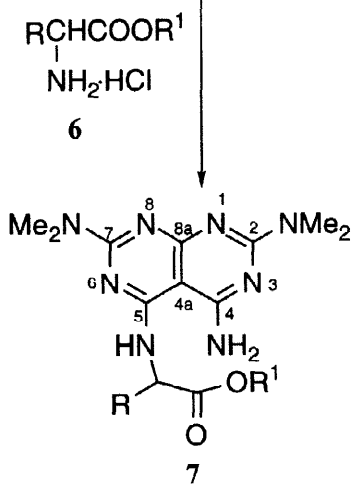
PII: S0040-4020(98)00588-2

3 with ammonium hydroxide in ethanol under reflux afforded 4-amino-5-chloro-2,7-bis(dimethylamino)pyrimido[4,5-*d*]pyrimidine (**5**) in satisfactory yield (61.5%), meanwhile 6-(amino-dimethylamino)azomethino-4-chloro-5-cyanopyrimidine (**4**) was isolated as minor product (3.8%) (as shown in Scheme 1). It is logical to consider that **3** reacted at first with ammonia to give **4**, which underwent

Scheme 1



6	R	R^1
a	H	C_2H_5
b(L-)	$(CH_3)_2CH-$	C_2H_5
c(L-)	$(CH_3)_2CHCH_2-$	CH_3
d(L-)	$H_3CSCH_2CH_2-$	C_2H_5
e(L-)	$PhCH_2-$	C_2H_5
f(L-)	$HOCH_2-$	CH_3



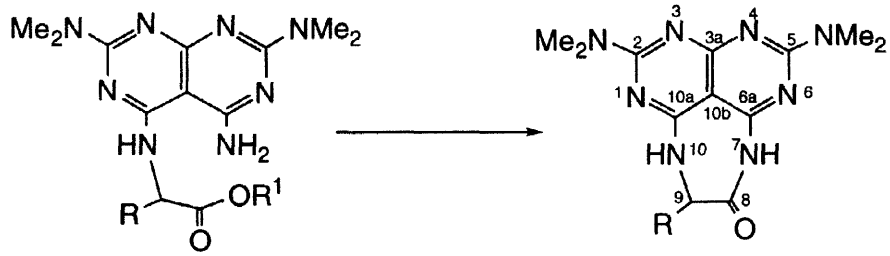
cyclization to afford **5**. In the ^{13}C-NMR spectrum of **4**, the C-atom signal of chloroazomethino group at about 142 ppm disappeared and a new signal due to this C-atom emerged in higher chemical shift region. The CN absorption (2204 cm^{-1}) in infrared and ^{13}C-NMR spectra as well as the NH_2 signal in ^{1}H-NMR spectrum provide other evidences for the structure of compound **4**. Even though **4** and **5** have the same molecular ion peak in mass spectrometry, the disappearance of the signals for chloroazomethino and cyano groups in ^{13}C-NMR spectrum of **5** makes it easy to confirm its structure. The observation that the chlorine in chloroazomethino group is easier to be displaced by an amino group than the other one is consistent with

our previous result[12].

α-Aminoacidic esters (**6a-f**) are strong nucleophiles and reacted with **5** in ethanol under reflux giving coresponding pyrimido[4,5-*d*]pyrimidines **7a-f** in good yields. The absence of the characteristic intensitivity proportion for chlorine-containing compounds in the mass spectrometries of **7** indicates that the chlorine in substrate was displaced by another group. The typical ester carbonyl absorption at about 1740 cm^{-1} in IR together with the microanalysis data are in accordance with the products.

After the treatment with sodium ethoxide in ethanol under reflux, **7a-e** were converted into tricyclic products **8a-e**, in which a [1,4]diazepine ring is *ortho-* and *peri*-fused to the pyrimido[4,5-*d*]pyrimidine skeleton (see Scheme 2). That the molecular ion peaks of the products are 46 or 30 fewer than those of corresponding substrates indicates the elimination of ethanol or methanol respectively. Now we take **8b** as

Scheme 2



7a-e **8a-e**

a representative to discuss these cyclization reactions. The carbonyl absorption in infrared spectrum moved from 1740 cm^{-1} to 1700 cm^{-1} indicating that the ester was converted into amide. Besides the evidence of molecular ion peak in mass spectrometry, the disappearance of the signals for ethyl group (1.27 ppm, 4.21 ppm in ^{1}H-NMR, 14.3 ppm(-), 61.1 ppm(+) in ^{13}C-NMR spectra due to $OCH_2\underline{CH_3}$ and $O\underline{CH_2}CH_3$ respectively) confirms that during the reaction ethanol is eliminated. There are two NH group signals in the ^{1}H-NMR spectrum of **8b**, one is a singlet at 10.67 ppm which should be due to amide proton, the other is a doublet at 8.09 ppm which should be due to the other NH proton. Because of the carbonyl absorption at 1700cm^{-1} in infrared and the NH group signal at 10.67 ppm in ^{1}H-NMR spectra, we consider that **8b** exists in DMSO-d_6 as cyclic amide instead of cyclic hydroxyimine structure. Unfortunately, except **8b** we cannot provide the satisfactory microanalysis data besides HRMS, even though they were treated under the same condition as **8b**. This may be due to their formation of hydrogen bond with water. The up to standard HRMS data and their good solubility in water support this explanation.

EXPERIMENTAL

Melting points were determined on a Reichert hot stage microscope and are uncorrected. IR spectra were measured with a Perkin-Elmer spectrophotometer 283 using potassium bromide and are given as cm^{-1}.

^{1}H- and ^{13}C-NMR spectra were recorded on either a Bruker WM-250 (^{1}H-NMR: 250.13 MHz, ^{13}C-NMR: 62.89 MHz), Bruker WM-360 (^{1}H-NMR: 360MHz, ^{13}C-NMR: 90.56 MHz) or a Varian XL 300 (^{1}H-NMR: 299.95 MHz, ^{13}C-NMR: 75.43 MHz) spectrometer in DMSO-d_6 or $CDCl_3$. The chemical shifts are reported in parts per million (ppm) downfield from internal tetramethylsilane. Electron impact MS spetra were obtained on a Varian MAT 311A instrument. Element analyses were performed on a Heraeus Vario EL CHNS apparatus.

6-(Amino-dimethylamino)azomethino-4-chloro-5-cyanopyrimidine (4) and 4-Amino-5-chloro-2,7-bis(dimethylamino)pyrimido[4,5-*d*]pyrimidine (5):

A mixture of 4-chloro-5-cyano-2-dimethylamino-6-(dimethylamino-chloro)azomethinopyrimidine (**3**) (2.87g, 10mmoles) and aqueous ammonium hydroxide (10ml, 25%aq) in ethanol (200ml) was refluxed for 19 hours, another portion of ammonia water (50ml, 25%aq) was dropped in during the reaction. After removal of the solvent and water under reduced pressure, the residue was chromatographed on a silica column (70-230 mesh) using ethyl acetate as eluent to give 0.1g **4** (3.8%) and 1.65g **5** (61.5%).

The analytical data of **4**: mp 215-218°C. IR (KBr): 3854, 3424, 3168 (NH); 2204 (CN); 1606, 1560, 1458 (C=N, C=C); 1388. ^{1}H-NMR (300 MHz, DMSO-d_6): δ = 3.04 (s, 6H, N(C**H**$_3$)$_2$); 3.11 (s, 6H, N(C**H**$_3$)$_2$); 7.7-9.0 (2H, N**H**$_2$). ^{13}C-NMR (75.43 MHz, DMSO-d_6): δ = 36.7 (-, N(**C**H$_3$)$_2$); 38.8 (-, N(**C**H$_3$)$_2$); 86.2 (+, C-5); 116.4 (+, **C**N); 157.7 (+, C$_{azometh.}$); 159.0 (+, C-4); 160.3 (+, C-6); 166.2 (+, C-2). MS m/z (%): [M+2]$^+$: 269 (23); M$^+$: 267 (74); 241 (26); 223 (27); 120 (13); 71 (39); 57 (36); 44 (100). HRMS: Calcd for $C_{10}H_{14}ClN_7$: 267.1000. Found: 267.1001. Anal. calcd for $C_{10}H_{14}ClN_7$: C, 44.86; H, 5.27; N, 36.62. Found: C, 45.11; H, 5.53; N, 36.34.

The analytical data of **5** : mp 229-232°C. IR (KBr): 3411, 3314, 3209 (NH); 1539, 1394. ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 3.25 (s, 12H, 2xN(C**H**$_3$)$_2$); 5.4-7.1 (2H, N**H**$_2$). ^{13}C-NMR (75.43 MHz, $CDCl_3$): δ = 37.0 (-, N(**C**H$_3$)$_2$); 37.2 (-, N(**C**H$_3$)$_2$); 92.8 (+, C-4a); 157.7 (+, C-5); 160.3 (+, C-4); 160.8 (+, C-8a); 162.2 (+, C-7); 167.5 (+, C-2). MS m/z (%): [M+2]$^+$: 269 (31); M$^+$: 267 (100); 254 (28); 252 (82); 224 (51); 134 (14); 71 (53); 44 (35). HRMS: Calcd for $C_{10}H_{14}ClN_7$: 267.1000. Found: 267.1001. Anal. calcd for $C_{10}H_{14}ClN_7$: C, 44.86; H, 5.27; N, 36.62. Found: C, 44.98; H, 5.62; N, 35.82.

General procedure for the preparation of 5-substituted 4-amino-2,7-bis(dimethylamino)pyrimido[4,5-*d*]pyrimidines (7a-f):

To a stirred solution of corresponding α-aminoacidic ester hydrochloride (**6a-f**) (10 mmoles) in waterfree chloroform (30 ml) barium hydroxide powder (8 mmoles) was added in several portions. After stirring at room temperature for 2.5 hours, the solid was filtered off, and the solvent was removed from the filtrate under reduced pressure. The resulting α-aminoacidic ester was dissolved in ethanol (30 ml), to this solution 4-amino-2,7-bis(dimehylamino)-5-chloropyrimido[4,5-*d*]pyrimidine (**5**) (1.2 mmoles) was added. After heating and refluxing for 5-7 hours the solvent was removed under reduced pressure, the residue was chromatographed on a silica column (70-230 mesh) using ethyl acetate as eluent to give **7a-f**.

4-Amino-2,7-bis(dimethylamino)-5-[(2-ethoxy-2-oxoethyl)amino]pyrimido[4,5-*d*]pyrimidine (7a) (88.6%). mp 240-242°C. IR (KBr): 3331, 3187 (NH); 1751 (C=O); 1653, 1539 (C=N, C=C); 1274, 1203 (C-

N); 1061 (C-O). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.29 (t, J = 7.2 Hz, 3H, CH_2CH_3); 1.85 (s, 2H, NH_2); 3.20 (s, 12H, 2xN(CH_3)$_2$); 4.37 (m, 4H, OCH_2, NCH_2CO); 5.22 (s, 1H, NH). ^{13}C-NMR (75.43 MHz, $CDCl_3$): δ = 13.9 (-, CH_2CH_3); 38.3 (-, m, 2xN(CH_3)$_2$); 43.7 (+, OCH_2); 62.5 (+, NCH_2CO); 81.2 (+, C-4a); 151.7 (+, C-5); 152.0 (+, C-4); 156.5 (+, C-8a); 158.0 (+, C-2); 159.6 (+, C-7); 168.9 (+, C=O). MS m/z (%): $[M+1]^+$: 335 (18); M^+: 334 (100); 319 (59); 261 (32); 245 (35); 218 (28); 162 (8); 71 (40). HRMS: Calcd for $C_{14}H_{22}N_8O_2$: 334.1865. Found: 334.1864. Anal. calcd for $C_{14}H_{22}N_8O_2$: C, 50.29; H, 6.63; N, 33.51. Found: C, 50.54; H, 6.80; N, 33.41.

4-Amino-2,7-bis(dimethylamino)-5-[(2-ethoxy-1-isopropyl-2-oxoethyl)amino]pyrimido[4,5-*d*] pyrimidine (7b) (86.5%). mp 202-205°C. IR (KBr): 3367, 3189 (NH); 1740 (C=O); 1646, 1541 (C=N, C=C); 1396; 1272 (C-N). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.04 (d, J = 6.9 Hz, 6H, CH(CH_3)$_2$); 1.27 (t, J = 7.2 Hz, 3H, CH_2CH_3); 2.27 (m, 1H, CH(CH_3)$_2$); 3.21 (s, 12H, 2xN(CH_3)$_2$); 4.21 (t, J = 7.2 Hz, 2H, OCH_2CH_3); 4.72 (s, 1H, NCHCO); 5.05 (s, 2H, NH_2); 6.04 (s, 1H, NH). ^{13}C-NMR (62.89 MHz, $CDCl_3$): δ = 14.3 (-, CH_2CH_3); 18.5 (-, CH(CH_3)$_2$); 19.3 (-, CH(CH_3)$_2$); 31.0 (-, CH(CH_3)$_2$); 37.1 (-, 2xN(CH_3)$_2$); 59.3 (-, NCHCO); 61.1 (+, OCH_2); 84.8 (+, C-4a); 160.7 (+, C-5); 162.0 (+, C-4); 162.5 (+, C-8a); 162.6 (+, C-2); 167.9 (+, C-7); 173.1 (+, C=O). MS m/z (%): $[M+1]^+$: 377 (21); M^+: 376 (100); 361 (45); 333 (23); 303 (44); 287 (30); 248 (29); 233 (32); 205 (16); 71 (60); 55 (18); 44 (17). HRMS: Calcd for $C_{17}H_{28}N_8O_2$: 376.2336. Found: 376.2337. Anal. calcd for $C_{17}H_{28}N_8O_2$: C, 54.24; H, 7.50; N, 29.77. Found: C, 54.37; H, 7.54; N, 29.45.

4-Amino-2,7-bis(dimethylamino)-5-[(1-isobutyl-2-methoxy-2-oxoethyl)amino]pyrimido[4,5-*d*] pyrimidine (7c) (57.4%). mp 244-246°C. IR (KBr): 3338, 3182 (NH); 1744 (C=O); 1653, 1647, 1541 (C=N, C=C); 1395; 1269 (C-N). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.99 (t, J = 6.0 Hz, 6H, CH(CH_3)$_2$); 1.74 (m, 3H, $CHCH_2$); 3.02 (s, 12H, 2xN(CH_3)$_2$); 3.72 (s, 3H, OCH_3); 4.87 (m, NCHCO); 5.05 (s, 2H, NH_2); 5.85 (1H, NH). ^{13}C-NMR (75.43 MHz, $CDCl_3$): δ = 22.2 (-, CH(CH_3)$_2$); 22.8 (-, CH(CH_3)$_2$); 25.1 (-, CH(CH_3)$_2$); 37.0 (-, 2xN(CH_3)$_2$); 41.4 (+, $CH_2CH(CH_3)_2$); 52.0 (-, NCHCO); 52.8 (-, OCH_3); 84.6 (+, C-4a); 160.2 (+, C-5); 161.6 (+, C-4); 162.2 (+, C-8a); 162.3 (+, C-2); 167.7 (+, C-7); 174.3 (+, C=O). MS m/z (%): $[M+1]^+$: 377 (13); M^+: 376 (100); 361 (28); 333 (21); 317 (23); 301 (9); 233 (11); 71 (34); 44 (100). HRMS: Calcd for $C_{17}H_{28}N_8O_2$: 376.2336. Found: 376.2337. Anal. calcd for $C_{17}H_{28}N_8O_2$: C, 54.24; H, 7.50; N, 29.77. Found: C, 54.06; H, 7.61; N, 28.60.

4-Amino-2,7-bis(dimethylamino)-5-[(2-ethoxy-1-methylmercaptoethyl-2-oxoethyl)amino]pyrimido [4,5-*d*]pyrimidine (7d) (83.9%). mp 232-234°C. IR (KBr): 3333, 3189 (NH); 1732 (C=O); 1646, 1542 (C=N, C=C); 1394; 1270 (C-N). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.27 (t, 3H, CH_2CH_3); 2.11 (s, 3H, SCH_3); 2.3 (m, 2H, $CH_2CH_2SCH_3$); 2.63 (t, 2H, $CH_2CH_2SCH_3$); 3.20 (s, 12H, 2xN(CH_3)$_2$); 4.21 (m, 2H, OCH_2); 4.88 (m, NCHCO); 5.32 (2H, NH_2); 6.3 (1H, NH). ^{13}C-NMR (62.89 MHz, $CDCl_3$): δ = 14.2 (-, OCH_2CH_3); 15.7 (-, SCH_3); 30.7 (+, $CH_2CH_2SCH_3$); 31.2 (+, $CH_2CH_2SCH_3$); 37.1 (-, 2xN(CH_3)$_2$); 53.9 (-, NCHCO); 61.5 (+, OCH_2); 84.6 (+, C-4a); 160.1 (+, C-5); 161.7 (+, C-4); 162.2 (+, C-8a); 162.3 (+, C-2); 167.6 (+, C-7); 173.0 (+, C=O). MS m/z (%): $[M+1]^+$: 409 (24); M^+: 408 (100); 393 (42); 347 (29); 334 (68); 259 (64); 233 (48); 162 (15); 120 (11); 71 (77); 61 (35); 44 (22). HRMS: Calcd for $C_{17}H_{28}N_8O_2S$:

408.2055. Found: 408.2054. Anal. calcd for $C_{17}H_{28}N_8O_2S$: C, 49.98; H, 6.91; N, 27.43; S, 7.85. Found: C, 49.71; H, 6.80; N, 26.77; S, 7.94.

4-Amino-5-[(1-benzyl-2-ethoxy-2-oxoethyl)amino]-2,7-bis(dimethylamino)pyrimido[4,5-*d*]pyrimidine (7e) (49.8%). mp 199-202°C. IR (KBr): 3334, 3186 (NH); 1730 (C=O); 1647, 1542, 1452 (C=N, C=C); 1394; 1271 (C-N). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.24 (t, 3H, OCH_2CH_3); 3.18 (s, 6H, $N(CH_3)_2$); 3.21 (s, 6H, $N(CH_3)_2$); 3.35 (m, 2H, $PhCH_2$); 4.18 (m, 2H, OCH_2CH_3); 4.75 (s, 2H, NH_2); 4.95 (m, NCHCO); 5.82 (d, 1H, NH); 7.15-7.33 (m, 5H, $H_{aroma.}$). ^{13}C-NMR (62.89 MHz, $CDCl_3$): δ = 14.2 (-, OCH_2CH_3); 37.1 (-, 2x$N(CH_3)_2$); 37.5 (+, $PhCH_2$); 55.4 (-, NCHCO); 61.4 (+, OCH_2); 84.6 (+, C-4a); 127.2 (-, C-4′); 128.7 (-, C-3′); 129.3 (-, C-2′); 136.5 (+, C-1′); 159.8 (+, C-5); 161.8 (+, C-4); 162.5 (+, C-8a); 162.6 (+, C-2); 167.9 (+, C-7); 172.6 (+, C=O). MS m/z (%): $[M+1]^+$: 425 (22); M^+: 424 (100); 409 (29); 351 (20); 333 (21); 259 (21); 248 (79); 233 (32); 219 (25); 205 (24); 162 (11); 91 (31); 71 (58); 44 (44). HRMS: Calcd for $C_{21}H_{28}N_8O_2$: 424.2334. Found: 424.2333. Anal. calcd for $C_{21}H_{28}N_8O_2$: C, 59.42; H, 6.65; N, 26.40. Found: C, 59.78; H, 6.88; N, 26.15.

4-Amino-2,7-bis(dimethylamino)-5-[(1-hydroxymethyl-2-methoxy-2-oxoethyl)amino]pyrimido[4,5-*d*] pyrimidine (7f) (65.5%). mp 225-227°C. IR (KBr): 3405, 3178 (NH, OH); 1739 (C=O); 1653, 1647, 1457 (C=N, C=C); 1395; 1272 (C-N). ^{1}H-NMR (300 MHz, DMSO-d_6): δ = 3.03 (s, 6H, $N(CH_3)_2$); 3.09 (s, 6H, $N(CH_3)_2$); 3.63 (s, 3H, OCH_3); 3.87 (t, 2H, $HOCH_2$); 4.57 (m, 1H, NCHCO); 5.21 (t, 1H, OH); 6.61 (s, 2H, NH_2); 6.72 (d, 1H, NH). ^{13}C-NMR (90.56 MHz, DMSO-d_6): δ = 36.2 (-, $N(CH_3)_2$); 36.4 (-, $N(CH_3)_2$); 57.1 (-, OCH_3); 56.9 (-, NCHCO); 60.7 (+, $HOCH_2$); 83.6 (+, C-4a); 159.7 (+, C-5); 161.5 (+, C-8a); 161.9 (+, C-4); 162.2 (+, C-2); 167.1 (+, C-7); 171.5 (+, C=O). MS m/z (%): $[M+1]^+$: 351 (18); M^+: 350 (100); 335 (42); 319 (19); 275 (16), 259 (12); 233 (10); 205 (9); 162 (7); 130 (7); 71 (28); 43 (5). HRMS: Calcd for $C_{14}H_{22}N_8O_3$: 350.1815. Found: 350.1815. Anal. calcd for $C_{14}H_{22}N_8O_3$: C, 47.99; H, 6.33; N, 31.98. Found: C, 48.18; H, 6.53; N, 31.70.

General procedure for the preparation of 9-sustituted 2,5-bis(dimethylamino)-9,10-dihydro-1,3,4,6,7,10-hexaazacyclohepta[*de*]naphthalen-8(7*H*)-ones (8a-e):

To a stirred solution of sodium ethoxide in ethanol, prepared by dissolving sodium (17 mg, 0.75 mmol) in ethanol (30 ml), the corresponding **7a-e** (0.4 mmol) was added. After heating and refluxing for 6 hours, the solvent was removed under reduced pressure. The residue was chromatographed on a silica column (70-230 mesh) using methanol as eluent to give **8a-e**.

2,5-Bis(dimethylamino)-9,10-dihydro-1,3,4,6,7,10-hexaazacyclohepta[*de*]naphthalen-8(7*H*)-one (8a) (69.4%). mp 209°C. IR (KBr): 3394 (NH); 1567, 1541 (C=N, C=C); 1397; 1336; 1296; 818. ^{1}H-NMR (300 MHz, DMSO-d_6): δ = 3.06 (s, 6H, $N(CH_3)_2$); 3.08 (s, 6H, $N(CH_3)_2$); 3.96 (s, 2H, NCH_2CO); 6.75 (2H. 2xNH). ^{13}C-NMR (75.43 MHz, DMSO-d_6): δ = 36.2 (-, $N(CH_3)_2$); 36.3 (-, $N(CH_3)_2$); 43.3 (+, C-9); 83.0 (+, C-10b); 159.3 (+, C-10a); 160.9 (+, C-3a); 161.1 (+, C-6a); 161.4 (+, C-2); 166.3 (+, C-5); 171.3 (+, C-8). MS m/z (%): $[M+1]^+$: 289 (2); M^+: 288 (97); 273 (100); 259 (15); 245 (65); 216 (18); 71 (94); 55 (34); 44 (63); 43 (44). HRMS: Calcd for $C_{12}H_{16}N_8O$: 288.1448. Found: 288.1449.

2,5-Bis(dimethylamino)-9,10-dihydro-9-isopropyl-1,3,4,6,7,10-hexaazacyclohepta[*de*]naphthalen-8(7*H*)-one (8b) (95%). mp 266°C (decomp.). IR (KBr): 3231 (NH); 1700 (C=O); 1609, 1581, 1539 (C=N, C=C); 1387; 1266, 1243, 1214 (C-N); 1153; 1101; 821. ^{1}H-NMR (250.13 MHz, DMSO-d_6): δ = 0.84 (d, J = 6.6 Hz, 3H, CHC**H**$_3$); 0.88 (d, J = 6.7 Hz, 3H, CHC**H**$_3$); 1.92 (m, 1H, C**H**(CH$_3$)$_2$); 3.11 (s, 12H, 2xN(C**H**$_3$)$_2$); 8.09 (d, 1H, H-10); 10.67 (s, 1H, H-7). ^{13}C-NMR (62.89 MHz, DMSO-d_6): δ = 19.0 (-, CH(**C**H$_3$)$_2$); 26.6 (-, **C**H(CH$_3$)$_2$); 36.3 (-, N(**C**H$_3$)$_2$); 36.4 (-, N(**C**H$_3$)$_2$); 64.2 (+, C-9); 87.5 (+, C-10b); 155.6 (+, C-10a); 160.5 (+, C-6a); 162.1 (+, C-3a); 162.4 (+, C-2); 167.4 (+, C-5); 170.0 (+, C-8). MS m/z (%): [M+1]$^+$: 331 (20); M$^+$: 330 (100); 315 (67); 301 (19); 287 (62); 259 (10); 165 (6); 91 (13); 71 (23); 55 (9); 44 (16). HRMS: Calcd for $C_{15}H_{22}N_8O$: 330.1917. Found: 330.1917. Anal. calcd for $C_{15}H_{22}N_8O$: C, 54.53; H, 6.71; N, 33.92. Found: C, 54.57; H, 6.86; N, 33.78.

2,5-Bis(dimethylamino)-9,10-dihydro-9-isobutyl-1,3,4,6,7,10-hexaazacyclohepta[*de*]naphthalen-8(7*H*)-one (8c) (58.2%). mp 250°C. IR (KBr): 3375 (NH); 1575; 1394; 1340; 1272 (C-N); 819. ^{1}H-NMR (250.13 MHz, DMSO-d_6): δ = 0.92 (d, J = 6.5 Hz, 6H, CH(C**H**$_3$)$_2$); 1.6-1.9 (m, 3H C**H**$_2$C**H**(CH$_3$)$_2$); 3.07 (s, 12H, 2xN(C**H**$_3$)$_2$); 4.42 (t, J = 6.2 Hz, 1H, H-9); 6.76 (2H, 2xN**H**). ^{13}C-NMR (90.56 MHz, DMSO-d_6): δ = 22.3 (-, CH**C**H$_3$); 23.0 (-, CH**C**H$_3$); 24.5 (-, **C**H(CH$_3$)$_2$); 36.3 (-, N(**C**H$_3$)$_2$); 41.8 (+, **C**H$_2$CH(CH$_3$)$_2$); 54.4 (-, C-9); 83.5 (+, C-10b); 160.2 (+, C-10a); 161.9 (+, C-6a); 162.0 (+, C-3a); 162.1(+, C-2); 167.0 (+, C-5); 175.6 (+, C-8). MS m/z (%): [M+1]$^+$: 345 (18); M$^+$: 344 (100); 329 (73); 315 (25); 301 (43); 259 (13); 216 (11); 71 (15); 44 (8). HRMS: Calcd for $C_{16}H_{24}N_8O$: 344.2072. Found: 344.2071.

2,5-Bis(dimethylamino)-9,10-dihydro-9-[(2-methylmercapto)ethyl]-1,3,4,6,7,10-hexaazacyclohepta[*de*]naphthalen-8(7*H*)-one (8d) (88.4%). mp 227°C. IR (KBr): 3349 (NH); 1623, 1569 (C=N, C=C); 1395; 1344; 1272 (C-N); 1060; 804. ^{1}H-NMR (250.13 MHz, DMSO-d_6): δ = 2.02 (s, 3H, SC**H**$_3$); 2.09 (m, 2H, C**H**$_2$CH$_2$SCH$_3$); 2.59 (t, 2H, CH$_2$C**H**$_2$SCH$_3$); 3.08 (s, 12H, 2xN(C**H**$_3$)$_2$); 4.41 (t, 1H, H-9); 6.6 (1H, N**H**). ^{13}C-NMR (90.56 MHz, DMSO-d_6): δ = 14.6 (-, S**C**H$_3$); 30.1 (+, **C**H$_2$CH$_2$SCH$_3$); 31.4 (+, CH$_2$**C**H$_2$SCH$_3$); 36.3 (-, N(**C**H$_3$)$_2$); 54.7 (-, C-9); 83.5 (+, C-10b); 159.7 (+, C-6a); 161.7 (+, C-3a); 161.9 (+, C-10a); 162.0(+, C-2); 166.9 (+, C-5); 173.7 (+, C-8). MS m/z (%): [M+1]$^+$: 363 (20); M$^+$: 362 (100); 347 (55); 319 (15); 301 (19); 245 (21); 157 (12); 71 (22); 61 (16); 44 (24). HRMS: Calcd for $C_{15}H_{22}N_8OS$: 362.1639. Found: 362.1641.

9-Benzyl-2,5-bis(dimethylamino)-9,10-dihydro-1,3,4,6,7,10-hexaazacyclohepta[*de*]naphthalen-8(7*H*)-one (8e) (98.8%). mp 248°C. IR (KBr): 3366 (NH); 1565; 1394; 1340; 1273 (C-N); 1062; 911; 820. ^{1}H-NMR (250.13 MHz, DMSO-d_6): δ = 1.87 (S, 2H, Ph**C**H$_2$); 3.06 (s, 12H, 2xN(C**H**$_3$)$_2$); 4.60 (m, 1H, H-9); 6.22 (S, 2H, 2xN**H**); 7.0-7.2 (m, 5H, H$_{aroma.}$). ^{13}C-NMR (62.89 MHz, DMSO-d_6): δ = 36.4 (-, N(**C**H$_3$)$_2$); 37.0 (+, Ph**C**H$_2$); 56.5 (-, C-9); 83.4 (+, C-10b); 125.7 (-, C-4′); 127.6 (-, C-3′); 129.4 (-, C-2′); 139.1 (+, C-1′); 159.6 (+, C-10a); 161.8 (+, C-6a); 162.1 (+, C-2, C-3a); 174.7 (+, C-8). MS m/z (%): [M+1]$^+$: 379 (23); M$^+$: 378 (100); 363 (45); 349 (14); 335 (34); 287 (13); 259 (18); 189 (6); 91 (12); 71 (9); 44 (4). HRMS: Calcd for $C_{19}H_{22}N_8O$: 378.1915. Found: 378.1913.

ACKNOWLEDGEMENTS

Generous support of this work by BASF AG, BAYER AG, HOECHST AG, Verband der Chemischen Industrie-Fond der Chemie-, and Deutsche Forschungsgemeinshaft is gratefully acknowledged. We are indebted to Dr. W. Kramer and Mrs. U. Hertle for recordering and discussing NMR spectra, to Mr. H. Rudy and Mr. P. Weyrich for mass spectra and elemental analysis, to Dr. R. Faust for help with nomenclature; we thank ICN Biomedicals GmbH (Eschwege) for providing us generously with sillica gel.

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