The '*t*-Amino Effect' of *ortho*-Nitroso Amines. Synthesis of 2,6-Diaminoadenine Derivatives from 6-(Dialkylamino)-5-nitrosopyrimidines

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The '*t*-amino effect' of amino-nitroso compounds was documented by preparing the (dialkylamino)-nitroso pyrimidines **4**–**18**, and cyclising them under thermal conditions in high yields to the purine derivatives **19**–**32**. The reactivity of the amino-nitroso-pyrimidines, particularly of **17** derived from diethyl iminodiacetate, and of **19**, derived from 1-phenylimidazolidine, correlates with the stability of the intermediate azomethine ylide. Thermolysis of the amino-nitroso-pyrimidines **34**–**37**, possessing dialkylamino substituents at C(4) and C(6), proceeded by protiodenitrosation, leading to **38**–**41**.

Introduction. – The thermal cyclisation of *N*,*N*-dialkylanilines possessing at least one *N*-methylene group and substituted in the *ortho*-position by a π-acceptor substituent, usually termed the '*t*-amino effect'[1]), has been known for a long time[2]), and was periodically reviewed [6–9]. A large number of *N*,*N*-dialkylanilines possessing an *ortho* π-acceptor substituent undergo the transformation. Among the most important *ortho*-substituents are the nitro, azo, imino, sulfimino, thionitroso, carbonyl, thiocarbonyl, and acceptor-substituted alkenyl groups. The cyclisation of *ortho*-nitroso anilines according to the *t*-amino effect has, however, to the best of our knowledge, never been unambiguously documented, although the intermediate formation of such nitroso derivatives in the course of the cyclisation of *ortho*-(*N*,*N*-dialkyl)(amino)anilines under oxidative conditions, or the cyclisation of *ortho*-(*N*,*N*-dialkyl)(nitro)anilines under reducing conditions was postulated, as discussed by *Meth-Cohn* and *Suschitzky* (see [7] and refs. cit. therein).

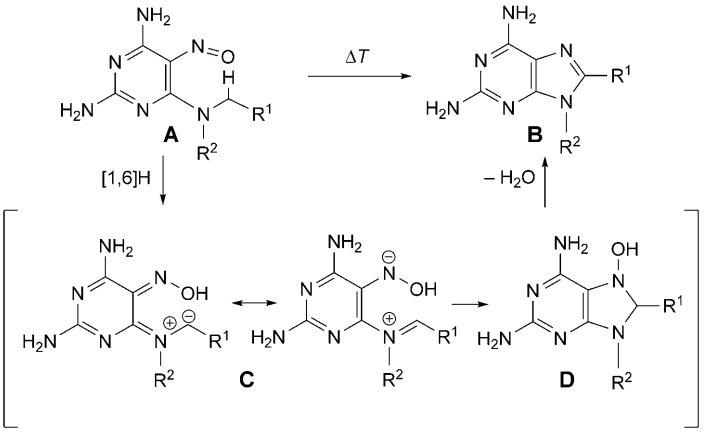
6-Amino-5-nitrosopyrimidines substituted at C(2) and C(4) are readily available, established intermediates in the synthesis of purine and pteridine derivatives [10][11]. We have developed new methods for the transformation of 6-(acylamino)-5-nitroso-pyrimidines into guanidines [12], pteridinones [13], pyrimido-diazepines, and diazepino-purines [14]. The thermal cyclisation of 6-(dialkylamino)-5-nitrosopyrimidines should provide unambiguous evidence for the *t*-amino effect of *ortho*-*N*,*N*-dialkyl-nitrosoanilines, and provide a ready access to purines and purine-derived ring systems that are of interest in view of the biological properties of many purine

1) The unsatisfactory designation of a reaction by the term 'effect' (*cf.* [1]) has led to the suggestion of replacing the expression by 'α-cyclisation of tertiary amines' [2][3] and 'T-reaction' [4].

2) The first reaction to be described by *Meth-Cohn* and *Suschitzky* as '*t*-amino effect' was reported by *Pinnow* [5].

derivatives[3]). We expected the thermal cyclisation of 6-(dialkylamino)-5-nitrosopyrimidines to follow the established reaction mechanism for the *t*-amino effect, as shown in *Scheme 1* [16][17].

Scheme 1



We assumed that formation of azomethine ylides (**C** in *Scheme 1*) is rate-determining, although the elimination of H_2O from the cyclisation product **D** is disfavoured for stereoelectronic reasons. The reactivity of the amino-nitroso-pyrimidines should then reflect the influence of the nature of the substituents on the relative stability of the azomethine ylides. We intended to evaluate the validity of this assumption, and to explore the scope of the expected cyclisation by examining the thermal cyclisation of open-chain and cyclic (dialkylamino)-nitroso-pyrimidines, varying the steric and electronic properties of the dialkylamino group.

Results and Discussion. – Scouting experiments to prepare the required amino-nitroso-pyrimidines by nitrosating 6-chloropyrimidine-2,4-diamine (**1**) [18] (*Scheme 2*), followed by treatment of the poorly stable product with secondary amines, resulted in no more than *ca.* 30% of the desired amino-nitroso-pyrimidines[4]).

For this reason, we turned towards 6-(phenylsulfanyl)pyrimidine-2,4-diamine (**2**) [19] to prepare the desired amino-nitroso-pyrimidines **4**–**18** (*Schemes 2–4*). Both the nitrosation of alkyl- and arylthio analogues and the subsequent substitution of the alkyl- or arylsulfanyl group by nitrogen nucleophiles are well known [20–22]. Replacement of the 6-Cl substituent **1** with a PhS group by improving a known procedure [19] afforded **2** in 92% yield. Nitrosation of **2** provided **3** in a yield of 85%.

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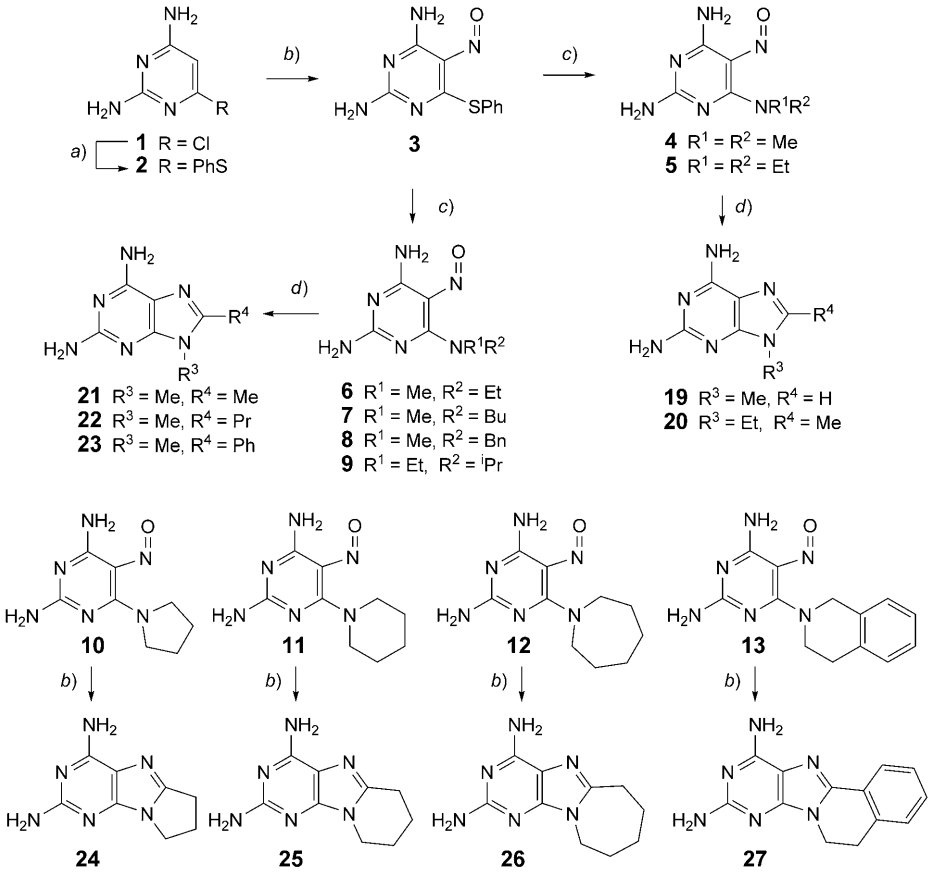
[3]) Consideration of the biological properties of similar ring systems has led *Ojea et al.* [15] to use the *t*-amino effect of 6-(dialkylamino)-5-(dicyanoethenyl)pyrimidines for the synthesis of fused pyrido[2,3-*d*]pyrimidines.

[4]) We thank *Fangli Zhang* for these experiments and for the first evidence that thermolysis of 2,4-diamino-5-nitroso-6-(pyrrolidin-1-yl)pyrimidines leads to the desired purine derivatives.

We first examined the synthesis and cyclisation of the (dimethylamino)- and (diethylamino)-nitroso pyrimidines **4** and **5**, and of the unsymmetrically substituted analogues **6**–**9** (*Scheme 2*).

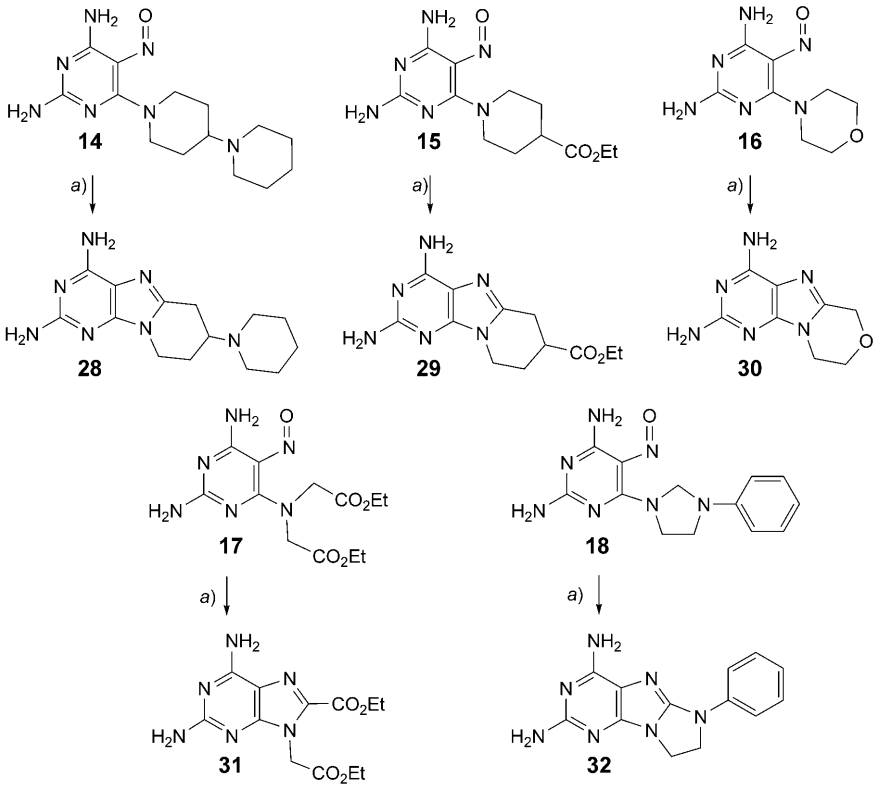
Scheme 2



a) NaOH, MeOH/H_2O, PhOH, 70°; 92%. *b*) $NaNO_2$, AcOH/H_2O, 50°; 85%. *c*) Secondary amine, EtOH, Δ; 72–95%. *d*) Ph_2O, Δ; 88–97%.

Treatment of **3** with 2 equiv. of each one of the selected acyclic secondary amines provided the desired amino-nitroso-pyrimidines **4**–**9** in yields between 68 and 87%. The substitution was conveniently followed by observing the colour change from purple to red-pink. The amino-nitroso-pyrimidines **10**–**13**, derived from cyclic amines, and **14**–**16**, derived from less strongly basic cyclic amines (*Scheme 3*) were prepared in the same way, and in similar yields. Only **17** (45%), derived from diethyl iminodiacetate, and **18** (32%), derived from 1-phenylimidazolidine [23], were obtained in lower yields. The IR spectra of all amino-nitroso-pyrimidines show the typical NO band between 1500 and 1600 cm^{-1}. A H-bond from C(4)NH_2 to the NO group is evidenced by the significant chemical-shift difference between the two C(4)N–H, one resonating at 10.70

Scheme 3



a) Ph_2O, 210°; 85–96%.

and the other at 7.60 ppm, and the C(2)NH_2 group resonating between 7.04 and 7.08 ppm.

Heating the 6-(dimethylamino)-pyrimidine **4** and the diethylamino analogue **5** in Ph_2O at 200 to 210° induced a rapid change of colour from reddish over green-brown to deep-brown and blackish. Liquid chromatography/mass spectrometry (LC/MS) of samples recorded before heating, and within 2 and 5 min from the beginning of heating exhibited two new peaks, one with the same mass as the starting material, and one with the mass expected for the final product that increased as the reaction proceeded, until it became the only peak, at which time heating was discontinued. The product was isolated and purified by column chromatography to provide the purines **19** (84%) and **20** (87%), respectively. The 6-(diethylamino)-pyrimidine **5** reacted slightly more rapidly than the 6-(dimethylamino) analogue **4**, reflecting the relative stability of the more highly substituted intermediate azomethine ylide and of the transition state leading to it. The regioselectivity of the cyclisation of the (ethyl)(methyl)amino derivative **6** and of the (butyl)(methyl)amino derivative **7** that yielded 95% exclusively of the purines **21** and **22**, respectively, is in keeping with this interpretation. Similarly,

cyclization of 6-[(benzyl)(methyl)amino]-pyrimidine **8** gave exclusively the 8-phenylpurine **23** in 88% yield.

Cyclisation of the azomethine ylide derived from **9** should lead to an *N*-hydroxy dihydropurine that cannot aromatize by simple dehydration; we expected the migration of a Me group. However, the starting material reacted much more slowly than **4**–**8**, forming a black, complex product mixture that was not analyzed.

The amino-nitroso-pyrimidines **10**–**13**, derived from cyclic amines, reacted very similarly to each other, although more slowly than **4**–**8**, derived from open-chain amines, to provide the cyclisation products **24**–**27**, all in high yields (see the *Table*).

Table. *Starting Amino-nitroso-pyrimidine, Temperature and Duration of the Thermal Cyclisation, Product, and Yield*

Starting material	Product	*T* [°]	Duration [min]	Yield [%]
4	**19**	185	10	97
5	**20**	185	5	95
6	**21**	190	35	95
7	**22**	190	30	94
8	**23**	175	15	88
10	**24**	210	90	97
11	**25**	210	40	95
12	**26**	210	30	95
13	**27**	210	20	95
14	**28**	210	50	89
15	**29**	210	35	92
16	**30**	210	90	85
17	**31**	210	3	96
18	**32**	185	10	96

The trend to a diminished reactivity was most clearly visible for the pyrrolidin-1-yl derivative **10**. Its cyclisation required *ca.* 90 min at 210°, whereas the 6-(dimethylamino)-pyrimidine reacted within 10 min at 185°. The piperidin-1-yl derivative **11** required less time for cyclization than **10**. Still milder conditions led to the cyclisation of the azepan-1-yl derivative **12** to **26** and, not surprisingly, particularly of the tetrahydroisoquinolin-2-yl derivative **13** to **27**. It reacted more rapidly than **11**, but still more slowly than the open-chain amino derivatives, indicating that the stability of the azomethine ylide is not the only factor determining the reactivity of these amino-nitroso-pyrimidines. The resulting purines were obtained in high yields, but proved poorly soluble, even in DMSO.

The azepanyl and the isoquinolinyl derivatives **26** and **27**, respectively, crystallized from DMSO, and their structures were established by X-ray analysis (*Figs. 1* and *2*)[5]).

[5]) The crystallographic data have been deposited with the *Cambridge Crystallographic Data Centre* as deposition No. CCDC-801183 for **26** and CCDC-801184 for **27**. Copies of the data can be obtained free of charge *via* http://www.ccdc.cam.ac.uk/data_request/cif (or from the *Cambridge Crystallographic Data Centre*, 12 Union Road, Cambridge CB2 1EZ (fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk)).

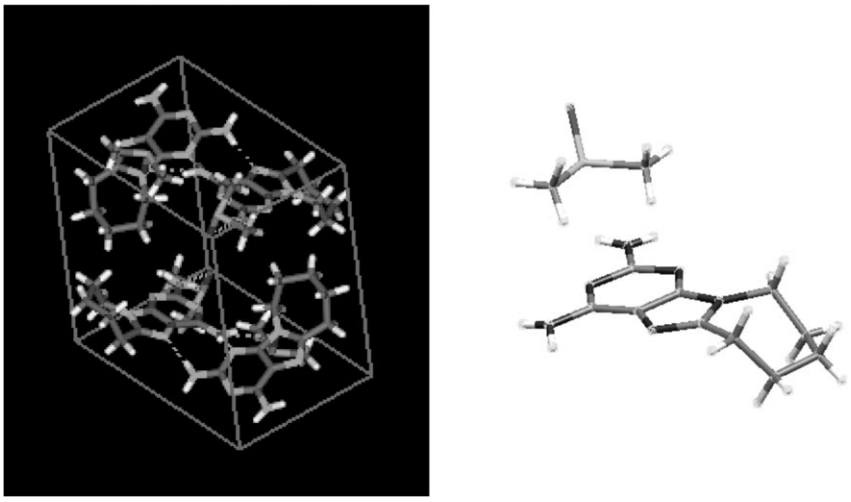


Fig. 1. *Crystal structure of 7,8,9,10-tetrahydro-6*H*-azepino[1,2-*e*]purine-2,4-diamine* (**26**·DMSO)

The amino-nitroso-pyrimidines **14**–**16** (*Scheme 3*) were prepared to examine the effect of the σ-acceptor substituents that are expected to disfavour the hydride shift. The effects of the π-acceptor and π-donor properties of the 6-amino substituents of **17** and **18**, respectively, on the reactivity of the amino-nitroso-pyrimidines were of interest, as both substituents should stabilize the assumed intermediate azomethine ylide, while hydride migration from **17** was expected to be disfavoured. We also expected a favourable effect of the substituents on the solubility of the resulting purine derivatives.

The amino-nitroso-pyrimidines **14** and **15** provided the cyclisation products **28** and **29**, respectively, under similar conditions as the piperidine derivative **11** gave **25**, while the morpholine derivative **16** required clearly harsher reaction conditions to yield **30** (*Table*). Cyclisation of the iminodiacetate **17** to **31** (96%) and of the imidazolidinyl derivative **18** to **32** (96%) proceeded at a lower temperature (185° for 10 min) and clearly more rapidly than cyclization of **14**–**16**, in keeping with the intermediate formation of an azomethine ylide. The cyclization under mild conditions of a glycine-substituted pyrimidine-carbaldehyde *via* an azomethine ylide was already reported [16], while the cyclization of *N*,*N*-acetals appears to be new.

Unfortunately, the effect of the nature of the amino group of the pyrimidines **14**–**18** on the solubility of the products **28**–**32** was rather small, all resulting purines proving poorly soluble at neutral pH, even in DMSO.

The rather high temperature required for the cyclization may result from the donor properties of the NH_2 groups at C(2) and C(4), reducing the electrophilic properties of the NO group and from the C(4)NH $\cdots$ ONC(5) H-bond, orienting the NO group in an unfavourable direction. To explore the effect of this H-bond, we wished to replace the NH_2 group at C(4) by a MeO or by a dialkylamino group, treating 4,6-dimethoxy-5-nitrosopyrimidin-2-amine[6]) (**33**) [24] with a selection of cyclic secondary amines (*Scheme 4*).

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[6]) We thank *Lonza AG*, Visp, for a generous gift of 4,6-dimethoxypyrimidin-2-amine.

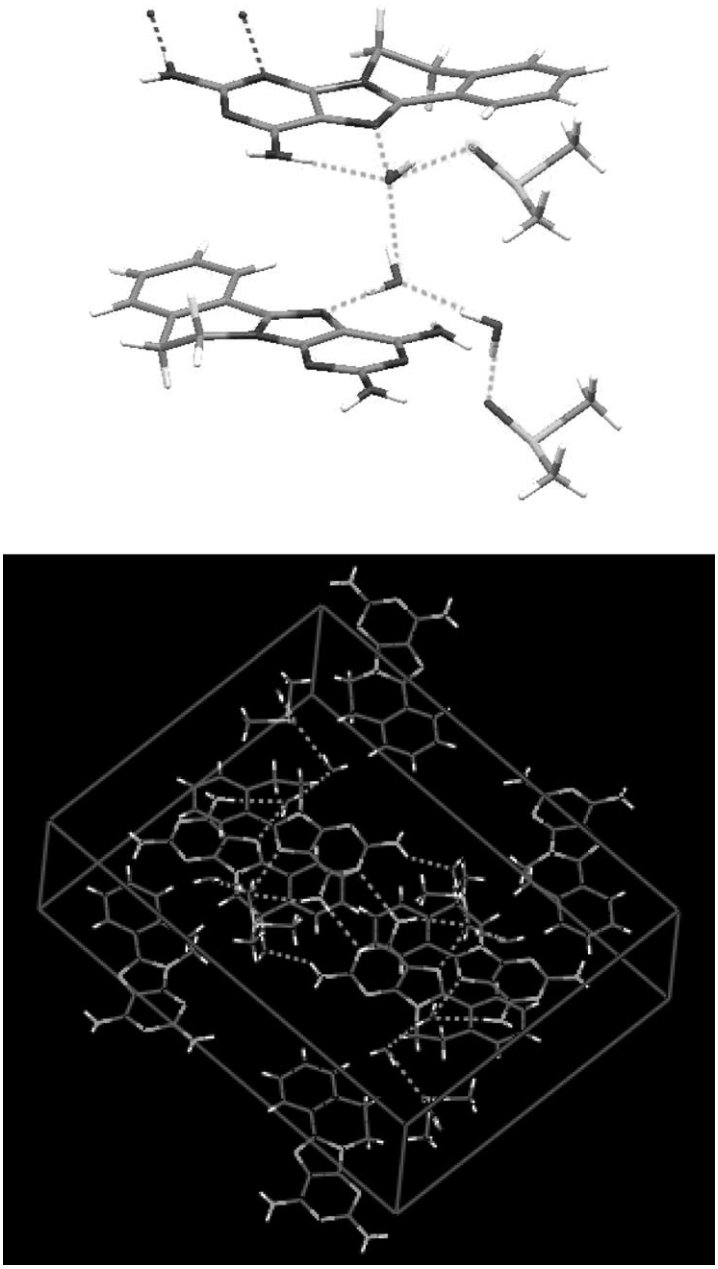
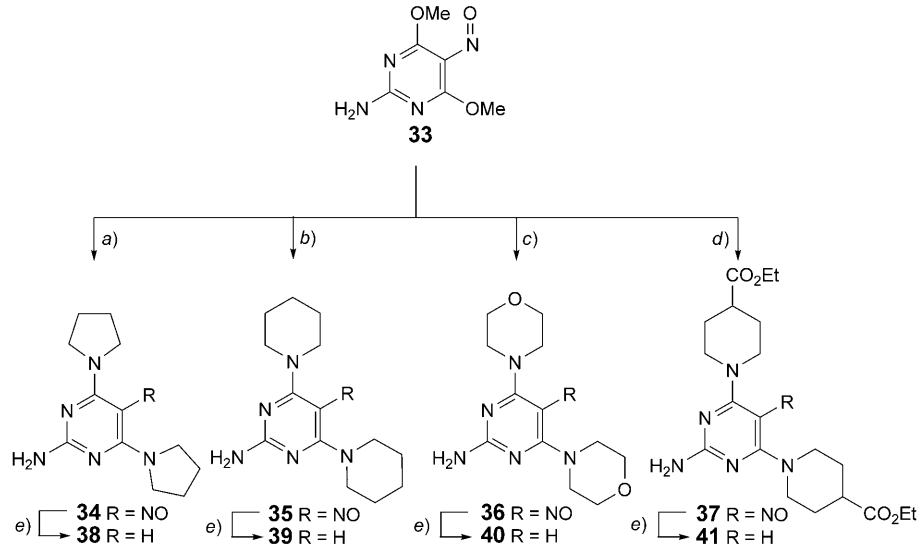


Fig. 2. *Crystal structure of 5,6-dihydropurino[8,9-*a*]isoquinoline-9,11-diamine* (**27** · 1.5 H_2O · 0.5 DMSO)

Scheme 4



a) Pyrrolidine, EtOH, r.t.; 88%. *b*) Piperidine, EtOH, r.t.; 93%. *c*) Morpholine, EtOH, r.t.; 80%. *d*) Ethyl isonipecotate (=ethyl piperidine-4-carboxylate), EtOH, r.t.; 85%. *e*) Ph_2O, 210°.

However, **33** reacted with either 1 or 2 equiv. of pyrrolidine, piperidine, morpholine, or ethyl piperidine-4-carboxylate (=ethyl isonipecotate) under a range of reaction conditions to consistently provide the disubstitution products **34**–**37**, respectively [25], although the reaction of the bis(benzyloxy) analogue with primary amines led to monosubstituted products [26], conceivably on account of the intramolecular H-bond between the first introduced C(4)NHR and the NO group.

Unexpectedly, heating the amino-nitroso-pyrimidines **34**–**37** in Ph_2O under the same reaction conditions as described before led exclusively to the products of denitrosation, **38**–**41** (*Scheme 4*). To confirm the structure of the denitrosation products that are known compounds [26], with the exception of **41**, we synthesised an authentic sample of the dimorpholino-pyrimidine **40** [27] from commercial 4,6-dichloropyrimidin-2-amine.

We assume that the steric interaction with the *ortho* amino groups forces the NO group out of the plane of the pyrimidine ring, so that, at the high temperature, protiodenitrosation takes place, with the rather acidic 2-NH_2 group acting as protonating agent[7]), suggesting a significant role of the H-bond from the neighbouring amino group in stabilizing the nitroso-pyrimidines.

We thank Dr. *B. Bernet* for double-checking the manuscript, Dr. *T. Steinlin* and Dr. *F.-L. Zhang* for useful discussions, and *Syngenta AG*, Basel, for generous support.

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[7]) We have not yet explored the effect of removing the NH_2 substituents at C(2).

Experimental Part

General: See [28].

6-(Phenylsulfanyl)pyrimidine-2,4-diamine (**2**) [19]. A soln. of 6-chloropyrimidine-2,4-diamine [18] (50 g, 0.36 mol) in MeOH/H_2O 3:2 (1.5 l) was treated with NaOH (18.14 g, 0.45 mol) at r.t. PhSH (53.5 ml, 0.52 mmol) was added dropwise. The soln. was stirred for 24 h at 100°, cooled to r.t., and evaporated. The residue was crystallized from MeOH/H_2O to afford **2** (69.4 g, 92%). White needles. A sample for analysis was obtained by sublimation at 135° and $< 10^{-3}$ bar. R_f (CH_2Cl_2/MeOH 9:1) 0.42. M.p. 158° ([19]: 156–157°). IR (ATR): 3415*w*, 3388*m*, 3170*m*, 3070*w*, 2185*w*, 1620*s*, 1541*s*, 1482*s*, 1443*m*, 1434*m*, 1364*s*, 1272*m*, 1164*w*, 1148*m*, 1091*w*, 1072*w*, 1022*w*, 972*w*, 921*w*, 894*m*, 791*m*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 7.59–7.47 (*m*, 5 arom. H); 6.21 (*s*, NH_2); 6.00 (*s*, NH_2); 5.11 (*s*, H–C(5)). ^{13}C-NMR (75 MHz, (D_6)DMSO): 168.75 (*s*, C(2)); 164.16 (*s*, C(6)); 162.55 (*s*, C(4)); 135.39 (2*d*); 129.76 (2*d*); 129.50 (2*d*); 129.25 (*s*); 89.44 (*d*, C(5)). HR-MALDI-MS: 219.0696 (100, $[M+H]^+$, $C_{10}H_{11}N_4S^+$; calc. 219.0704).

5-Nitroso-6-(phenylsulfanyl)pyrimidine-2,4-diamine (**3**). A soln. of **2** (2 g, 9.16 mmol) in H_2O/AcOH 8:2 (50 ml) was treated with $NaNO_2$ (758 mg, 11 mmol), stirred overnight at 50°, and cooled to 0°. The purple precipitate was filtered off and recrystallized in PrOH to afford **3** (1.92 g, 85%). R_f (CH_2Cl_2/MeOH 10:1) 0.50. M.p. 190°. IR (ATR): 3478*w*, 3309*m*, 3269*m*, 3119*m*, 3071*s*, 1661*m*, 1626*s*, 1536*s*, 1495*s*, 1474*s*, 1458*s*, 1437*s*, 1375*s*, 1331*s*, 1242*s*, 1141*s*, 1065*m*, 999*s*, 914*s*, 806*m*, 787*m*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 9.68 (br. *d*, $J = 3.0$, NH); 8.16 (br. *d*, $J = 3.0$, NH); 7.84 (br. *s*, NH); 7.67–7.63 (*m*, 2 arom. H); 7.59 (br. *s*, NH); 7.51–7.40 (*m*, 3 arom. H). ^{13}C-NMR (75 MHz, (D_6)DMSO): 181.00 (*s*, C(6)); 161.01 (*s*, C(2)); 149.03 (*s*, C(4)); 144.87 (*s*, C(5)); 135.64 (2*d*); 129.27 (2*d*); 129.09 (2*d*); 127.94 (*s*). HR-MALDI-MS: 248.0601 (72, $[M+H]^+$, $C_{10}H_{10}N_5OS^+$; calc. 248.0606), 217.0548 (100, $[M-NO]^+$, $C_{10}H_9N_4S^+$; calc. 217.0548).

General Procedure for the Preparation of the Amines **4**–**18** (*GP 1*). A suspension of **3** (1 equiv.) in EtOH or BuOH (for **9** and **16**–**18**) (5 ml) was treated with the suitable secondary amine (2 equiv.) and stirred for periods and at temps. indicated. The coloured precipitates were filtered off and dried under vacuum.

N^4,N^4-*Dimethyl-5-nitrosopyrimidine-2,4,6-triamine* (**4**) [21][22]. Prepared according to *GP 1* from **3** (500 mg, 2.02 mmol) and Me_2NH (205 µl, 4.04 mmol) at 60° for 60 min. Yield: 320 mg (87%). Dark-pink powder. R_f (CH_2Cl_2/MeOH 9:1) 0.56. M.p. 259° [21][22]: 258–259°). IR (ATR): 3107*s*, 1670*m*, 1631*m*, 1553*s*, 1479*s*, 1403*s*, 1347*s*, 1323*s*, 1227*s*, 1155*s*, 1095*s*, 1042*s*, 1000*m*, 880*m*, 835*m*, 787*s*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 10.65, 7.65 (2 br. *s*, H_2N–C(6)); 7.08 (br. *s*, H_2N–C(2)); 3.33 (*s*, NMe_2). ^{13}C-NMR (75 MHz, (D_6)DMSO): 162.81, 161.96 (2*s*, C(2), C(4)); 151.51 (*s*, C(6)); 141.15 (*s*, C(5)); 41.86 (*q*, NMe_2). HR-MALDI-MS: 183.0975 (100, $[M+H]^+$, $C_6H_{11}N_6O^+$; calc. 183.0994).

N^4,N^4-*Diethyl-5-nitrosopyrimidine-2,4,6-triamine* (**5**). Prepared similarly to **4** according to *GP 1* from **3** (500 mg, 2.02 mmol) and Et_2NH (416 µl, 4.04 mmol). Yield: 358 mg (84%). Dark-pink powder. R_f (CH_2Cl_2/MeOH 9:1) 0.37. M.p. 215°. IR (ATR): 3335*w*, 3272*w*, 3125*s*, 1621*m*, 1538*s*, 1482*s*, 1457*s*, 1439*m*, 1428*w*, 1377*w*, 1364*w*, 1313*s*, 1244*s*, 1196*s*, 1157*s*, 1111*s*, 1073*s*, 1050*s*, 1010*s*, 813*w*, 789*s*, 752*m*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 10.78, 7.63 (2 br. *s*, H_2N–C(6)); 7.04 (br. *s*, H_2N–C(2)); 3.74 (*q*, $J = 6.7$, $N(CH_2Me)_2$); 1.19 (*t*, $J = 6.9$, $N(CH_2Me)_2$). ^{13}C-NMR (75 MHz, (D_6)DMSO): 162.10 (*s*, C(2)); 161.37 (*s*, C(4)); 151.58 (*s*, C(6)); 104.90 (*s*, C(5)); 45.36 (*t*, $N(CH_2Me)_2$); 13.42 (*q*, $N(CH_2Me)_2$). HR-MALDI-MS: 211.298 (100, $[M+H]^+$, $C_8H_{15}N_6O^+$; calc. 211.1307), 193.1201 (49, $[M-OH]^+$, $C_8H_{13}N_6^+$; calc. 193.1202).

N^4-*Ethyl*-N^4-*methyl-5-nitrosopyrimidine-2,4,6-triamine* (**6**). Prepared according to *GP 1* from **3** (500 mg, 2.02 mmol) and ethyl(methyl)amine (351 µl, 4.04 mmol) at 60° for 75 min. Yield: 314 mg (79%). Dark-pink powder. R_f (CH_2Cl_2/MeOH 9:1) 0.38. M.p. 235°. IR (ATR): 3278*m*, 3096*s*, 1671*m*, 1633*m*, 1539*s*, 1490*s*, 1458*w*, 1407*m*, 1361*m*, 1340*s*, 1317*s*, 1222*s*, 1199*s*, 1156*s*, 1099*m*, 1068*m*, 1049*s*, 1033*m*, 1003*s*, 853*w*, 823*m*, 787*s*, 752*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 10.72, 7.64 (2 br. *s*, H_2N–C(6)); 7.07 (br. *s*, H_2N–C(2)); 3.81 (*q*, $J = 7.1$, NCH_2Me); 3.31 (*s*, NMe); 1.18 (*t*, NCH_2Me). ^{13}C-NMR (75 MHz, (D_6)DMSO): 162.13, 162.04 (2*s*, C(2), C(4)); 151.55 (*s*, C(6)); 141.09 (*s*, C(5)); 47.77 (*t*, NCH_2Me); 43.13 (*q*, NMe); 12.94 (*q*, NCH_2Me). HR-MALDI-MS: 197.1145 (100, $[M+H]^+$, $C_7H_{13}N_6O^+$; calc. 197.1151), 179.1040 (54, $[M-OH]^+$, $C_7H_{11}N_6^+$; calc. 179.1040).

N^4-*Butyl*-N^4-*methyl-5-nitrosopyrimidine-2,4,6-triamine* (**7**). Prepared similarly to **6** according to *GP 1* from **3** (500 mg, 2.02 mmol) and butyl(methyl)amine (482 µl, 4.04 mmol). Yield: 355 mg (78%). Pink powder. R_f (CH_2Cl_2/MeOH 9:1) 0.59. M.p. 204°. IR (ATR): 3499*s*, 3140*s*, 2951*s*, 2928*m*, 2869*w*, 1599*m*, 1543*s*, 1484*s*, 1461*s*, 1407*m*, 1344*s*, 1311*s*, 1266*w*, 1226*s*, 1173*m*, 1144*s*, 1102*s*, 1058*w*, 1033*w*, 990*s*, 878*w*, 849*m*, 789*s*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 10.71, 7.63 (2 br. *s*, H_2N–C(6)); 7.05 (br. *s*, H_2N–C(2)); 3.78 (*t*, *J* = 7.5, NCH_2); 3.33 (*s*, NMe); 1.02 (*quint.*, *J* = 6.9, NCH_2CH_2); 1.27 (*sext.*, *J* = 7.3, CH_2Me); 0.89 (*t*, *J* = 7.2, CH_2Me). ^{13}C-NMR (75 MHz, (D_6)DMSO): 161.99, 161.95 (2*s*, C(2), C(4)); 151.63 (*s*, C(6)); 150.43 (*s*, C(5)); 52.60 (*t*, NCH_2); 39.82 (*q*, NMe); 29.38 (*t*, NCH_2CH_2); 19.40 (*t*, CH_2Me); 13.75 (*q*, CH_2Me). HR-MALDI-MS: 225.1458 (100, $[M+H]^+$, $C_9H_{17}N_6O^+$; calc. 225.1464), 207.1352 (88, $[M-OH]^+$, $C_9H_{15}N_6^+$; calc. 207.1358), 194.1400 (74, $[M-NO]^+$, $C_9H_{16}N_5^+$; calc. 194.1406). Anal. calc. for $C_9H_{16}N_6O$ (224.27): C 48.20, H 7.19, N 37.47; found: C 48.09, H 7.14, N 37.29.

N^4-*Benzyl*-N^4-*methyl-5-nitrosopyrimidine-2,4,6-triamine* (**8**). Prepared according to *GP 1* from **3** (250 mg, 1.01 mmol) and benzyl(methyl)amine (260 µl, 2.02 mmol). Yield: 193 mg (74%). Pink powder. R_f (CH_2Cl_2/MeOH 9:1) 0.44. M.p. 227°. IR (ATR): 3446*m*, 3291*w*, 3253*w*, 3145*s*, 1588*s*, 1538*s*, 1486*s*, 1453*m*, 1408*m*, 1377*m*, 1343*s*, 1316*w*, 1228*s*, 1143*s*, 1082*m*, 1041*w*, 1026*w*, 998*s*, 961*m*, 884*m*, 837*w*, 812*w*, 789*s*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 10.66, 7.72 (2 br. *s*, H_2N–C(6)); 7.36–7.25 (*m*, 5 arom. H); 7.19 (br. *s*, H_2N–C(2)); 5.15 (*s*, PhCH_2); 3.35 (*s*, NMe). ^{13}C-NMR (75 MHz, (D_6)DMSO): 162.83, 162.11 (2*s*, C(2), C(4)); 151.54 (*s*, C(6)); 141.27 (*s*, C(5)); 137.33 (*s*, C(1′)); 128.09 (*d*, C(2′), C(6′)); 126.92 (*d*, C(3′), C(5′)); 126.64 (*d*, C(4′)); 63.39 (*t*, PhCH_2); 39.99 (*q*, NMe). HR-MALDI-MS: 225.1304 (39, $[M+H]^+$, $C_{12}H_{15}N_6O^+$; calc. 259.1307), 241.1201 (99, $[M-OH]^+$, $C_{12}H_{13}N_6^+$; calc. 241.1202), 228.1249 (100, $[M-NO]^+$, $C_{12}H_{14}N_5^+$; calc. 228.1249). Anal. calc. for $C_{12}H_{14}N_6O$ (258.28): C 55.80, H 5.46, N 32.54; found: C 55.91, H 5.37, N 32.21.

N^4-*Ethyl*-N^4-*(1-methylethyl)-5-nitrosopyrimidine-2,4,6-triamine* (**9**). Prepared according to *GP 1* from **3** (500 mg, 2.02 mmol) and ethyl(isopropyl)amine (488 µl, 4.04 mmol) at 60° for 90 min. Yield: 312 mg (68%). R_f (CH_2Cl_2/MeOH 9:1) 0.51. M.p. 214°. IR (ATR): 3301*w*, 3142*s*, 1629*s*, 1531*w*, 1504*w*, 1378*m*, 1322*s*, 1250*s*, 1203*w*, 1151*s*, 1104*s*, 1044*m*, 994*m*, 916*w*, 792*s*, 751*m*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 10.78, 7.63 (2 br. *s*, H_2N–C(6)); 7.04 (br. *s*, H_2N–C(2)); 5.22 (br. *s*, CHMe$_2$); 3.74 (br. *q*, *J* = 6.9, CH_2Me); 1.22–1.15 (*m*, NHMe_2, NCH_2Me). ^{13}C-NMR (75 MHz, (D_6)DMSO): 161.88, 161.72 (2*s*, C(2), C(4)); 151.67 (*s*, C(6)); 141.06 (*s*, C(5)); 40.13 (*d*, CHMe$_2$); 39.56 (*t*, CH$_2$Me): 20.54 (*q*, CHMe_2); 15.66 (*q*, CH_2Me). HR-MALDI-MS: 225.1461 (48, $[M+H]^+$, $C_9H_{17}N_6O^+$; calc. 225.1464), 207.1352 (100, $[M-OH]^+$, $C_9H_{15}N_6^+$; calc. 207.1358), 194.1400 (14, $[M-NO]^+$, $C_9H_{16}N_5^+$; calc. 194.1406).

5-Nitroso-6-(pyrrolidin-1-yl)pyrimidine-2,4-diamine (**10**) [21]. Prepared similarly to **4** according to *GP 1* from **3** (500 mg, 2.02 mmol) and pyrrolidine (332 µl, 4.04 mmol). Yield: 361 mg (86%). Red powder. R_f (CH_2Cl_2/MeOH 9:1) 0.46. M.p. 254° ([21]: 233–234°). IR (ATR): 3146*w*, 2972*s*, 2873*w*, 1606*m*, 1539*s*, 1476*s*, 1371*s*, 1337*m*, 1310*s*, 1256*m*, 1227*m*, 1206*s*, 1141*s*, 1054*m*, 1033*m*, 996*s*, 921*w*, 881*m*, 838*w*, 789*s*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 10.76, 7.63 (2 br. *s*, H_2N–C(4)); 7.05 (br. *s*, H_2N–C(2)); 3.77 (br. *s*, 2 H–C(2′), 2 H–C(5′)); 1.88 (br. *s*, 2 H–C(3′), 2 H–C(4′)). ^{13}C-NMR (75 MHz, (D_6)DMSO): 162.17 (*s*, C(2)); 160.59 (*s*, C(6)); 151.46 (*s*, C(4)); 141.14 (*s*, C(5)); 52.67, 49.73 (2*t*, C(2′), C(5′)); 26.32, 23.34 (2*t*, C(3′), C(4′)). HR-MALDI-MS: 209.1145 (53, $[M+H]^+$, $C_8H_{13}N_6O^+$; calc. 209.1151), 191.1043 (100, $[M-OH]^+$, $C_8H_{11}N_6^+$; calc. 191.1045).

5-Nitroso-6-(piperidin-1-yl)pyrimidine-2,4-diamine (**11**) [21][22][29]. Prepared similarly to **4** according to *GP 1* from **3** (500 mg, 2.02 mmol) and piperidine (399 µl, 4.04 mmol) (192 mg, 85%). Pink powder. R_f (CH_2Cl_2/MeOH 9:1) 0.52. M.p. 210° ([21][22][29]: 211.5–214°). IR (ATR): 3477*m*, 3404*m*, 3253*w*, 3049*s*, 2937*w*, 2850*w*, 1648*w*, 1610*m*, 1536*s*, 1478*s*, 1442*s*, 1436*s*, 1337*s*, 1301*s*, 1237*s*, 1179*m*, 1154*s*, 1108*s*, 1068*w*, 1051*m*, 1008*m*, 982*s*, 869*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 10.56, 7.64 (2 br. *s*, H_2N–C(4)); 7.11 (br. *s*, H_2N–C(2)); 3.98 (*d*, *J* = 5.1, 2 H–C(2′), 2 H–C(6′)); 1.68–1.59 (*m*, 2 H–C(3′), 2 H–C(4′), 2 H–C(5′)). ^{13}C-NMR (75 MHz, (D_6)DMSO): 162.23, 161.95 (2*s*, C(2), C(6)); 151.58 (*s*, C(4)); 140.67 (*s*, C(5)); 49.19 (*t*, C(2′), C(6′)); 26.31 (*t*, C(3′), C(5′)); 24.37 (*t*, C(4′)). HR-MALDI-MS: 223.1302 (72, $[M+H]^+$, $C_9H_{15}N_6O^+$; calc. 223.1307), 191.1047 (100, $[M-HNO]^+$, $C_9H_{13}N_5^+$; calc. 191.1171).

6-(Azepan-1-yl)-5-nitrosopyrimidine-2,4-diamine (**12**). Prepared according to *GP 1* from **3** (500 mg, 2.02 mmol) and azepane (455 µl, 4.04 mmol) at 60° for 50 min. Yield: 335 mg (72%). Pink powder. R_f (CH_2Cl_2/MeOH 9:1) 0.55. M.p. 224°. IR (ATR): 3315*m*, 3145*s*, 2980*w*, 2934*m*, 2857*w*, 1629*s*, 1555*w*, 1535*s*,

1475*s*, 1460*w*, 1431*s*, 1374*m*, 1364*w*, 1332*s*, 1314*s*, 1283*w*, 1252*w*, 1241*s*, 1223*s*, 1186*w*, 1173*w*, 1136*s*, 1101*m*, 1064*m*, 1033*m*, 1011*m*, 999*s*, 978*m*, 902*m*, 863*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 10.65, 7.63 (2 br. *s*, H_2N–C(4)); 7.04 (br. *s*, H_2N–C(2)); 3.95 (*t*, *J* = 6.0, 2 H–C(2′), 2 H–C(7′)); 1.72 (br. *s*, 2 H–C(3′), 2 H–C(6′)); 1.54 (br. *s*, 2 H–C(4′), 2 H–C(5′)). ^{13}C-NMR (75 MHz, (D_6)DMSO): 162.02, 161.79 (2*d*, C(2), C(6)); 151.60 (*d*, C(4)); 141.98 (*d*, C(5)); 52.60 (*t*, C(2′), C(7′)); 27.79 (*t*, C(3′), C(6′)); 26.09 (*t*, C(4′), C(5′)). HR-MALDI-MS: 237.1849 (50, $[M+H]^+$, $C_{10}H_{17}N_6O^+$; calc. 237.1853), 219.1363 (100, $[M-OH]^+$, $C_{10}H_{15}N_6^+$; calc. 219.1358).

*6-(3,4-Dihydroisoquinolin-2(1*H*)-yl)-5-nitrosopyrimidine-2,4-diamine* (**13**). Prepared similarly to **4** according to *GP 1* from **3** (500 mg, 2.02 mmol) and 1,2,3,4-tetrahydroquinoline (508 µl, 4.04 mmol). Yield: 518 mg (95%). Pink powder. R_f (CH_2Cl_2/MeOH 9 :1) 0.47. M.p. 130°. IR (ATR): 3394*w*, 3317*m*, 3135*s*, 2833*w*, 1652*s*, 1595*s*, 1523*s*, 1490*s*, 1457*w*, 1440*s*, 1428*w*, 1381*w*, 1342*s*, 1316*s*, 1281*m*, 1219*s*, 1197*m*, 1141*s*, 1052*s*, 999*s*, 978*s*, 932*m*, 883*w*, 862*w*, 832*w*, 809*w*, 789*s*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 10.55, 7.73 (2 br. *s*, H_2N–C(4)); 7.26 – 7.16 (*m*, 4 arom. H, H_2N–C(2)); 5.12 (*s*, 2 H–C(1′)); 4.16 (*t*, *J* = 5.7, 2 H–C(3′)); 2.94 (*t*, *J* = 5.7, 2 H–C(4′)). ^{13}C-NMR (75 MHz, (D_6)DMSO): 162.59, 162.14 (2*s*, C(2), C(6)); 151.51 (*s*, C(4)); 140.93 (*s*, C(5)); 134.68, 133.54 (2*s*, C(4a′), C(8a′)); 128.01, 126.18 (2*d*, C(5′), C(8′)); 125.89, 125.78 (2*d*, C(6′), C(7′)); 55.03 (*t*, C(1′)); 46.75 (*t*, C(3′)); 28.72 (*t*, C(4′)). HR-MALDI-MS: 271.1302 (45, $[M+H]^+$, $C_{13}H_{15}N_6O^+$; calc. 271.1307), 253.1198 (73, $[M-OH]^+$; $C_{13}H_{13}N_6^+$; calc. 253.1202), 240.1244 (100, $[M-NO]^+$, $C_{13}H_{14}N_5^+$; calc. 240.1249).

6-(1,4′-Bipiperidin-1′-yl)-5-nitrosopyrimidine-2,4-diamine (**14**). Prepared according to *GP 1* from **3** (500 mg, 2.02 mmol) and 4-(piperidin-1-yl)piperidine (700 µl, 4.04 mmol) at 60° for 120 min. Yield: 587 mg (95%). Pink powder. R_f (CH_2Cl_2/MeOH 9 :1) 0.60. M.p. 235°. IR (ATR): 3220*m*, 3138*m*, 2972*s*, 2846*w*, 2800*w*, 1651*w*, 1612*s*, 1537*s*, 1483s, 1450*s*, 1425*m*, 1394*w*, 1330*s*, 1236*s*, 1216*m*, 1166*w*, 1143*s*, 1120*s*, 1057*m*, 1033*m*, 1013*s*, 986*s*, 932*w*, 873*m*, 829*m*, 788*s*, 749*m*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 10.53, 7.67 (2 br. *s*, H_2N–C(4)); 7.14 (br. *s*, H_2N–C(2)); 4.91 (br. *d*, *J* = 12.3, H_a–C(2′), H_a–(C6′)); 3.08 (br. *t*, *J* = 12.3, H_b–C(2′), H_b–C(6′)); 2.64 – 2.45 (*m*, H–C(4′), 2 H–C(2″), 2 H–C(6″)); 1.79 (*d*, *J* = 11.7, H_a–C(3′), H_a–C(5′)); 1.45 – 1.38 (*m*, H_b–C(3′), H_b–C(5′), 2 H–C(3″), 2 H–C(4″), 2 H–C(5″)). ^{13}C-NMR (75 MHz, (D_6)DMSO): 162.28 (*s*, C(2)); 161.99 (*s*, C(6)); 151.54 (*s*, C(4)); 140.67 (*s*, C(5)); 61.60 (*t*, C(2′), C(6′)); 49.60 (*t*, C(2″), C(6″)); 47.67 (*d*, C(4′)); 28.32 (*t*, C(3′), C(5′)); 26.09 (*t*, C(3″), C(5″)); 24.58 (*t*, C(4″)). HR-MALDI-MS: 306.2038 (100, $[M+H]^+$, $C_{14}H_{24}N_7O^+$; calc. 306.2042), 288.1922 (54, $[M-OH]^+$, $C_{14}H_{22}N_7^+$; calc. 288.1937), 275.1978 (54, $[M-NO]^+$, $C_{14}H_{23}N_6^+$; calc. 275.1984). Anal. calc. for $C_{14}H_{23}N_7O$ (305.38): C 55.06, H 7.59, N 32.11; found: C 54.78, H 7.41, N 31.75.

Ethyl 1-(2,6-Diamino-5-nitrosopyrimidin-4-yl)piperidine-4-carboxylate (**15**). Compound **15** was prepared similarly to **14** according to *GP 1* from **3** (500 mg, 2.02 mmol) and ethyl isonipecotate (611 µl, 4.04 mmol). Yield: 389 mg (65%). Red powder. R_f (CH_2Cl_2/MeOH 9 :1) 0.62. M.p. 247°. IR (ATR): 3428*m*, 3305*m*, 3174*m*, 2981*s*, 2765*w*, 1716*s*, 1606*s*, 1537*s*, 1476*m*, 1394*w*, 1375*w*, 1318*s*, 1204*s*, 1177*m*, 1138*s*, 1095*m*, 1046*m*, 1033*s*, 1012*s*, 948*w*, 936*w*, 865*m*, 826*w*, 789*s*, 692*s*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 10.51, 7.69 (2 br. *s*, H_2N–C(6)); 7.17 (br. *s*, H_2N–C(2)); 4.07 (*q*, *J* = 7.2, O*C*H_2Me); 3.59 – 3.29 (*m*, 2 H–C(2′), 2 H–C(6′)); 2.75 – 2.73 (*m*, H–C(4′)); 1.92 (*t*, *J* ≈ 9.9, H_a–C(3′), H_a–C(5′)); 1.63 (*q*, *J* = 10.2, H_b–C(3′), H_b–C(5′)); 1.19 (*t*, *J* = 7.2, OCH_2*Me*). ^{13}C-NMR (75 MHz, (D_6)DMSO): 173.38 (*s*, C=O); 162.33, 162.28 (2*s*, C(2), C(4)); 151.51 (*s*, C(6)); 140.70 (*s*, C(5)); 59.86 (*t*, O*C*H_2Me); 47.39 (*t*, C(2′), C(6′)); 28.43 (*t*, C(3′), C(5′)); 26.31 (*d*, C(4′)); 14.15 (*q*, OCH_2*Me*). HR-MALDI-MS: 295.1516 (50, $[M+H]^+$, $C_{12}H_{19}N_6O_3^+$; calc. 295.1519), 277.1409 (100, $[M-OH]^+$, $C_{12}H_{17}N_6O_2^+$; calc. 277.1408), 264.1459 (18, $[M-NO]^+$, $C_{12}H_{18}N_5O_2^+$; calc. 264.1460). Anal. calc. for $C_{12}H_{18}N_6O_3$ (294.31): C 48.87, H 6.16, N 28.55; found: C 48.47, H 6.35, N 28.27.

6-(Morpholin-4-yl)-5-nitrosopyrimidine-2,4-diamine (**16**) [21]. Compound **16** was prepared according to *GP 1* from **3** (500 mg, 2.02 mmol) and morpholine (355 µml, 4.04 mmol) at 60° for 150 min. Yield: 361 mg (68%). Red-orange powder. R_f (CH_2Cl_2/MeOH 9 :1) 0.40. M.p. 246° ([21]: 225 – 226°). IR (ATR): 3488*s*, 3430*m*, 3316*m*, 3030*m*, 2919*s*, 2851*m*, 1604*s*, 1546*w*, 1517*m*, 1487*s*, 1461*w*, 1421*w*, 1374*s*, 1324*s*, 1267*m*, 1225*w*, 1216*s*, 1159*s*, 1111*m*, 1099*s*, 1059*w*, 1026*m*, 987*s*, 919*w*, 865*s*, 827*w*, 787*s*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 10.52, 7.74 (2 br. *s*, H_2N–C(4)); 7.29 (br. *s*, H_2N–C(2)); 4.04 (*t*, *J* = 4.5, 2 H–C(2′), 2 H–C(6′)); 3.69 (*t*, *J* = 4.6, 2 H–C(3′), 2 H–C(5′)). ^{13}C-NMR (75 MHz, (D_6)DMSO): 165.22 (*s*, C(6)); 162.19 (*s*, C(2)); 151.49 (*s*, C(4)); 140.78 (*s*, C(5)); 66.34 (*t*, C(2′), C(6′)); 48.58 (*t*, C(3′), C(5′)).

HR-MALDI-MS: 225.1092 (78, $[M+H]^+$, $C_8H_{13}N_6O_2^+$; calc. 225.1100), 207.0989 (100, $[M-OH]^+$, $C_8H_{11}N_6O^+$, calc. 207.0994).

Diethyl 2,2′-[(2,6-Diamino-5-nitrosopyrimidin-4-yl)imino]diacetate (**17**). Compound **17** was prepared according to *GP 1* from **3** (100 mg, 0.4 mmol) and diethyl iminodiacetate (142 µl, 0.81 mmol) at 90° for 140 min. Yield: 59.5 mg (45%). Pink powder. R_f (CH_2Cl_2/MeOH 9:1) 0.63. M.p. 150°. IR (ATR): 3400*m*, 3275*m*, 3125*s*, 2998*w*, 2928*w*, 1733*s*, 1625*s*, 1527*s*, 1489*w*, 1441*w*, 1407*w*, 1370*m*, 1353*w*, 1315*m*, 1238*m*, 1210*s*, 1187*s*, 1140*s*, 1057*m*, 1016*s*, 980*s*, 869*w*, 788*m*, 748*m*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 10.46, 7.82 (2 br. *s*, H_2N–C(6)); 7.30, 7.19 (2 br. *s*, H_2N–C(2)); 4.54 (*s*, $N(CH_2)_2$); 4.13, 4.03 (2*q*, $J=7.2$, 2 OCH_2Me); 1.23–1.13 (*m*, 2 OCH$_2$*Me*). ^{13}C-NMR (75 MHz, (D_6)DMSO): 168.56, 168.23 (2*s*, 2 C=O); 162.82, 161.80 (2*s*, C(2), C(4)); 151.17 (*s*, C(6)); 140.90 (*s*, C(5)); 60.43, 60.01 (2*t*, $N(CH_2)_2$, 2 OCH_2Me); 14.16 (*q*, 2 OCH$_2$*Me*). HR-MALDI-MS: 327.1407 (35, $[M+H]^+$, $C_{12}H_{19}N_6O_5^+$; calc. 327.1417), 309.1297 (17, $[M-OH]^+$, $C_{12}H_{17}N_6O_4^+$; calc. 309.1311), 296.1348 (100, $[M-NO]^+$, $C_{12}H_{18}N_5O_4^+$; calc. 296.1359).

1-Phenylimidazolidine. According to [23], a soln. of *N*-phenylethane-1,2-diamine (1 g, 7.34 mmol) in EtOH (2 ml) was treated dropwise at r.t. with 37% aq. HCHO (3.30 g, 11 mmol), and stirred for 10 min until TLC showed disappearance of the diamine. Upon cooling to 5°, a pale precipitate was formed which was filtered off, washed with H_2O, and dried under vacuum to afford the title compound (856 mg, 80%). R_f (CH_2Cl_2/MeOH 9:1) 0.48. M.p. 120°. IR (ATR): 3344*s*, 3054*s*, 2920*w*, 2859*w*, 2796*s*, 2709*w*, 1661*s*, 1599*s*, 1568*w*, 1509*s*, 1462*m*, 1415*w*, 1384*m*, 1367*m*, 1323*w*, 1258*w*, 1230*s*, 1207*w*, 1191*w*, 1154*m*, 1104*w*, 1075*w*, 1033*m*, 982*s*, 967*w*, 923*m*, 859*m*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 7.24 (*t*, $J=7.6$, H–C(3′), H–C(5′)); 6.71 (*t*, $J=7.5$, H–C(4′)); 6.53 (*d*, $J=7.8$, H–C(2′), H–C(6′)); 4.17 (*s*, 2 H–C(2)); 3.44 (*t*, $J=6.6$, 2 H–C(5)); 3.14 (*t*, $J=6.3$, 2 H–C(4)); 2.18 (br. *s*, NH). ^{13}C-NMR (75 MHz, (D_6)DMSO): 146.3 (*s*, C(1′)); 129.26 (*d*, C(3′), C(5′)); 116.41 (*d*, C(4′)); 111.74 (*d*, C(2′), C(6′)); 69.07 (*t*, C(2)); 50.95 (*t*, C(5)); 45.73 (*t*, C(4)). HR-MALDI-MS: 149.1072 (100, $[M+H]^+$, $C_9H_{13}N_2^+$; calc. 149.1079).

5-Nitroso-6-(3-phenylimidazolidin-1-yl)pyrimidine-2,4-diamine (**18**). Compound **18** was prepared according to *GP 1* from **3** (100 mg, 0.4 mmol) and 1-phenylimidazolidine (120 mg, 0.81 mmol) at 90° for 120 min. Yield: 37 mg (32%). Pink-violet powder. R_f (CH_2Cl_2/MeOH 9:1) 0.49. M.p. 182°. IR (ATR): 3310*m*, 3131*s*, 3070*s*, 2985*s*, 1666*w*, 1629*s*, 1539*s*, 1496*s*, 1367*w*, 1322*s*, 1247*s*, 1145*s*, 997*w*, 916*m*, 808*w*, 788*s*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 10.64, 7.80 (br. *s*, H_2N–C(4)); 7.40–7.20 (*m*, H_2N–C(2), H–C(3″), H–C(5″)); 6.79 (*t*, $J=7.2$, H–C(4″)); 6.69 (br. *s*, H–C(2″), H–C(6″)); 5.03 (*s*, 2 H–C(2′)); 4.14 (br. *s*, H–C(5′)); 3.54 (br. *s*, H–C(4′)). ^{13}C-NMR (75 MHz, (D_6)DMSO): 162.27 (br. *s*, C(2), C(4)); 151.25 (*s*, C(6)); 145.99 (*s*, C(1″)); 140.85 (*s*, C(5)); 128.82 (*d*, C(3″), C(5″)); 117.91 (*d*, C(4″)); 113.19 (*d*, C(2″), C(6″)); 68.22 (*t*, C(2′)); 47.39 (*t*, C(5′)); 44.09 (*t*, C(4′)). HR-MALDI-MS: 268.1311 (30, $[M-OH]^+$, $C_{13}H_{14}N_7^+$; calc. 268.1305), 255.1442 (100, $[M-NO]^+$, $C_{13}H_{16}N_6^+$; calc. 255.1431).

General Procedure for Thermal Cyclisation of 4-(Dialkylamino)-5-nitroso-pyrimidines (*GP 2*). A suspension of the nitroso amines **4**–**18** in Ph_2O (1–3 ml) was heated to 175–210° until LC/MS showed completion of the reaction (see the *Table*). Flash column chromatography (pentane for removal of Ph_2O, then MeCN/EtOH 1:2 to 1:1) gave the products **19**–**32**.

*9-Methyl-9*H*-purine-2,6-diamine* (**19**) [10]. Yield: 97%. R_f (CH_2Cl_2/MeOH 5:1) 0.29. M.p. 290° ([10]: 314–316 (dec.)). IR (ATR): 3312*m*, 3109*s*, 2929*w*, 1662*w*, 1631*m*, 1587*s*, 1527*m*, 1474*w*, 1454*w*, 1429*m*, 1404*s*, 1336*s*, 1284*m*, 1216*m*, 1102*m*, 1053*m*, 977*m*, 860*w*, 833*w*, 790*s*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 7.64 (*s*, H–C(8)); 6.61 (br. *s*, H_2N–C(6)); 5.76 (br. *s*, H_2N–C(2)); 3.53 (*s*, MeN). ^{13}C-NMR (75 MHz, (D_6)DMSO): 159.80 (*s*, C(6)); 155.55 (*s*, C(2)); 151.65 (*s*, C(4)); 137.54 (*d*, C(8)); 112.78 (*s*, C(5)); 28.95 (*q*, NMe). HR-MALDI-MS: 165.0885 (100, $[M+H]^+$, $C_6H_9N_6^+$; calc. 165.0889).

*9-Ethyl-8-methyl-9*H*-purine-2,6-diamine* (**20**). Yield: 95%. R_f (CH_2Cl_2/MeOH 5:1) 0.43. M.p. 252°. IR (ATR): 3492*m*, 3293*w*, 3114*m*, 2971*w*, 2937*w*, 1663*m*, 1630*s*, 1589*s*, 1479*s*, 1446*m*, 1417*s*, 1384*s*, 1371*s*, 1337*s*, 1273*w*, 1249*w*, 1167*w*, 1065*w*, 1035*w*, 1005*m*, 961*w*, 829*w*, 792*s*, 771*m*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 6.46 (br. *s*, H_2N–C(6)); 5.65 (br. *s*, H_2N–C(2)); 3.94 (*q*, $J=7.2$, NCH_2Me); 2.39 (*s*, Me); 1.23 (*t*, $J=7.1$, NCH$_2$*Me*). ^{13}C-NMR (75 MHz (D_6)DMSO): 159.22 (*s*, C(6)); 154.62 (*s*, C(2)); 152.00 (*s*, C(4)); 143.96 (*s*, C(8)); 111.55 (*s*, C(5)); 36.24 (*t*, NCH_2Me); 14.97 (*q*, NCH$_2$*Me*); 13.39 (*q*, Me). HR-MALDI-MS: 193.1106 (100, $[M+H]^+$, $C_8H_{13}N_6^+$; calc. 193.1206).

*8,9-Dimethyl-9*H*-purine-2,6-diamine* (**21**). Yield: 95%. R_f (CH_2Cl_2/MeOH 5:1) 0.35. M.p. 292°. IR (ATR): 3314*m*, 3126*s*, 1630*w*, 1593*s*, 1432*w*, 1406*s*, 1380*s*, 1357*w*, 1335*m*, 1065*w*, 986*m*, 788*s*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 6.46 (br. *s*, H_2N–C(6)); 5.64 (br. *s*, H_2N–C(2)); 3.27 (*s*, NMe); 2.36 (*s*,

Me–C(8)). ^{13}C-NMR (75 MHz, (D_6)DMSO): 159.16 (*s*, C(6)); 154.55 (*s*, C(2)); 152.49 (*s*, C(4)); 144.82 (*s*, C(8)); 111.44 (*s*, C(5)); 27.89 (*q*, NMe); 13.39 (*q*, *Me*–C(8)). HR-MALDI-MS: 179.1088 (100, $[M+H]^+$, $C_7H_{11}N_6^+$; calc. 179.1045).

*9-Methyl-8-propyl-9*H*-purine-2,6-diamine* (**22**). Yield: 94%. R_f (CH_2Cl_2/MeOH 5:1) 0.65. M.p. 245°. IR (ATR): 3312*m*, 3144*m*, 2961*w*, 2929*w*, 2876*w*, 1627*w*, 1589*s*, 1437*s*, 1403*m*, 1380*s*, 1333*m*, 1284*w*, 1156*w*, 1082*w*, 993*m*, 938*w*, 790*s*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 6.47 (br. *s*, H_2N–C(6)); 5.65 (br. *s*, H_2N–C(2)); 3.46 (*s*, MeN); 2.69 (*t*, $J = 7.5$, CH_2–C(8)); 1.72 (*sext.*, $J = 7.5$, CH_2Me); 0.97 (*t*, $J = 7.3$, CH_2Me). ^{13}C-NMR (75 MHz, (D_6)DMSO): 155.97 (*s*, C(6)); 154.66 (*s*, C(2)); 152.53 (*s*, C(4)); 147.90 (*s*, C(8)); 111.61 (*s*, C(5)); 28.62 (*q*, MeN); 27.84 (*t*, CH_2–C(8)); 20.28 (*t*, CH_2Me); 13.86 (*q*, CH_2Me). HR-MALDI-MS: 207.1353 (100, $[M+H]^+$, $C_9H_{15}N_6^+$; calc. 207.1358).

*9-Methyl-8-phenyl-9*H*-purine-2,6-diamine* (**23**). Yield: 88%. R_f (CH_2Cl_2/MeOH 5:1) 0.71. M.p. 292°. IR (ATR): 3465*m*, 3331*m*, 3172*m*, 2989*w*, 2916*w*, 1655*w*, 1622*s*, 1588*s*, 1517*m*, 1503*m*, 1462*s*, 1431*s*, 1406*s*, 1340*s*, 1313*w*, 1289*w*, 1211*w*, 1184*w*, 1149*w*, 1100*w*, 1061*m*, 1024*m*, 974*m*, 920*w*, 850*w*, 790*s*, 775*s*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 7.78 (*d*, $J = 6.9$, H–C(2′), H–C(6′)); 7.55–7.40 (*m*, H–C(3′), H–C(4′), H–C(5′)); 6.73 (br. *s*, H_2N–C(6)); 5.84 (br. *s*, H_2N–C(2)); 3.64 (*s*, MeN). ^{13}C-NMR (75 MHz, (D_6)DMSO): 159.78 (*s*, C(6)); 155.46 (*s*, C(2)); 153.53 (*s*, C(4)); 146.01 (*s*, C(8)); 130.10 (*d*, C(4′)); 128.54 (*s*, C(1′)); 128.18 (*d*, C(2′), C(6′)); 128.05 (*d*, C(3′), C(5′)); 112.81 (*s*, C(5)); 30.08 (*q*, MeN). HR-MALDI-MS: 241.1198 (100, $[M+H]^+$, $C_{12}H_{13}N_6^+$; calc. 241.1202).

*7,8-Dihydro-6*H*-pyrrolo[1,2-*e*]purine-2,4-diamine* (**24**). Yield: 92%. R_f (CH_2Cl_2/MeOH 5:1) 0.29. M.p. 334°. IR (ATR): 3476*m*, 3286*m*, 3107*s*, 1671*m*, 1633*m*, 1582*s*, 1466*m*, 1424*s*, 1383*s*, 1329*w*, 1302*m*, 1272*w*, 1173*w*, 1062*m*, 1018*m*, 784*s*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 6.44 (br. *s*, H_2N–C(4)); 5.64 (br. *s*, H_2N–C(2)); 3.85 (*t*, $J = 6.7$, 2 H–C(8)); 2.77 (*t*, $J = 7.5$, 2 H–C(6)); 2.55 (*quint.*, $J = 6.9$, 2 H–C(7)). ^{13}C-NMR (75 MHz, (D_6)DMSO): 158.94 (*s*, C(4)); 154.75 (*s*, C(2)); 153.77 (*s*, C(9a)); 149.59 (*s*, C(5a)); 117.11 (*s*, C(4a)); 41.1 (*t*, C(8)); 25.86 (*t*, C(6)); 22.42 (*t*, C(7)). HR-MALDI-MS: 191.1039 (100, $[M+H]^+$, $C_8H_{11}N_6^+$; calc. 191.1045).

*6,7,8,9-Tetrahydropyrido[1,2-*e*]purine-2,4-diamine* (**25**). Yield: 95%. R_f (CH_2Cl_2/MeOH 5:1) 0.35. M.p. 309°. IR (ATR): 3483*m*, 3297*m*, 3122*s*, 2945*w*, 1671*m*, 1632*m*, 1585*s*, 1474*w*, 1457*w*, 1417*s*, 1387*s*, 1350*s*, 1325*s*, 1272*m*, 1240*w*, 1171*w*, 1148*w*, 1109*w*, 1074*w*, 1022*w*, 965*w*, 954*m*, 914*w*, 870*w*, 822*w*, 788*s*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 6.47 (br. *s*, H_2N–C(4)); 5.66 (br. *s*, H_2N–C(2)); 3.82 (*t*, $J = 5.7$, 2 H–C(9)); 2.79 (*t*, $J = 6.1$, 2 H–C(6)); 1.93–1.88 (*m*, 2 H–C(7), 2 H–C(8)). ^{13}C-NMR (75 MHz, (D_6)DMSO): 159.09 (*s*, C(4)); 154.61 (*s*, C(2)); 151.55 (*s*, C(10a)); 144.27 (*s*, C(5a)); 111.72 (*s*, C(4a)); 41.04 (*t*, C(9)); 24.92 (*t*, C(6)); 22.04 (*t*, C(8)); 20.43 (*t*, C(7)). HR-MALDI-MS: 205.1197 (100, $[M+H]^+$, $C_9H_{13}N_6^+$; calc. 205.1202).

*7,8,9,10-Tetrahydro-6*H*-azepino[1,2-*e*]purine-2,4-diamine* (**26**). Yield: 96%. R_f (CH_2Cl_2/MeOH 5:1) 0.34. M.p. 305°. IR (ATR): 3472*m*, 3296*m*, 3108*s*, 2927*s*, 2852*w*, 1668*m*, 1610*m*, 1583*s*, 1469*m*, 1430*w*, 1417*s*, 1389*s*, 1361*w*, 1348*s*, 1322*m*, 1279*w*, 1257*w*, 1226*m*, 1190*m*, 1141*w*, 1085*m*, 1067*w*, 1029*w*, 1006*w*, 965*s*, 893*w*, 883*w*, 837*w*, 823*w*, 790*s*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 6.47 (br. *s*, H_2N–C(4)); 5.62 (br. *s*, H_2N–C(2)); 4.01 (br. *s*, 2 H–C(10)); 2.88–2.80 (*m*, 2 H–C(6)); 1.83–1.76 (*m*, 2 H), 1.65–1.60 (*m*, 4 H) (2 H–C(7), 2 H–C(8), 2 H–C(9)). ^{13}C-NMR (75 MHz, (D_6)DMSO): 159.19 (*s*, C(4)); 154.87 (*s*, C(2)); 152.13 (*s*, C(5a)); 150.19 (*s*, C(11a)); 117.14 (*s*, C(4a)); 41.62 (*t*, C(10)); 30.27 (*t*, C(6)); 29.40, 28.51, 25.78 (3*t*, C(7), C(8), C(9)). HR-MALDI-MS: 219.1350 (100, $[M+H]^+$, $C_{10}H_{15}N_6^+$; calc. 219.1358).

X-Ray Data of **26**·*DMSO*. Crystals of **26**·DMSO suitable for X-ray analysis were obtained by isothermal distillation of H_2O in a soln. of **26** in DMSO. Crystal data at 123 K for $C_{10}H_{14}N_6 \cdot C_2H_6OS$ (296.4); monoclinic $P2_1/c$; $a = 12.9469(6)$, $b = 8.4516(4)$, $c = 13.1139(7)$ Å, $\beta = 90.320(2)°$. $V = 1434.93(12)$ Å^3; $Z = 4$; $D_{calc} = 1.372$ Mg/m^3. *Bruker-Nonius Kappa-CCD* with MoK_α radiation ($\lambda = 0.71073$ Å). The structure was solved by direct methods [30] and refined by full-matrix least-squares analysis [31] including an isotropic extinction correction. All heavy atoms were refined anisotropically (H-atoms isotropic, whereby H-positions are based on stereochemical considerations). $R = 0.0994$, $R_w = 0.1756$ for 261 parameters and 3254 reflections with $I > 2\sigma(I)$.

*5,6-Dihydropurino[8,9-*a*]isoquinoline-9,11-diamine* (**27**). Yield: 95%. R_f (CH_2Cl_2/MeOH 5:1) 0.58. M.p. 302°. IR (ATR): 3309*w*, 3124*s*, 1633*m*, 1587*s*, 1574*s*, 1527*m*, 1477*w*, 1452*w*, 1418*s*, 1385*s*, 1333*s*, 1299*w*, 1278*w*, 1154*w*, 1074*w*, 1047*m*, 984*s*, 903*s*, 805*m*, 789*s*, 773*s*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 7.93 (*d*, $J = 7.5$, H–C(1)); 7.39 (*t*, $J = 7.5$, H–C(3)); 7.13 (*t*, $J = 7.4$, H–C(2)); 7.01 (*d*, $J = 7.5$, H–C(4)); 6.76 (br. *s*,

H_2N–C(11)); 5.88 (br. *s*, H_2N–C(9)); 4.11 (*t*, *J* = 6.9, 2 H–C(6)); 3.17 (*t*, *J* = 6.8, 2 H–C(5)). ^{13}C-NMR (75 MHz, (D_6)DMSO): 159.51 (*s*, C(11)); 155.17 (*s*, C(9)); 151.49 (*s*, C(7a)); 141.97 (*s*, C(4a)); 134.13 (*s*, C(12a)); 128.65, 128.12 (2*d*, C(2), C(3)); 126.86, 123.02 (2*d*, C(1), C(4)); 113.58 (*s*, C(11a)); 55.93 (*t*, C(6)); 27.45 (*t*, C(5)). HR-MALDI-MS: 253.1194 (100, $[M+H]^+$, $C_{13}H_{13}N_6^+$; calc. 253.1202).

X-Ray Data of **27**·*1.5 H*$_2$*O*·*0.5 DMSO*. Crystals of **27**·1.5 H_2O·0.5 DMSO suitable for X-ray analysis were obtained upon storing a soln. of **27** in DMSO for an extended period of time. Crystal data at 100 K for 2 $C_{13}H_{12}N_6$·3 H_2O·C_2H_6OS (636.749); monoclinic $P2_1/c$; $a = 18.0070(6)$, $b = 6.9897(3)$, $c = 23.4261(9)$ Å, $\beta = 90.8293(12)^\circ$. $V = 2948.2(2)$ Å^3; $Z = 4$. *Bruker-Nonius Kappa-CCD* with MoK_α radiation ($\lambda = 0.7107$ Å). The structure was solved by direct methods [30] and refined by full-matrix least-squares analysis [31] including an isotropic extinction correction. All heavy atoms were refined anisotropically (H-atoms isotropic, whereby H-positions are based on stereochemical considerations). $R = 0.0813$, $R_w = 0.1612$ for 550 parameters and 4512 reflections with $I > 2\sigma(I)$.

*(±)-6,7,8,9-Tetrahydro-7-(piperidin-1-yl)pyrido[1,2-*e*]purine-2,4-diamine* ((±)-**28**). Yield: 89%. R_f (CH_2Cl_2/MeOH 5:1) 0.36. M.p. 252°. IR (ATR): 3315*m*, 3113*m*, 2926*s*, 1727*w*, 1667*w*, 1631*m*, 1593*s*, 1478*m*, 1421*m*, 1387*s*, 1333*s*, 1269*w*, 1205*m*, 1151*w*, 1072*m*, 1017*m*, 1000*s*, 995*m*, 789*s*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 6.46 (br. *s*, H_2N–C(4)); 5.64 (br. *s*, H_2N–C(2)); 4.01–3.96 (*m*, H_a–C(9)); 3.68 (*td*, $J \approx 10.6, 4.8$, H_b–C(9)); 2.87 (narrow *AB*, 2 H–C(6)); 2.59–2.46 (*m*, H–C(7), 2 H–C(2′), 2 H–C(6′)); 2.18–2.08 (*m*, 1 H); 2.00–1.85 (*m*, 1 H); 1.55–1.35 (*m*, 6 H). ^{13}C-NMR (75 MHz, (D_6)DMSO): 159.16 (*s*, C(4)); 154.61 (*s*, C(2)); 151.41 (*s*, C(10a)); 144.33 (*s*, C(5a)); 112.05 (*s*, C(4a)); 57.85 (*d*, C(7)); 49.64 (*t*, C(2′), C(6′)); 27.56 (*t*, C(8)); 25.85 (*t*, C(3′), C(5′)); 24.34 (*t*, C(4′)); signals for C(6) and C(9) hidden by the solvent signals. HR-MALDI-MS: 288.1930 (100, $[M+H]^+$, $C_{14}H_{22}N_7^+$; calc. 288.1937).

*Ethyl (±)-2,4-Diamino-6,7,8,9-tetrahydropyrido[1,2-*e*]purine-7-carboxylate* ((±)-**29**). Yield: 92%. R_f (CH_2Cl_2/MeOH 5:1) 0.32. M.p. 279°. IR (ATR): 3421*m*, 3300*w*, 3180*s*, 2989*w*, 1714*s*, 1645*w*, 1628*m*, 1590*s*, 1526*w*, 1470*s*, 1436*m*, 1422*s*, 1391*s*, 1369*m*, 1331*s*, 1294*m*, 1254*s*, 1209*m*, 1122*w*, 1071*w*, 1036*m*, 1017*w*, 936*w*, 904*m*, 871*m*, 847*w*, 790*s*, 775*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 6.52 (br. *s*, H_2N–C(4)); 5.68 (br. *s*, H_2N–C(2)); 4.13 (*q*, *J* = 6.9, OCH_2Me)); 4.00–3.90 (*m*, H_a–C(9)); 3.90–3.75 (*m*, H_b–C(9)); 3.07–2.88 (*m*, 2 H–C(6), H–C(7)); 2.33–2.29 (*m*, H_a–C(8)); 2.09–2.03 (*m*, H_b–C(8)); 1.21 (*t*, *J* = 7.1, OCH_2Me). ^{13}C-NMR (75 MHz, (D_6)DMSO): 172.63 (*s*, C=O); 159.22 (*s*, C(4)); 154.71 (*s*, C(2)); 151.45 (*s*, C(10a)); 142.78 (*s*, C(5a)); 111.96 (*s*, C(4a)); 60.33 (*t*, OCH_2Me); 40.13 (*t*, C(9)); 36.94 (*d*, C(7)); 27.08, 24.80 (2*t*, C(6), C(8)); 14.14 (*q*, OCH_2Me). HR-MALDI-MS: 277.1405 (100, $[M+H]^+$, $C_{12}H_{17}N_6O_2^+$; calc. 277.1413).

*8,9-Dihydro-6*H*-[1,4]oxazino[4,3-*e*]purine-2,4-diamine* (**30**). Yield: 85%. R_f (CH_2Cl_2/MeOH 10:1) 0.29. M.p. 362°. IR (ATR): 3384*w*, 3223*s*, 3173*s*, 2957*w*, 2884*w*, 2843*w*, 1638*m*, 1585*s*, 1464*s*, 1421*s*, 1393*s*, 1337*s*, 1291*w*, 1262*w*, 1221*w*, 1147*w*, 1107*m*, 1092*s*, 1024*w*, 1000*w*, 974*s*, 946*m*, 872*m*, 858*m*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 6.59 (br. *s*, H_2N–C(4)); 5.77 (br. *s*, H_2N–C(2)); 4.78 (*s*, 2 H–C(6)); 4.05 (br. *t*, *J* = 5.4, 2 H–C(8)); 3.92 (br. *t*, *J* = 5.1, 2 H–C(9)). ^{13}C-NMR (75 MHz, (D_6)DMSO): 159.04 (*s*, C(4)); 154.76 (*s*, C(2)); 151.15 (*s*, C(10a)); 141.69 (*s*, C(5a)); 109.95 (*s*, C(4a)); 78.63 (*t*, C(6)); 64.23 (*t*, C(8)); 63.17 (*t*, C(9)). HR-MALDI-MS: 207.0993 (100, $[M+H]^+$, $C_8H_{11}N_6O^+$; calc. 207.0994).

*Ethyl 2,6-Diamino-9-(2-ethoxy-2-oxoethyl)-9*H*-purine-8-carboxylate* (**31**). Yield: 96%. R_f (CH_2Cl_2/MeOH 5:1) 0.51. M.p. 224°. IR (ATR): 3421*m*, 3300*m*, 3180*s*, 2923*s*, 2853*w*, 1714*s*, 1645*m*, 1628*m*, 1590*s*, 1469*s*, 1435*m*, 1422*s*, 1391*s*, 1369*m*, 1331*m*, 1294*m*, 1254*s*, 1208*s*, 1122*w*, 1071*m*, 1036*s*, 1016*w*, 981*w*, 936*w*, 905*m*, 870*w*, 828*w*, 790*s*, 775*m*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 6.24 (br. *s*, H_2N–C(6)); 5.64 (br. *s*, H_2N–C(2)); 5.04 (*s*, NCH_2); 4.29, 4.15 (2*q*, *J* = 7.1, 2 OCH_2Me); 1.29, 1.20 (2*t*, *J* = 7.2, 2 OCH_2Me). ^{13}C-NMR (75 MHz, (D_6)DMSO): 167.47, 161.41 (2*s*, 2 C=O); 158.54 (*s*, C(6)); 156.96 (*s*, C(2)); 152.57 (*s*, C(4)); 133.85 (*s*, C(8)); 113.01 (*s*, C(5)); 61.61, 61.13 (2*t*, 2 OCH_2Me); 44.55 (*t*, NCH_2); 14.12 (*q*, 2 OCH_2Me). HR-MALDI-MS: 309.1309 (100, $[M+H]^+$, $C_{12}H_{17}N_6O_4^+$; calc. 309.1311).

*7,8-Dihydro-6-phenyl-6*H*-imidazo[1,2-*e*]purine-2,4-diamine* (**32**). Yield: 94%. R_f (CH_2Cl_2/MeOH 5:1) 0.70. M.p. 196°. IR (ATR): 3313*m*, 3161*s*, 1614*m*, 1592*s*, 1506*s*, 1456*w*, 1409*s*, 1330*s*, 1249*m*, 1136*w*, 1019*m*, 955*w*, 883*w*, 782*m*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 7.75 (*d*, *J* = 7.8, H–C(2′), H–C(6′)); 7.36 (*t*, *J* = 7.2, H–C(3′), H–C(5′)); 6.96 (*t*, *J* = 7.2, H–C(4′)); 6.20 (br. *s*, H_2N–C(4)); 5.59 (br. *s*, H_2N–C(2)); 4.46, 4.19 (2*dd*, *J* = 9.6, 6.3, 2 H–C(7), 2 H–C(8)). ^{13}C-NMR (75 MHz, (D_6)DMSO): 158.28 (*s*, C(4)); 152.96 (*s*, C(2)); 150.37 (*s*, C(9a)); 149.14 (*s*, C(1′)); 139.88 (*s*, C(5a)); 128.28 (*d*, C(3′), C(5′)); 120.02 (*d*, C(4′));

114.43 (*d*, C(2′), C(6′)); 111.71 (*s*, C(4a)); 50.44, 48.53 (2*t*, C(7), C(8)). HR-MALDI-MS: 268.1198 (100, $[M+H]^+$, $C_{13}H_{14}N_7^+$; calc. 268.1311).

Diethyl 1,1′-(2-Amino-5-nitrosopyrimidine-4,6-diyl)dipiperidine-4-carboxylate (**37**). A suspension of *2-amino-4,6-dimethoxy-5-nitrosopyrimidine* (**33**; 250 mg, 1.36 mmol) in EtOH (3 ml) was treated with ethyl isonipecotate (412 µl, 2.72 mmol) and stirred at r.t. for 2 h until TLC and LC/MS showed disappearance of the starting material. After evaporation, the residue was suspended in Et_2O. The precipitate was filtered off, washed with Et_2O, and dried under vacuum to afford **37** (512 mg, 85%). Dark violet powder. R_f (CH_2Cl_2/MeOH 9:1) 0.43. M.p. 98°. IR (ATR): 3325*w*, 3186*w*, 2936*m*, 2865*w*, 1722*s*, 1628*m*, 1556*w*, 1511*s*, 1442*s*, 1373*m*, 1316*s*, 1271*s*, 1202*s*, 1154*s*, 1109*w*, 1095*w*, 1034*s*, 995*s*, 936*m*, 889*w*, 859*m*, 832*w*, 797*m*, 766*m*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 7.93 (br. *s*, H_2N–C(2)); 4.08 (*q*, *J* = 7.2, 2 OCH_2Me); 2.98 (br. *t*, *J* = 9.9, 4 H–C(2′), 4 H–C(6′)); 2.76–2.65 (*m*, 2 H–C(4′)); 1.97–1.17 (*m*, 4 H–C(3′), 4 H–C(5′)); 1.14 (*t*, *J* = 7.2, 2 OCH$_2$*Me*). ^{13}C-NMR (75 MHz, (D_6)DMSO): 173.35 (*s*, 2 C=O); 165.00 (*s*, C(2)); 161.63, 150.28 (2*s*, C(4), C(6)); 140.15 (*s*, C(5)); 59.89 (*t*, 2 O*C*H$_2$Me); 49.88 (*t*, 2 C(2′), 2 C(6′)); 42.81 (*t*, 2 C(4′)); 27.67 (*t*, 2 C(3′), 2 C(5′)); 14.67 (*q*, 2 OCH$_2$*Me*). HR-MALDI-MS: 435.2350 (100, $[M+H]^+$, $C_{20}H_{31}N_6O_5^+$; calc. 435.2356), 417.2244 (13, $[M-OH]^+$, $C_{20}H_{29}N_6O_4^+$; calc. 417.2250), 404.2289 (43, $[M-NO]^+$, $C_{20}H_{30}N_5O_4^+$; calc. 404.2298).

General Procedure for the Denitrosation of the 4,6-Bis(dialkylamino)-5-nitrosopyrimidines **34**–**37** (*GP 3*). A suspension of the nitroso amines **34**–**37** in Ph_2O (1 ml) was heated to 210°. Progress of the reaction was monitored by LC/MS. After a few min of heating, a new peak corresponding to the loss of the NO group was formed in all cases. Upon continued heating, LC/MS analysis showed the progressive disappearance of starting material, and, as based on the mass, formation of denitrosated products. Purification by flash column chromatography (pentane for removal of Ph_2O, then MeCN/EtOH 1:2 to 1:1) gave **38**–**41**.

4,6-Di(morpholin-4-yl)pyrimidin-2-amine (**40**). Morpholine (135 µl, 1.53 mmol) was added dropwise at r.t. to a suspension of NaH (60% dispersion in oil, 58 mg, 1.52 mmol) in DMSO (5 ml), and the mixture was stirred for 15 min. 2-Amino-4,6-dichloropyrimidine (100 mg, 0.61 mmol) was added, and the mixture was heated at 80° for 3 h. Progress of the reaction was monitored by LC/MS. After 40 min, LC/MS showed two peaks, corresponding to starting material and to the product of monosubstitution. Heating was continued until consumption of starting material. After cooling, MeOH was added, morpholine was removed *in vacuo*, and the residue was extracted with CH_2Cl_2. Evaporation of the solvent and purification by flash column chromatography (CH_2Cl_2) provided **40** (113 mg, 70%). R_f (CH_2Cl_2/MeOH 9:1) 0.60. ^{1}H-NMR (300 MHz, $CDCl_3$): 5.13 (*s*, H–C(5)); 4.50 (br. *s*, H_2N–C(2)); 3.73 (br. *s*, 4 H–C(2′), 4 H–C(6′)); 3.48 (br. *s*, 4 H–C(3′), 4 H–C(5′)). ^{13}C-NMR (75 MHz, $CDCl_3$): 163.99 (2*s*, C(4), C(6)); 161.61 (*s*, C(2)); 73.13 (*s*, C(5)); 65.85 (2*t*, 2 C(2′), 2 C(6′)); 44.25 (2*t*, 2 C(3′), 2 C(5′)).

Diethyl 1,1′-(2-Aminopyrimidine-4,6-diyl)dipiperidine-4-carboxylate (**41**). Prepared according to *GP 3* (15 min at 210°). Yield: 75%. R_f (CH_2Cl_2/MeOH 9:1) 0.64. ^{1}H-NMR (300 MHz, $CDCl_3$): 5.60 (br. *s*, H_2N–C(2)); 5.20 (*s*, H–C(5)); 3.74 (*q*, *J* = 7.1, 2 OCH_2Me); 2.92 (br. *t*, *J* = 11.1, 4 H–C(2′), 4 H–C(6′)); 2.65–2.46 (*m*, 4 H–C(3′), 4 H–C(5′)); 1.15 (*t*, *J* = 7.1, 2 OCH$_2$*Me*). ^{13}C-NMR (75 MHz, $CDCl_3$): 174.63 (*s*, 2 C=O); 164.24 (*s*, C(2)); 160.80 (2*s*, C(4), C(6)); 74.10 (*s*, C(5)); 60.74 (*t*, 2 O*C*H$_2$Me)); 44.02, 41.40 (2*t*, 2 C(2′), 2 C(6′)); 29.70, 27.70 (2*t*, 2 C(3′), 2 C(5′)); 14.22 (*q*, 2 OCH$_2$*Me*).

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