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# Electrophilic Amination of Pyrimidine-2-thiones - Synthesis of Zwitterionic 2-Aminothiopyrimidinium-N-ylides, Pyrimidine-2-ones and Bicyclic Pyrimidinium Compounds

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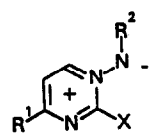
**Abstract:** 1-Amino-pyrimidine-2-thiones **2** or **11** and 1-acylmethyl-pyrimidine-2-thiones **13** react with 3,3-pentamethyleneoxaziridine **3** or hydroxylamine-O-sulfonic acid by electrophilic amination of the sulfur atom yielding zwitterionic 2-amino-1-imidothiopyrimidinium-N-ylides **4** and **12** or 1-aminopyrimidine-2-ones **5** and 1-acylmethylpyrimidine-2-ones **14**. The pyrimidine-2-ones **5** and **14** can be cyclized by dehydration to 1,3,4-oxadiazolo[3,2-a]pyrimidinium salts **6** and oxazolo[3,2-a]pyrimidinium salts **15**.

## Introduction

Earlier studies[1] conducted by our group involved 1-aminopyrimidine-2-hydrazones having a deep purple or violet color that might be attributed to the formation of zwitterionic 1-amido-2-hydrazinopyrimidinium ylides **1** (X = $NHNH_2$, $R^2$ = aryl or acyl). We wished to test this hypothesis by the synthesis of structurally related S-analogous compounds **4** and **12** [**1** (X = $SNH_2$)] in order to examine their absorption behavior. 1-Amido-3-aminothio-pyrimidinium ylides **4** are generally unknown. A possible route to ylides of structure **4** is the deprotonation of corresponding 1-amino-3-aminothiopyrimidinium salts, which might be available by electrophilic amination of pyrimidine-2-thiones **2** or **11** with pentamethyleneoxaziridine. The latter is reported[2] to aminate thiouracils that do not form ylides, but instead either neutral pyrimidines (through deprotonation of a ring nitrogen atom) or benzylideneaminothiopyrimidinones.

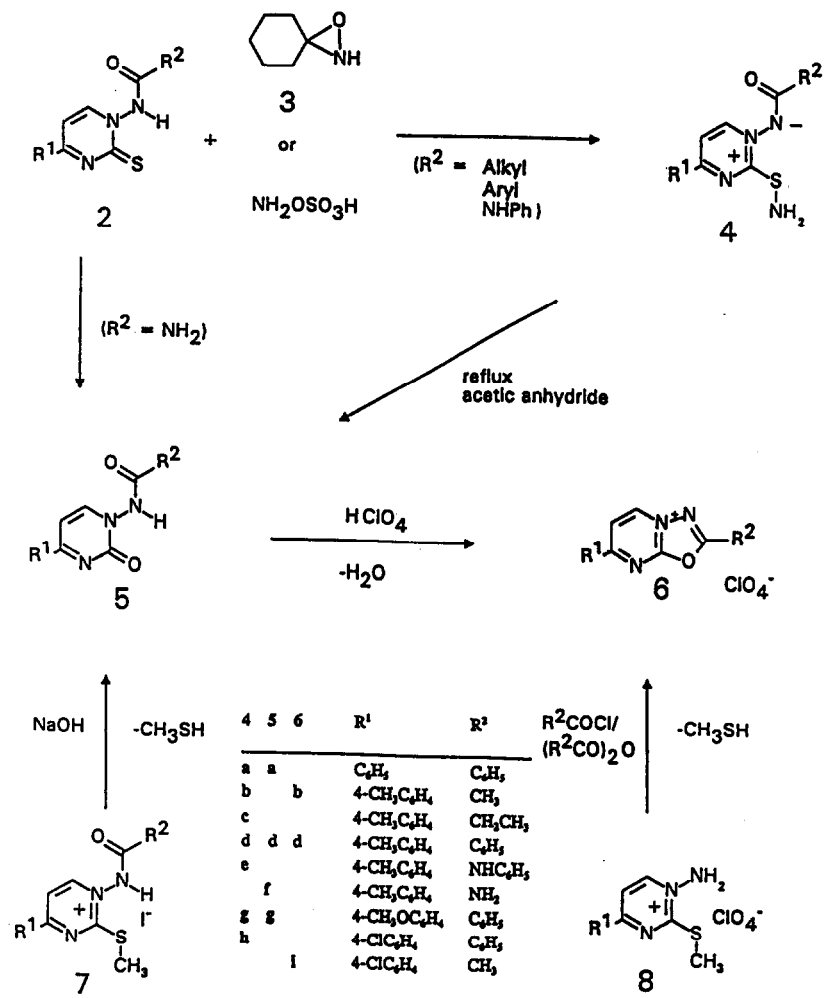



**1**

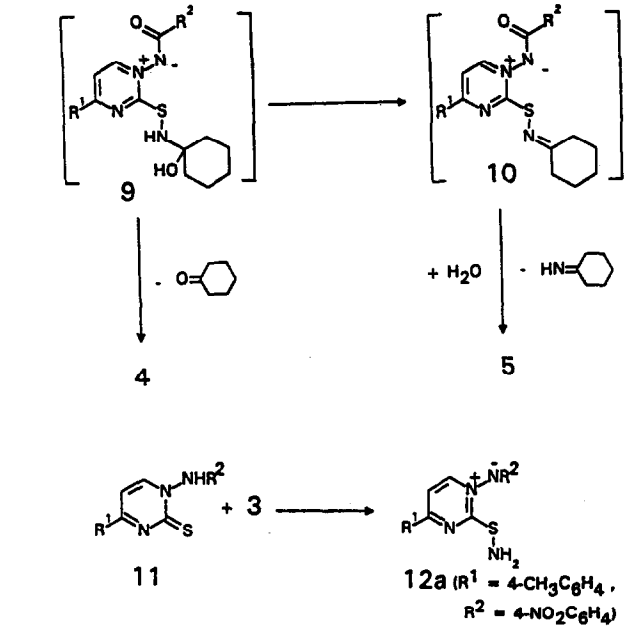
Another goal of our investigation was to carry out the quantum chemical calculation of the anticipated 1-amido-3-aminothiopyrimidinium ylide moiety (in **4**).

**Results and Discussion**

*Synthesis*. Reacting 3,3-pentamethyleneoxaziridine **3** or hydroxylamine-O-sulfonic acid with 1-acylamino or 1-phenylureido-pyrimidine-2-thiones **2** ($R^2$ = aryl, alkyl or anilino) at room temperature produces the target products **4** in a clean reaction. Intermediates (e. g. **9** or 2-aminothiopyrimidinium salts) were not isolated. This transformation was extended to 1-arylamino substituted pyrimidine-2-thiones **11** giving 2-amino-1-arylimidothiopyrimidinium-N-ylides **12**. The structure of the N-ylide **4d** in solid state was examined by X-ray analysis. The pyrimidine ring (see Figure 1) is nearly planar (mean deviation 0.4 pm); the exocyclic heteroatoms S and N1 are located 6 and 14 pm, respectively, outside the ring plane. The bond length N2-C8 (136.1 pm) between position 1 and 2 of the ring corresponds to some double bond character. The N1-N2 bond length (139.8 pm) is similar to the value (141.3) in a known 1-aminopyrimidine-2-imine[4] lies between the values for N-N single and double bonds.




| 4 | 5 | 6 | $R^1$ | $R^2$ |
|---|---|---|---|---|
| a | a | | $C_6H_5$ | $C_6H_5$ |
| b | | b | 4-$CH_3C_6H_4$ | $CH_3$ |
| c | | | 4-$CH_3C_6H_4$ | $CH_2CH_3$ |
| d | d | d | 4-$CH_3C_6H_4$ | $C_6H_5$ |
| e | | | 4-$CH_3C_6H_4$ | $NHC_6H_5$ |
| | f | | 4-$CH_3C_6H_4$ | $NH_2$ |
| g | g | | 4-$CH_3OC_6H_4$ | $C_6H_5$ |
| h | | | 4-$ClC_6H_4$ | $C_6H_5$ |
| | | I | 4-$ClC_6H_4$ | $CH_3$ |



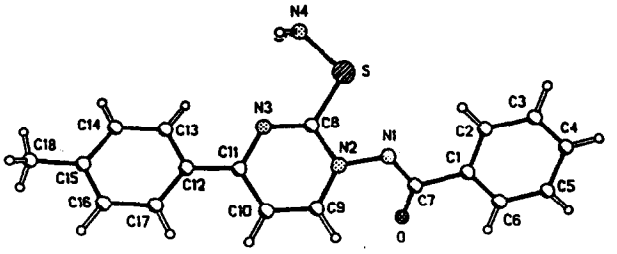




Fig. 1: Molecular structure of the N-ylide 4d[3]

The $NH_2$ group does not appear to be involved in strong hydrogen bonding; the short non-bonded contacts N4...N3 286 pm (intramolecular) and N4...N1 (1-x, 1-y, 1-z) 312 pm may correspond to weak hydrogen bonds.

The $^1H$ and $^{13}C$-NMR spectroscopic data (see Table 2) also correspond to structures **4** and **12**. The pale yellow color of 2-aminothio-1-imidopyrimidinium ylides **4** and **12** differs from the deep violet or purple color observed in the assumed 1-amido-2-hydrazinopyrimidinium-N-ylides **1** (X = $NH_2$)[1], thus not supporting the proposed structure of the latter compounds.

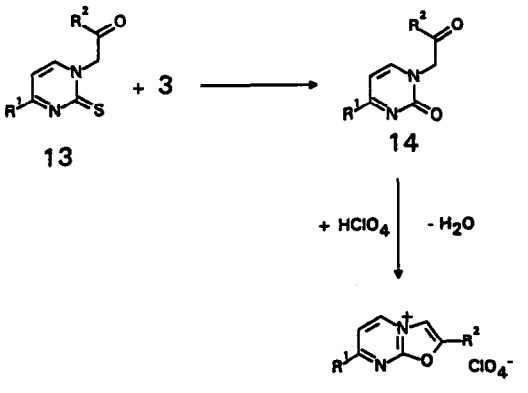
When the 1-ureidopyrimidine-2-thione **2** ($R^1$ = 4-$CH_3C_6H_4$, $R_2$ = $NH_2$) was treated with 3,3-pentamethyleneoxaziridine **3**, the 1-ureido-pyrimidine-2-one **5f** was isolated instead of the S-amination product **4**. The formation of this product can be explained via a similar intermediate **9**, which loses water rather

than cyclohexanone (formation of **4**). The water hydrolyzes the resulting 2-cyclohexylidenaminothiopyrimidinium-N-ylide **10**.

We further explored the possibility of cyclizing the 1-acylamido-2-aminothiopyrimidinium ylides **4** to condensed pyrimidines. Since facile dehydration occurs in the mass spectrometer (electron impact) giving [$M^+ - H_2O$] rather than the molecular ion in a number of cases (see Table 2), preparative dehydration was attempted. The desired pyrimido[1,2-e]1,2,4,5-thiatriazinium salts, however, could not be synthesized. Compounds **4**, when melted or heated in PPA, yielded complex mixtures of decomposition products. Heating in acetic anhydride surprisingly provides the 1-acylamino-pyrimidine-2-ones **5** by exchanging the aminothio group for oxygen, a formal hydrolysis. It is possible that a nucleophilic attack of the amino nitrogen atom of **4** on acetic anhydride is involved, since acetamide is an expected by-product (TLC).

The structure of 2-acylaminopyrimidine-2-ones **5** could be demonstrated by spectroscopic data (see Table 2) and by an independent synthesis, viz. hydrolysis of the corresponding 1-amino-2-methylthiopyrimidinium salt **7**[1]. When the 1-acylamido-2-aminothiopyrimidinium-N-ylide **4d** was treated with a mixture of acetic anhydride and perchloric acid, 1,3,4-oxadiazolo[3,2-a]pyrimidinium perchlorate **6d** was obtained (method E) rather than the corresponding pyrimidine-2-one **5d**. Since isolated 1-acylaminopyrimidine-2-one **5d** also gave 1,3,4-oxadiazolo[3,2-a]pyrimidinium perchlorate **6d** under these conditions, the former can be expected to be an intermediate in the synthesis starting from **4**. 1,3,4-Oxadiazolo[3,2-a]-pyrimidinium salts **6** can independently be synthesized by refluxing 1-amino-2-methylthiopyrimidinium iodides **8**[5] with acetic anhydride/acetyl chloride (method F). Known syntheses of the 1,3,4-oxadiazolo[3,2-a]pyrimidine system are usually based on a final assembly of the pyrimidine ring rather than the oxadiazole ring[6].

In reactions of 3,3-pentamethyleneoxaziridine **3** with 1-acylmethyl-pyrimidine-2-thiones **13**, which are C-analogues of **2**, no S-amination products could be isolated, but only 1-acylmethyl-pyrimidine-2-ones **4**. Obviously these products were formed in a similar manner to the pyrimidine-2-ones **5**. 1-Phenacyl-pyrimidine-2-one **14b** could be dehydrated with acetic anhydride/perchloric acid giving the oxazolo[3,2-a]pyrimidinium perchlorate **15**. This product was identical with the compound prepared earlier[7] starting from 2-methylthio-1-phenacyl-pyrimidinium iodide by elimination of methylthiol in the presence of pyridine.




13 14 15

The above-mentioned results demonstrate that pentamethyleneoxaziridine or hydroxylamine-O-sulfonic acid are able to S-aminate 1-aminopyrimidine-2-thiones that cannot be stabilized by deprotonation of a ring NH group as was known for thiouracils. The expected 1-amino-2-aminothiopyrimidinium salts cannot be isolated but react further to provide either 1-amido-2-aminothiopyrimidinium N-ylides by deprotonation of the NH substituent attached to position 1, or pyrimidine-2-ones by hydrolysis.

*Quantum Chemical Studies on N-Ylides of Type 4.* The parent system of **4d** is an ylide of typ **A**. Ab initio calculations[8,9] (HF/4-31G) reveal that there are at least 4 different rotamers (**A-D**) with E(**A**) < E(**C**)< E(**B**) < E**D**); the results of PM3[10,11] are at variance with these data (see Table 4, $\Delta H_f$(**C**) < $\Delta H_f$(**A**) < $\Delta H_f$(**D**) < $H_f$(**B**)), but it should be borne in mind that $\Delta\Delta H_f$(**A-C**) is quite small (4.6 kcal/mol). Interestingly, annelation of an aromatic ring does not change this sequence considerably: With a 3-21G basis conformer **E** is most stable compared with **F**, **G**, and **H**. A similar result is obtained with PM3; $\Delta\Delta H_f$(**E-G**)(PM3) is of course insignificant. The potential hypersurface $\Delta H_f$(PM3) = $\Delta H_f(\Theta_1, \Theta_2)$ with $0 \leq \Theta_1 \leq 180°$ and $180° \leq \Theta_2 \leq 360°$ ($\Theta_1$ = Θ(1-2-3-4), Θ(4-5-6-7) is shown in Fig. 2 (56 data points, polynomial interpolation). For obvious reasons no detailed ab initio investigations have been undertaken

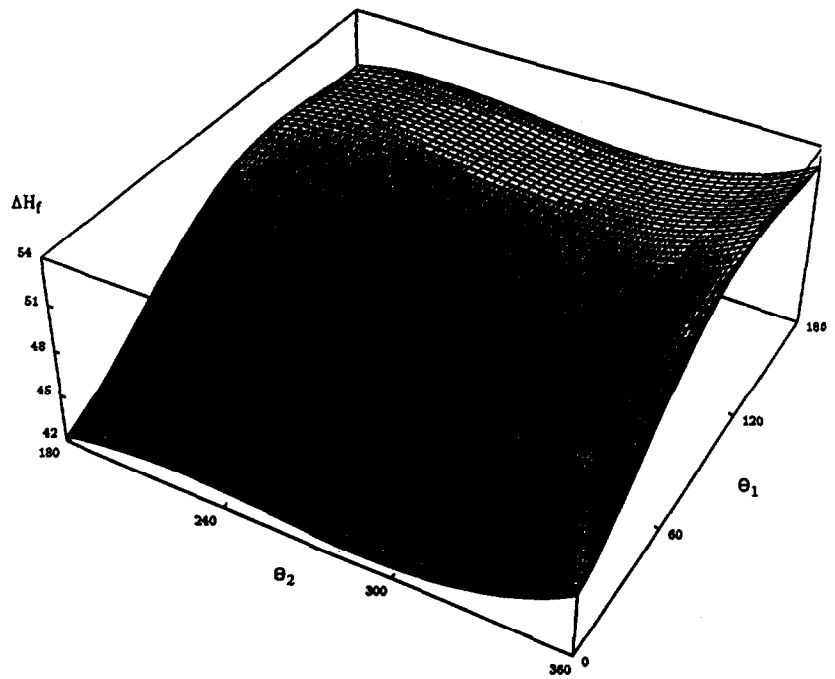
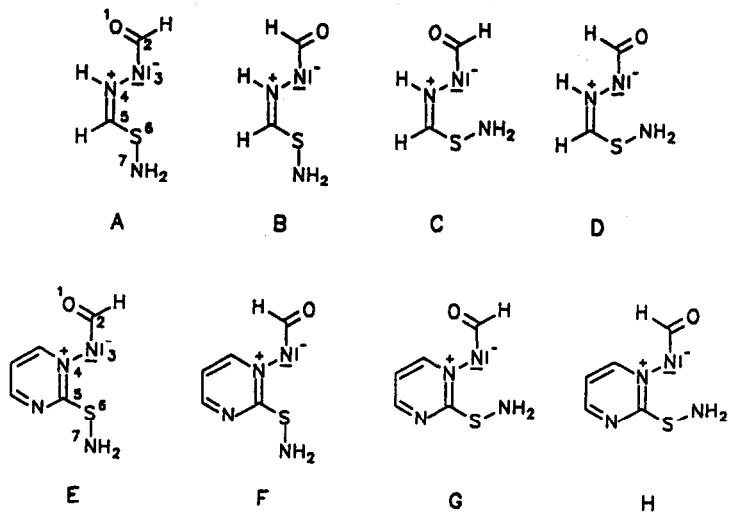
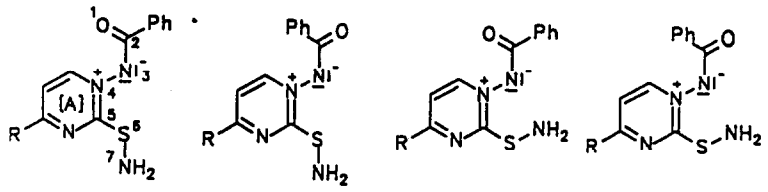



Fig. 2: Potential hypersurface of **E** (PM3 values; $\Theta_1$ = Θ(1-2-3-4), $\Theta_2$ = Θ(4-5-6-7); polynomial interpolation

for **4d**. Semiempirical calculations again reveal that there are at least 4 different rotamers on the energy hypersurface (**I** (Fig. 3), **J** (Fig. 4), **K** (Fig. 5), and **L** (Fig. 6)) with **I** and **J** of comparable stability. But as ab initio results on the model compounds **A** and **D** have shown (vide supra) the PM3 calculations probably overestimate the thermodynamic stability of **D** (= **H** = **L**). As shown above both ab initio and semiempirical energies (enthalpies) differ considerably for different rotamers as do calculated rotational barriers. In Fig. 7 the rotational barrier for **A** (ab initio values with a 4-31G basis, fully optimized; $0 \leq \Theta(1\text{-}2\text{-}3\text{-}4) \leq 180°$ is drawn; a value of $\Delta E = 34.4$ kcal/mol is obtained. Single point calculations with extended basis sets (Table 5) do not alter this result considerably. In contrast to these data PM3 yields (Fig. 8, Table 5) $\Delta\Delta H_f = 11.0$ kcal/mol, which seems to be more reliable. The rotational barrier for **E** ($0 \leq \Theta(1\text{-}2\text{-}3\text{-}4) \leq 180°$) resembles this value quite closely (Fig. 9, $\Delta\Delta H_f = 8.6$ kcal/mol). In conclusion it may be remarked that the preferred occurrence of a rotamer of type **A** (**E**, **I**) is in accord with the X-ray investigation an **4d**. These X-ray results make it possible to compare geometrical data (bond lengths, bond angles) with those calculated for **A**, **E**, and **I**. The main points are as follows: On the ab initio level the model system **A** seems to be unsuitable when $r(4\text{-}5)_{calc}$ amd $r(4\text{-}5)_{obs}$ (for **4d**) are compared. The reason is obvious; the anellation of a benzenoid ring casts off this disagreement. On the 3-21G level there is a slight difference between $r(6\text{-}7)_{calc}$ and $r(6\text{-}7)_{obs}$. PM3 calculations lead to a very short N(3)-N(4)-distance as do the AM1 and MNDO models: the variation of $\Delta H_f$with r(3-4) is remarkable (Fig. 10; AM1 data; $\Delta\Delta H_f = \Delta H_f$ (1.398 Å) - $\Delta H_f$(min) = 3.3 kcal/mol). On the AM1 level an S-N distance (r(6-7)) of 1.639 Å is obtained, but the variation of $\Delta H_f$ with r(6-7) in this region ($\Delta\Delta H_f = \Delta H_f$(1.682 Å) - $\Delta H_f$(1.636 Å)) amounts to only 0.9 kcal/mol. Obviously calculated bond lengths of the ylides (and of other dipolar compounds)[12] should be treated with some caution.





4

I J K L

R=(4-$CH_3$)$C_6H_4$

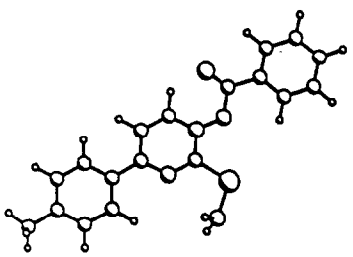


Fig.3: Calculated structure of I (PM3)

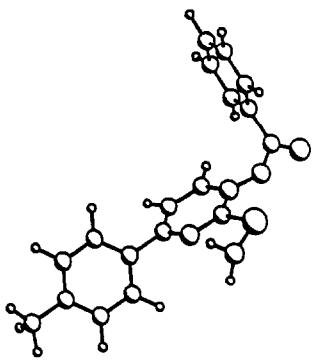


Fig.4: Calculated structure of J (PM3)

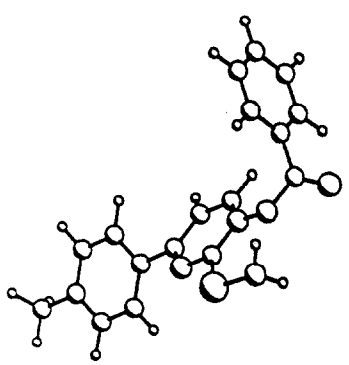


Fig.5: Calculated structure of K (PM3)

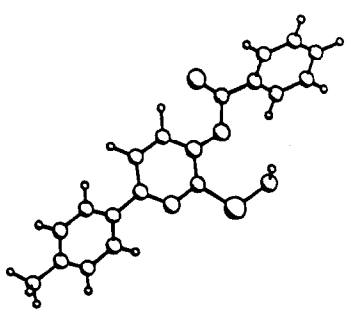


Fig.6: Calculated structure of L (PM3)

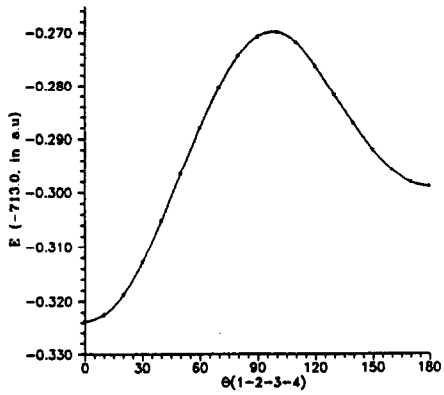



Fig.7: Variation of E(a.u.) with Θ(1-2-3-4) for A (ab initio values with a 4-31G basis, spline interpolation)

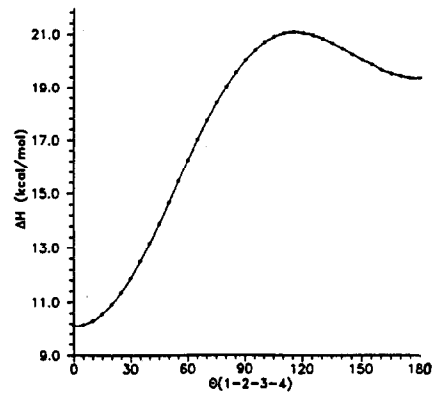



Fig.8: Variation of $\Delta H_f$ with Θ(1-2-3-4) for A (PM3, spline interpolation)

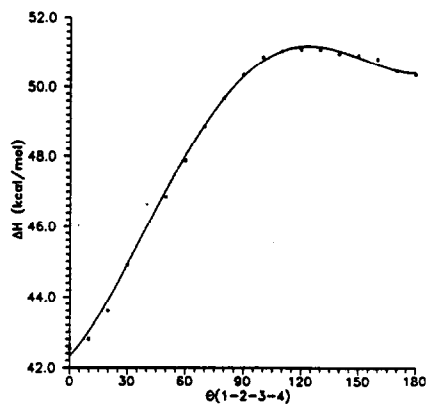



Fig.9: Variation of $\Delta H_f$ with Θ(1-2-3-4) for E (PM3, polynomial approximation of 4th order)

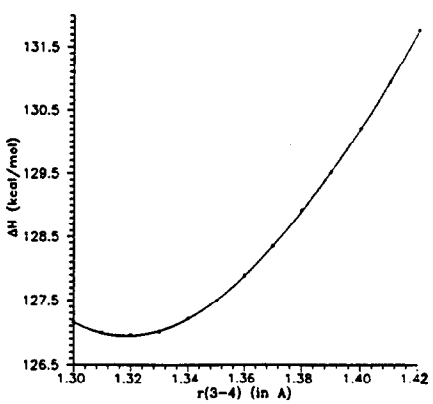



Fig.10: Variation of $\Delta H_f$ with r(3-4) for 4d (rotamer 1, polynomial approximation of 3rd order)

Table 1: 1-Acylimido-2-aminothiopyrimidinium-N-ylides 4, 1-Acylaminopyrimidine-2-ones 5, 1,3,4-Oxadiazolo[3,2-a]pyrimidinium Salts 6 and 2-Aminothio-1-(4-nitrophenylimido)-pyrimidinium-N-ylide 12, 1-Acylmethylpyrimidine-2-ones 14 and Oxazolo[3,2-a]pyrimidinium Salts 15

| | Yield [%]/ Method | m.p. [°C] | Molecular formula Elemental analysis Calcd. C H N Found | $^1$H-NMR (DMSO-$d_6$) |
|---|---|---|---|---|
| 4a | 71/A | 140-143 (toluene) | $C_{17}H_{14}N_4OS$ (322.4) 63.34 4.38 17.38 63.36 4.41 17.18 | 7.17 - 7.65 (m, 5H, $C_6H_5$); 7.68 - 7.97 (m, 5H, $C_6H_5$); 8.08 (d, J = 7.1 Hz, 1H, NCCH); 8.38 (d, J = 7.1 Hz, 1H, CHN) |
| 4b[a] | 78/A | 192-195 (toluene) | $C_{13}H_{14}N_4OS$ (274.3) 56.92 5.14 20.42 | 2.05 (s, 3H, $CH_3CO$); 2.35 (s, 3H, $CH_3$phenyl); 7.05 - 7.36 (m, 2H, $C_6H_4$); 7.49 (d, J = 7.1 Hz, |

| | | | | |
|---|---|---|---|---|
| | | | 57.00 5.17 20.14 | 1H, CHCN); 8.00 - 8.17 (m, 2H, $C_6H_4$); 8.40 (d, J = 7.1 Hz, 1H, CHN); 11.67 (s, 2H, $NH_2$) |
| 4c | 86/A | 143-145 (toluene) | $C_{14}H_{16}N_4OS$ (288.4) 58.31 5.59 19.43 58.33 5.64 19.55 | 1.12 (t, J = 7.3 Hz, 3H, $\underline{CH_3}CH_2$); 2.11 (q, J = 6.9 Hz, 2H, $CH_3\underline{CH_2}$); 2.48 (s, 3H, $CH_3$phenyl); 7.42 (d, J = 8Hz, 2H, $C_6H_4$); 8.05 (d, J = 6.9 Hz, 1H, CHCN); 8.32 (d, J = 8 Hz, $C_6H_4$); 9.13(d, J = 6.9 Hz, 1H, CHN) |
| 4d[b] | 77/A 61/B | 180-182 (aceto-nitrile) | $C_{18}H_{16}N_4OS$ (336.4) 64.27 4.79 16.65 64.32 4.76 16.72 | 2.48 (s, 3H, $CH_3$); 7.40 (m, 2H, $C_6H_4$); 7.52-7.60 (m, 3H, $C_6H_5$); 8.07 (m, 2H, $C_6H_4$); 8.15 (d, J = 6.9 Hz, 1H, CHCN); 8.18 (m, 2H, $C_6H_5$); 9.44 (d, J = 6.9 Hz, 1H, CHN); 12.34 (s, 2H, $NH_2$) |
| 4e | 69/A | 200-202 (aceto-nitrile) | $C_{18}H_{17}N_3OS$ (351.4) 61.52 4.88 19.93 61.45 4.80 19.96 | 3.34 (s, 3H, $CH_3$); 7.25 - 7.60 (m, 5H, $C_6H_5$); 8.15 (d, J = 7.1 Hz, 1H, CHCN); 8.35 (m, 4H, $C_6H_4$); 9.4 (d, J = 7.1 Hz, 1H, CHN) |
| 4g[c] | 40/A | 160-162 (toluene) | $C_{18}H_{16}N_4O_2S$ (352.4) 61.35 4.58 15.90 61.10 4.54 15.70 | 2.48 (s, 3H, $CH_3$); 7.11 (m, 2H, $C_6H_4$); 7.38-7.47 (m, 3H, $C_6H_5$); 7.52-8.03 (m, 2H, $C_6H_4$); 8.10 (d, J = 6.9 Hz, 1H, HCN); 8.45 (m, 2H, $C_6H_5$); 9,36 (d, J = 6.9 Hz, 1H, CHN) |
| 4h | 51/A | 187-190 (aceto-nitrile) | $C_{17}H_{13}N_4OSCl$ (356.9) 57.22 3.67 15.70 57.86 3.45 16.40 | 7.5 (m, 3H, $C_6H_5$); 7.72 (m, 2H,$C_6H_4$); 7.9(m,2H, $C_6H_4$); 8.25 (d,1H,J=7 Hz,CHCN); 8.4(m,2H,$C_6H_5$); 8.86 (d, J = 7 Hz, 1H, CHN); 11.5(s,2H, $NH_2$) |
| 5a | 67/C | 167-169 (ethanol) | $C_{17}H_{13}N_3O_2$ (291.3) 70.09 4.50 14.42 69.94 4.29 14.37 | 7.17 (d, J = 7.09 Hz, 1H, CHN); 7.45 (m, 3H, $C_6H_5CO$); 7.56-7.6 (m, 3H, $C_6H_5$); 7.7-7.9 (m, 2H, $C_6H_5CO$); 8.03-8.18 (m, 2H, $C_6H_5$); 8.38 (d, J = 7.09 Hz, 1H, CHCN) |
| 5d[d] | 74/C 83/D | 282-283 (ethanol) | $C_{18}H_{15}N_3O_2$ (305.3) 70.81 4.95 13.76 70.88 4.98 13.57 | 2,48 (s, 3H, $CH_3$); 7.25 (d, J = 7.09 Hz, 1H, CHN); 7.39-7.45 (m, 3H, $C_6H_5$); 7.52 (m, 2H, $C_6H_4$); 7.63-7.69 (m, 2H,$C_6H_5$ ); 7.76-8.00 (m, 2H, $C_6H_4$); 8.58(d, J = 7.2 Hz, 1H, CHN) |
| 5f[e] | 93/A | 209-211 (aceto-nitrile) | $C_{12}H_{12}N_4O_2$ (244.2) 59.01 4.95 22.94 59.04 5.15 23.05 | 2.49 (s, 3H, $CH_3$); 6.84 (s, 2H, $NH_2$); 7.48 (d, J = 7.3 Hz, 1H, CHCN); 8.04 (m, 2H, $C_6H_4$); 8.14 -8.36 (m, 2H,$C_6H_4$); 8.40 (d, J=6.9 Hz, 1H, CHN) |
| 5g[f] | 82/D | 254-255 (ethanol) | $C_{18}H_{15}N_3O_3$ (321.3) 67.28 4.70 13.08 67.15 4.87 13.17 | 3.38 (s, 3H, $CH_3O$); 7.14 (d, J = 7.1Hz,1H,CHN) 7.55 (m, 3H,$C_6H_5$); 7.59-7.66 (m, 2H,$C_6H_4$); 7.97-8.00 (m, 2H,$C_6H_5$); 8.19 (m, 2H,$C_6H_4$); 8.31 (d, J = 7.1 Hz, 1H, CHCN); 11.88 (s, 1H, NH) |

| | | | | |
|---|---|---|---|---|
| **6d**[h] | 96/E[i]<br>69/E[j] | 333-335<br>(acetan-<br>hydride)<br>319-320<br>(aceto-<br>nitrile) | $C_{18}H_{14}N_3O_5Cl$ (387.1)<br>55.75 3.64 10.84<br>55.97 3.58 10.71 | 2.51 (s, 3H, $CH_3$); 7.50-7.76 (m, 3H, $C_6H_5$); 7.82-7.87 (m, 2H, $C_6H_4$); 8.18-8.28 (m, 2H, $C_6H_5$); 8.41-8.52 (m, 2H, $C_6H_4$); 8.89 (d, J=7.28 Hz, 1H, CH); 10.20 (d, J = 7.28 Hz,1H, CHN) |
| **6i** | 32/F | 256-283[g]<br>(acetic<br>acid) | $C_{12}H_9Cl_2N_3O_5$ (346.1)<br>41.64 2.62 12.14<br>41.53 2.69 11.97 | 3.22 (s, 3H, $CH_3$); 8.05 (d, J = 8 Hz, 2H, $C_6H_4$), 8.75 (d, J = 8 Hz, 2H, $C_6H_4$), 9.16 (d, J = 7 Hz, 1H, CH), 10.40 (d, J = 7 Hz, 1H, CHN) |
| **12a**[b] | 98 | 233-235<br>(aceto-<br>nitrile) | $C_{17}H_{15}N_4O_2S$ (339.4)<br>60.16 4.46 16.51<br>60.21 4.37 16.51 | 2.38 (s, 3H, $CH_3$); 6.82 (m, 2H, $C_6H_4$); 7.37 (m, 2H, $C_6H_4$-$NO_2$); 7.61 (d, J = 7.1 Hz, 1H, CHCN); 8.10-8.15 (m, 4H, $C_6H_4$, $C_6H_4NO_2$); 8.64 (d, J = 7.1 Hz, 1H, CHN); 10.60 (s, 2H, $NH_2$) |
| **14a** | 70 | 209-210<br>(aceto-<br>nitrile) | $C_{18}H_{14}N_2O_2$ (290.3)<br>74.47 4.87 9.65<br>74.70 4.83 9.91 | 3.32 (s,2H,$CH_2$); 7.17 (d,J=6.9Hz,1H,CHCN);7.48-7.59(m,3H,$C_6H_5CO$);7.66(m,3H,$C_6H_5$),7.77(m,2H, $C_6H_5CO$);8.1(m,2H,$C_6H_5$),8.25(d,J=6.9Hz,1H,CHN) |
| **14b** | 68 | 268-270<br>(aceto-<br>nitrile) | $C_{19}H_{16}N_2O_2$ (304.4)<br>74.96 5.31 9.20<br>74.78 5.34 8.93 | 2.4 (s, 3H, $CH_3$), 3.30 (s, 2H, $CH_2$), 7.14 (d, J = 6.9 Hz, 1H, CHCN), 7.31 (m, 3H, $C_6H_5$), 7.41 - 7.59 (m, 2H, $C_6H_4$), 7.70 (m, 2H, $C_6H_5$), 8.00 (m, 2H, $C_6H_4$), 8.20 (d, J = 7.1 Hz, 1H, CHN) |
| **15b** | 76 | 255-257[l]<br>(ethanol) | | |

[a] $^{13}$C-NMR ([D$_6$]DMSO): 20.85, 21.11, 105.43, 128.28, 129.72, 131.76, 143.16, 152.16, 163.68, 168.81, 180.40; MS (70 eV) *m/z* (%): 256 ($M^+$-$H_2O$, 100), 224 (43), 201 (26), 185 (33), 184 (29), 116 (25), 115 (36), 91 (41), 65 (31),44 (46), 43 (57), 42 (25), 39 (31), 28 (26), 18 (46)

[b] $^{13}$C-NMR ([D$_6$]DMSO): 21.13, 105.63, 127.94, 128.37, 128.66, 129.77, 131.37, 131.75, 132.74, 143.28, 152.51, 163.86, 165.41, 180.81; MS (70 eV) *m/z* (%): 318 ($M^+$-$H_2O$, 100), 182 (15), 121 (19), 115 (19) 105 (67), 103 (21), 91 (24), 89 (16), 77 (79), 65 (20), 63 (18), 51 (28), 39 (16);
UV (acetonitrile) $\lambda_{max}$(nm) (log $\epsilon$): 290 (4.24), 390 (4.29)

[c] MS (70 eV) *m/z* (%): 334($M^+$-$H_2O$,42), 318(16), 200(21), 105(100), 91(26), 86(17), 77(65), 51 (27)

[d] $^{13}$C-NMR ([D$_6$]DMSO): 21.23, 100.73, 127.98, 128.14, 128.85, 129.75, 131.25, 132.85, 133.04, 142.77, 151.75, 153.82, 166.37, 170.99; MS (70 eV) *m/z* (%): 305 ($M^+$, 2), 226 (15), 184 (22), 105 (100), 77 (35), 43 (19). - [e] MS (70 eV) *m/z* (%): 244 ($M^+$, 16), 243 (100), 217 (46), 216 (25), 202 (30), 201 (55), 129 (85), 128 (39), 115 (28); UV (acetonitrile) $\lambda_{max}$(nm) (log $\epsilon$): 295 (4.37), 388 (3.26)

[f] $^{13}$C-NMR ([D$_6$]DMSO): 55.5, 100.29, 114.37, 127.71, 127.81, 128.72, 130.01, 131.22, 132.75, 151.30, 153.68, 162.82, 166.18; 170.18; MS (70 eV) *m/z* (%): 321 ($M^+$, 3), 200 (46), 105 (100), 77 (59), 51 (17);

[g] decomposition. - [h] $^{13}$C-NMR ([D$_6$]DMSO): 21.26, 101.08, 128.00, 128.39, 128.47, 130.30, 131.34, 132.11, 132.96, 143.37, 152.70, 163.49, 166.37, 170.69; MS (70 eV) *m/z* (%): 288 ($M^+$-$ClO_4$, 4), 201 (16), 200 (25), 105 (100), 77 (57), 51 (20), 44 (16), 40 (54); UV (acetonitrile) $\lambda_{max}$ (nm): 254, 354. - [i] starting from 5d

[j] starting from 4d. - [k] $^{13}$C-NMR ([D$_6$]DMSO): 21.13, 106.45, 112.94, 125.62, 128.42, 129.74, 131.72, 140.44, 143.28, 151.90, 152.72, 163.80, 180.52; MS (70 eV) *m/z* (%): 339 ($M^+$, 15), 338 (70), 305 (24), 259 (24), 202 (37), 201 (91), 169 (27), 143 (22), 142 (21), 118 (22), 117 (29), 116 (37), 115 (100), 91 (61), 90

(30), 89 (34), 65 (74), 64 (46), 63 (69), 52 (25), 51 (24), 39 (51), 30 (76); UV (acetonitrile) $\lambda_{max}$ (nm): 305 (4.58), 402 (3.59). - [D] Ref.[4] mp 255-258°C

Table 2: Calculated Bond Lengths, Bond Angles, and Dihedral Angles of A - L [Semiempirical (PM3, AM1, MINDO/3) and Ab Initio Values

| | A[a] | B[a] | C[a] | D[a] | E[b] | F[b] | G[b] | H[b] | I[c] | J | K | L | exp[d] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| r(1-2) | 1.220 (1.241) | 1.207 (1.217) | 1.219 (1.239) | 1.208 (1.216) | 1.226 (1.239) | 1.206 (1.214) | 1.225 (1.238) | 1.206 (1.214) | 1.234 (1.258, 1.240) | 1.210 | 1.212 | 1.232 | 1.246 |
| r(2-3) | 1.415 (1.339) | 1.431 (1.350) | 1.413 (1.343) | 1.425 (1.353) | 1.406 (1.336) | 1.434 (1.371) | 1.407 (1.339) | 1.434 (1.372) | 1.419 (1.398, 1.402) | 1.448 | 1.435 | 1.423 | 1.347 |
| r(3-4) | 1.319 (1.397) | 1.309 (1.382) | 1.333 (1.395) | 1.324 (1.374) | 1.336 (1.446) | 1.310 (1.456) | 1.335 (1.451) | 1.310 (1.460) | 1.329 (1.318, 1.325) | 1.298 | 1.321 | 1.351 | 1.398 |
| r(4-5) | 1.324 (1.258) | 1.328 (1.256) | 1.321 (1.262) | 1.324 (1.269) | 1.409 (1.347) | 1.418 (1.336) | 1.407 (1.353) | 1.417 (1.344) | 1.406 (1.424, 1.406) | 1.421 | 1.413 | 1.403 | 1.361 |
| r(5-6) | 1.750 (1.790) | 1.748 (1.785) | 1.734 (1.802) | 1.733 (1.799) | 1.787 (1.821) | 1.788 (1.817) | 1.788 (1.829) | 1.788 (1.824) | 1.787 (1.739, 1.702) | 1.785 | 1.788 | 1.787 | 1.753 |
| r(6-7) | 1.757 (1.762) | 1.756 (1.765) | 1.741 (1.762) | 1.741 (1.761) | 1.750 (1.739) | 1.749 (1.734) | 1.753 (1.746) | 1.753 (1.751) | 1.739 (1.629, 1.636) | 1.739 | 1.737 | 1.736 | 1.682 |
| e(2-3-4) | 121.1 (109.0) | 120.0 (112.5) | 120.6 (108.7) | 120.2 (112.5) | 123.7 (115.4) | 122.3 (109.5) | 123.8 (116.2) | 122.6 (109.3) | 123.5 (123.4, 122.6) | 124.9 | 126.0 | 122.4 | 113.8 |
| e(5-6-7) | 98.4 ( 95.9) | 98.3 ( 95.6) | 111.9 (105.6) | 112.2 (106.2) | 102.4 (100.0) | 102.4 (100.3) | 102.6 (107.8) | 102.2 (106.2) | 105.9 (117.2, 118.8) | 105.9 | 113.3 | 122.4 | 102.3 |
| \|e(1-2-3-4)\| | 0.1 (0.0) | 177.2 (180.0) | 0.3 (0.9) | 179.3 (180.3) | 0.1 (0.0) | 179.6 (183.4) | 1.2 (1.8) | 179.4 (177.0) | 0.1 (0.0, 9.3) | 126.7 | 142.4 | 2.0 | 3.4 |
| \|e(4-5-6-7)\| | 179.6 (180.0) | 179.8 (180.0) | 0.8 (31.3) | 0.1 (33.2) | 177.9 (180.0) | 178.4 (176.8) | 49.1 (40.7) | 55.0 (41.5) | 179.9 (179.9, 175.5) | 177.5 | 4.6 | 2.7 | 173.0 |
| E(a.u.) | -713. 32379 | -713. 29893 | -713. 31970 | -713. 29584 | -878. 22884 | -878. 20144 | -878. 22180 | -878. 19949 | | | | | |
| $E_{rel}$[f] | 0.0 | 15.6 | 2.6 | 17.5 | 0.0 | 17.2 | 4.5 | 18.4 | | | | | |
| $H_f$[g] | 10.1 | 19.4 | 5.5 | 13.5 | 42.5 | 50.4 | 42.6 | 49.2 | 82.7 (126.9, 99.3 | 89.4 | 87.9 | 81.4 | |
| $\mu$ (D) | 4.235 | 6.731 | 1.187 | 5.387 | 3.272 | 5.447 | 1.122 | 4.389 | 4.492 (5.799, 6.210) | 7.306 | 6.352 | 21.88 | |

[a] Values in parenthesis: 4-31G (fully optimized);values in parenthesis: 3-21G (fully optimized); values in parenthesis: AM1, MNDO (fully optimized); 4d; in A; energy of the most stable conformer: 0.0 kcal/mol (rel.); in kcal/mol

Table 3: Energies of Conformers of Type A (ab initio [a], PM3)

| | E(Θ(1-2-3-4)=0°) | E(Θ(1-2-3-4)=100°) | E (kal/mol) |
|---|---|---|---|
| 4-31G | -713.32379 | -713.26987 | 34.4 |
| D95//4-31G | -714.12696 | -714.07387 | 33.3 |
| 6-31G*//4-31G | -714.26659 | -714.21546 | 32.1 |
| 6-311G**//4-31G | -714.37568 | -714.32523 | 31.7 |
| MP2/6-31g*//4-31G | -715.31073 | -715.26759 | 27.1 |
| PM3 | 10.1 | 20.7[b] | 10.6 |

[a] in a.u.; [b] $H_f$(max) = 21.1 kcal/mol (Θ(1-2-3-4) = 115°)

## Experimental

IR spectra: IR-Specord 71 Carl-Zeiss-Jena. - $^1$H NMR: BS 487/c (80 MHz) Tesla Brno, WP 200 (300 MHz) Bruker. - $^{13}$C NMR: WP 300 (50 MHz) Bruker. - MS (70eV): HP 5995 A Hewlett Packard. - UV spectra: UV/VIS spectrometer Specord, Carl-Zeiss-Jena.
Known syntheses of the starting pyrimidines **2**[1], **13**[6] and the 3,3-pentamethyleneoxaziridine **3**[2] were used.

### 1-Acylamido-2-aminothiopyrimidinium-N-ylides 4 and 12, 1-Ureidopyrimidine-2-one 5f and 1-Acylmethylpyrimidine-2-ones 14 - General Procedures

*Method A.* 3 mmol 1-Acylaminopyrimidine-2-thione **2**, 1-arylaminopyrimidine-2-thione **11**, or 1-acylmethylpyrimidine-2-thione **13** were added to 50 ml of 0.1 mol solution of 3,3-pentamethyleneoxaziridine **3** in toluene. After stirring the mixture at room temperature for 1 h, the precipitate was filtered off and recrystallized. If no precipitate was obtained, the toluene was evaporated in vacuum. The remaining oil was crystallized by addition of ether.

*Method B.* 0.36 g (3 mmol) Hydroxylamine-O-sulfonic acid were added to a solution of 3 mmol of **2** in 20 ml 4% ethanolic NaOH. A yellow precipitate appeared immediately. After 20 min the reaction mixture was diluted with water and acidified with HCl. The precipitate was filtered and recrystallized.

### 1-Acylaminopyrimidine-2-ones 5

*Method C.* A mixture of 3 mmol 1-acylamido-2-aminothiopyrimidinium-N-ylide **4** and 10ml acetic anhydride was refluxed for 10 min. The resulting colorless solution was allowed to cool to room tem-

perature and was diluted with about 30 ml water. The product was filtered and recrystallized.

*Method D.* A mixture of 1.0 g (2.1 mmol) of 4-(4-anisyl)-1-benzoylamino-2-methylthiopyrimidinium iodide **7** ($R^1$ = 4-$CH_3OC_6H_4$, $R^2$ = $C_6H_5$), 20 ml ethanol, and 0.3 g (6.3 mmol) NaOH in 5 ml water was refluxed for 4 h. The ethanol was evaporated in vacuum. A small amount of water was added to dissolve the NaI formed. The resulting solution was acidified to pH 1 by adding concentrated HCl while cooling with ice. The yellow precipitate was filtered by suction, washed with ethanol and recrystallized.

**1,3,4-Oxadiazolo[3,2-a]pyrimidinium Perchlorates 6 and Oxazolo[3,2-a]pyrimidinium Perchlorate 15b**

*Method E.* 0.3 g 70% $HClO_4$ were added to 10 ml acetic anhydride under intensive ice cooling and stirring. After 10 min, 3 mmol 1-acylamido-2-aminothiopyrimidinium-N-ylide **4d**, 1-acylimidopyrimidine-2-one **5**, or 1-acylmethylpyrimidine-2-one **14** were added. After 30 min stirring at ambient temperature the solution was allowed to stand until a colorless precipitate occurred (30 min). It was filtered by suction and recrystallized.

*Method F.* A mixture of 0.01 mol 1-amino-2-methylthiopyrimidinium perchlorate **8**, 2ml acetyl chloride, and 20 ml acetic anhydride was refluxed for 1 h. The mixture was concentrated in vacuum. The product crystallized after adding a few drops of acetonitrile or ethanol. It was filtered by suction and recrystallized.

**Molecular Structure of N-Ylide 4d.**

*Crystal data:* $C_{18}H_{16}N_4OS$, M= 336.4. Triclinic, space group P1,$a$ = 955.2(2), $b$ = 983.5(2), $c$= 1027.5(3) pm, $\alpha$= 87.99(2), ß= 67.59(2), $\gamma$= 67.02(2)°,
$U$ = 0.8142 nm$^3$, $Z$ = 2, $D_x$ = 1.372 Mg m$^{-3}$, (Mo $K_\alpha$) = 0.71069 A, $\mu$ = 0.2 mm$^{-1}$,
$T$ = 178 K, F(000) = 352.

*Data collection and refinement*: A pale yellow prism 0.7 x 0.35 x 0.3 mm was mounted on a glass fibre in inert oil and transferred to the cold gas stream of the diffractometer (Siemens R3 with LT-2 low-temperature attachment). Data were collected to $2\Theta_{max}$ 50° with monochromated Mo $K_\alpha$ radiation. Of 3044 measured intensities, 2863 were unique ($R_{int}$ 0.021) and 2181 > 4 ($\sigma F$) used for all calculations (program system "Siemens SHELXTL PLUS").

*Structure solution and refinement:* The structure was solved by direct methods and subjected to anisotropic full-matrix least-squares refinement on $F$. Hydrogen atoms of the $NH_2$ group were refined freely; others were included using a riding model. Refinement proceeded to $R$ 0.036, $wR$ 0.041. The weighting scheme was $w^1$ = $\sigma^2(F)$ + 0.0003 $F^2$. 228 parameters; $S$ 1.4; max. $\Delta/\sigma$ 0.002; max.$\Delta\rho$ 0.2 x 10$^{-6}$ e pm$^{-3}$. Final atom coordinates are given in Table 3.

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## References


1. Liebscher, J.; Hassoun, A.; Fabian, J. *Monatsh. Chem.* **1989**, *120*, 749-758.
2. Andreae, S,: Schmitz, E. *Synthesis* 1991, 327-341.
3. Full details of the structural determination (complete bond lengths, H atom coordinates, structure factors, temperature factors) were submitted to the Fachinformationszentrum Karlsruhe, Gesellschaft für Wissenschaftlich-technische Information mbH, W-7514 Eggenstein-Leopoldshafen 2, Germany. Any request for this material should quote a full literature citation and the reference number CSD-56914.
4. Liebscher, J.; Hassoun, A.; Van der Plas, H. *J. Heterocycl. Chem.* **1990**, *27*, 1441-1445.
5. Liebscher, J.; Hartmann, H. *J. Prakt. Chem.* **1982**, *324*, 942-946.
6. Hill, J.; In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.: Pergamon Press, Oxford, Toronto, Sidney, Paris, Frankfurt, **1984**, volume 6, part 4B, chapter 4.23, page 427.
7. Liebscher, J.; Hassoun, A. *Synthesis* **1988**, 816-820.
8. 8a. Hehre, W. J.; Radom, L.; v. Schleyer, P. R.; Pople, J. A. *Ab initio Molecular Orbital Theory.* Wiley, New York **1986**.-8b. Lawley, K. P., Ed.; *Ab initio Methods in Quantum Chemistry* , Part I. *Advances in Chemical Physics.*, Vol.LXVII. Wiley, New York **1987**.-8c. Lawley, K. P., Ed.; *Ab initio Methods in Quantum Chemistry*, Part I. *Advances in Chemical Physics*, Vol.LXIX. Wiley, New York **1987**.
9. The Gaussian program package was used: Gaussian 90, Revision F, Frisch, M. J.; Head-Gordon, M; Trucks, G. W.; Foresman, F. B.; Schlegel, H. B.; Raghavachari, K.: Robb, M.; Binkley, J. S.; Gonzalez, C., Defrees, D. J.; Fox, D. J.; Whiteside, R. A.; Seeger, R.; Melius, C. F.; Baker, J.; Martin, R. L.; Kahn, L. R.; Stewart, J. J. P.; Topiol, S; Pople, J. A., Gaussian, Inc., Pittsburgh PA, 1990.
10. 10a. Stewart, J. J. P. *J. Comp.-Aid. Mol. Design* **1990**, *4*,1. - 10b. Stewart, J. J. P. *J. Comput. Chem.* **1989**, *10*, 209. - 10c. Stewart, J. J. P. *J. Comput. Chem.* **1989**, *10*, 221. - 10d. Dewar, M. J. S.; Healy, E. F.; Holder, A. J.; Yuan, Y.-C. *J. Comput. Chem.* **1990**, *11*, 543. - 10e. Buß, V.; Messinger, J.; Heuser, N. *QCPE Bulletin* **1991**, *11*, 5. - 10f. Stewart, J. J. P. *J. Comput. Chem.* **1991**, *11*, 543. - 10g. Coolidge, M. B.; Martin, J. E.; Stewart, J. J. P. *J. Comput. Chem.* **1991**, *12*, 948 (calculation of molecular vibrational frequencies using semiempirical methods, comparison of MINDO/3, MNDO, AM1; and PM3; both AM1 and PM3 gave fairly accurate results). - 10h. Seeger, D. M., Korzeniewski, C., Kowalchyk, W. *J. Phys. Chem.* **1991**, *95*, 6871 (force constants derived by AM1, PM3, MNDO, and 4-21G).
11. The program package MOPAC (version 6.00, QCPE 455) has been used: *QCPE Bulletin* **1990**, *10*, 86 (VAX version; for usage on a CRAY X-MP minor changes had to be made).
12. 12a. Ollis, W. D., Ramsden, C. A. *Adv. Heterocycl. Chem.* **1976**, *19*, 1. - 12b. Newton, C. G.; Ramsden, C. A.*Tetrahedron* **1982**, *38*, 2965. - 12c. Ollis, W. D.; Stanforth, S. P.; Ramsden, C. A. *Tetrahedron* **1985**, *41*, 2239. - 12d. Zagravescu, I.; Petrovanu, P. *N-Ylid Chemistry*, McGraw-Hill: New York, **1976**. - 12e. Böttger, A.; Debaerdemaeker, T.; Radziszewski; Friedrichsen, W. *Chem. Ber.***1988**, *121*, 895.