Ring Transformations of Semicyclic 1,3-Dicarbonyl Heteroanalogs; I. Synthesis of Semicyclic *N*-Acyl- and *N*-(Aminocarbonyl)amidine Derivatives and Their Ring Transformation to 5-(ω-Aminoalkyl)-1,2,4-triazoles

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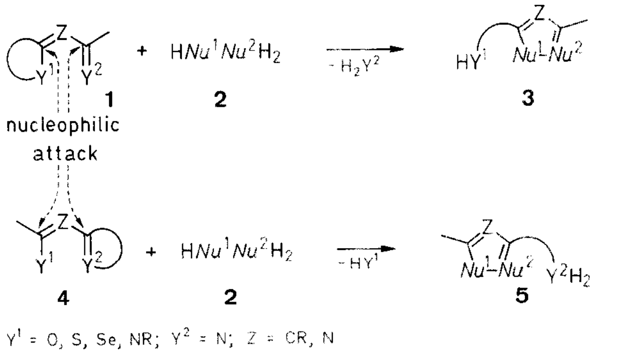
The semicyclic *N*-(thioacyl)- or *N*-(aminothiocarbonyl)amidines **11** are readily available through reaction of *O*-methyllactims **9** or *in situ* generated lactam acetales **10** with aminothiocarbonyl compounds **7** or with carboxamides or ureas **8** and sulfurization of the resultant semicyclic *N*-acyl- or *N*-(aminocarbonyl)amidines **12** with P_4S_{10}. The semicyclic *N*-(thioacyl)- or *N*-(aminothiocarbonyl)amidines **11** are converted into the *S*-alkylation products **13**. Reaction of **13** with hydrazines gives rise to ring transformation resulting in 5-(ω-aminoalkyl)-1,2,4-triazoles **17**. The same products **17** can be obtained by treating semicyclic *N*-acyl- or *N*-(aminocarbonyl)amidines **12** first with $POCl_3$ and then with hydrazines. Similarly, reaction of the *N*-phenyl-*N'*-(thiazolidin-2-yliden)thiourea (**20**) with methyl iodide and hydrazine yields 3-(2-mercaptoethylamino)-5-(phenylamino)-1,2,4-triazole (**22**).

Alkylheterocycles such as **3** or **5** which are substituted by a heteroatom in the ω-position of the alkyl chain can be synthesized in different ways:

- Cyclization of open-chain precursors already possessing the ω-substituted alkyl chain;[1]
- Introduction of the ω-substituted alkyl chain into a heterocyclic substrate;[2]
- Modification of a side chain of an alkylheterocycle.[3]

Another interesting approach to ω-substituted *C*-alkylheterocycles, which is particularly useful in the case of longer alkyl chains, is based on ring transformations of heteroanalogs of β-dicarbonyl compounds such as **1** or **4** in which one of the leaving groups Y^1 or Y^2 is connected to the corresponding carbonyl C-atom by an alkanediyl or other saturated bridge. When such a 1,3-bifunctional electrophile **1** or **4** reacts with bifunctional nucleophiles **2**, only the leaving group X or Y which is not incorporated in the starting ring will leave the molecule. However, nucleophilic $C-Y^1$ (in **1**) or $C=Y^2$ bond scission (in **4**) at the bridged leaving group leads to ring opening. Hence, this leaving group is not eliminated but remains connected, via the previous bridge, to the resultant heterocyclic product **3** or **5**, respectively (Scheme **A**). In the course of this ring transformation, the final heterocyclic ring is formed by condensation while the starting saturated ring system is opened to give the ω-substituted side chain. Only few examples of the transformation of Scheme **A** have hitherto been described.[4–12]



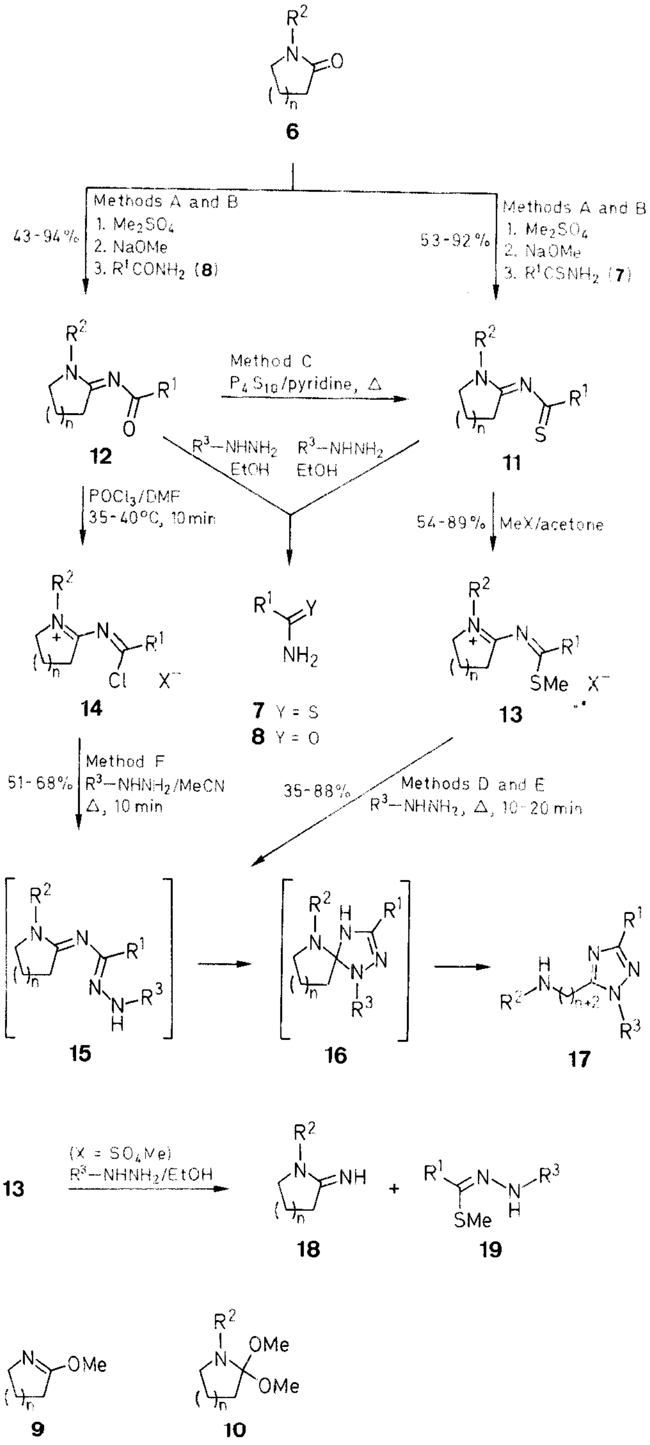
Scheme A

In the course of our studies on the synthesis of heterocycles starting from open-chain heteroanalogs of β-dicarbonyl compounds,[13,14] we tried to apply the general approach of Scheme **A** to the synthesis of a number of heterocyclic products. We now report on the synthesis of 5-(ω-aminoalkyl)-1,2,4-triazoles starting from semicyclic *N*-thioacylamidines **11** or semicyclic *N*-acylamidines **12**. As we have recently shown,[15] compounds **11** are easily available by the reaction of thioamides **7** with *O*-methyllactims **9** (Method A) or lactam acetales **10** (Method B), the latter being used as isolated compounds or generated *in situ* by treating lactams **6** first with dimethyl sulfate and then with sodium methoxide (for some additional examples, see Table 1). We further found that semicyclic thioacylamidines **11** can also be obtained by sulfurization of semicyclic *N*-acylamidines **12** with phosphorus(V) sulfide in pyridine[16] (Method C) (see Table 1). All starting *N*-acyllactamimines **12** (Table 1) are new[17] and were synthesized from the corresponding amides **8** and *O*-methyllactims **9** or *in situ* generated lactam acetals **10**.

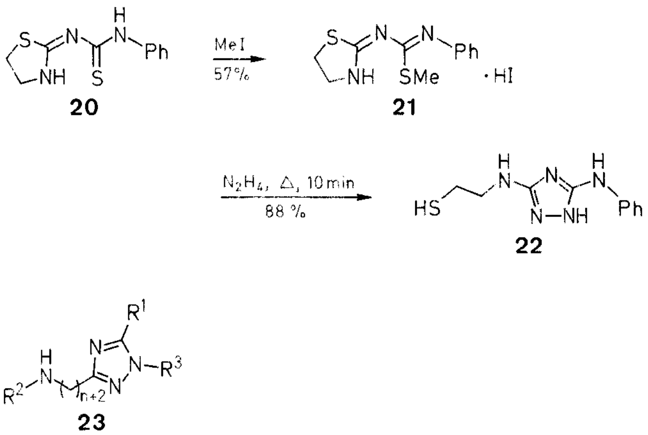
First attempts to react semicyclic thioacylamidines **11** or acylamidines **12** with hydrazines in ethanol lead to cleavage of the C—N—C skeleton with formation of thioamides **7** or amides **8**, respectively, rather than the expected triazoles. We therefore used activated derivatives of **11** and **12**. *N'*-(Thiocarbonyl)lactamimines **11**, for example, can be *S*-alkylated. Usually the resultant semicyclic 3-alkylthio-2-aza-2-propeniminium salts **13** (for some examples see Table 1) could be reacted with hydrazines (Methods D and E) without prior purification. The 5-(ω-aminoalkyl)-1,2,4-triazoles **17**[18] could thus be obtained as free bases (R^3 = H or phenyl) or as hydroiodides (R^3 = 4-nitrophenyl). It is also possible to use dimethyl sulfate as methylating agent for **11**. The *S*-methylation products **13** (X = $MeSO_4$) usually do not crystallize as well as the corresponding iodides; hence, they were reacted with hydrazines without prior isolation to give triazoles **17**. However, use of this procedure (Method D) in some cases (e.g., reaction of **11 b** with dimethyl sulfate and 4-nitrophenyl- or 2,4-dinitrophenylhydrazine) again leads to cleavage of the C—N—C unit resulting in the formation of a lactam imine **18** and a methyl hydrazonothioate **19** (i.e. R^1 = 4-methoxyphenyl, R^3 = 4-nitrophenyl; yield 71%; mp 126–128°C) (Scheme **B**). It appears that this type of competing reaction depends on both, the substituent R^3 and on the methylating agent MeX.

A second route to 5-(ω-aminoalkyl)-1,2,4-triazoles **17** uses semicyclic *N*-acylamidines **12** as starting material. These compounds can be further activated by treatment with phosphoryl chloride to give semicyclic 3-chloro-2-aza-2-propeniminium salts **14** as crude products, which can be converted into the desired 5-(ω-aminoalkyl-1,2,4-triazole hydrochlorides **17** · HCl by reaction with hydrazines (Method F). As shown by the transformation of *N*-phenyl-*N'*-(thiazolidin-2-ylidene)thiourea **20** to 5-(2-mercaptoethylamino)triazole **22** by methylation (formation of **21** see Table 1) and subsequent reaction with hydrazine (Method E), the general ring transformation of Scheme **A** can also be applied to semicyclic 1,3-dicarbonyl heteroanalogs possessing two heteroatoms in the bridge. In this case, however, an ω-mercaptoalkyl-triazole **22** is formed (Scheme **C**), not an ω-aminoalkyl derivative.

The structures of the functionalized 1,2,4-triazoles **17** and **21** (Table 3) were proven by microanalyses and spectrometric methods. The ω-aminoalkyl chain of **17** gives rise to the following order of increasing chemical shifts in the ^{1}H-NMR spectra: $CH_2-(CH_2)_nCH_2$ < NR^2 < NCH_2 ≈ CH_2 triazole. The differences in the shifts of these groups are significantly smaller in the products **17** as compared with the reactants **11** and **12**. In the MS spectra, typical fragment peaks of R^2NHCH_2 (α-cleavage) and $R^2NH(CH_2)_2$ are found. These data rule out spiro or lactam imine isomers such as **16**[19] or **15**. For example, isomers **15** would be expected to show chemical shifts similar to those of the starting materials **11**[15] in the order $CH_2-(CH_2)_n-CH_2$ < $CH_2C{=}N$ < CH_2N. Further, the isomers **23** have to be taken into consideration. However, diaryl-



Scheme **B**



Scheme **C**

Footnotes to Scheme **B**

12	R^1	R^2	n
a	Ph	CH_3	1
b	$4\text{-}CH_3OC_6H_4$	CH_3	1
c	PhNH	CH_3	1
d	$3\text{-}C_5H_4N$	CH_3	1
e	$4\text{-}CH_3OC_6H_4$	C_2H_5	2
f	Ph	H	3
g	Ph	CH_3	3
h	$3\text{-}CH_3C_6H_4$	H	3
i	$3\text{-}CH_3C_6H_4$	CH_3	3
j	$4\text{-}CH_3OC_6H_4$	CH_3	3
k	$4\text{-}CH_3OC_6H_4$	H	3
l	PhNH	CH_3	3

11	13	R^1	R^2	n
a		Ph	CH_3	1
b	b	$4\text{-}CH_3OC_6H_4$	CH_3	1
c	c	$4\text{-}ClC_6H_4$	CH_3	1
d		NH_2	CH_3	1
e	e	PhNH	CH_3	1
f		$4\text{-}CH_3OC_6H_4$	C_2H_5	2
g		$4\text{-}ClC_6H_4$	C_2H_5	2
h		Ph	CH_3	3
i		$4\text{-}CH_3OC_6H_4$	H	3
j		$4\text{-}CH_3OC_6H_4$	CH_3	3
k	k	$4\text{-}ClC_6H_4$	CH_3	3
l	l	PhNH	CH_3	3

17	R^1	R^2	n	R^3
a HI	$4\text{-}CH_3OC_6H_4$	CH_3	1	$4\text{-}NO_2C_6H_4$
b HCl	$4\text{-}CH_3OC_6H_4$	CH_3	1	$4\text{-}NO_2C_6H_4$
c	$4\text{-}ClC_6H_4$	CH_3	1	Ph
d	NH_2	CH_3	1	Ph
e	PhNH	CH_3	1	H
f HI	$4\text{-}CH_3OC_6H_4$	C_2H_5	2	$4\text{-}NO_2C_6H_4$
g HCl	$3\text{-}CH_3C_6H_4$	CH_3	3	$4\text{-}NO_2C_6H_4$
h HI	$4\text{-}ClC_6H_4$	CH_3	3	$4\text{-}NO_2C_6H_4$
i	PhNH	CH_3	3	H

substituted compounds **17** (R^1, R^3 = aryl) show downfield shifts for *ortho*-protons, which are characteristic of planar 1,3-diaryl-1,2,4-triazoles rather than of the 1,5-diaryl isomers in which the aryl substitutes are not in the same plane as the triazole ring.[20] The 5-(2-mercaptoethylamino)-1,2,4-triazole **22** exhibits a characteristic 3-amino-5-anilino-1,3,5-triazole fragment (m/z = 175) derived from a McLafferty rearrangement. Hence, the less probable isomeric 3-(2-aminoethylthio)-5-anilino-1,2,4-triazole structure can be ruled out. The mechanism of the formation of 5-(ω-aminoalkyl)-1,2,4-triazoles starting from semicyclic 2-aza-2-propeniminium salts **13**, **14**, and **21** probably starts with attack of the hydrazine upon position 3 and elimination of the leaving group. Cyclization of the resultant products, i.e. **15**, gives spiro intermediates, i.e. **16**, which undergo ring opening by C−N bond cleavage. The syntheses depicted in Schemes **B** and **C** represent convenient and effective approaches to hitherto unknown 5-(ω-aminoalkyl)-1,2,4-triazoles. They make possible the preparation of compounds possessing alkyl side chains having at least three C-atoms.

Semicyclic *N'*-Thioacyl- or *N'*-(Aminothiocarbonyl)amidines 11 and *N'*-Acyl- or *N'*-(Aminocarbonyl)amidines 12; General Procedures:

Method A: A solution of thiocarboxamide or thiourea **7** (0.01 mol) or of carboxamide or urea **8** (0.01 mol) in *O*-methyllactim **9**[21] (0.05 mol) is refluxed for 45 min. The cold mixture is poured into H_2O (12 mL). The product **11** (R^2 = H) or **12** (R^2 = H) is isolated by suction and recrystallized (Tables 1 and 2).

Method B: A mixture of lactam **6** (0.1 mol) and dimethyl sulfate (1.26 g, 0.1 mol) is either heated at 80 °C for 2 h or is kept at room

Table 1. Compounds **11**, [a] **13**, and **21** Prepared

Product	Method	Yield (%)	mp (°C)[b] (Solvent)	Molecular Formula[c] or Lit. mp (°C)	MS (70 eV)[d] m/z (%)	UV (MeOH)[e] λ_{max} (nm) (log ε)	^{1}H-NMR (DMSO-d_6/TMS)[f] δ, J(Hz)
11a	C	45	94–96 (MeOH)	$C_{12}H_{14}N_2S$ (218.3)	218 (M^+, 60); 121 (100); 115 (47); 77 (66); 55 (68); 51 (42); 41 (52)		
11b	C	73	78–80 (MeOH)	80–81[15]			
11f	B	83	93–95 (MeOH)	$C_{15}H_{20}N_2OS$ (276.4)	276 (M^+, 23); 243 (100); 169 (54); 138 (22); 125 (10); 55 (47)		
11g	B	89	102–103 (EtOH)	$C_{14}H_{17}ClN_2S$ (280.8)	280 (M^+, 12); 247 (100); 169 (13); 155 (66); 142 (14); 125 (20); 111 (24); 82 (45); 55 (56)	270 (4.20); 346 (3.72)	1.2 (t, 3H, CH_3); 1.85 [m, 4H, $(CH_2)_2$]; 3.1 (t, 2H, $CH_2C{=}N$); 3.5 (m, 4H, CH_2NCH_2); 7.2 (d, 2H, C_6H_4); 8.2 (d, 2H, C_6H_4)[g]
11h	C	63	88–90 (MeOH)	$C_{14}H_{18}N_3S$ (246.4)			
11i	A	53	124–126 (EtOH)	$C_{14}H_{18}N_2OS$ (262.4)	262 (M^+, 34); 229 (38); 219 (15); 151 (74); 139 (14); 134 (30); 129 (22); 96 (100); 82 (14)	276 (4.50); 333 (2.18)	1.7 [m, 6H, $(CH_2)_3$]; 2.8 (m, 2H, $CH_2C{=}N$); 3.5 (m, 2H, CH_2N); 3.8 (s, 3H, CH_3O); 6.9 (d, 2H, C_6H_4); 8.1 (d, 2H, C_6H_4); 10.7 (br, 1H, NH)
11j	C	44	128–130 (MeOH)	$C_{15}H_{20}N_2OS$ (276.4)	276 (M^+, 17); 243 (60); 115 (90); 110 (46); 108 (55); 55 (87); 42 (100); 41 (80)		
11k[h]	A	53	124–126 (EtOH)	$C_{14}H_{17}ClN_2S$ (280.8)	280 (M^+, 12); 247 (100); 155 (63); 110 (41); 68 (32)	281 (4.24); 352 (3.87); 433s (2.28)	
11l[i]	B	92	177–178 (EtOH)	$C_{14}H_{19}N_3S$ (261.4)	261 (M^+, 8); 169 (65); 135 (100); 126 (25); 77 (52); 44 (64)	242s (4.01); 298 (4.33)	
13b[j]		87	167–169 (EtOH)	$C_{14}H_{19}IN_2OS$ (390.3)			2.1 (m, 2H, CH_2); 2.5 (s, 3H, SCH_3); 2.75 (m, 2H, $CH_2C{=}$); 3.1 (s, 3H, NCH_3); 3.6 (m, 2H, CH_2N); 3.8 (s, 3H, OCH_3); 7.1 (d, 2H, C_6H_4); 8.2 (d, 2H, C_6H_4)
13c[j]		89	172–173 (EtOH)	$C_{13}H_{16}ClIN_2S$ (394.7)	267 ($M^+ - I$, 10); 220 (24); 156 (13); 109 (100); 55 (48)		2.0 (m, 2H, CH_2); 2.6 (s, 3H, SCH_3); 2.75 (m, 2H, $CH_2C{=}$); 3.2 (s, 3H, NCH_3); 3.9 (t, 2H, NCH_2); 7.6 (s, 4H, C_6H_5)
13e[j]		54	137–138 (EtOH)	$C_{13}H_{18}IN_3S$ (375.3)			
13k[j]		67	192–193 (EtOH)	$C_{15}H_{20}ClIN_2S$ (422.8)			
13l[j]		64	168–170 (EtOH)	$C_{15}H_{22}IN_3S$ (403.3)			
21		57	161–163 (EtOH)	$C_{11}H_{14}IN_3S_2$ (379.3)			

[a] For compounds **11c**, **11d**, and **11e**, see Ref. 15.
[b] Uncorrected, measured with heating block Boetius.
[c] Satisfactory microanalyses: C ∓0.4, H ∓0.21, N ∓0.31.
[d] Recorded on a Hewlett Packard 5995A spectrometer.
[e] Measured using a Specord UV spectrometer (Carl Zeiss Jena).
[f] Obtained on a Tesla BS 587 (80 MHz) FT-spectrometer.
[g] In $CDCl_3$.
[h] ^{13}C-NMR (DMSO-d_6): δ = 24.3; 25.5; 28.2; 31.2; 39.1; 53.0; 126.8 129.1; 134.9; 140.5; 173.7; 195.5.
[i] ^{13}C-NMR (DMSO-d_6): δ = 24.2; 26.5; 28.2; 30.2; 38.0; 51.8; 121.0 123.0; 128.1; 140.1; 166.7; 186.3.
[j] X = I.

temperature for 12 h. It is then cooled to a temperature below 15 °C and a solution of NaOMe [from Na (2.3 g, 0.1 mol) and MeOH (15 mL)] is added with stirring. After 5 min the aminothiocarbonyl **7** (0.1 mol) or aminocarbonyl **8** (0.1 mol) compound is added at room temperature and stirring is continued until the reactant **7** or **8** has completely dissolved. In most cases, the product **11** or **12** precipitates from the mixture. H_2O (15 mL) is then added and the product is isolated by suction. Otherwise, the solvent is evaporated under reduced pressure and the product is precipitated by adding a few drops of H_2O. The product is recrystallized (Tables 1 and 2).

Method C: A solution of the semicyclic *N*-acyl- or *N*-(aminocarbonyl)amidine **12** (0.01 mol) in pyridine (10 mL) is heated to boiling and P_4S_{10} (1.5 g, 0.0034 mol) is added in portions. After cooling to room temperature, the mixture is diluted with H_2O (about 5 mL). In the case of compounds **11a** and **11j**, MeOH (7 mL) and cyclohexane (7 mL) are added in addition. The product is isolated by suction and recrystallized (Tables 1 and 2).

Semicyclic 3-Methylthio-2-aza-2-propenium Salts 13 and Thiazolidine Derivative 21; General Procedure:

Methyl iodide (28.6 g, 0.2 mol) is added to a stirred solution of the semicyclic *N*-thioacyl- or *N*-(aminothiocarbonyl)amidine **11** (0.1 mol) or the thiourea derivative **20**[22] (23.8 g, 0.01 mol) in acetone (200 mL). Products **13** (R^1 = aryl), and **21** precipitate within a few minutes. They are isolated by suction and recrystallized. They can be used in further reactions without prior purification. Products **13** (R^1 = NHR^3) do not precipitate from the mixture; they can be isolated as crude products by evaporating the solvent (Table 1).

ω-Functionalized 1,2,4-Triazoles 17 and 22; General Procedures:

Method D: The respective hydrazine (0.01 mol) is added to a stirred solution of the semicyclic 3-methylthio-2-aza-2-propeniminium salt **13** (0.01 mol) in EtOH (20 mL). The mixture is heated to reflux for 20 min, then cooled to room temperature. The product either crystallizes directly from the mixture or is precipitated by the addition of H_2O (a few mL). It is isolated by suction and recrystallized (Table 3).

Method E: A mixture of the semicyclic 3-methylthio-2-aza-2-propeniminium salt **13** (0.01 mol) and hydrazine hydrate (72%; 6.95 g, 0.1 mol) is refluxed for 10 min, then cooled to room temperature. Water (1–2 mL) is added. The product is isolated by suction and recrystallized (Table 3).

Method F: $POCl_3$ (6 mL) is added dropwise to a stirred solution of the semicyclic *N*-acyl- or *N*-(aminocarbonyl)amidine **12** (0.01 mol) in DMF

Table 2. Compounds **12** Prepared

Product	Method	Yield (%)	mp (°C)[a] (Solvent)	Molecular Formula[b]	MS (70 eV)[c] m/z (%)	IR (KBr)[d] ν (cm⁻¹)	¹H-NMR (DMSO-d_6/TMS)[e] δ
12a	B	70	63–64 (cyclohexane)	$C_{12}H_{14}N_2O$ (202.3)		1630	2.13 (m, 2H, CH_2); 3.18 (m, 5H, CH_2, CH_3); 3.44 (m, 2H, CH_2); 7.38 (m, 3H, C_6H_5); 8.27 (m, 2H, C_6H_5)
12b	B	67	92–93 (cyclohexane)	$C_{13}H_{16}N_2O_2$ (232.3)	232 (M⁺, 13); 135 (100); 125 (53); 107 (17); 77 (39); 64 (21); 42 (27)	1660	2.13 (m, 2H, CH_2); 3.13 (t, 2H, CH_2); 3.25 (s, 3H, NCH_3); 3.69 (t, 2H, CH_2); 4.0 (s, 3H, OCH_3); 7.25 (d, 2H, C_6H_4); 8.25 (d, 2H, C_6H_4)
12c	B	59	142–143 (EtOH)	$C_{12}H_{15}N_3O$ (217.3)	217 (M⁺, 4); 125 (100); 83 (6); 42 (7); 41 (6); 39 (5)	1650	
12d	B	71	81–82 (cyclohexane)	$C_{11}H_{13}N_3O$ (203.2)	203 (M⁺, 5); 172 (8); 125 (100); 106 (25); 83 (18); 78 (42); 57 (84); 51 (42); 42 (30)	1640	2.0 (m, 2H, CH_2); 3.0 (t, 2H, CH_2); 3.1 (s, 3H, CH_3); 3.5 (t, 2H, CH_2); 7.4 (m, 1H, C_5H_4N); 8.4 (d, 1H, C_5H_4N); 8.6 (d, 1H, C_5H_4N); 9.3 (s, 1H, C_5H_4N)
12e	B	74	63–65 (cyclohexane)	$C_{15}H_{20}N_2O_2$ (260.3)	260 (M⁺, 8); 135 (71); 125 (100); 107 (17); 92 (26); 77 (34); 55 (17); 44 (55)	1620	1.23 (t, 3H, CH_3C); 1.8 (m, 4H, CH_2, CH_2); 3.0 (t, 2H, CH_2N); 3.6 (q, 2H, CH_2N); 3.8 (s, 3H, CH_3O); 6.8 (d, 2H, C_6H_4); 8.1 (d, 2H, C_6H_4)
12f	B	83	78–80 (cyclohexane)	$C_{13}H_{16}N_2O$ (216.3)	217 (5); 216 (M⁺, 38); 215 (50); 139 (43); 105 (100); 77 (71); 55 (18); 51 (26)	1660	1.68 [m, 6H, $(CH_2)_3$]; 3.34 (s, 2H, $CH_2C{=}N$); 2.69 (m, 2H, CH_2N); 7.44 (m, 3H, C_6H_5); 7.97 (m, 2H, C_6H_5); 11.1 (s, 1H, NH)
12g	B	43	66–68 (EtOH)	$C_{14}H_{18}N_2O$ (230.3)	230 (M⁺, 17); 153 (44); 125 (45); 105 (97); 77 (100); 51 (40); 42 (42)	1620	1.69 [m, 6H, $(CH_2)_3$]; 2.82 (m, 2H, $CH_2C{=}N$); 3.18 (s, 3H, CH_3); 3.43 (m, 2H, NCH_2); 7.3 (m, 3H, C_6H_5); 8.2 (m, 2H, C_6H_5)
12h	A	87	64–66 (cyclohexane)	$C_{14}H_{18}N_2O$ (230.3)	230 (M⁺, 21); 229 (26); 139 (42); 119 (100); 91 (72); 65 (29); 55 (17)	1650	1.68 [m, 6H, $(CH_2)_3$]; 2.5 (m, 2H, $CH_2C{=}N$); 3.34 (m, 2H, NCH_2); 7.3 (m, 2H, C_6H_4); 7.82 (m, 2H, C_6H_4)
12i	B	91	52–53 (cyclohexane)	$C_{15}H_{20}N_2O$ (244.3)	244 (M⁺, 20); 153 (47); 125 (47); 119 (87); 91 (100); 65 (54); 44 (45); 42 (63); 39 (36)	1625	
12j	B	44	100–102 (cyclohexane)	$C_{15}H_{20}N_2O_2$ (260.3)	260 (M⁺, 9); 135 (100); 125 (42); 92 (27); 77 (35); 44 (20); 42 (27)	1610	1.64 [m, 6H, $(CH_2)_3$]; 2.8 (m, 2H, $CH_2C{=}N$); 3.2 (s, 3H, NCH_3); 3.37 (s, 2H, NCH_2); 3.8 (s, 3H, OCH_3); 6.95 (d, 2H, C_6H_4); 8.0 (d, 2H, C_6H_4)
12k	A	82	135–137 (EtOH)	$C_{14}H_{18}N_2O_2$ (246.3)	246 (M⁺, 90); 135 (100); 107 (15); 92 (21); 77 (31); 64 (13); 55 (14); 41 (19)		1.8 [m, 6H, $(CH_2)_3$]; 2.75 (m, 2H, $CH_2C{=}N$); 3.29 (m, 2H, CH_2N); 4.0 (s, 3H, OCH_3); 7.13 (d, 2H, C_6H_4); 8.25 (d, 2H, C_6H_4); 11.25 (br, 1H, NH)
12l	B	70	132–134 (EtOH)	$C_{14}H_{19}N_3O$ (245.3)	245 (M⁺, 1); 153 (100); 92 (7); 65 (10); 55 (16); 42 (20)	1670	

[a] Uncorrected, measured with heating block Boetius.
[b] Satisfactory microanalyses: C ∓0.36, H ∓0.25, N ∓0.38.
[c] Recorded on a Hewlett-Packard 5995A spectrometer.
[d] Recorded on a Specord 71 Infrared spectrophotometer (Carl Zeiss Jena).
[e] Obtained on a Tesla BS 587 (80 MHz) FT-spectrometer.

Table 3. Compounds **17** or **17** · HX and **22** Prepared

Product	Method	Yield (%)	mp (°C)[a] (Solvent)	Molecular Formula[b]	^{1}H-NMR (DMSO-d_6/TMS)[c] δ	MS (70 eV)[d] m/z (%)
17a · HI	D	72	230–232 (EtOH)	$C_{19}H_{21}N_5O_3 \cdot HI$ (495.3)	1.91 (m, 2H, CH_2); 2.5 (s, 3H, CH_3N); 3.15 (m, 4H, CH_2N, CH_2C); 3.8 (s, 3H, OCH_3); 7.0 (d, 2H, C_6H_4); 7.9 (m, 4H, C_6H_4); 8.5 (d, 2H, C_6H_4)	
17b · HCl	F	68	285–287 (DMF)	$C_{19}H_{21}N_5O_3 \cdot HCl$ (403.9)		367 (M^+ – HCl, 1); 323 (19); 310 (94); 90 (34); 44 (100)
17c	D	35	146–148 (EtOH)	$C_{18}H_{19}ClN_4$ (326.8)	2.12 (m, 2H, CH_2); 2.5 (s, 3H, CH_3N); 3.0 (m, 4H, CH_2N, CH_2C); 7.4 (d, 2H, C_6H_4); 7.5 (s, 5H, C_6H_5); 8.0 (d, 2H, C_6H_4); 8.25 (s, 1H, NH)	268 (100); 268 (52); 91 (40); 72 (30); 58 (40); 44 (39)
17d	D	49	83–85 (H_2O)	$C_{18}H_{19}ClN_3$ (312.8)		231 (40); 174 (100); 91 (45); 77 (15); 44 (43)
17e[e]	E	61	184–185 (H_2O)	$C_{12}H_{17}N_5$ (231.3)		231 (M^+, 12); 187 (35); 174 (100); 77 (23); 44 (27)
17f · HI	D	72	182–184 (EtOH)	$C_{21}H_{25}N_5O_3 \cdot HI$ (523.4)		395 (M^+ – HI, 5); 394 (12); 350 (47); 336 (87); 252 (19); 137 (21); 58 (100); 44 (12)
17g · HCl	F	51	207–209 (DMF)	$C_{21}H_{25}N_5O_2 \cdot HCl$ (415.9)	1.8 [m, 6H, $(CH_2)_3$]; 2.39 (s, 3H, CCH_3); 2.95 (s, 3H, CH_3N); 3.8 (m, 4H, CH_2N, CH_2C); 7.35 (m, 2H, C_6H_4); 7.94 (m, 5H, C_6H_4); 8.46 (d, 2H, C_6H_4)	379 (M^+ – Cl, 1); 362 (31); 307 (16); 249 (13); 90 (13); 63 (11); 44 (100)
17h · HI[f]	D	75	205–206 (MeCN)	$C_{20}H_{22}ClN_5O_2 \cdot HI$ (526.7)		382 (13); 327 (10); 297 (6); 269 (3); 128 (33); 106 (18); 90 (10); 44 (100)
17i	E	82	140–141 (H_2O)	$C_{14}H_{21}N_5$ (259.4)	1.6 [m, 6H, $(CH_2)_3$]; 2.5 (s, 3H, CH_3); 2.8 (m, 4H, CH_2N, CH_2C); 6.5 (br, 2H, NH, NH); 7.0 (m, 1H, C_6H_5); 7.4 (m, 2H, C_6H_5); 7.7 (d, 2H, C_6H_5); 9.2 (br, 1H, NH)	259 (M^+, 15); 227 (11); 216 (35); 187 (100); 174 (60); 77 (25); 55 (10); 44 (82)
22[g]	E	88	150–151 (n-BuOH)	$C_{10}H_{13}N_5S$ (235.3)	2.9 (t, 2H, SCH_2); 3.6 (t, 2H, NCH_2); 7.1 (br, 1H, NH); 7.3 (d, 1H, C_6H_5); 7.4 (t, 2H, C_6H_5); 7.7 (d, 2H, C_6H_5); 8.7 (s, 1H, NH); 11.3 (s, 1H, NH)	235 (M^+, 28); 188 (100); 175 (31); 144 (15); 119 (26); 103 (20); 91 (20); 77 (62)

[a] Uncorrected, measured with heating block Boetius.
[b] Satisfactory microanalyses: C ∓0.34, H ∓0.23, N ∓0.26.
[c] Obtained on a Tesla BS 587 (80 MHz) FT-spectrometer.
[d] Recorded on a Hewlett Packard 5995A spectrometer.
[e] IR (KBr): ν = 3250, 2910, 1600, 1540, 1500 cm^{-1}.
UV (MeOH):[h] λ_{max} (log ε) = 257 nm (4.61).
^{13}C-NMR (DMSO-d_6): δ = 24.3 (t); 27.6 (t); 36.2 (q); 51.0 (t); 116.0 (d); 119.4 (d); 129.0 (d); 142 (s); 156.1 (s); 159.5 (s).
Recorded on a Tesla BS 587 (20 MHz) spectrometer.
[f] ^{13}C-NMR (DMSO-d_6): δ = 24.8; 25.2; 26.0; 26.6; 32.4; 47.9; 124.9; 125.3; 127.7; 128.9; 129.0; 134.2; 141.7; 146.7; 157.5; 159.8.
[g] UV (MeOH):[h] λ_{max} (log ε) = 258 nm (4.24).
[h] Measured using a Specord UV spectrometer.

(7 mL) at a temperature below 40 °C (cooling). The temperature is then kept between 35 and 40 °C for 10 min by slight warming whereafter the mixture is allowed to cool to room temperature. Then, Et_2O (20 mL) is added and the mixture stirred for 2 min. The Et_2O layer is decanted, another portion of Et_2O (20 mL) is added, the mixture stirred, and the Et_2O layer decanted. The remaining oil (3-chloro-2-aza-2-propeniminium salt **14**) is dissolved in MeCN (10 mL) and this solution is combined with the respective hydrazine (0.011 mol). The solution is refluxed for 10 min, then cooled to room temperature. The product is precipitated by the addition of H_2O (about 5 mL), isolated by suction, and recrystallized (Table 3).

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