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# Chiral 2-(ω-Aminoalkyl)-oxazolines by Ring Transformation of Lactam Derivatives [1])

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*Dedicated to Professor Dr. Rudolf Gompper on the Occasion of his 70th Birthday*

**Abstract.** 2-(ω-Aminoalkyl)-oxazolines **7** as starting materials for further asymmetric synthesis can be prepared in enantiomerically pure form by ring transformation of lactim ethers **1** or lactam acetals **2** with chiral 2-aminoalcohols **3**. Hydroxyethyllactam imines **5**, lactamimino-alkyloxazolines **8**, or ω-aminoalkaneamides **9** can be formed as by-products by condensation without ring transformation, by further reaction with lactim ether **1**, or by hydrolysis, respectively.

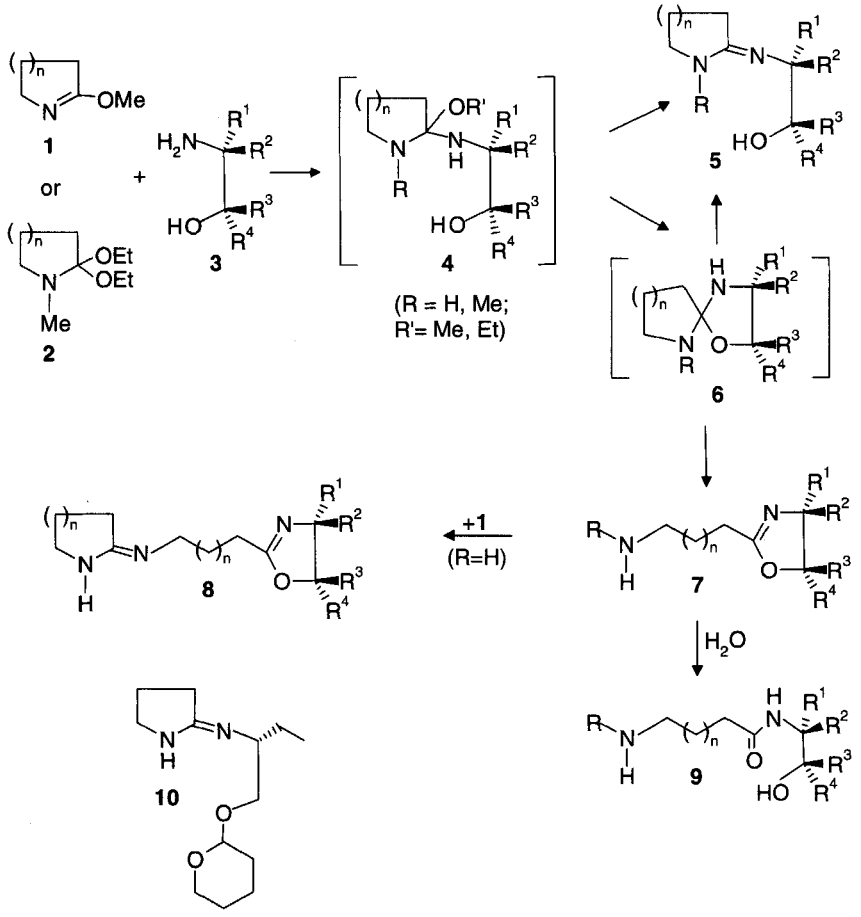
Recently chiral 2-(ω-aminoalkyl)-oxazolines such as **7** have gained interesting application in the asymmetric synthesis of ω-aminobutyric acids based on α-alkylation and subsequent hydrolytic cleavage of the oxazoline ring [1]. We now report a useful access to the starting 2-(ω-aminoakyl)-oxazolines **7**.

A. Botta reported [2] a general method for the synthesis of ω-aminoalkylazolines by ring transformation of lactams and their derivatives e. g. lactim ethers **1** or lactam acetals **2** with diamines [2, 3], aminothiols [2] and aminoalcohols [2]. This ring transformation looked promising to generate the desired enantiomerically pure aminoalkyloxazolines **7** if corresponding chiral aminoalcohols **3** were used as binucleophiles. The ring transformation method however can be encountered with several problems such as formation of mixtures of isomeric ring-transformed and not ring-transformed products (e. g. oxazolines **7** were generally observed [2] as mixtures with **5**) or competing reactions leading to 2 : 1 products [2]. Furthermore, recent investigations of such ring transformations with certain amino acids as binucleophiles revealed the danger of subsequent reactions of ω-aminoalkylazoline-4-carboxylic acids with starting lactim ether **1** giving corresponding 2-(ω-lactamiminoalkyl)-azoline-4-carboxylic acids [4].

Facing these problems and taking into account that no detailed information (spectra, ratios of isomeric products) was given [2] for the formation of the only example of a chiral but racemic ω-aminoalkyl-oxazoline **7** ($R^1 = R^2 = R^3 = H$, $R^4 = Me$) we investigated the ring transformation of lactim ethers **1** or lactam acetals **2** with chiral amino alcohols **3** in detail. We envisaged to develop a reliable access to a variety of enantiomerically pure ω-aminoalkyl-oxazolines **7** in order to study the effect of substituents $R^1$, $R^2$, $R^3$, $R^4$ in the oxazoline ring on the stereoselectivity of the asymmetric side chain alkylation mentioned above [1].

Our investigations of reactions of lactam derivatives **1** or **2** with chiral aminoalcohols **3** revealed that in addition to products **5** and **7** two further types of products (**8** and **9**) can be formed (see Table 1). Often just one product was found. In a number of cases mixtures were obtained which could be separated by Kugelrohr distillation. The lactamimino-alkyloxazolines **8** derived from further reactions of ω-aminoalkyl-oxazolines **7** with unreacted lactim ether **1** while the N-(2-hydroxyethyl)-amides **9** arose from hydrolytic cleavage of the oxazoline ring. The reaction of lactam acetals **2** afforded the envisaged ring transformed ω-methylaminoalkyl-oxazolines **7** as sole products in most cases (for one exception see formation of non-ringtransformed **5p**). The easiness of subsequent hydrolytic cleavage of the 2-(ω-methylaminoalkyl)-oxazolines **7** (R = Me) giving ω-aminoalkaneamids **9** depends on the chain length. While

[1]) Presented in part at the 2nd Iminiumsalz-Tagung in Stimpfach-Rechenberg, Germany (September 20–22, 1995)



**Scheme 1**

the ω-methylaminopropyl-oxazolines **7** (n = 1) are stable, the homologous ω-methylaminopentyl compounds **7** (n = 3) can be isolated but are cleaved on standing in the open air. ω-Methylaminobutyl-oxazolines **7** (n = 2) however suffer hydrolytic cleavage already during isolation. Reactions of aminoalcohols **3** with lactim ethers **1** show a higher tendency to give not ring-transformed lactam imines **5**, especially if the butyrolactim ether **1** (n = 1) and in part if valerolactim ether **1** (n = 2) are used. Regardless of this trend a certain extend of ring transformation could be achieved in almost all cases (see Table 1), however, the expected ω-aminoalkyloxazolines can suffer further transformation to the corresponding lactam imines **8**. As demonstrated in some cases (compounds **5a**, **7a** and **8d**) the application of high pressure (10 kbar) improves the yields of ring transformation products.

From the mechanistic point of view the reaction of lactam derivatives **1** or **2** with aminoalcohols **3** can be understood by a primary attack of the amino group affording semicyclic aminal esters **4** which either give lactam imines **5** by elimination of alcohol or can cyclize to spiro compounds **6**. The latter act as intermediates in the ring transformation to ω-aminoalkyloxazolines **7** or could alternatively cleave the C-O-bond to form lactam imines **5**. The formation of spiro intermediates **6** *via* lactam imines **5** is improbable since the latter could not be transformed to ω-aminoalkyloxazolines **7** or their derivatives under similar conditions.

The structure elucidation of all compounds was possible by spectroscopic methods (see Tables 2 and 3) in a similar way as shown [4] for 2-(ω-aminoalkyl)-oxazoline-4-carboxylic acids. Thus, compounds containing an ω-aminoalkyl chain (e. g. **7**, **8**, **9**) exhibit typical fragment peaks in the mass spectra derived from an onium cleavage. The N–$CH_3$ $^1$H-NMR signal of *N*-methyl substituted derivatives (R = Me) are downfield shifted (> 3 ppm) in lactam imines **5** as compared with ring transformed aminoalkyloxazolines **7** (δ = 2.2–2.9 ppm). The $^{13}$C-NMR shift of the CH-N carbon atom of the oxazoline ring in compounds **7** and **8** appear at δ = 62–75 ppm while the corresponding signals of the non-oxazoline compounds **5** and **9** appear at 50–60 ppm. The lactam imine **10** derived from reaction of the corresponding O-protected aminoalcohol and butyrolactim ether **1** (n = 1) served as unambiguous reference compound for interpretation of spectra of lactam imines **5**. All chiral products **7** are optically active (see Table 2). HPLC-

**Table 1** Reaction of Lactam Derivatives **1** and **2** with Aminoalcoholes **3**

| R | $R^1$ | $R^2$ | $R^3$ | $R^4$ | n | time [a] | yield % of isolated product 5 | 7 | 8 | 9 |
|---|---|---|---|---|---|---|---|---|---|---|
| H | Et | H | H | H | 1 | 6h | **a**(25) | **a**(30) | | |
| | | | | | | 12h [b] | **a**(34) | **a**(45) | | |
| H | H | Me | Ph | H | 1 | 14h | **b**(15) | **b**(33) | | |
| H | H | Mom | H | Ph | 1 | 24h | | **c**(44) | | |
| H | Me | Me | H | H | 1 | 24h | | | **d**(35) | |
| | | | | | | 12h [b] | | | **d**(86) [c] | |
| Me | Et | H | H | H | 1 | 12h | | **e**(76) | | |
| Me | H | Me | Ph | H | 1 | 16h | | **f** (51) | | |
| Me | H | Mom | H | Ph | 1 | 20h | | **g**(70) | | |
| Me | Me | Me | H | H | 1 | 12h | | **h**(49) | | |
| H | Et | H | H | H | 2 | 16h | **i** (31) | **i**(34) | | |
| H | H | Me | Ph | H | 2 | 18h | | | | **j**(35) |
| H | H | Mom | H | Ph | 2 | 16h | **k**(25) [d] | **k**(7) [d] | | **k**(58) [d] |
| H | Me | Me | H | H | 2 | 20h | | | **l** ( 24) | |
| Me | Et | H | H | H | 2 | 20h | | | | **m**(31) |
| Me | H | Me | Ph | H | 2 | 20h | | | | **n**(38) |
| Me | H | Mom | H | Ph | 2 | 22h | | | | **o**(27) |
| Me | Me | Me | H | H | 2 | 14h | **p**(23) | **p**(67) | | |
| H | Et | H | H | H | 3 | 24h | | **q**(70) | | |
| H | H | Me | Ph | H | 3 | 20h | | **r**(65) | | |
| H | H | Mom | H | Ph | 3 | 48h | | **s**(28) | | |
| H | Me | Me | H | H | 3 | 18h | | | **t** (26) | |
| Me | Et | H | H | H | 3 | 18h | | **u**(76) | | |
| | | | | | | [e] | | | | **u**(>95) |
| Me | H | Me | Ph | H | 3 | 17h | | **v**(41) | | |
| | | | | | | [e] | | | | **v**(>95) |
| Me | H | Mom | H | Ph | 3 | 18h | | **w**(36) | | |
| | | | | | | [e] | | | | **w**(>95) |
| Me | Me | Me | H | H | 3 | 16h | | **x** (79) | | |
| H | Et | H | H | H | 9 | 12h | | **y** (48) | | |
| H | H | Me | Ph | H | 9 | 18h | | **yy**(61) | | |
| H | H | Mom | H | Ph | 9 | 36h | | **z** (48) | | |
| H | Me | Me | H | H | 9 | 18h | | **zz**(32) | **zz**(25) | |

[a]) Method A [b]) Method B [c]) ratio of aminoalcohol **3** : lactim ether **1** = 1 : 2 [d]) unseparable mixture [e]) after keeping **7** on air

investigations of selected examples revealed a complete retention of the configuration of the starting aminoalcohols **3** in all transformations.

The aforementioned results demonstrate that the ring transformation of lactam derivatives **1** and **2** with aminoalcohols **3** is an useful method to synthesize a variety of enantiomerically pure ω-aminoalkyloxazolines **7** which are useful starting materials for asymmetric synthesis of chiral α-alkyl-ω-aminoacids [1]. The previous results reported by Botta [2] could only show a part of the complexity of the reaction of lactam derivatives **1** and **2** with amino alcohols. Realizing this fact we further investigated the reaction of lactim ethers **1** and lactam acetals **2** with racemic 1,2-diaminopropane, which according to the same author give ω-aminoalkylimidazolines **12** as sole products. Our detailed investigations with lactam derivatives **1** and **2** of various ring sizes revealed a higher tendency to give ring transformation products as compared with corresponding reactions with aminoalcohols **3** (see Tables 4 and 5). 5- and 6-membered lactim ethers **1** however gave further ring modification of the resulting ω-aminoalkylimidazolines **12** to the corresponding lactam imines **13**.

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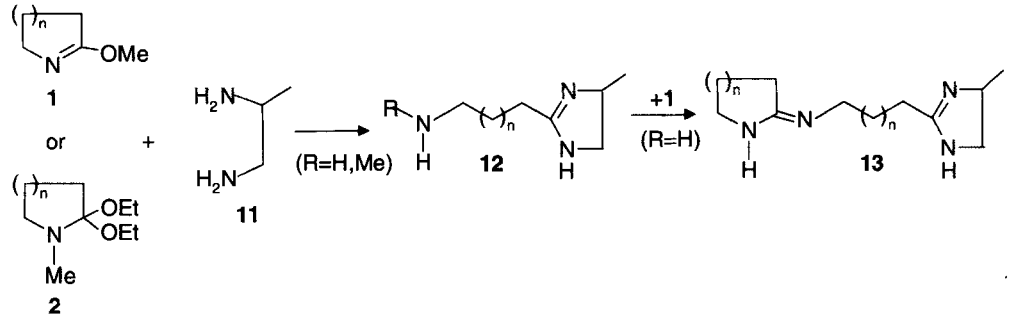
## Experimental

Melting points are uncorrected. $^1$H-NMR and $^{13}$C-NMR spectra were recorded at 300 and 75.5 MHz respectively on a BRUKER AC-300 with TMS as internal standard. Mass spectra (HP 5995 A) were measured at 70 eV. Enantiomeric purity of products **7** was proved by analytical HPLC (KONTRON INSTRUMENTS) on cellulose carbamate (CHIRALCEL OD-R; Daicel). Optical rotation was determined with a PERKIN ELMER polarimeter 241. Lactim ethers **1** [5] and lactam acetals **2** [6] were prepared according to known procedures.

### General Procedure for the Synthesis of N'-Hydroxyethyllactam-2-imines (5 and 10), 2-(ω-Aminoalkyl)-Δ$^2$-azolines (7) and (12), 2-(ω-Lactamiminoalkyl)-Δ$^2$-azolines (8) and (13) and *N*-(2-Hydroxyethyl)-ω-aminoalkanamides (9) (Method A)

A solution of lactam derivative **1** or **2** (0.01 mol) in dry methanol (40 ml) or ethanol (40 ml) respectively was dropped into a solution of aminoalcohol **3** (0.015 mol) in the same solvent (50 ml) during 15 min. After the addition of *p*-




**Scheme 2**

**Table 2** Physical and Spectroscopic Data of 2-(ω-Amino-alkyl)-$\Delta^2$-oxazolines (**7**)

| Nr. | m.p.°C | b.p °C/mbar | $[\alpha]_D^{20}$ [a] | $^1$H-NMR [b] | $^{13}$C-NMR [c] | MS *m/z* (%) |
|---|---|---|---|---|---|---|
| **7a** | 71–73 | 150/0.5 | + 62.0 (1.0) | 0.94–0.99 (t, J=7.4, 3H, $CH_3$); 1.43–1.63 (m, 2H, $CH_2$); 1.90–2.00 (quint, 2H, J=7.2, 7.8, $CH_2$); 2.42–2.47 (t, 2H, J=8.1, $CH_2$-N); 3.49–3.70 (m, 3H, CH, $CH_2$-O) | 9.9 $CH_3$; 23.4 $CH_2$; 25.7 $CH_2$; 32.9 $CH_2$; 55.6 $CH_2$-N; 67.3 CH-N; 71.9 $CH_2$-O; 167.4 C=N | 156 ($M^+$, 1,0); 155 (M-1, 2.8); 125 (89); 111 (45); 54 (53); 41 (62); 30 (100) |
| **7b** | 118–120 | 175/0.5 | − 260 (0.75) | 4.11–4.14 (d, J=6.7, 1H,CH-N); 4.76–4.79 (d, J=6.1, 1H, CH-O) 5.00–5.55 (br s, 2H,$NH_2$) | 5.2 $CH_2$-N; 64.9 CH-N; 78.5 5 CH-O | 30 (100) |
| **7c** | – | 200–225/0.5 | + 19.2 (0.64) | 3.50–3.62 (m, 2H, $CH_2$-O); 4.06–4.1152.6 $CH_2$-N; 74.2 CH-N; (q, J=5.7, 1H, CH-N); 5.25–5.27 (d, J=7.0, 1H,CH-O) | 52.6 $CH_2$-N; 74.2 CH-N; 83.2 CH-O | 141 (100); 30 (70) |
| **7e** | 34–38 | 125/0.2 | + 40.9 (1.0) | 2.72 (s, 3H, $CH_3$-N); 2.94–3.08 (m, 1H, CH-N); 3.33–3.48 (m, 2H, $CH_2$-O) | 31.4 $CH_3$-N; 50.9 $CH_2$-N; 63. 1 CH-N; 66.1 $CH_2$-O | 44 (100) |
| **7f** | 55–60 | 200/0.5 | + 32.3 (0.75) | 2.82 (s, 3H, N-$CH_3$); 3.37–3.45 (dd, J=4.1,6.1, 1H, CH-N); 4.62–4.63 (d, J=6.0, 1H,CH-O) | 31.1 $CH_3$-N; 60.5 CH-N; 76.7 CH-O | 44 (100) |
| **7g** | ~ 30 | 220/0.5 | + 151.5 (0.40) | 2.77 (s, 3H, $CH_3$-N); 4.03–4.09 (q, J=6.5,12.5, 1H, CH-N); 5.22-5.24 (d, J=6.9, 1H, CH-O) | 30.4 $CH_3$-N; 50.1 $CH_2$-N; 65.0 CH-N; 71.7 $CH_2$-O; 83.2 CH-O | 155 (100); 44 (95) |
| **7h** | – | 65/0.5 | – | 2.20 (s, 3H, $CH_3$-N); 3.69 (s, 2H, $CH_2$-O) | 36.1 $CH_3$-N; 50.9 $CH_2$-N; 66.7 C; 78.7 $CH_2$-O | 44 (100) |
| **7i** | ~ 50 | 175/0.5 | + 50.0 (1.0) | 3.22–3.66 (m, 5H, CH, $CH_2$-N, $CH_2$-O) | 45.4 $CH_2$-N; 67.3 CH-N; 71.8 $CH_2$-O | 30 (100) |
| **7p** | – | 45/0.8 | – | 2.13 (s, 3H, $CH_3$-N); 3.61 (s, 2H, $CH_2$-O) | 36.2 N-$CH_3$; 51.4 $CH_2$-N; 66.6 C; 76.9 $CH_2$-O | 44 (100) |
| **7q** | | 150/0.5 | + 39.0 (1.0) | 3.78–3.84 (t, J=7.8, 1H, $CH_2$-O); 3.96–4.04 (quint, J=6.6, 7.0, 1H, CH-N); 4.24–4.27 (t, J=8.1, 1H, $CH_2$-O) | 41.5 $CH_2$-N; 67.3 CH-N; 71.7 $CH_2$-O | 30 (100) |
| **7r** | | 220/0.5 | − 165.2 (0.85) | 4.34–4.44 (sext, 1H, CH-N); 5.52–5.56 (d, J=9.2, 1H, CH-O) | 30.8 $CH_2$-N; 64.8 CH-N; 83.6 CH-O | 30 (100) |
| **7s** | – | 240/0.5 | + 35.6 (1.0) | 2.57–2.61 (t, J=6.7, 2H,$CH_2$-N); 3.99–4.05 (dd, J=4.5, 6.6, 1H, CH-N); 5.18–5.21 (d, J=6.8, 1H, CH-O) | 41.8 $CH_2$-N; 74.2 CH-N; 83.2 CH-O | 30 (100) |
| **7u** | – | 125/2.0 | + 36.2 (1.0) | 2.34 (s, 3H, $CH_3$-N); 3.74–3.79 (t, J=7.8, 1H, $CH_2$-O); 3.88–3.98 (m, 1H, CH-N); 4.16–4.22 (sext, J=1.2, 8.1, 1H, $CH_2$-O) | 35.9 $CH_3$-N; 51.4 $CH_2$-N; 67.0 CH-N; 71.5 $CH_2$-O | 44 (100) |
| **7v** | – | 145/0.5 | + 53.5 (1.0) | 2.36 (s, 3H, N-$CH_3$); 4.28–4.39 (m, 1H,CH-N); 5.47–5.51 (d, J=9.8, 1H,CH-O) | 36.3 $CH_3$-N; 51.7 $CH_2$-N; 64.7 CH-N; 83.6 CH-O | 44 (100) |
| **7w** | – | 170–190/0.5 | − 59.0 (0.1) | 2.30 (s, 3H, $CH_3$-N); 3.35–3.52 (m, 2H, $CH_2$-O); 3.99–4.01 (m, 1H, CH-N); 5.17–5.19 (d, J=6.8, 1H, CH-O) | 35.9 $CH_3$-N; 51.3 $CH_2$-N; 73.9 CH-N; 71.8 $CH_2$-O; 82.9 CH-O | 44 (100) |
| **7x** | – | 75–90/0.5 | – | 2.02 (s, 3H, $CH_3$-N); 3.49 (s, 2H, $CH_2$-O) | 36.1 N-$CH_3$; 51.5 $CH_2$-N; 66.4 C; 78.4 $CH_2$-O | 44 (100) |
| **7y** | ~ 45 | 170/0.5 | + 43.0 (1.0) | 4.38–4.40 (sext, 1H, CH-N); 5.52–5.55 (d, J=9.8, 1H, CH-O) | 41.6 $CH_2$-N; 67.2 CH-N; 71.6 $CH_2$-O | 113 (100); 30 (81) |
| **7yy** | – | 250/0.5 | − 60.0 (1.0) | 4.38–4.40 (sext, 1H, CH-N); 5.52–5.55 (d, J=9.8, 1H, CH-O) | 64.8 CH-N; 83.5 CH-O | 30 (100) |
| **7z** | – | 220–250/0.5 | − 21.1 (1.0) | 3.07–3.11 (t, J=7.1, 2H, $CH_2$-N); 3.82 (s, 2H, $CH_2$-O) | 29.1 $CH_2$-N; 59.2 $CH_3$-O; 74.3 $CH_2$-O; 74.3 CH-N; 83.2 CH-O | 30 (100) |
| **7zz** | – | 215–235/0.5 | – | 3.07–3.11 (t, J=7.1, 2H, $CH_2$-N); 3.82 (s, 2H, $CH_2$-O) | 29.6 $CH_2$-N; 66.8 C; 78.8 $CH_2$-O | 30 (100) |

[a]) in brackets: c in g/100 mg $CHCl_3$
[b]) δ/ppm, J/Hz, $CDCl_3$
[c]) δ/ppm, $CDCl_3$, with the exception of **7a** only selected data

**Table 3** Physical and Spectroscopic Data of Lactam-2-hydroxyethylimines (**5** and **10**), 2-ω-Lactamiminoalkyl)-$\Delta^2$-oxazolines (**8**), *N*-(2-Hydroxyethyl)-ω-aminoalkaneamides (**9**)

| Nr. | m.p. °C | b.p. °C [a] | $^1$H-NMR (δ/ppm, J/Hz, $CDCl_3$) | $^{13}$C-NMR (δ/ppm, $CDCl_3$) [b] | MS *m/z* (rel. int. %) [b] |
|---|---|---|---|---|---|
| **5a** | – | 225/0.5 | 0.94–0.99 (t, J=7.4, 3H, $CH_3$); 1.43–1.63 (m, 2H, $CH_2$); 1.90–2.00 (quint 2H, J= 7.2, 7.8, $CH_2$); 2.42–2.47 (t, 2H,J=8.1, $CH_2$-N) 3.49–3.70 (m, 3H, CH, $CH_2$-O) | 10.5 $CH_3$; 23.4 $CH_2$; 24.8 $CH_2$; 31.8 $CH_2$; 42.7 $CH_2$-N); 57.8 CH-N; 66.9 $CH_2$-O 167.6 C=N | 156 ($M^+$+1, 8); 155 ($M^+$,1); 125 (97); 111 (70); 85(100); 68 (33); 41 (62); 30 (64) |
| **5b** | – | 220/0.5 | 4.11–4.14 (d, J=6.7, 1H,CH-N); 4.73–4.75 (d, J=2.0, 1H,CH-O) | 43.5 $CH_2$-N; 54.3 CH-N; 73.6 CH-O | 111 (100); 30 (35) |
| **5i** | – | 240/0.5 | 3.22–3.66 (m, 5H, CH, $CH_2$-N, $CH_2$-O) | 40.7 $CH_2$-N; 56.4 CH-N; 68.0 $CH_2$-O | 99 (100); 30 (34) |
| **5p** | – | 85/0.5 | 2.95 (s, 3H, $CH_3$-N); 2.99 (br s, 2H, $CH_2$-N); 3.01 (s, 2H, $CH_2$-O) | 34.3 N-$CH_3$; 49.7 $CH_2$-N; 66.6 C; 71.6 $CH_2$-O | |
| **10** | – | Öl | 3.33–3.40 (m, 1H, CH-N); 3.45–3.47 (m, 2H, $CH_2$-O); 3.59–3.63 (t, J=6.8, 2H, $CH_2$-O); 4.50–4.58 (m, 1H, CH-O) | 42.2 $CH_2$-N; 49.8 CH-N; 62.1 $CH_2$-O; 69.0 $CH_2$-O; 98.7 CH-O | 85 (100); 30 (19) |
| **8d** | – | 125/0.1 | 1.20 (s, 6H, 2x$CH_3$); 1.75–1.87 (m, 4H, 2x$CH_2$); 2.21–2.30 (m, 2H, $CH_2$); 2.35–2.41 (m, 2H, $CH_2$); 3.22–3.27 (t, J=6.8, 2H, $CH_2$-N); 3.54–3.59 (t, J=6.1, 2H, $CH_2$-N); 3.85 (s, 2H, $CH_2$-O) | 22.9 $CH_2$; 23.2 $CH_2$; 25.4 $CH_2$; 25.5 $CH_2$; 28.4 2x$CH_3$; 42.7 $CH_2$-N; 56.1 $CH_2$-N; 66.8 C; 79.0 $CH_2$-O; 165.5 C=N; 165.9 C=N | 224 ($M^+$+1, 0.8); 223 ($M^+$, 1.2); 111 (44); 85 (42); 83 (41); 58 (100); 41 (51); 28 (55) |
| **8l** | – | 160/0.5 | 2.94–2.99 (t, J=6.9, 2H, $CH_2$-N); 3.21–3.25 (t, J=6.3, 2H, $CH_2$-N); 3.71 (s, 2H, $CH_2$-O) | 40.5 $CH_2$-N; 46.1 $CH_2$-N; 66.7 C; 78.7 $CH_2$-O | 99 (100); 30 (99) |
| **8t** | – | 150–175/0.5 | 2.89–2.94 (t, J=7.1, 2H, $CH_2$-N); 3.20–3.23 (t, J=4.8, 2H, $CH_2$-N); 3.77 (s, 2H, $CH_2$-O) | 36.3 $CH_2$-N; 42.6 $CH_2$-N; 66.7 C; 78.8 $CH_2$-O | 55 (100); 30 (70) |
| **8zz** | – | 175–200/0.5 | 2.48–2.53 (t, J=6.9, 2H, $CH_2$-N); 3.10–3.11 (m, 2H, $CH_2$-N); 3.73 (s, 2H, $CH_2$-O) | 33.4 $CH_2$-N; 41.9 $CH_2$-N; 66.6 C; 78.7 $CH_2$-O | 126 (100); 30 (85) |
| **9j** | 110–115 | – | 1.06–1.08 (d, J=6.8, 3H, $CH_3$); 1.43–1.65 (m, 4H, 2x$CH_2$); 2.16–2.20 (t, J=7.1, 2H, $CH_2$); 3.13–3.19 (t, J=6.7, 2H,$CH_2$-N); 4.08–4.17 (sext, 1H, CH-N); 4.63–4.66 (d, J=4.3, 1H, CH-O); 7.19–7.41 (m, 5H, Ph) | 15.2 $CH_3$; 24.1 $CH_2$; 31.18 $CH_2$; 36.54 $CH_2$; 49.9 $CH_2$-N; 51.86 CH-N; 76.9 CH-O; 127.5 2x$CH_{Ph}$; 128.2 $CH_{Ph}$; 129.0 2x$CH_{Ph}$; 143.7 $C_{Ph}$; 175.7 C=O | 250($M^+$, 0.8); 126 (24); 100 (74); 56 (45); 44 (100); 30 (84) |
| **9m** | 55–57 | 110–120/0.9 | 2.35 (s, 3H, $CH_3$-N); 3.43–3.75–3.79 (m, 1H, CH-N); 6.22–6.25 (br s, 1H, NH) | 35.9 $CH_3$-N; 51.0 $CH_2$-N; 53.1 CH-N; 64.5 $CH_2$-O | 44 (100) |
| **9n** | ~ 91 | 200/0.5 | 2.29 (s, 3H, N-$CH_3$); 4.21–4.26 (m, 1H, CH-N); 4.82–4.83 (d, J=2.8, 1H, CH-O); 6.27–6.28 (d, J=8.3, 1H, NH) | 36.9 $CH_3$-N; 51.7 CH-N; 52.0 $CH_2$-N; 76.4 CH-O | 44 (100) |
| **9o** | 95–105 | 205/0.5 | 2.37 (s, 3H, $CH_3$-N); 4.17–4.21 (m, 1H, CH-N); 4.95–4.97 (d, J=4.3, 1H, CH-O); 6.35–6.38 (d, J=7.7, 1H, NH) | 36.1 $CH_3$-N; 51.2 $CH_2$-N; 59.2 CH-N; 73.3 $CH_2$-O; 74.3 CH-O | 44 (100) |
| **9u** | 35–37 | – | 35.5 $CH_3$-N; 51.0 $CH_2$-N; 52.8 CH-N; 63.8 $CH_2$-O | | 44 (100) |
| **9v** | ~ 65 | – | 2.27 (s, 3H, N-$CH_3$); 3.07–3.18 (m, 1H CH-N); 4.76 (s, 1H, CH-O); 6.37–6.43 (t, J=8.3, 1H, NH) | 35.2 $CH_3$-N; 50.7 CH-N; 50.7 $CH_2$-N; 75.1 CH-O | 44 (100) |
| **9w** | 70–80 | – | | | 44 (100) |

[a] pressure/mbar [b] with the exception of **5a**, **8f**, and **9j** only selected data

**Table 4** Reaction of Lactam Derivatives **1** and **2** with 1,2-Diaminopropane **11**

| R | n | Method | **12**(% yield) [a] | **13**(% yield) [a] |
|---|---|---|---|---|
| H | 1 | A, 8h | | **a** (33) |
| | | C | | **a** (55) |
| Me | 1 | A, 8h | **b** (54) | |
| | | C | **b** (60) | |
| H | 2 | C | | **c** (30) |
| Me | 2 | C | **d** (53) | |
| H | 3 | C | **e** (80) | |
| H | 9 | C | **f** (98) | |

[a] of isolated product

**Table 5** Physical and Spectroscopic Data of 2-(ω-Aminoalkyl)-$\Delta^2$-imidazolines (**12**) and 2-(ω-Lactamiminoalkyl)-$\Delta^2$-imidazolines (**13**)

| Nr. | m.p. °C | b.p. °C [a] | $^1$H-NMR (δ/ppm, J/Hz, $CDCl_3$) | $^{13}$C-NMR (δ/ppm, $CDCl_3$) [b] | MS *m/z* (rel. int. %) [b] |
|---|---|---|---|---|---|
| **12b** | – | 125/0.8 | 0.76–0.79 (d, J=6.3, 3H, $CH_3$); 1.63–1.68 (t, J=7.4, 2H, $CH_2$); 1.96–2.08 (m, 2H, $CH_2$); 2.53 (s, 3H, N-$CH_3$); 2.85–2.91 (dd, J=4.2, 12.3, 1H, $CH_2$-N); 2.92–2.97 (t, J=6.8 2H, $CH_2$-N); 3.09-3.14 (t, J=11.5, 1H, $CH_2$-N); 3.36–3.44 (m, 1H, CH-N) | 19.5 $CH_2$; 21.0 $CH_3$; 26.2 $CH_2$; 31.0 N-$CH_3$; 48.1 CH-N; 50.8 $CH_2$-N; 59.9 $CH_2$-N; 163.8 C=N | 155 ($M^+$, 6.9); 125 (43); 111 (61); 98 (66); 44 (100); 42 (54); 30 (43); 28 (74) |
| **12d** | – | 250/0.5 | 2.85–2.89 (t, J=6.7, 2H, $CH_2$-N); 3.14–3.21 (dd, J=7.6, 11.2, 1H, $CH_2$-N); 3.72–3.79 (t, J=11.2, 1H, $CH_2$-N); 2.46 (s, 3H, N-$CH_3$); 4.02–4.09 (m, 1H, CH-N) | 33.7 N-$CH_3$; 48.5 $CH_2$-N; 53.2 CH-N; 57.9 $CH_2$-N | 111(100); 44 (80) |
| **12e** | – | 150/0.15 | 2.35–2.40 (t, J=6.7, 2H, $CH_2$-N); 2.80–2.86 (dd, J=7.3, 11.1, 1H, $CH_2$-N); 3.35–3.42 (t, J=11.1, 1H, $CH_2$-N); 3.58–3.64 (m, 1H, CH-N) | 41.3 $CH_2$-N; 56.0 CH-N; 56.7 $CH_2$-N | 30 (100) |
| **12f** | 44–49 | 215–230/0.3 | 2.57–2.65 (m, 4H, $CH_2$-N, $CH_2$); 3.07–3.13 (dd, J=7.3, 11.2, 1H, $CH_2$-N); 3.61–3.68 (t, J=11.0, 1H, $CH_2$-N); 3.86–3.89 (m, 1H, CH-N) | 42.1 $CH_2$-N; 55.9 CH-N; 56.5 $CH_2$-N | 30 (100) |
| **13a** | – | 180–200/0.1 | [c] 3.64-3.80 (m, 1H, CH-N) 2.89-2.95 (dd, J=7.3, 11.3, 1H, $CH_2$-N); 3.04–3.09 (t, J=6.9, 2H, N-$CH_2$); 3.38-3.42 (t, J=6.7, 2H, N-$CH_2$); 3.45–3.52 (t, J=11.0, 1H, $CH_2$-N); 3.64–3.80 (m, 1H, CH-N) | [c] 42.0 $CH_2$-N; 54.4 $CH_2$-N; 55.7 CH-N; 56.9 $CH_2$-N | 111 (100); 30 (25); 28 (33) |
| **13c** | 62–71 | 210–220/0.5 | 3.69–3.77 (m, 1H, CH-N) 2.90–3.01 (m, 3H, 2×$CH_2$-N); 3.18–3.23 (t, J=5.7, 2H, N-$CH_2$); 3.45–3.52 (t, J=11.0, 1H, $CH_2$-N); 3.69–3.77 (m, 1H, CH-N) | 40.6 $CH_2$-N; 44.9 $CH_2$-N; 54.4 $CH_2$-N; 56.4 CH-N; 56.9 $CH_2$-N | 125 (100); 30 (43) |

[a]) pressure/mbar [b]) with the exception of **12b** and **13a** only selected data [c]) in DMSO-$d_6$

toluenesulfonic acid (0.017 g, 0.0001 mol), the mixture was kept at room temperature overnight and was then refluxed for several hours (see Table 1). After evaporation of the solvent in vacuum the oily residue was purified by bulb to bulb vacuum distillation (first fraction contained excess aminoalcohol **3**).

### Synthesis of 5a, 7a, and 8d under high pressure conditions (Method B)

Aminoalcohol **3** (0.0005 mol) and butyrolactim ether **1** (0.05g, 0.0005 mol) were dissolved in dry methanol (5 ml). The mixture was filled into a Teflon-tube (diameter 5 mm; length: 20 cm). After sealing the tube was immersed into the transmitter liquid of a high pressure apparatus (HOFER), and the pressure was raised to 10 kbar. The mixture was kept under these conditions at room temperature for 2 d. After decompression the mixture was worked up as described in Method A.

### Synthesis of 2-(ω-Aminoalkyl)-$\Delta^2$-imidazolines (12) and 2-(ω-Lactamiminoalkyl)-$\Delta^2$-imidazolines (13) (Method C) [2]

Lactam derivative **1** or **2** (0.05 mol), 1,2-diaminopropane (5.50 g, 0.075 mol) and *p*-toluenesulfonic acid (0.87g, 0.005 mol) were heated with stirring in a distillation apparatus first to 00 °C. The temperature was gradually raised to 160 °C during 30 min. The corresponding alcohol (2 ml) distilled off. After heating the mixture to 160 °C for 2 h and to 190 °C for 1 h the crude mixture was purified as described in Method A.

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