(DIETHYLAMINO)SULFUR TRIFLUORIDE (DAST) AS A USEFUL REAGENT FOR THE PREPARATION OF 2-OXAZOLINES FROM 1,2-AMIDO ALCOHOLS

Pierre Lafargue, a Pierre Guenot, b and Jean-Paul Lellouche a *

(a) CEA, CE-Saclay, Département de Biologie Cellulaire et moléculaire, Service des Molécules Marquées, B 1547, F-91191 Gif-sur-Yvette Cedex, France
(b) Centre Régional de Mesures Physiques de l'Ouest, Université de Rennes I, Campus de Beaulieu, 35042 Rennes, France

Abstract- Acyclic 1,2-amido alcohols (6) react efficiently with a slight excess of (diethylamino)sulfur trifluoride (DAST) to afford the corresponding 2-oxazolines (10) in good yields ranging between 57-95%. Even at the low temperature of -78 °C, a rapid (<1 h) and stereoselective amide cyclization is observed without formation of acylaziridine by-products. The scope of this cyclization is discussed.

The synthetic potential of 2-oxazoline nucleus relies essentially on its specific chemical properties. Particularly attractive is its easy transformation or elaboration into conventional functional groups. It acts for example as a masked carboxylic group and as an efficient ortho-metallation directing moiety. Moreover, this nucleus showed interesting potentials in the field of asymmetric synthesis. Thus, C2-symmetrical bis(4,5-dihydrooxazolyl)methanes have been used successfully in the asymmetric version of numerous reactions like Diels-Alder reaction, hydrosilylation of ketones, olefin cyclopropanation and aziridination. Further interest arose recently from the discovery of oxazolines incorporated as peptide mimetics into the backbone of biologically active compounds isolated from marine sources. Synthetic procedures leading to 2-oxazolines include bimolecular reactions such as the reaction of amino alcohols with imidates, unimolecular rearrangements of acylaziridines, or cyclizations of hydroxy amides and related compounds.
Our interest in this field originates from an unsuccessful fluorodehydroxylation encountered with the two 1,2-acetamido alcohols (1) and (2) (1.0 equivalent) using (diethylamino)sulfur trifluoride \(^\text{12}\) in slight excess (SF\(_3\)NET\(_2\), DAST: 1.1 equivalents, -78°C, 1 h, Scheme 1). \(^\text{13}\) Under these conditions, an intramolecular participation of the amide produced the corresponding 2-oxazolines (3) (82%) and (4) (83%) rather than the expected fluorinated acetamides (5) (Entries 1 and 2 in Table).

A careful literature survey revealed surprisingly that DAST has only been made to react with cyclic 1,2-amido alcohols (6) (R\(_5\) = Ph or Me) in CH\(_2\)Cl\(_2\) at room temperature (16 h) affording the cyclic 2-oxazolines (7) \(^\text{14}\) (left part of Scheme 2). Modest yields of products were observed depending on the structure of 6.
Considering the preparation of 2-oxazolines (10) from acyclic 1,2-hydroxy amides (6), the goal of this work is to show that our new experimental conditions represent an improvement both in terms of DAST stoichiometry, low cyclization temperature and short reaction times. The case of variously substituted acyclic precursors of type (6) has been especially examined.

The starting 1,2-amido alcohols were obtained using the Schotten-Baumann procedure (unoptimized yields, see Table and Experimental). They were submitted to our standard protocol and the cyclization monitored by tlc until completion (30 min to 1 h). Hydrolysis of the reaction mixture must be conducted at -78 °C under basic conditions (4M NH₄OH) in order to minimize HF mediated ring-opening of the oxazolines. Purification by flash chromatography, performed on silica gel deactivated by triethylamine, affords the corresponding pure 2-oxazolines. The results shown in the Table enabled us to make some useful comments:

1) The cyclization can be conducted at the low temperature of -78 °C using only a slight excess of DAST (1.1 equivalents) without formation of aziridine (9) resulting from a possible N-cyclization. The reaction is complete within 1 h, and the product is obtained in fair to good yield (Entries 1-11, 57-95 %). Lower yields are observed when the starting amido alcohols are partially insoluble (heterogeneous media, Entries 3 and 6: 62 and 57 % in 12 and 20), or when the resulting 2-oxazoline is still labile even on deactivated silica gel (Entry 5, 76 % in 17),

2) Variable structural patterns in 6 are well tolerated. Primary and secondary amido alcohols are activated in the same manner towards amide participation. Moreover, a tetrasubstituted acylamino (Entries 1 and 2) or a quaternary carbon located close to the nucleophilic amide carbonyl in 6 (Entries 4, 8 and 11) did not impede the cyclization. Interestingly, cyclization of 13 to 14 (Entry 4, 70 %) is accompanied by the fluorinated amide (15) (one diastereoisomer, 28 %). In this case, fluorination of 13 competes with the formation of 14. tert-Butyl substituents which might be expected to cause a decrease in reactivity in fact do not hinder the reaction at all since 2-oxazolines (24) and (30) were isolated in nearly quantitative yield.

3) Proceeding probably through intermediate (8), 13 the depicted O-cyclization is totally diastereoselective with inversion at C(2) of 6. Only one diastereoisomeric 2-oxazoline has been isolated as judged by high-field ¹H- and ¹³C-nmr (diastereoisomeric purity of crude 12, 14 and 17 ≥ 97 %, Entries 3-5). The depicted absolute stereochemistry of these adducts relies on several experimental data:

Crude 17, even purified on deactivated silica gel, affords the opened 1,2-amido alcohol (18) (20 %). The latter
Table: DAST mediated cyclization of 1,2-amido alcohols (6)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Amido alcohol</th>
<th>(Yield)</th>
<th>2-Oxazoline</th>
<th>(Yield)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>1&lt;sup&gt;13&lt;/sup&gt;</td>
<td>3 (82 %)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>2&lt;sup&gt;13&lt;/sup&gt;</td>
<td>4 (83 %)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td><img src="image" alt="" /> R = Ph</td>
<td>11 (95 %)</td>
<td>R = Ph</td>
<td>12 (62 %)</td>
</tr>
<tr>
<td>4</td>
<td><img src="image" alt="" /> R = t-C&lt;sub&gt;4&lt;/sub&gt;H&lt;sub&gt;9&lt;/sub&gt;</td>
<td>13 (82 %)</td>
<td>R = t-C&lt;sub&gt;4&lt;/sub&gt;H&lt;sub&gt;9&lt;/sub&gt;</td>
<td>14 (70 %)</td>
</tr>
<tr>
<td>5</td>
<td><img src="image" alt="" /></td>
<td>16 (50 %)</td>
<td>17 (76 %)</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td><img src="image" alt="" /> R = Ph</td>
<td>19 (62 %)</td>
<td>R = Ph</td>
<td>20 (57 %)</td>
</tr>
<tr>
<td>7</td>
<td><img src="image" alt="" /> R = CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>21 (66 %)</td>
<td>R = CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>22 (75 %)</td>
</tr>
<tr>
<td>8</td>
<td><img src="image" alt="" /> R = t-C&lt;sub&gt;4&lt;/sub&gt;H&lt;sub&gt;9&lt;/sub&gt;</td>
<td>23 (85 %)</td>
<td>R = t-C&lt;sub&gt;4&lt;/sub&gt;H&lt;sub&gt;9&lt;/sub&gt;</td>
<td>24 (95 %)</td>
</tr>
<tr>
<td>9</td>
<td><img src="image" alt="" /> R = Ph</td>
<td>25 (70 %)</td>
<td>R = Ph</td>
<td>26 (90 %)</td>
</tr>
<tr>
<td>10</td>
<td><img src="image" alt="" /> R = CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>27 (55 %)</td>
<td>R = CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>28 (76 %)</td>
</tr>
<tr>
<td>11</td>
<td><img src="image" alt="" /> R = t-C&lt;sub&gt;4&lt;/sub&gt;H&lt;sub&gt;9&lt;/sub&gt;</td>
<td>29 (56 %)</td>
<td>R = t-C&lt;sub&gt;4&lt;/sub&gt;H&lt;sub&gt;9&lt;/sub&gt;</td>
<td>30 (93 %)</td>
</tr>
<tr>
<td>12</td>
<td><img src="image" alt="" /></td>
<td>31</td>
<td>32 (48 %)</td>
<td></td>
</tr>
</tbody>
</table>
can also be obtained by direct acidic hydrolysis of 17 (0.1 M HCl, 77 %). Comparison of the spectral analyses performed on 16 and 18 shows that they are epimeric at C(2). Additionally, magnetization transfer (NOEDIFF experiments) is observed between Me at C(4) and H(5) in 12 and 14. This is only compatible with a trans relationship of substituents and an inversion of configuration at C(2) of 11 and 13,

4) A limitation of DAST as an hydroxyl activating agent has been also encountered (Entry 12). The threonine containing dipeptide (31) gave rise to the known Z-dehydropeptide (32)\(^\text{11f}\) (Entry 12, 48 %) accompanied by starting material (35 %). In agreement with previous observations, a trans E2-elimination involving the acidic α-proton accounts for this alkene stereochemistry.\(^\text{11f,15}\)

Since evidence of structural misassignments between 2-oxazolines (10) and acylaziridines (9) have recently been published,\(^\text{11f,16}\) the 2-oxazoline nature of the products needs to be established. By ir spectroscopy, the presence of the imino stretching band in 10 versus the amido one in isomeric 9 does not constitute a reliable proof.\(^\text{17}\) The exclusive formation of 10 rather than 9 relies on significant spectroscopic and literature data.\(^\text{18}\) Elms of 10 show the characteristic fragmentation of a 2-oxazoline nucleus ([M-R₄CHO]⁺ ion)\(^\text{19}\) providing conclusive structural evidence.

In conclusion, DAST, in only a slight excess, was shown to be a very powerful hydroxyl activating reagent towards variously substituted acyclic 1,2-amido alcohols (6), even at the low temperature of -78 °C. Following activation, a stereoselective and rapid S_N2-type intramolecular amide cyclization (< 1 h) led to the corresponding 2-oxazolines (10) in good yields (57-95 %) without formation of any of the corresponding aziridines (9).

**EXPERIMENTAL SECTION**

The melting points of compounds were taken in capillary tubes using a Büchi 535 apparatus and were uncorrected. Ir spectra of samples were obtained as KBr or KCl pellets. \(^\text{1H-Nmr}\) (300 MHz) and \(^\text{13C-nmr}\) (75 MHz) spectra were obtained in CD₂Cl₂ unless otherwise noted. Chemical shifts are given as δ values (ppm). Mass spectra were done on a Finnigan-Mat 4600 spectrometer. HRms spectra were recorded on a Varian MAT mass spectrometer at CRMPO (University of Rennes I). Specific rotations were determined using a Jobin-Yvon RJ micropolarimeter. Elemental analyses were performed at the ICSN, CNRS, Gif-sur-Yvette. The products were purified by flash chromatography on Merck silica gel (40-60 mesh) at medium pressure (200 mbar). Tlc
was done on Merck silica gel plates (60F254) with a fluorescent indicator. DAST (commercially available from Janssen Chimica) was used as received without prior purification.

**Preparation of Amido Alcohols (6) : A General Procedure.** Excess amount of an acid chloride (4.0 mmol) was slowly added to a 2-amino alcohol (1.0 mmol) dissolved in a 1/1 mixture of H2O/CH2Cl2 (20 ml) containing K2CO3 (12.0 mmol) at 20 °C. The mixture was vigorously stirred for 1.5 h to 5.0 h then diluted with CH2Cl2 (20 ml). The organic layer was washed (3 x 20 ml of 10% NaHCO3), dried (MgSO4), filtered and then concentrated to an oil. Purification of the crude amidoalcohol was conducted by flash chromatography on silica gel. The unoptimized yields are compiled in the Table.

**DAST Mediated Cyclization Of Amido Alcohols (6) : A Typical Experimental Procedure.** The amido alcohol (6) (1.5 mmol) dissolved in CH2Cl2 (8-15 ml) was cooled at -78 °C under nitrogen and DAST (1.65 mmol) was slowly added. After completion of the reaction (< 1 h, tlc control), the medium was hydrolysed with crushed ice added with 4M NH4OH (1.0 ml) at -78 °C. The aqueous layer was then extracted with CH2Cl2 (3 x 15 ml), and the combined organic layers dried (MgSO4), filtered and concentrated leaving an oily residue, which was subjected to flash chromatography on silica gel deactivated with TEA (eluted with the solvent mixture indicated in the respective column), to give the purified oxazolines in the yields shown in the Table.

4-(4-Benzzyloxybenzyl)-4-methoxycarbonyl-2-methyl-2-oxazoline (3). Solvent mixture: AcOEt/pentane/TEA 50/50/0.5; 1H-nmr δ 1.90 (s, 3H), 3.00 (s, 2H, CH2Ar), 3.70 (s, 3H, CH3OOC), 4.10 and 4.50 (2d, 2H, J = 9.1 Hz, CH2-O), 5.00 (s, 2H, O-CH3Ph), 6.90 and 7.10 (2d, 4H, Ph, J = 8.5 Hz), 7.30-7.50 (m, 5H, Ph); 13C-nmr δ 13.9 (CH3), 42.9 (CH2Ar), 52.6 (C=N), 70.3 (CH3-O), 73.0 (CH2-O), 78.8 (PhCH2-O), [114.8, 127.9, 128.2, 128.8, 131.7, 137.6, 158.2] (Phenyl groups), 166.1 (N=O), 173.5 (COO); ms (CI, NH3) m/z: 340.0 [MH]+, 357.0 [M+NH4]+; HRms m/z calcd for C20H21N04 339.1471. Found 339.147 [M]+; m/z calcd for C19H17N03 307.1208. Found: 307.112 [M-CH30]+; m/z 298.0 [M-CH3CN]+; Anal. Calcd for C20H21N04: C, 70.73; H, 6.23; N, 4.13. Found: C, 70.28; H, 5.96; N, 4.14.

4-(4-Benzzyloxybenzyl)-4-hydroxymethyl-2-methyl-2-oxazoline (4). Solvent mixture: acetone/hexane/TEA 70/30/0.5; ir (KBr) 3200 (vOH), 1650 (vC=O, amide), 1600, 1495 (vC=N), 1440, 1375 (vCN), 1285, 1240, 1165
HETEROCYCLES, Vol. 41, No. 5, 1995 953

\[ \text{cm}^{-1}; 1^H-\text{nmr} \delta 1.87 (s, 3H, CH}_3\text{), 2.69 and 2.82 (2d, 2H, J = 13.6 Hz, CH}_2\text{Ar), 3.45 and 3.67 (2d, 2H, J = 11.4 Hz, CH}_2\text{OH), 4.07 and 4.12 (2d, 2H, J = 8.4 Hz, CH}_2\text{O), 5.06 (s, 2H, O-CH}_2\text{Ph), 6.93 and 7.10 (2d, 4H, J = 8.5 Hz, Ph), 7.30-7.50 (m, 5H, Ph); 1^3C-\text{nmr} \delta 13.8 (CH}_3\text{), 41.3 (CH}_2\text{Ar), 66.9 (C-N), 70.3 (CH}_2\text{OH), 72.4 (CH}_2\text{O), 75.6 (O-CH}_2\text{Ph), [115.0, 127.9, 128.2, 129.2, 131.9, 132.5, 137.7, 158.0] (Phenyl groups), 166.1 (N=C-0); ms (Cl, NH}_3) m/z: 312.0 [MH]+; HRms m/z calcd for C\text{19H}_2\text{1N}_3\text{O}_3 311.1521. Found 311.151 [M]+; m/z 281.0 [M-CH}_2\text{OH (weak intensity)]; Anal. Calcd for C\text{19H}_2\text{1N}_3\text{O}_3: C, 73.29; H, 6.97.

(4R,5S)-4-Methyl-2,5-diphenyl-2-oxazoline (12). Solvent mixture: CH\text{2Cl}_2/TEA 99/1; ir (NaCl) 1640 (\nu\text{N=C-O}), 1485, 1445, 1320, 1100 cm\text{^{-1}; 1^H-}\text{nmr} \delta 1.47 (d, 3H, CH}_3\text{), 4.19 (m, 1H, CH-N), 5.12 (d, 1H, CH-Ph, J = 7.5 Hz), 7.32-7.55 (m, 8H, Ph), 8.20 (d, 2H, Ph, J = 6.7 Hz); 1^3C-\text{nmr} \delta 21.9 (CH}_3\text{), 71.0 (CH-N), 88.9 (CH-O), [126.7, 129.3, 129.5, 129.8, 132.4, 141.3] (Phenyl groups), 162.0 (N=C-0); ms (Cl, NH}_3) m/z : 238.0 [MH]+; HRms m/z calcd for C\text{16H}_1\text{5N}_3\text{O} 237.1154. Found 237.116 [M]+; m/z calcd for C\text{7H}_1\text{3N} 111.0735. Found 111.073 [M-PhCHO]+; Anal. Calcd for C\text{16H}_1\text{5NO: C, 80.98; H, 6.37; N, 5.90. Found: C, 81.02; H, 6.47; N, 5.96; \alpha\text{D}= -149.7 \text{ (c 2.54, MeOH).}

(4R,5S)-4-Methyl-5-phenyl-2-tert-butyl-2-oxazoline (14). Solvent mixture: pentane/acetone/TEA 92/8/0.5; ir (NaCl) 1655 (\nu\text{N=C-O}), 1475 (\nu\text{C=O}), 1450, 1135 cm\text{^{-1}; 1^H-}\text{nmr} \delta 1.27 (s, 9H, C(CH}_3\text{)\text{3}), 1.32 (d, 3H, CH)_3\text{), 4.86 (d, 1H, CH-O, J = 7.4 Hz), 7.25-7.40 (m, 5H, Ph); 1^3C-\text{nmr} \delta 21.9 (C(CH}_3\text{)\text{3}), 28.1 (CH}_3\text{), 33.6 (C(CH}_3\text{)\text{3}), 71.5 (CH-N), 88.5 (CH-O), [126.3, 129.0, 129.7, 142.8] (Phenyl group), 173.8 (N=C-0); ms (Cl, NH}_3) m/z : 218.0 [MH]+; HRms m/z calcd for C\text{14H}_1\text{9NO} 217.1467. Found 217.146 [M]+; m/z calcd for C\text{7H}_1\text{3N} 111.1048. Found 111.105 [M-PhCHO]+; \alpha\text{D}= +5.7 \text{ (c 0.51, MeOH).}

(1R)-N-(2-Fluoro-2-phenyl-1-methyl) ethyl-pivaloylamine (15). Solvent mixture: pentane/acetone 92/8; ir (NaCl) 3340 (\nu\text{NH}), 1630 (\nu\text{CO}), 1525 (\delta\text{NH}), 1200 (\nu\text{C-F}) cm\text{^{-1}; 1^H-}\text{nmr} \delta 1.10 (d, 3H, CH}_3\text{), 1.20 (s, 9H, t-Bu), 4.30 (m, 1H, CH-N), 5.60 (d, 1H, CH-F, J_{HF} = 48.0 Hz and J = 5.4 Hz), 5.80 (s, 1H, NH), 7.25-7.40 (m, 5H, Ph); 1^3C-\text{nmr} \delta 13.5 (C(CH}_3\text{)\text{3}), 27.7 (CH}_3\text{), 38.5 (C(CH}_3\text{)\text{3}), 49.7-50.1 (CH-N, 2J_{CF} = 24.7 Hz), 95.1-97.5 (CH-F, J_{CF} = 175.3 Hz), [126.2, 126.3, 129.2, 129.4, 138.8] (Phenyl group), 178.9 (N=C-0); ms (Cl,
NH₃) m/z: 255.0 [M+NH₄⁺], 238.0 [MH⁺]; HRms m/z calcd for C₁₄H₂₀NOF 237.1529. Found 237.153 [M]⁺; HRms m/z calcd for C₁₄H₁₉NO 217.1467. Found 217.146 [M-HF]⁻.

(4S,5R)-2,4-Dimethyl-5-phenyl-2-oxazoline (17). Solvent mixture: MeOH/CH₂Cl₂/TEA 3/97/1; ¹H-nmr (CDCl₃) δ 1.37 (d, 3H, CH₃, J = 6.7 Hz), 2.07 (s, 3H, CH₃-C=N), 3.97 (m, 1H, CH-N), 4.90 (d, 1H, CH-O, J = 7.8 Hz), 7.27-7.42 (m, 5H, Ph); ¹³C-nmr δ 13.0 (CH₃-C=N), 20.4 (CH₃), 70.4 (CH-N), 87.6 (CH-O), [125.4, 128.0, 128.6, 140.3] (Phenyl group), 162.5 (N=C=O); IR (KBr) 3400 (νOH), 3295 (νNH), 1635 (νC=O), 1530 (δNH), 1445, 1370, 1260 cm⁻¹; ¹H-nmr δ 1.07 (d, 3H, CH₃, J = 7.1 Hz), 1.89 (s, 3H, CH₃-C≡N), 3.73 (s, 1H, OH), 4.08 (m, 1H, CH-N), 4.56 (d, 1H, CH-Ph, J = 5.3 Hz), 5.82 (s, 1H, NH), 7.26-7.37 (m, 5H, Ph); ¹³C-nmr δ 17.6 (CH₃), 23.3 (NHCOC₃H₃), 52.1 (CH-N), 78.1 (CH-O), [126.7, 127.9, 128.5, 142.5] (Phenyl group), 171.1 (C=O); ms (CI, NH₃) m/z: 176.0 [MH]⁺; HRms m/z calcd for C₁₁H₁₃NO 175.0997. Found 175.100 [M]⁺; m/z calcd for C₄H₇N 69.0579. Found 69.058 [M-PhCHO]⁺.

(1S,2S)-N-(2-Hydroxy-2-phenyl-1-methyl)ethylacetylamine (18). Obtained by acidic hydrolysis of 17. Compound (17) (50.0 mg, 0.29 mmol) was dissolved and agitated at 20 °C in 5 ml of 0.1 N HCl for 24 h. After reaction, CH₂Cl₂ (5 ml) and 10 % Na₂CO₃ (5 ml) were added to the reaction medium. The separated organic phase was dried (MgSO₄), filtered and concentrated under vacuum. Crude 18 was purified by flash chromatography on silica gel eluted by the mixture ether/pentane 1/4 (77 %). IR (KBr) 3400 (νOH), 3295 (νNH), 1635 (νCO), 1530 (δNH), 1445, 1370, 1260 cm⁻¹; ¹H-nmr δ 1.07 (d, 3H, CH₃, J = 7.1 Hz), 1.89 (s, 3H, CH₃-C≡N), 3.73 (s, 1H, OH), 4.08 (m, 1H, CH-N), 4.56 (d, 1H, CH-Ph, J = 5.3 Hz), 5.82 (s, 1H, NH), 7.26-7.37 (m, 5H, Ph); ¹³C-nmr δ 17.6 (CH₃), 23.3 (NHCOC₃H₃), 52.1 (CH-N), 78.1 (CH-O), [126.7, 127.9, 128.5, 142.5] (Phenyl group), 171.1 (C=O); ms (CI, NH₃) m/z: 211.0 [M+NH₄⁺], 194.0 [MH⁺], 176.0 [M-·OH]⁺; HRms m/z calcd for C₁₁H₁₃NO 175.0997. Found 175.099 [M-H₂O]⁺.

(4R)-2,4-Diphenyl-2-oxazoline (20). Solvent mixture: CH₂Cl₂/TEA 100/0.5; mp 112 °C; ir (NaCl) 1635 (νN=C-O), 1490, 1445, 1350 cm⁻¹; ¹H-nmr δ 4.26 (t, 1H, CH₂-O, J = 8.8 Hz), 4.80 (t, 1H, CH₂-O, J = 8.8 Hz), 5.37 (dd, 1H, CH-N, J = 8.8 and 9.5 Hz), 7.31-7.54 (m, 8H, Ph), 8.04 (d, 2H, Ph, J = 7.5 Hz); ¹³C-nmr δ 71.0 (CH-N), 75.2 (CH₂-O), [127.1, 127.8, 128.2, 128.7, 128.9, 131.8, 143.1] (Phenyl groups), 164.6 (N=C-O); ms (Cl, NH₃) m/z : 224.0 [MH]⁺; HRms m/z calcd for C₁₅H₁₃NO 223.0998. Found 223.099 [M]⁺; m/z calcd for C₁₄H₁₁N 193.0891. Found 193.089 [M-CH₂O]⁺; Anal. Calcd for C₁₅H₁₃NO: C, 80.69; H, 5.87; N, 6.27. Found: C, 80.96; H, 6.06; N, 5.98; [α]²³D = +12.0 ° (c 1.55, MeOH).
(4R)-2-Methyl-4-phenyl-2-oxazoline (22). Solvent mixture: MeOH/CH$_2$Cl$_2$/TEA 1/99/1; ir (NaCl) 1655 (v$_{N=C-O}$), 1375, 1220, 1200 cm$^{-1}$; $^1$H-nmr $\delta$ 2.08 (s, 3H, CH$_3$), 4.04 (t, 1H, CH$_2$-O, J = 8.6 Hz), 4.60 (t, 1H, CH$_2$-O, J = 8.6 Hz), 5.16 (dd, 1H, CH-N, J = 8.6 and 8.4 Hz), 7.26-7.40 (m, 5H, Ph); $^{13}$C-nmr $\delta$ 14.0 (CH$_3$), 70.2 (CH-N), 75.0 (CH$_2$-O), [126.9, 127.6, 128.9, 143.3] (Phenyl group), 165.7 (N=C=O); ms (CI, NH$_3$) m/z: 179.0 [M+NH$_4$]+, 162.0 [MH]+; HRms m/z calcd for C$_{10}$H$_{11}$NO 161.0841. Found 161.084 [M]+; m/z calcd for C$_9$H$_9$N 131.0735. Found 131.073 [M-CH$_2$O]+; Anal. Calcd for C$_{10}$H$_{11}$NO: C, 74.5; H, 6.88; N, 8.69. Found: C, 74.78; H, 6.89; N, 8.48; $[\alpha]_{23}^{23}$D = +107.9 $^\circ$ (c 3.75, MeOH).

(4R)-4-Phenyl-2-tert-butyl-2-oxazoline (24). Solvent mixture: MeOH/CH$_2$Cl$_2$/TEA 1/99/1; ir (NaCl) 1645 (v$_{N=C-O}$), 1470, 1445, 1130 cm$^{-1}$; $^1$H-nmr $\delta$ 1.35 (s, 9H, CH$_3$), 4.07 (t, 1H, CH$_2$-O, J = 8.1 Hz), 4.60 (t, 1H, CH$_2$-O, J = 9.2 Hz), 5.15 (dd, 1H, CH-N, J = 8.1 and 8.3 Hz), 7.25-7.41 (m, 5H, Ph); $^{13}$C-nmr $\delta$ 26.8 (C(CH$_3$)$_3$), 32.5 (C(CH$_3$)$_3$), 68.7 (CH-N), 74.0 (CH$_2$-O), [125.7, 126.5, 127.8, 142.5] (Phenyl group), 173.9 (N=C=O); ms (Cl, NH$_3$) m/z: 221.0 [M+NH$_4$]+, 204.0 [MH]+; HRms m/z calcd for C$_{13}$H$_{17}$NO 203.1310. Found 203.130 [M]+; m/z 173.0 [M-CH$_2$O]⁺ (weak intensity); m/z calcd for 117.0579. Found 117.058 [M-CH$_2$O-CH$_2$=CH$_2$]+; Anal. Calcd for C$_{13}$H$_{17}$NO: C, 76.8; H, 8.43; N, 6.89. Found: C, 76.41; H, 8.81; N, 6.71; $[\alpha]_{23}^{23}$D = +89.2 $^\circ$ (c 4.54, MeOH).

(4S)-4-Benzyl-2-phenyl-2-oxazoline (26). Solvent mixture: CH$_2$Cl$_2$/TEA 99/1; ir (KBr) 1640 (v$_{N=C-O}$), 1485, 1445, 1350 cm$^{-1}$; $^1$H-nmr $\delta$ 2.79 (dd, 1H, CH$_2$-Ph, J = 7.5 and 13.6 Hz), 3.12 (dd, 1H, CH$_2$-Ph, J = 6.0 and 13.6 Hz), 4.12 and 4.38 (2dd, 1H, CH$_2$-O, J = 8.5 and 8.0 Hz), 4.56 (m, 1H, CH-N), 7.23-7.52 (m, 8H, Ph), 7.94 (d, 2H, Ph, J = 7.5 Hz); $^{13}$C-nmr $\delta$ 42.2 (CH$_2$-Ph), 68.3 (CH-N), 72.3 (CH$_2$-O), [126.7, 128.5, 128.6, 128.7, 129.7, 131.5] (Phenyl groups), 164.0 (N=C=O); ms (Cl, NH$_3$) m/z: 238.0 [MH]$^+$; HRms m/z calcd for C$_{16}$H$_{15}$NO 237.1154. Found 237.115 [M]+; m/z 207.0 [M-CH$_2$O]⁺ (weak intensity); Anal. Calcd for C$_{16}$H$_{15}$NO: C, 80.98; H, 6.37; N, 5.90. Found: C, 81.02; H, 6.47; N, 5.96; $[\alpha]_{23}^{23}$D = +22.9 $^\circ$ (c 1.23, MeOH).

(4S)-4-Benzyl-2-methyl-2-oxazoline (28). Solvent mixture: MeOH/CH$_2$Cl$_2$/TEA 99/1; ir (NaCl) 1670 (v$_{N=C-O}$), 1380, 1225 cm$^{-1}$; $^1$H-nmr $\delta$ 1.91 (s, 3H, CH$_3$), 2.66 (dd, 1H, CH$_2$-Ph, J = 7.4 and 13.5 Hz), 2.96 (dd, 1H, CH$_2$-Ph, J = 6.1 and 13.5 Hz), 3.89 and 4.17 (2t, 2H, CH$_2$-O, J = 8.6 Hz), 4.35 (m, 1H, CH-N), 7.19-7.32 (m, 5H, Ph); $^{13}$C-nmr $\delta$ 14.3 (CH$_3$), 42.6 (CH$_2$-Ph), 68.4 (CH-N), 72.5 (CH$_2$-O), [126.9, 129.0, 130.0, 132.9, 139.3] (Phenyl group), 165.2 (O=C=O); ms (Cl, NH$_3$) m/z: 176.0 [MH]$^+$; HRms m/z calcd for C$_{11}$H$_{13}$NO
175.0997. Found 175.100 [M]+, \( m/z \) calcd for C\(_{10}\)H\(_{11}\)N 145.0891. Found 145.090 [M-CH\(_2\)O]; Anal. Caled for C\(_{11}\)H\(_{13}\)NO: C, 75.46; H, 7.48. Found: C, 75.50; H, 7.26; \([\alpha]_{D}^{23} = -47.9^\circ\) (c 1.70, MeOH).

\((4S)-4\text{-Benzyl-2-tert-butyl-2-oxazoline}\) (30). Solvent mixture: MeOH/CH\(_2\)Cl\(_2\)/TEA 1/99/1; ir (NaCl) 1650 (\( \nu_{\text{C=O}} \)), 1135 cm\(^{-1}\); \( ^1\text{H-nmr} \) \( \delta \) 1.16 (s, 3H, CH\(_3\)), 2.66 (dd, 1H, CH\(_2\)-Ph, \( J = 7.4 \) and 13.5 Hz), 2.94 (dd, 1H, CH\(_2\)-Ph, \( J = 5.6 \) and 13.5 Hz), 3.91 and 4.13 (2t, 2H, CH\(_2\)-O, \( J = 10.0 \) Hz), 4.30 (m, 1H, CH-N), 7.19-7.31 (m, 5H, Ph); \( ^{13}\text{C-nmr} \) \( \delta \) 28.3 (C(CH\(_3\))\(_3\)), 33.7 (C(CH\(_3\))\(_3\)), 42.4 (CH\(_2\)-Ph), 67.8 (CH-N), 72.2 (CH\(_2\)-O), 1127.0, 129.0, 130.3 (Phenyl group), 174.4 (N=C-O); ms (Cl, NH\(_3\)) \( \text{m/z:} \ 218.0 \ [\text{MH}]^+; \text{HRms m/z calcd for C}_{14}\text{H}_{19}\text{NO 217.1467. Found 217.147 [M]+; m/z 187.0 [M-CH\(_2\)O] (weak intensity); [\alpha]_{D}^{23} = -50.2^\circ\) (c 1.20, MeOH).

**Dehydropeptide** (32). Solvent mixture: pentane/AcOEt 3/1; \( ^1\text{H-nmr} \) \( \delta \) 1.40 (s, 9H, C(CH\(_3\))\(_3\)), 1.67 (d, 3H, CH\(_3\)-CH, \( J = 7.0 \) Hz), 3.02 (dd, 1H, CH\(_2\)-Ph, \( J = 7.4 \) and 14.1 Hz), 3.17 (dd, 1H, CH\(_2\)-Ph, \( J = 6.4 \) and 14.1 Hz), 3.71 (s, 3H, CH\(_3\)-O), 4.43 (m, 1H, CH-N), 5.00 (s, 2H, NH), 6.70-6.77 (m, 1H, CH=C), 7.26-7.33 (m, 5H, Ph); \( ^{13}\text{C-nmr} \) \( \delta \) 14.5 (C(CH\(_3\))\(_3\)), 28.3 (CH\(_3\)-CH), 38.0 (CH\(_2\)-Ph), 52.4 (CH\(_3\)-O), 54.5 (C(CH\(_3\))\(_3\)), 56.3 (CH-N), 126.4, 127.2, 128.9, 129.7 (Phenyl group), 134.2 (C=C-N), 136.8 (C=CH), 156.0 (OCON), 165.0 (C=C-CO\(_2\)), 170.0 (N-C=O); ms (Cl, NH\(_3\)) \( \text{m/z:} \ 380.0 \ [\text{M+NH}_4]^+; \ 363.0 \ [\text{MH}]^+.

**REFERENCES AND NOTES**


18. The resonance signals of CH(5)-O and C(5)H-O in 10 appear more deshielded than the corresponding expected signals of CH(3)-N and C(3)H-N in 9. Moreover, the 2-oxazolines (26), (28) and (30) and the acylaziridines (9) (R2 = Bn, R3 = R4 = H, R5 = Ph, Me or t-Bu) are known compounds. Our 1H-nmr data fit well a 2-oxazoline structure. The other adducts are attributed the 2-oxazoline structure based on similar nmr resonances for H(4), C(4) and H(5), C(5).


Received, 17th November, 1994