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

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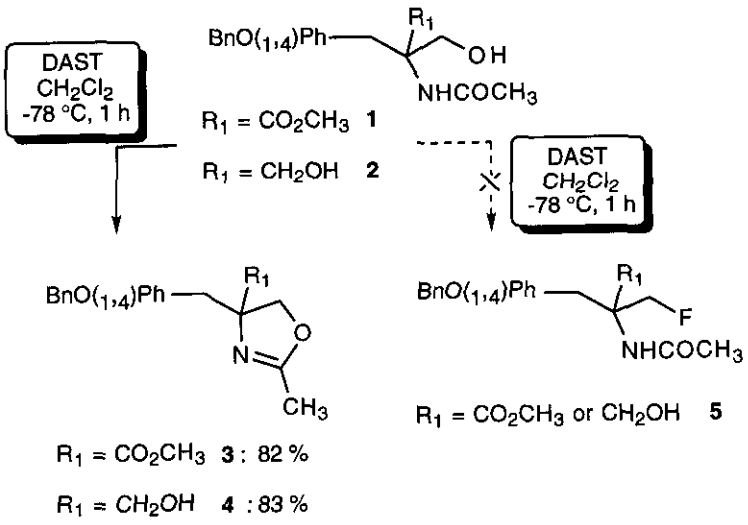
Abstract- Acyclic 1,2-amido alcohols (**6**) react efficiently with a slight excess of (diethylamino)sulfur trifluoride (DAST) to afford the corresponding 2-oxazolines (**10**) in good yields ranging between 57-95 %. *Even at the low temperature of -78 °C*, a rapid (< 1 h) and stereoselective amide cyclization 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. [1] It acts for example as a masked carboxylic group [1b-d,2] and as an efficient ortho-metallation directing moiety. [1d,3] Moreover, this nucleus showed interesting potentials in the field of asymmetric synthesis. [1d] Thus, C_2-symmetrical bis(4,5-dihydrooxazolyl)methanes have been used successfully in the asymmetric version of numerous reactions like Diels-Alder reaction, [4] hydrosilylation of ketones, [5] olefin cyclopropanation [6] and aziridination. [7] Further interest arose recently from the discovery of oxazolines incorporated as peptide mimetics into the backbone of biologically active compounds isolated from marine sources. [8] Synthetic procedures leading to 2-oxazolines include bimolecular reactions such as the reaction of amino alcohols with imidates, [1,9] unimolecular rearrangements of acylaziridines, [1,10] or cyclizations of hydroxy amides and related compounds. [1,8d,11]

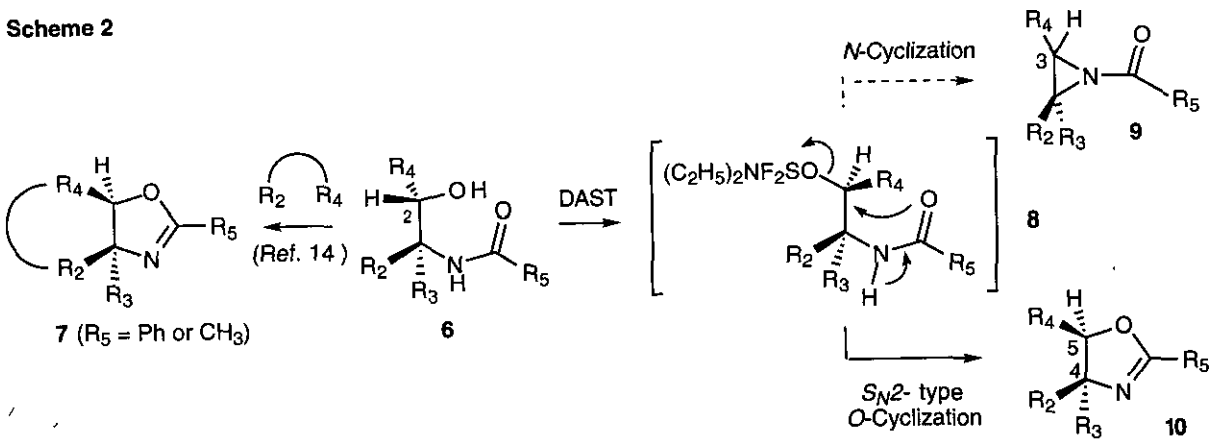
Our interest in this field originates from an unsuccessful fluorodehydroxylation encountered with the two 1,2-acetamido alcohols (**1**) and (**2**) (1.0 equivalent) using (diethylamino)sulfur trifluoride [12] in slight excess (SF_3NEt_2, DAST: 1.1 equivalents, -78°C, 1 h, Scheme 1). [13] Under these 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).

Scheme 1



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_2Cl_2 at *room temperature (16 h)* affording the *cyclic* 2-oxazolines (**7**) [14] (left part of Scheme 2). Modest yields of products were observed depending on the structure of **6**.

Scheme 2



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 NH_4OH) 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:

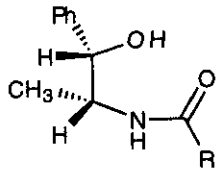
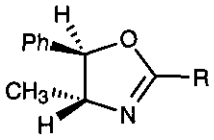
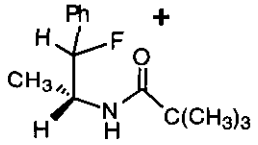
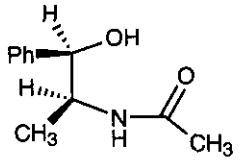
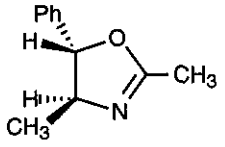
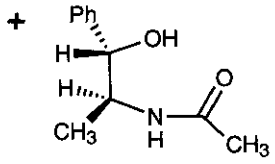
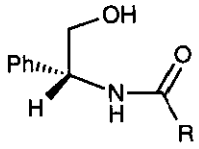
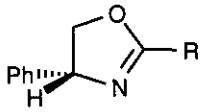
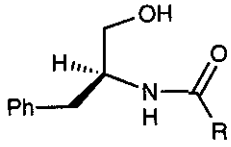
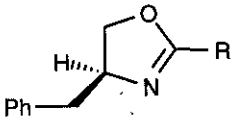
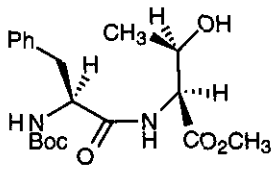
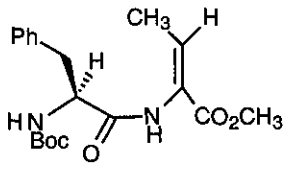
1) The cyclization can be conducted *at the low temperature of -78 °C* using only a slight excess of DAST (1.1 equivalents) without formation of aziridine (**9**) resulting from a possible *N*-cyclization. The reaction is complete *within 1 h*, and the product is obtained in fair to good yield (Entries 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 ^{13}C-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**)

Entry	Amido alcohol		(Yield)	2-Oxazoline		(Yield)
1			**1** [13]			**3** (82 %)
2			**2** [13]			**4** (83 %)
3		R = Ph	**11** (95 %)		R = Ph	**12** (62 %)
4		R = *t*-C_4H_9	**13** (82 %)		R = *t*-C_4H_9	**14** (70 %)
						**15** (28 %)
5			**16** (50 %)			**17** (76 %)
						**18** (20 %)
6		R = Ph	**19** (62 %)		R = Ph	**20** (57 %)
7		R = CH_3	**21** (66 %)		R = CH_3	**22** (75 %)
8		R = *t*-C_4H_9	**23** (85 %)		R = *t*-C_4H_9	**24** (95 %)
9		R = Ph	**25** (70 %)		R = Ph	**26** (90 %)
10		R = CH_3	**27** (55 %)		R = CH_3	**28** (76 %)
11		R = *t*-C_4H_9	**29** (56 %)		R = *t*-C_4H_9	**30** (93 %)
12			**31**			**32** (48 %)

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**) [11f] (Entry 12, 48 %) accompanied by starting material (35 %). In agreement with previous observations, a trans E_2-elimination involving the acidic α-proton accounts for this alkene stereochemistry. [11f,15]

Since evidence of structural misassignments between 2-oxazolines (**10**) and acylaziridines (**9**) have recently been published, [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. [17] The *exclusive formation* of **10** rather than **9** relies on significant spectroscopic and literature data. [18] EIms of **10** show the characteristic fragmentation of a 2-oxazoline nucleus ($[M-R_4CHO]^+$ ion) [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. ^{1}H-Nmr (300 MHz) and ^{13}C-nmr (75 MHz) spectra were obtained in CD_2Cl_2 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 ($60F_{254}$) 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 H_2O/CH_2Cl_2 (20 ml) containing K_2CO_3 (12.0 mmol) at 20 °C. The mixture was vigourously stirred for 1.5 h to 5.0 h then diluted with CH_2Cl_2 (20 ml). The organic layer was washed (3 x 20 ml of 10% $NaHCO_3$), dried ($MgSO_4$), 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 CH_2Cl_2 (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 NH_4OH (1.0 ml) at -78 °C. The aqueous layer was then extracted with CH_2Cl_2 (3 x 15 ml), and the combined organic layers dried ($MgSO_4$), 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-Benzyloxybenzyl)-4-methoxycarbonyl-2-methyl-2-oxazoline (3). Solvent mixture: AcOEt/pentane/TEA 50/50/0.5; ^{1}H-nmr δ 1.90 (s, 3H), 3.00 (s, 2H, C$\underline{H}_2$Ar), 3.70 (s, 3H, C$\underline{H}_3$OOC), 4.10 and 4.50 (2d, 2H, J = 9.1 Hz, C$\underline{H}_2$-O), 5.00 (s, 2H, O-C$\underline{H}_2$Ph), 6.90 and 7.10 (2d, 4H, Ph, J = 8.5 Hz), 7.30-7.50 (m, 5H, Ph); ^{13}C-nmr δ 13.9 (C$\underline{H}_3$), 42.9 (C$\underline{H}_2$Ar), 52.6 (C-N), 70.3 (C$\underline{H}_3$-O), 73.0 (C$\underline{H}_2$-O), 78.8 (PhC$\underline{H}_2$-O), [114.8, 127.9, 128.2, 128.8, 131.7, 137.6, 158.2] (Phenyl groups), 166.1 (N=C-O), 173.5 (COO); ms (CI, NH_3) *m / z:* 340.0 $[MH]^+$, 357.0 $[M+NH_4]^+$; HRms *m/z* calcd for $C_{20}H_{21}NO_4$ 339.1471. Found 339.147 $[M]^+$; *m/z* calcd for $C_{19}H_{17}NO_3$ 307.1208. Found 307.112 $[M-CH_3OH]^+$; *m/z* 298.0 $[M-CH_3CN]^+$; Anal. Calcd for $C_{20}H_{21}NO_4$: C, 70.73; H, 6.23; N, 4.13. Found: C, 70.28; H, 5.96; N, 4.14.

4-(4-Benzyloxybenzyl)-4-hydroxymethyl-2-methyl-2-oxazoline (4). Solvent mixture: acetone/hexane/TEA 70/30/0.5; *ir* (KBr) 3200 (ν_{OH}), 1650 ($\nu_{C=O}$, amide), 1600, 1495 ($\nu_{C=C}$), 1440, 1375 (ν_{CN}), 1285, 1240, 1165

cm^{-1}; ^{1}H-nmr δ 1.87 (s, 3H, C<u>H</u>$_3$), 2.69 and 2.82 (2d, 2H, J = 13.6 Hz, C<u>H</u>$_2$Ar), 3.45 and 3.67 (2d, 2H, J = 11.4 Hz, C<u>H</u>$_2$-OH), 4.07 and 4.12 (2d, 2H, J = 8.4 Hz, C<u>H</u>$_2$-O), 5.06 (s, 2H, O-C<u>H</u>$_2$Ph), 6.93 and 7.10 (2d, 4H, J = 8.5 Hz, Ph), 7.30-7.50 (m, 5H, Ph); ^{13}C-nmr δ 13.8 (<u>C</u>H$_3$), 41.3 (<u>C</u>H$_2$Ar), 66.9 (<u>C</u>-N), 70.3 (<u>C</u>H$_2$-OH), 72.4 (<u>C</u>H$_2$-O), 75.6 (O-<u>C</u>H$_2$Ph), [115.0, 127.9, 128.2, 129.2, 131.9, 132.5, 137.7, 158.0] (Phenyl groups), 166.1 (N=<u>C</u>-O); ms (CI, NH_3) *m / z:* 312.0 $[MH]^+$; HRms *m/z* calcd for $C_{19}H_{21}NO_3$ 311.1521. Found 311.151 $[M]^+$; *m/z* 281.0 $[M\text{-}CH_2O]^+$ (weak intensity); Anal. Calcd for $C_{19}H_{21}NO_3$: C, 73.29; H, 6.97. Found: C, 73.5; H, 6.97.

(*4R,5S*)-4-Methyl-2,5-diphenyl-2-oxazoline (12). Solvent mixture: CH_2Cl_2/TEA 99/1; ir (NaCl) 1640 ($\nu_{N=C-O}$), 1485, 1445, 1320, 1100 cm^{-1}; ^{1}H-nmr δ 1.47 (d, 3H, C<u>H</u>$_3$, J = 7.2 Hz), 4.19 (m, 1H, C<u>H</u>-N), 5.12 (d, 1H, C<u>H</u>-Ph, J = 7.5 Hz), 7.32-7.55 (m, 8H, Ph), 8.20 (d, 2H, Ph, J = 6.7 Hz); ^{13}C-nmr δ 21.7 (<u>C</u>H$_3$), 71.0 (<u>C</u>H-N), 88.9 (<u>C</u>H-O), [126.7, 129.3, 129.5, 129.8, 132.4, 141.3] (Phenyl groups), 162.0 (N=<u>C</u>-O); ms (CI, NH_3) *m/z* : 238.0 $[MH]^+$; HRms *m/z* calcd for $C_{16}H_{15}NO$ 237.1154. Found 237.116 $[M]^+$; *m/z* calcd for C_9H_9N 131.0735. Found 131.073 $[M\text{-}PhCHO]^+$; 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; $[\alpha]^{23}_D$ = -149.7 ° (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 ($\nu_{N=C-O}$), 1475 ($\nu_{C=C}$), 1450, 1135 cm^{-1}; ^{1}H-nmr δ 1.27 (s, 9H, C(C<u>H</u>$_3$)$_3$), 1.32 (d, 3H, C<u>H</u>$_3$, J = 7.1 Hz), 3.89 (m, 1H, C<u>H</u>-N), 4.86 (d, 1H, C<u>H</u>-O, J = 7.4 Hz), 7.25-7.40 (m, 5H, Ph); ^{13}C-nmr δ 21.9 (C(<u>C</u>H$_3$)$_3$), 28.1 (<u>C</u>H$_3$), 33.6 (<u>C</u>(CH$_3$)$_3$), 71.5 (<u>C</u>H-N), 88.5 (<u>C</u>H-O), [126.3, 129.0, 129.7, 142.8] (Phenyl group), 173.8 (N=<u>C</u>-O); ms (CI, NH_3) *m/z* : 218.0 $[MH]^+$; HRms *m/z* calcd for $C_{14}H_{19}NO$ 217.1467. Found 217.146 $[M]^+$; *m/z* calcd for $C_7H_{13}N$ 111.1048. Found 111.105 $[M\text{-}PhCHO]^+$; $[\alpha]^{23}_D$ = +5.7 ° (c 0.51, MeOH).

***(1R)-N*-(2-Fluoro-2-phenyl-1-methyl) ethyl-pivaloylamine (15).** Solvent mixture: pentane/acetone 92/8; ir (NaCl) 3340 (ν_{NH}), 1630 (ν_{CO}), 1525 (δ_{NH}), 1200 (ν_{C-F}) cm^{-1}; ^{1}H-nmr δ 1.10 (d, 3H, C<u>H</u>$_3$, J = 7.0 Hz), 1.20 (s, 9H, *t*-Bu), 4.30 (m, 1H, C<u>H</u>-N), 5.60 (d, 1H, C<u>H</u>-F, J_{HF} = 48.0 Hz and J = 5.4 Hz), 5.80 (s, 1H, N<u>H</u>), 7.25-7.40 (m, 5H, Ph); ^{13}C-nmr δ 13.5 (C(<u>C</u>H$_3$)$_3$), 27.7 (<u>C</u>H$_3$), 38.5 (<u>C</u>(CH$_3$)$_3$), 49.7-50.1 (<u>C</u>H-N, $^2J_{CF}$ = 24.7 Hz), 95.1-97.5 (<u>C</u>H-F, J_{CF} = 175.3 Hz), [126.2, 126.3, 129.2, 129.4, 138.8] (Phenyl group), 178.9 (N=<u>C</u>-O); ms (CI,

NH_3) *m/z*: 255.0 $[M+NH_4]^+$, 238.0 $[MH]^+$; HRms *m/z* calcd for $C_{14}H_{20}NOF$ 237.1529. Found 237.153 $[M]^+$; HRms *m/z* calcd for $C_{14}H_{19}NO$ 217.1467. Found 217.146 $[M-HF]^+$.

(*4S,5R*)-2,4-Dimethyl-5-phenyl-2-oxazoline (17). Solvent mixture: $MeOH/CH_2Cl_2$/TEA 3/97/1; ^{1}H-nmr ($CDCl_3$) δ 1.37 (d, 3H, $C\underline{H}_3$, J = 6.7 Hz), 2.07 (s, 3H, $C\underline{H}_3$-C=N), 3.97 (m, 1H, C<u>H</u>-N), 4.90 (d, 1H, C<u>H</u>-O, J = 7.8 Hz), 7.27-7.42 (m, 5H, Ph); ^{13}C-nmr δ 13.0 ($\underline{C}H_3$-C=N), 20.4 ($\underline{C}H_3$), 70.4 (<u>C</u>H-N), 87.6 (<u>C</u>H-O), [125.4, 128.0, 128.6, 140.3] (Phenyl group), 162.5 (N=<u>C</u>-O); ^{13}C-nmr ($CDCl_3$) δ 13.9 ($\underline{C}H_3$-C=N), 21.1 ($\underline{C}H_3$), 70.2 (<u>C</u>H-N), 88.0 (<u>C</u>H-O), [125.3, 128.0, 128.5, 140.3] (Phenyl group), 163.5 (N=<u>C</u>-O); ms (CI, 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_4H_7N 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, CH_2Cl_2 (5 ml) and 10 % Na_2CO_3 (5 ml) were added to the reaction medium. The separated organic phase was dried ($MgSO_4$), 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 (ν_{OH}), 3295 (ν_{NH}), 1635 (ν_{CO}),1530 (δ_{NH}), 1445, 1370, 1260 cm^{-1}; ^{1}H-nmr δ 1.07 (d, 3H, $C\underline{H}_3$, J = 7.1 Hz), 1.89 (s, 3H, $C\underline{H}_3$-CO), 3.73 (s, 1H, O<u>H</u>), 4.08 (m, 1H, C<u>H</u>-N), 4.56 (d, 1H, C<u>H</u>-Ph, J = 5.3 Hz), 5.82 (s, 1H, N<u>H</u>), 7.26-7.37 (m, 5H, Ph); ^{13}C-nmr δ 17.6 ($\underline{C}H_3$), 23.3 (NHCO$\underline{C}H_3$), 52.1 (<u>C</u>H-N), 78.1 (<u>C</u>H-O), [126.7, 127.9, 128.5, 142.5] (Phenyl group), 171.1 (<u>C</u>=O); ms (CI, NH_3) *m/z*: 211.0 $[M+NH_4]^+$, 194.0 $[MH]^+$, 176.0 $[M-{}^{\bullet}OH]^+$; HRms *m/z* calcd for $C_{11}H_{13}NO$ 175.0997. Found 175.099 $[M-H_2O]^+$.

(*4R*)-2,4-Diphenyl-2-oxazoline (20). Solvent mixture: CH_2Cl_2/TEA 100/0.5; mp 112 °C; ir (NaCl) 1635 ($\nu_{N=C-O}$), 1490, 1445, 1350 cm^{-1}; ^{1}H-nmr δ 4.26 (t, 1H, $C\underline{H}_2$-O, J = 8.8 Hz), 4.80 (t, 1H, $C\underline{H}_2$-O, J = 8.8 Hz), 5.37 (dd, 1H, C<u>H</u>-N, J = 8.8 and 9.5 Hz), 7.31-7.54 (m, 8H, Ph), 8.04 (d, 2H, Ph, J = 7.5 Hz); ^{13}C-nmr δ 71.0 (<u>C</u>H-N), 75.2 ($\underline{C}H_2$-O), [127.1, 127.8, 128.2, 128.7, 128.9, 131.8, 143.1] (Phenyl groups), 164.6 (N=<u>C</u>-O); ms (CI, NH_3) *m/z* : 224.0 $[MH]^+$; HRms *m/z* calcd for $C_{15}H_{13}NO$ 223.0998. Found 223.099 $[M]^+$; *m/z* calcd for $C_{14}H_{11}N$ 193.0891. Found 193.089 $[M-CH_2O]^+$; Anal. Calcd for $C_{15}H_{13}NO$: *C, 80.69; H, 5.87; N, 6.27.* Found: C, 80.96; H, 6.06; N, 5.98; $[\alpha]^{23}_D$ = +12.0 ° (c 1.55, MeOH).

(*4R*)-2-Methyl-4-phenyl-2-oxazoline (22). Solvent mixture: MeOH/CH_2Cl_2/TEA 1/99/1; ir (NaCl) 1655 ($\nu_{N=C-O}$), 1375, 1220, 1200 cm^{-1}; ^{1}H-nmr δ 2.08 (s, 3H, C<u>H</u>$_3$), 4.04 (t, 1H, C<u>H</u>$_2$-O, J = 8.6 Hz), 4.60 (t, 1H, C<u>H</u>$_2$-O, J = 8.6 Hz), 5.16 (dd, 1H, C<u>H</u>-N, J = 8.6 and 8.4 Hz), 7.26-7.40 (m, 5H, Ph); ^{13}C-nmr δ 14.0 (<u>C</u>H$_3$), 70.2 (<u>C</u>H-N), 75.0 (<u>C</u>H$_2$-O), [126.9, 127.6, 128.9, 143.3] (Phenyl group), 165.7 (N=<u>C</u>-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_9H_9N 131.0735. Found 131.073 $[M-CH_2O]^+$; 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; $[\alpha]^{23}_D$ = +107.9 ° (c 3.75, MeOH).

(*4R*)-4-Phenyl-2-*tert*-butyl-2-oxazoline (24). Solvent mixture: MeOH/CH_2Cl_2/ TEA 1/99/1; ir (NaCl) 1645 ($\nu_{N=C-O}$), 1470, 1445, 1130 cm^{-1}; ^{1}H-nmr δ 1.35 (s, 9H, C<u>H</u>$_3$), 4.07 (t, 1H, C<u>H</u>$_2$-O, J = 8.1 Hz), 4.60 (t, 1H, C<u>H</u>$_2$-O, J = 9.2 Hz), 5.15 (dd, 1H, C<u>H</u>-N, J = 8.1 and 8.3 Hz), 7.25-7.41 (m, 5H, Ph); ^{13}C-nmr δ 26.8 (C(<u>C</u>H$_3$)$_3$), 32.5 (<u>C</u>(CH$_3$)$_3$), 68.7 (<u>C</u>H-N), 74.0 (<u>C</u>H$_2$-O), [125.7, 126.5, 127.8, 142.5] (Phenyl group), 173.9 (N=<u>C</u>-O); ms (CI, 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 $[M-CH_2O]^+$ (weak intensity); *m/z* calcd for 117.0579. Found 117.058 $[M-CH_2O-CH_2=CMe_2]^+$; Anal. Calcd for $C_{13}H_{17}NO$: C, 76.81; H, 8.43; N, 6.89. Found: C, 76.41; H, 8.81; N, 6.71; $[\alpha]^{23}_D$ = +89.2 ° (c 4.54, MeOH).

(*4S*)-4-Benzyl-2-phenyl-2-oxazoline (26). Solvent mixture: CH_2Cl_2/TEA 99/1; ir (KBr) 1640 ($\nu_{N=C-O}$), 1485, 1445 , 1350 cm^{-1}; ^{1}H-nmr δ 2.79 (dd, 1H, C<u>H</u>$_2$-Ph, J = 7.5 and 13.6 Hz), 3.12 (dd, 1H, C<u>H</u>$_2$-Ph, J = 6.0 and 13.6 Hz), 4.12 and 4.38 (2dd, 1H, C<u>H</u>$_2$-O, J = 8.5 and 8.0 Hz), 4.56 (m, 1H, C<u>H</u>-N), 7.23-7.52 (m, 8H, Ph), 7.94 (d, 2H, Ph, J = 7.5 Hz); ^{13}C-nmr δ 42.2 (<u>C</u>H$_2$-Ph), 68.3 (<u>C</u>H-N), 72.3 (<u>C</u>H$_2$-O), [126.7, 128.5, 128.6, 128.7, 129.7, 131.5] (Phenyl groups), 164.0 (N=<u>C</u>-O); ms (CI, 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 $[M-CH_2O]^+$ (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; $[\alpha]^{23}_D$ = +22.9 ° (c 1.23, MeOH).

(*4S*)-4-Benzyl-2-methyl-2-oxazoline (28). Solvent mixture: MeOH/CH_2Cl_2/TEA 1/99/1; ir (NaCl) 1670 ($\nu_{N=C-O}$), 1380, 1225 cm^{-1}; ^{1}H-nmr δ 1.91 (s, 3H, C<u>H</u>$_3$), 2.66 (dd, 1H, C<u>H</u>$_2$-Ph, J = 7.4 and 13.5 Hz), 2.96 (dd, 1H, C<u>H</u>$_2$-Ph, J = 6.1 and 13.5 Hz), 3.89 and 4.17 (2t, 2H, C<u>H</u>$_2$-O, J = 8.6 Hz), 4.35 (m, 1H, C<u>H</u>-N), 7.19-7.32 (m, 5H, Ph); ^{13}C-nmr δ 14.3 (<u>C</u>H$_3$), 42.6 (<u>C</u>H$_2$-Ph), 68.4 (<u>C</u>H-N), 72.5 (<u>C</u>H$_2$-O), [126.9, 129.0, 130.0, 132.9, 139.3] (Phenyl group), 165.2 (O=<u>C</u>-N); ms (CI, 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 $[M-CH_2O]^+$; Anal. Calcd for $C_{11}H_{13}NO$: C, 75.46; H, 7.48. Found: C, 75.50 ; H, 7.26; $[\alpha]^{23}_D$ = -47.9 ° (c 1.70, MeOH).

(*4S*)-4-Benzyl-2-*tert*-butyl-2-oxazoline (30). Solvent mixture: MeOH/CH_2Cl_2/ TEA 1/99/1; ir (NaCl) 1650 ($\nu_{N=C-O}$), 1135 cm^{-1}; ^{1}H-nmr δ 1.16 (s, 3H, C$\underline{H}_3$), 2.66 (dd, 1H, C$\underline{H}_2$-Ph, J = 7.4 and 13.5 Hz), 2.94 (dd, 1H, C$\underline{H}_2$-Ph, J = 5.6 and 13.5 Hz), 3.91 and 4.13 (2t, 2H, C$\underline{H}_2$-O, *J = 10.0* Hz), 4.30 (*m, 1H,* C$\underline{H}$-N), 7.19-7.31 (*m,* 5H, Ph); ^{13}C-nmr δ 28.3 (C($\underline{C}H_3)_3$), 33.7 ($\underline{C}(CH_3)_3$), 42.4 ($\underline{C}H_2$-Ph), 67.8 ($\underline{C}$H-N), 72.2 ($\underline{C}H_2$-O), [127.0, 129.0, 130.3] (Phenyl group), 174.4 (N=$\underline{C}$-O); ms (CI, NH_3) *m/z*: 218.0 $[MH]^+$; HRms *m/z* calcd for $C_{14}H_{19}NO$ 217.1467. Found 217.147 $[M]^+$; *m/z* 187.0 $[M-CH_2O]^+$ (weak intensity); $[\alpha]^{23}_D$ = -50.2 ° (c 1.20, MeOH).

Dehydropeptide (32). Solvent mixture: pentane/AcOEt 3/1; ^{1}H-nmr δ 1.40 (s, 9H, C(C$\underline{H}_3)_3$), 1.67 (d, 3H, C$\underline{H}_3$-CH, *J = 7.0* Hz), 3.02 (dd, 1H, C$\underline{H}_2$-Ph, *J = 7.4 and* 14.1 Hz), 3.17 (dd, 1H, C$\underline{H}_2$-Ph, J = 6.4 and 14.1 Hz), 3.71 (s, 3H, C$\underline{H}_3$-O), 4.43 (m, 1H, C$\underline{H}$-N), 5.00 (s, 2H, N$\underline{H}$), 6.70-6.77 (m, 1H, C$\underline{H}$=C), 7.26-7.33 (m, 5H, Ph); ^{13}C-nmr δ 14.5 (C($\underline{C}H_3)_3$), 28.3 ($\underline{C}H_3$-CH), 38.0 ($\underline{C}H_2$-Ph), 52.4 ($\underline{C}H_3$-O), 54.5 ($\underline{C}(CH_3)_3$), 56.3 ($\underline{C}$H-N), [126.4, 127.2, 128.9, 129.7] (Phenyl group), 134.2 (C=$\underline{C}$-N), 136.8 (C=$\underline{C}$H), 156.0 (O$\underline{C}$ON), 165.0 (C=C-$\underline{C}O_2$), 170.0 (N-$\underline{C}$=O); ms (CI, NH_3) *m/z*: 380.0 $[M+NH_4]^+$, 363.0 $[MH]^+$.

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18. The resonance signals of C<u>H</u>(5)-O and <u>C</u>(5)H-O in **10** appear more deshielded than the corresponding expected signals of C<u>H</u>(3)-N and <u>C</u>(3)H-N in **9**. [20] Moreover, the 2-oxazolines (**26**), (**28**) and (**30**) and the acylaziridines (**9**) (R_2 = Bn, R_3 = R_4 = H, R_5 = Ph, Me or *t*-Bu) are known compounds. [21] Our ^{1}H-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).

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