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STEREOSELECTIVE SYNTHESIS OF *TRANS*-4,5-DISUBSTITUTED OXAZOLIDIN-2-ONES BY INTRAMOLECULAR CONJUGATE ADDITION OF *N*- *p*-TOLUENESULFONYL CARBAMATES

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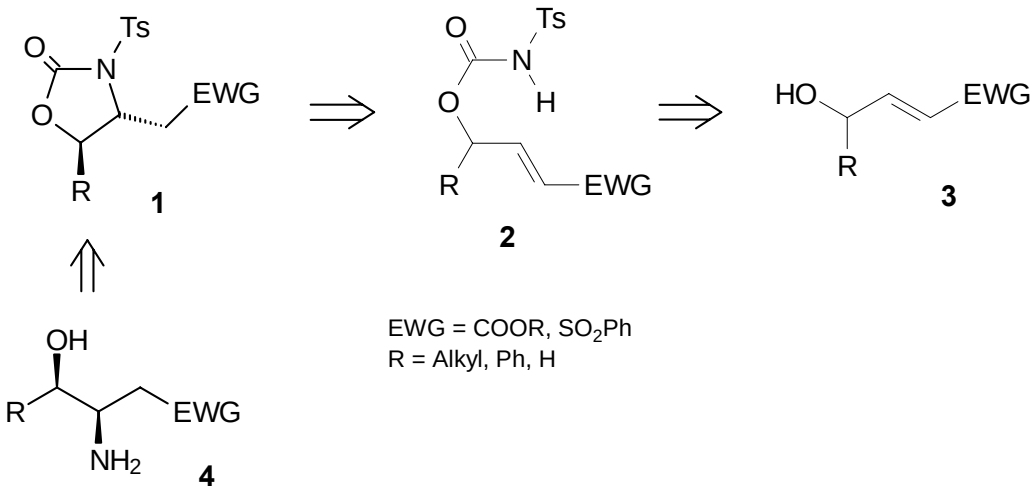
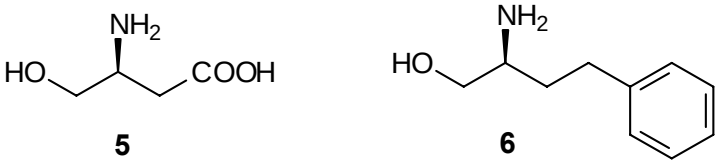
Abstract – *p*-Toluenesulfonyl carbamates **(2a-d)** were prepared starting from allylic alcohols **(3)**, in which the double bond is conjugated with an electron withdrawing group. In the presence of a catalytic amount of DBU, an intramolecular cyclisation occurred, leading to *trans*-4,5-disubstituted oxazolidin-2-ones **(1a-d)** with total stereoselection, which can be precursors of *syn*-4-hydroxy-3-amino acids.

Intramolecular conjugated addition of nitrogen nucleophiles to activated double bonds has been scarcely reported and in some cases the reaction must be carried out under an inert atmosphere.[1-9] In this field one of us [10] has already obtained enantiomerically pure diamino acids by cyclisation of a chiral 4-*p*-toluenesulfonylamino-2- butenoate, leading to an equimolar, easily separable diastereomeric mixture of imidazolidin-2-ones. Within a project directed towards the synthesis of non-proteinogenic amino acids,[11-17] we report here a convenient approach to *trans*-4,5-disubstituted oxazolidin-2-ones **(1)** by intramolecular conjugate addition of *N*-*p*-toluenesulfonyl carbamates **(2)** (Scheme 1).



Scheme 1

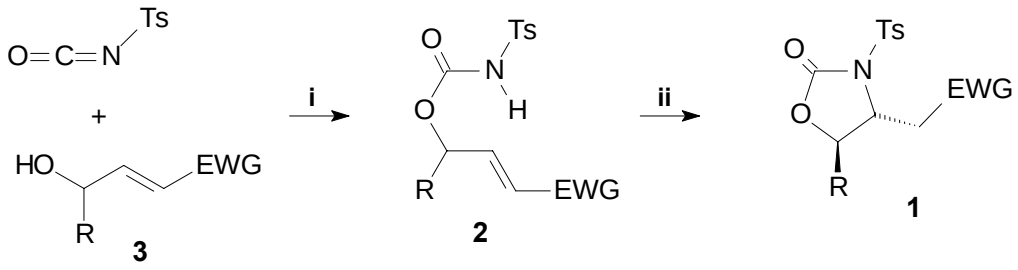
In fact, *trans*-4,5-disubstituted oxazolidin-2-ones **(1)** can be precursors of the *syn*-1-hydroxy-2-amino moiety **(4)** (EWG = COOR), a functional pattern which occurs in γ-substituted β-amino-γ-hydroxy acids with biological activity as subunits of antibiotic peptides, like tuberactinomycins A and N,[18,19] or gastroprotective natural products such as aminocoumacin C and AI-77-B.[20-23] Moreover, the 2-amino alcohol unit occurs as a sub-structure in β-amino-γ-hydroxy acids biologically active such as **5** [24-26] and in inhibitors of proteases, such as **6** (Scheme 2).[27,28]



Scheme 2

First, hydroxy derivatives **(3a-f)** were prepared according literature methods.[8,29,30] These compounds were subsequently treated with *p*-toluenesulfonyl isocyanate in DCM to give the corresponding *N*-*p*-toluenesulfonyl carbamates **(2a-f)** which were directly used in the following step without further purification (Scheme 3). In the presence of a catalytic amount of DBU in dichloromethane at room temperature, carbamates **(2)** underwent intramolecular conjugated addition to the activated double bond affording oxazolidin-2-ones **(1a-f)** in good yield, the ring size being determined by IR absorption of the carbonyl (1750 cm^{-1}).[31-35] When R was an alkyl or an aryl group, total stereoselection was observed, and *trans*-4,5-disubstituted oxazolidin-2-ones **(1a-d)** were isolated as the sole products, whose configuration was assigned on the basis of the $J_{4,5}$ value (about 4.0 Hz) in the ^1H NMR spectrum and n.O.e. experiments.[31-35] The exclusive formation of the *trans*-isomer can be explained by the reaction conditions,

an equilibrium occurring in the presence of DBU, leading to the most stable product. These compounds could be precursors of *syn*-3-amino-4-hydroxy acids after removal of the *p*-toluenesulfonyl group and cleavage of the heterocyclic ring carried out following literature methods.[10]

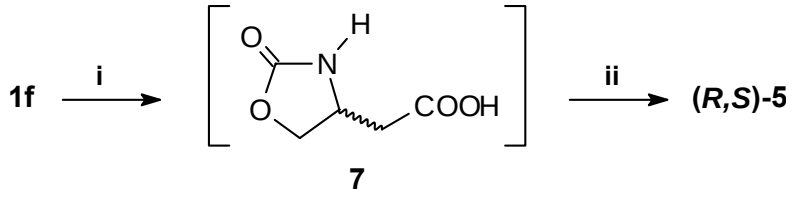


a. R = n-Bu, EWG = COOMe, 76%
b. R = Ph, EWG = COOEt, 88%
c. R = Me, EWG = SO_2Ph, 75%
d. R = Et, EWG = COOBn, 78%
e. R = H, EWG = SO_2Ph, 75%
f. R = H, EWG = COOBn, 78%

Reagents and conditions: i: DCM, rt, quantitative yield; ii: DBU (10 mol%), DCM, rt.

Scheme 3

However, when R = H **(1e,f)**, only a regioselective functionalisation of the double bond was observed, no matter of stereoselection. Nevertheless, the usefulness of compound **(1f)** was proven by conversion into racemic **5** through simple steps. In fact, simply by treating **1f** with Li in liquid NH_3, followed by cleavage of the heterocyclic ring under basic conditions,[10] racemic **5** was obtained in good yield.



Reagents and conditions: i: Li, NH_3, -78 °C; ii: NaOH, refluxing H_2O; Dowex AG 50W-X2, 1M NH_4OH as eluant, 52%.

Scheme 4

In conclusion, *N*-*p*-toluenesulfonyl carbamates **(2)** were disclosed to be useful starting material in order to prepare *trans*-4,5-disubstituted oxazolidin-2-ones with total stereoselection by intramolecular conjugated addition. Given the mild conditions required for the cyclisation, together with the access to an interesting class of compounds, the reported strategy would provide valuable intermediates for synthetic applications.

EXPERIMENTAL

Melting points were measured on a Electrothermal IA 9000 apparatus and are uncorrected. IR spectra were recorded in $CHCl_3$ on a Nicolet Fourier Transform Infrared 20-SX spectrophotometer. GC analyses were

performed using a Chrompack 9001 instrument equipped with a Chrompack 7720 capillary column (50 m x 0.25 mm i.d.; stationary phase CP-Sil-5 CB). ^{1}H and ^{13}C NMR spectra were recorded at 200 MHz and 50 MHz, respectively, on a Varian Gemini 200 spectrometer, using $CDCl_3$ as a solvent. Chemical shifts (δ) are reported in ppm relative to TMS and coupling constants (*J*) in Hz. Assignments were aided by decoupling and homonuclear two-dimensional experiments. GC-MS spectral analyses were performed with a Hewlett-Packard spectrometer 5890, series II, using a HP-5 capillary column (30 m x 0.25 mm i.d.; stationary phase 5% phenyl methyl silicone). MS spectral analysis was performed with a Fisons VG Autospec TRIO 1000 instrument.

Methyl (*E*)-4-hydroxy-2-octenoate (3a).

To a solution of methyl (*E*)-4-bromo-2-octenoate (4.7 g; 20 mmol) in DMF (10 mL) anhydrous sodium acetate was added (2.5 g; 30 mmol) and the mixture was heated for 4 h at 70 °C. After cooling, H_2O (40 mL) was added and the mixture was extracted with ethyl acetate (2 x 150 mL). After drying (Na_2SO_4) and removal of the solvent under reduced pressure, the residue was purified by silica gel chromatography (cyclohexane:ethyl acetate 60:40) to give the corresponding 4-acetoxy derivative (3.6 g; 85% yield) as a colorless oil. IR ($CHCl_3$): 1744, 1715 cm^{-1}; ^{1}H NMR: 0.86 (t, 3H, *J* = 6.2), 1.21 - 1.39 (m, 4H), 1.56 - 1.73 (m, 2H), 2.08 (s, 3H), 3.73 (s, 3H), 5.37 (dt, 1H, *J* = 5.3, *J* = 5.3), 5.91 (d, 1H, *J* = 15.8), 6.83 (dd, 1H, *J* = 5.3, *J* = 15.8); ^{13}C NMR: 14.3, 21.4, 22.8, 27.5, 33.9, 52.1, 72.9, 121.5, 146.3, 166.9, 170.5. A solution containing this compound (4.2 g; 20 mmol) in methanol (30 mL) was slowly added to the resin IRA 900 (5.0 g) in the methoxide form [35] suspended in methanol (30 mL). The mixture was stirred at rt for 1 h, then the resin was filtered off and washed with methanol (10 mL). After removal of the solvent under reduced pressure, the title product was obtained in a quantitative yield (3.4 g) as a colorless oil. IR ($CHCl_3$): 3351, 1718 cm^{-1}; ^{1}H NMR: 0.89 (t, 3H, *J* = 6.2), 1.21 - 1.48 (m, 4H), 1.51 - 1.68 (m, 2H), 1.89 (br s, 1H, OH), 3.73 (s, 3H), 4.23 - 4.37 (m, 1H), 6.04 (d, 1H, *J* = 15.8), 6.95 (dd, 1H, *J* = 5.0, *J* = 15.8); ^{13}C NMR: 14.4, 23.0, 27.8, 36.8, 52.1, 71.6, 120.1, 151.1, 167.5; GC-MS (EI, 70 eV): 172 (M^+), 157, 139, 113. Anal. Calcd for $C_9H_{16}O_3$: C, 62.77; H, 9.36. Found: C, 62.74; H, 9.40.

Ethyl (*E*)-4-phenyl-4-hydroxy-2-butenoate (3b).

To a solution containing ethyl (*E*)-4-phenyl-4-oxo-2-butenoate (2.0 g; 10 mmol) in dry methanol (50 mL) at -15 °C KBH_4 (0.7 g; 10 mmol) was added and the mixture was stirred for 1 h. Solid NH_4Cl (2.0 g) was added, then the mixture was poured in H_2O (40 mL) and extracted with ethyl acetate (3 x 100 mL). After drying (Na_2SO_4) and removal of the solvent under reduced pressure, the residue was purified by silica gel chromatography (cyclohexane:ethyl acetate 80:20) to give the title compound (1.9 g; 91% yield) as a colorless oil. IR ($CHCl_3$): 3352, 1711 cm^{-1}; ^{1}H NMR: 1.26 (t, 3H, *J* = 7.2), 3.02 (br s, 1H, OH), 4.16 (q, 2H,

J = 7.2), 5.29 (m, 1H), 6.12 (dd, 1H, *J* = 1.7, *J* = 15.7), 7.02 (dd, 1H, *J* = 3.0, *J* = 15.7), 7.33 (m, 5 ArH); ^{13}C NMR: 14.6, 61.1, 73.7, 120.3, 127.1, 128.0, 128.6, 128.9, 129.2, 141.6, 149.8, 167.3; GC-MS (EI, 70 eV): 206 (M^+), 177, 128, 77. Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.89; H, 6.84. Found: C, 69.85; H, 6.81.

Preparation of compounds (3c-f). General Procedure.

To a solution of the appropriate 2-alkenyl phenyl sulphone or benzyl 3-alkenoate (20 mmol) in chloroform (100 mL), *m*-chloroperbenzoic acid (50%; 8.6 g; 25 mmol) was added and the suspension was refluxed for 5 h. After cooling and removal of the solvent under reduced pressure, the residue was dissolved in ethyl acetate (100 mL) and the organic layer was washed with aqueous saturated Na_2CO_3 (2 x 50 mL). After drying (Na_2SO_4), the solvent was removed in vacuo and the residue was purified by silica gel chromatography (cyclohexane:ethyl acetate 50:50) to give the corresponding epoxide. To a solution of the epoxide (18 mmol) in dichloromethane (100 mL) DBU (0.3 mL) was added and the mixture was stirred for 2 h at rt. The organic phase was then washed with 1 M HCl (40 mL) and water (2 x 100 mL) and after drying (Na_2SO_4) the solvent was removed under reduced pressure. The residue was purified by silica gel chromatography (cyclohexane:ethyl acetate 60:40) to give compounds **(3c-f)**.

(*E*)-1-Benzenesulfonyl-1-buten-3-ol (3c).

Starting from (*E*)-(2-butenyl)phenylsulfone the title compound was prepared in 79% overall yield as a low melting solid. IR ($CHCl_3$): 3345 cm^{-1}; ^{1}H NMR: 1.26 (d, 3H, *J* = 6.9), 2.94 (br s, 1H. OH), 4.29 - 4.57 (m, 1H), 6.55 (dd, 1H, *J* = 1.8, *J* = 14.9), 6.94 (dd, 1H, *J* = 3.6, *J* = 14.9), 7.46 - 7.65 (m, 3 ArH), 7.78 - 7.92 (m, 2 ArH); ^{13}C NMR: 22.8, 66.7, 128.1, 129.3, 129.8, 134.0, 140.1, 149.9; GC-MS (EI, 70 eV): 212 (M^+), 194, 141, 77, 70. Anal. Calcd for $C_{10}H_{12}O_3S$: C, 56.59; H, 5.70. Found: C, 56.54; H, 5.66.

Benzyl (*E*)-4-hydroxy-2-hexenoate (3d).

Starting from benzyl (*E*)-3-hexenoate, the title compound was prepared in 81% overall yield as a colorless oil. IR ($CHCl_3$): 3348, 1721 cm^{-1}; ^{1}H NMR: 0.97 (t, 3H, *J* = 7.4), 1.55 - 1.75 (m, 2H), 4.21 - 4.32 (m, 1H), 4.45 (br s, 1H, OH), 5.20 (s, 2H), 6.10 (dd, 1H, *J* = 1.8, *J* = 15.8), 7.02 (dd, 1H, *J* = 4.8, *J* = 15.8), 7.31 - 7.43 (m, 5 ArH); ^{13}C NMR: 10.0, 29.9, 66.9, 72.8, 120.5, 128.7, 129.1, 130.3, 131.7, 134.1, 151.0, 167.0; GC-MS (EI, 70 eV): 220 (M^+), 202, 129, 91, 77. Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 70.84; H, 7.35.

(*E*)-3-Benzenesulfonyl-2-propenol (3e).

Starting from allyl phenylsulfone, the title compound was prepared in 77% overall yield as a colorless oil. IR ($CHCl_3$): 3351 cm^{-1}; ^{1}H NMR: 1.88 (br s, 1H, OH), 4.41 (m, 2H), 6.67 (dt, 1H, *J* = 2.2, *J* = 14.9), 7.07

(dt, 1H, *J* = 3.3, *J* = 14.9), 7.48 - 7.71 (m, 3 ArH), 7.85 - 7.97 (m, 2 ArH); ^{13}C NMR: 60.5, 127.8, 129.1, 129.7, 133.9, 140.4, 147.1; GC-MS (EI, 70 eV): 198 (M^+), 141, 77, 57. Anal. Calcd for $C_9H_{10}O_3S$: C, 54.53; H, 5.08. Found: C, 54.48; H, 5.04.

Benzyl (*E*)-4-hydroxy-2-butenoate (3f).

Starting from benzyl 3-butenoate, the title compound was prepared in 78% overall yield as a colorless oil. IR ($CHCl_3$): 3347, 1698 cm^{-1}; ^{1}H NMR: 1.78 (br s, 1H, OH), 4.36 (dd, 2H, *J* = 2.2, *J* = 3.9), 5.20 (s, 2H), 6.16 (dt, 1H, *J* = 2.2, *J* = 15.8), 7.09 (dt, 1H, *J* = 3.9, *J* = 15.8), 7.29 - 7.42 (m, 5 ArH); ^{13}C NMR: 62.3, 66.7, 120.3, 128.6, 128.7, 128.9, 129.0, 136.4, 148.0, 166.7; GC-MS (EI, 70 eV): 192 (M^+), 190, 101, 91, 77. Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.74; H, 6.29. Found: C, 68.79; H, 6.25.

Preparation of *N*-*p*-toluenesulfonyl carbamates (2a-f). General Procedure.

To a solution containing the compounds **(3a-f)** (15 mmol) in dichloromethane (50 mL) *p*-toluenesulfonyl isocyanate (3.2 g; 16 mmol) dissolved in dichloromethane (10 mL) was added at rt. The solution was stirred for 4 h and then the solvent was removed under reduced pressure. The residue was purified by silica gel chromatography (cyclohexane:ethyl acetate 80:20) to give the pure compounds **(2a-f)**.

Methyl (*E*)-4-*p*-toluenesulfonylaminocarbonyloxy-2-octenoate (2a).

Starting from compound **(3a)**, the title compound was prepared in 86% yield as a colorless oil. IR ($CHCl_3$): 3332, 1742, 1714 cm^{-1}; ^{1}H NMR: 0.84 (t, 3H, *J* = 6.6), 1.12 - 1.34 (m, 4H), 1.53 - 1.67 (m, 2H), 2.45 (s, 3H), 3.73 (s, 3H), 5.28 (dt, 1H, *J* = 5.2, *J* = 5.3), 5.81 (d, 1H, *J* = 15.7), 6.73 (dd, 1H, *J* = 5.3, *J* = 15.7), 7.35 (d, 2 ArH, *J* = 8.1), 7.61 (s, 1H, NH), 7.91 (d, 2 ArH, *J* = 8.1); ^{13}C NMR: 14.1, 21.9, 22.6, 27.0, 33.8, 52.2, 75.7, 121.6, 128.6, 130.0, 136.3, 145.3, 145.4, 150.6, 167.0; GC-MS (EI, 70 eV): 369 (M^+), 214, 155, 91. Anal. Calcd for $C_{17}H_{23}NO_6S$: C, 55.27; H, 6.28; N, 3.79. Found: C, 55.24; H, 6.31; N, 3.81.

Ethyl (*E*)-4-phenyl-4-*p*-toluenesulfonylaminocarbonyloxy-2-butenoate (2b).

Starting from compound **(3b)**, the title compound was prepared in 85% yield as a colorless oil. IR ($CHCl_3$): 3349, 1746, 1712 cm^{-1}; ^{1}H NMR: 1.25 (t, 3H, *J* = 7.0), 2.38 (s, 3H), 4.18 (q, 2H, *J* = 7.0), 5.99 (dd, 1H, *J* = 1.6, *J* = 15.6), 6.25 (dd, 1H, *J* = 1.6, *J* = 5.0), 6.91 (dd, 1H, *J* = 5.0, *J* = 15.6), 7.12 - 7.32 (m, 7 ArH), 7.87 (d, 2 ArH, *J* = 8.3); ^{13}C NMR: 14.6, 22.0, 61.4, 77.1, 122.3, 127.7, 128.6, 129.3, 129.4, 130.1, 136.2, 136.6, 144.3, 145.4, 150.4, 166.6; GC-MS (EI, 70 eV): 403 (M^+), 246, 155, 91. Anal. Calcd for $C_{20}H_{21}NO_6S$: C, 59.54; H, 5.25; N, 3.47. Found: C, 59.50; H, 5.27; N, 3.44.

(*E*)-1-Benzenesulfonyl-3-*p*-toluenesulfonylaminocarbonyloxy-1-butene (2c).

Starting from compound **(3c)**, the title compound was prepared in 82% yield as a colorless oil. IR ($CHCl_3$): 3347, 1746 cm^{-1}; ^1H NMR: 1.32 (d, 3H, *J* = 6.8), 2.45 (s, 3H), 5.41 (ddq, 1H, *J* = 6.8, *J* = 4.1, *J* = 1.6), 6.45 (dd, 1H, *J* = 15.1, *J* = 1.6), 6.82 (dd, 1H, *J* = 15.1, *J* = 4.1), 7.30 (d, 2 ArH, *J* = 8.2), 7.49 - 7.68 (m, 4H, 3 ArH + NH), 7.74 - 7.93 (m, 4 ArH); ^{13}C NMR: 22.2. 71.3, 126.8, 128.3, 128.5, 128.7, 128.8, 129.7, 129.9, 130.2, 131.1, 134.2, 140.0, 143.7, 145.7, 150.0, 169.3; GC-MS (EI, 70 eV): 409 (M^+), 254, 208, 155, 125, 91, 77. Anal. Calcd for $C_{18}H_{19}NO_6S_2$: C, 52.80; H, 4.68; N, 3.42. Found: C, 52.77; H, 4.65; N, 3.45.

Benzyl (*E*)-4-*p*-toluensulfonylaminocarbonyloxy-2-hexenoate (2d).

Starting from compound **(3d)**, the title compound was prepared in 86% yield as a colorless oil. IR ($CHCl_3$): 3347 cm^{-1}; ^1H NMR: 0.83 (t, 3H, *J* = 7.4), 1.53 - 1.76 (m, 2H), 2.40 (s, 3H), 5.17 (s, 2H), 5.18 - 5.29 (m, 1H), 5.83 (dd, 1H, *J* = 1.5, *J* = 15.8), 6.77 (dd, 1H, *J* = 5.2, *J* = 15.8), 7.31 (d, 2 ArH, *J* = 8.1), 7.36 (m, 5 ArH), 7.89 (d, 2 ArH, *J* = 8.1), 7.98 (s, 1H, NH); ^{13}C NMR: 9.5, 22.1, 67.1, 77.0, 122.2, 128.8, 129.0, 129.1, 130.2, 135.9, 136.1, 145.0, 145.7, 150.5, 166.2; GC-MS (EI, 70 eV): 417 (M^+), 262, 202, 170, 155, 91, 77. Anal. Calcd for $C_{21}H_{23}NO_6S$: C, 60.42; H, 5.55; N, 3.36. Found: C, 60.38; H, 5.57; N, 3.33.

(*E*)-1-Benzenesulfonyl-3-*p*-toluenesulfonylaminocarbonyloxy-1-propene (2e).

Starting from compound **(3e)**, the title compound was prepared in 88% yield as a white solid. mp 69-71 °C (ethyl acetate); IR ($CHCl_3$): 3335, 1744 cm^{-1}; ^1H NMR: 2.37 (s, 3H), 4.69 (dd, 2H, *J* = 2.0, *J* = 3.7), 6.46 (dt, 1H, *J* = 2.0, *J* = 15.1), 6.82 (dt, 1H, *J* = 3.7, *J* = 15.1), 7.24 (d, 2 ArH, *J* = 8.9), 7.46 - 7.65 (m, 3 ArH), 7.74 - 7.84 (m, 4 ArH); ^{13}C NMR: 22.0, 63.4, 128.1, 128.4, 129.9, 130.0, 131.7, 134.2, 136.3, 139.3, 139.9, 145.3, 151.1; GC-MS (EI, 70 eV): 395 (M^+), 240, 155, 91. Anal. Calcd for $C_{17}H_{17}NO_6S_2$: C, 51.63; H, 4.33; N, 3.54. Found: C, 51.58; H, 4.28; N, 3.50.

Benzyl (*E*)-4-*p*-toluenesulfonylaminocarbonyloxy-2-butenoate (2f).

Starting from compound **(3e)**, the title compound was prepared in 92% yield as a colorless oil. IR ($CHCl_3$): 3343, 1745, 1704 cm^{-1}; ^1H NMR: 2.42 (s, 3H), 4.74 (dd, 2H, *J* = 1.9, *J* = 4.6), 5.18 (s, 2H), 5.95 (dt, 1H, *J* = 1.9, *J* = 15.8), 6.86 (dt, 1H, *J* = 4.6, *J* = 15.8), 7.35 (d, 2 ArH, *J* = 8.4), 7.37 (m, 5 ArH), 7.63 (br s, 1H, NH), 7.92 (d, 2 ArH, *J* = 8.4); ^{13}C NMR: 22.2, 65.0, 67.1, 122.9, 128.8, 129.1, 130.2, 135.7, 136.1, 140.9, 145.8, 150.5, 165.9; GC-MS (EI, 70 eV): 389 (M^+), 234, 155, 91. Anal. Calcd for $C_{19}H_{19}NO_6S$: C, 58.60; H, 4.92; N, 3.60. Found: C, 58.55; H, 4,87; N, 3.65.

Preparation of oxazolidin-2-ones (1a-f). General procedure.

To a solution containing compounds **(2a-f)** (5 mmol) in dichloromethane (50 mL) DBU (0.3 mL) was added and the mixture was stirred for 12 h. Most of the solvent was removed under reduced pressure, ethyl

acetate (150 mL) was added and the organic phase was washed with 1 M HCl (50 mL) and subsequently with water (100 mL). After drying (Na_2SO_4), the solvent was removed under reduced pressure and the residue was purified by silica gel chromatography (cyclohexane:ethyl acetate 70:30), to give the pure oxazolidin-2-ones **(1a-f)**.

Methyl *trans*-(5-butyl-3-*p*-toluenesulfonyl-1,3-oxazolidin-2-on-4-yl)acetate (1a).

Starting from **2a**, the title compound was prepared in 76% yield as a colorless oil. IR ($CHCl_3$): 1748, 1740 cm^{-1}; ^1H NMR: 0.83 (t, 3H, *J* = 6.3), 1.14 - 1.41 (m, 4H), 1.42 - 1.73 (m, 2H), 2.44 (s, 3H), 2.78 (dd, 1H, *J* = 9.5, *J* = 16.9), 3.16 (dd, 1H, *J* = 3.2, *J* = 16.9), 3.68 (s, 3H), 4.26 (dt, 1H, *J* = 4.9, *J* = 2.9), 4.33 (ddd, 1H, *J* = 2.9, *J* = 3.2, *J* = 9.5), 7.37 (d, 2 ArH, *J* = 8.2), 7.94 (d, 2 ArH, *J* = 8.2); ^{13}C NMR: 14.2, 22.2, 22.6, 26.3, 34.8, 38.9, 52.6, 58.4, 80.8, 128.8, 128.9, 129.0, 130.3, 135.2, 146.3, 151.9, 170.5; GC-MS (EI, 70 eV): 369 (M^+), 214, 155, 91. Anal. Calcd for $C_{17}H_{23}NO_6S$: C, 55.27; H, 6.28; N, 3.79. Found: C, 55.31; H, 6.24; N, 3.75.

Ethyl *trans*-(5-phenyl-3-*p*-toluenesulfonyl-1,3-oxazolidin-2-on-4-yl)acetate (1b).

Starting from **2d**, the title compound was prepared in 88% yield as a white solid. mp 78-80 °C (ethyl acetate); IR ($CHCl_3$): 1748, 1741 cm^{-1}; ^1H NMR: 1.28 (t, 3H, *J* = 7.1), 2.45 (s, 3H), 2.98 (dd, 1H, *J* = 9.8, *J* = 17.1), 3.22 (dd, 1H, *J* = 3.5, *J* = 17.1), 4.57 (ddd, 1H, *J* = 2.6, *J* = 3.5, *J* = 9.8), 5.34 (d, 1H, *J* = 2.6), 7.12 - 7.38 (m, 7 ArH), 7.81 (d, 2 ArH, *J* = 8.4); ^{13}C NMR: 14.6, 22.2, 39.1, 61.8, 61.9, 80.6, 125.5, 127.8, 128.6, 128.8, 129.5, 130.1, 130.3, 134.8, 137.9, 143.7, 146.3, 152.1, 170.2; GC-MS (EI, 70 eV): 403 (M^+), 248, 155, 91. Anal. Calcd for $C_{20}H_{21}NO_6S$: C, 59.54; H, 5.25; N, 3.47. Found: C, 59.49; H, 5.29; N, 3.44.

***Trans*-3-*p*-toluenesulfonyl-4-benzenesulfonylmethyl-5-methyl-1,3-oxazolidin-2-one (1c).**

Starting from **2c**, the title compound was prepared in 75% yield as a colorless oil. IR ($CHCl_3$): 1748 cm^{-1}; ^1H NMR: 1.33 (d, 3H, *J* = 6.5), 2.46 (s, 3H), 3.50 (dd, 1H, *J* = 10.9, *J* = 13.6), 3.93 (dd, 1H, *J* = 2.1, J = 13.6), 4.28 (ddd, 1H, *J* = 2.1, *J* = 2.4, *J* = 10.9), 4.93 (dq, 1H, *J* = 6.5, *J* = 2.4), 7.32 (d, 2 ArH, *J* = 8.2), 7.62 - 7.75 (m, 3 ArH), 7.67 - 7.75 (m, 2 ArH), 7.96 (d, 2 ArH, *J* = 8.2); ^{13}C NMR: 22.0, 22.2, 58.4, 58.9, 76.9, 126.9, 128.4, 129.6, 129.9, 130.2, 130.3, 130.6, 134.3, 135.2, 139.1, 146.8, 151.2; GC-MS (EI, 70 eV): 409 (M^+), 254, 155, 91. Anal. Calcd for $C_{18}H_{19}NO_6S_2$: C, 52.80: H, 4.68; N, 3.42. Found: C, 52.74; H, 4.64; N, 3.45.

Benzyl *trans*-(5-ethyl-3-*p*-toluenesulfonyl-1,3-oxazolidin-2-on-4-yl)acetate (1d).

Starting from **2d**, the title compound was prepared in 78% yield as a colorless oil. IR ($CHCl_3$): 1746, 1741 cm^{-1}; ^1H NMR: 0.85 (t, 3H, *J* = 7.3), 1.49 - 1.73 (m, 2H), 2.42 (s, 3H), 2.83 (dd, 1H, *J* = 9.6, *J* = 17.0), 3.20

(dd, 1H, *J* = 3.3, *J* = 17.0), 4.22 (ddd, 1H, *J* = 3.0, *J* = 4.8, *J* = 7.4), 4.37 (ddd, 1H, *J* = 3.0, *J* = 3.3, *J* = 9.6), 5.12 (ABq, 2H, *J* = 12.1), 7.35 (d, 2 ArH, *J* = 8.4), 7.36 (m, 5 ArH), 7.92 (d, 2 ArH, *J* = 8.4); ^{13}C NMR: 8.8, 22.2, 28.2, 39.0, 58.1, 67.5, 81.8, 128.8, 129.0, 129.1, 129.2, 130.0, 130.4, 130.6, 135.2, 135.6, 146.3, 152.0, 169.9; GC-MS (EI, 70 eV): 417 (M^+), 162, 155, 91. Anal. Calcd for $C_{21}H_{23}NO_6S$: C, 60.42: H, 5.55; N, 3.36. Found: C, 60.37; H, 5.51; N, 3.40.

3-*p*-Toluenesulfonyl-4-benzenesulfonylmethyl-1,3-oxazolidin-2-one (1e).

Starting from **2e,** the title compound was prepared in 75% yield as a white solid. mp 75-77 °C (ethyl acetate); IR ($CHCl_3$): 1744 cm^{-1}; ^{1}H NMR: 2.45 (s, 3H), 3.49 (dd, 1H, *J* = 10.5, *J* = 13.7), 4.12 (dd, 1H, *J* = 2.0, *J* = 13.7), 4.48 - 4.76 (m, 3H), 7.28 - 7.39 (m, 3 ArH), 7.62 - 7.85 (m, 4 ArH), 7.96 (d, 2 ArH, *J* = 6.8); ^{13}C NMR: 22.2, 52.4, 59.2, 67.9, 126.9, 128.4, 128.9, 130.2, 130.3, 130.5, 135.2, 139.0, 143.5, 146.9; GC-MS (EI, 70 eV): 395 (M^+), 240, 155, 91. Anal. Calcd for $C_{17}H_{17}NO_6S_2$: C, 51.63; H, 4.33; N, 3.54. Found: C, 51.58; H, 4.39; N, 3.51.

Benzyl (3-*p*-toluenesulfonyl-1,3-oxazolidin-2-on-4-yl)acetate (1f).

Starting from **2f**, the title product was obtained in 78% yield as a colorless oil. IR ($CHCl_3$): 1751 cm^{-1}; ^{1}H NMR: 2.44 (s, 3H), 2.83 (dd, 1H, *J* = 9.7, *J* = 17.1), 3.35 (dd, 1H, *J* = 3.3, *J* = 17.1), 4.13 (dd, 1H, *J* = 4.4, *J* = 9.2), 4.51 (dd, 1H, *J* = 8.9, *J* = 9.2), 4.75 (dddd, 1H, *J* = 3.3, *J* = 4.4, *J* = 8.9, *J* = 9.7), 5.13 (ABq, 2H, *J* = 12.2), 7.35 (d, 2 ArH, *J* = 8.4), 7.37 (m, 5 ArH), 7.93 (d, 2 ArH, *J* = 8.4); ^{13}C NMR: 22.2, 39.0, 53.7, 67.5, 68.6, 128.9, 129.1, 129.2, 130.4, 135.0, 135.6, 146.4, 152.6, 170.0; GC-MS (EI, 70 eV): 389 (M^+), 234, 155, 91. Anal. Calcd for $C_{19}H_{19}NO_6S$: C, 58.60; H, 4.92; N, 3.60. Found: C, 58.55; H, 4.86; N, 3.65.

(*R,S*)-3-Amino-4-hydroxybutanoic acid (5).

In a flask under inert atmosphere NH_3 (about 50 mL) was condensed at -78 °C and then Li (210 mg; 30 mmol) was added. When the metal dissolved in NH_3, a solution containing **1f** (1.9 g; 5 mmol) in THF-*t*-BuOH 9:1 (20 mL) was quickly added. After 15 min NH_3 was removed , H_2O (15 mL) was slowly dropped and then the mixture was extracted with ethyl acetate (2 x 50 mL). To the solution NaOH (1.5 g) was added and the mixture was heated under reflux for 12 h. After removal of the H_2O under reduced pressure, the residue was redissolved in H_2O (5 mL) and the solution was adsorbed on ion-exchange resin Dowex AG 50W-X2. The resin was washed with distilled water and then eluted with 1 M NH_4OH to give the compound **(5)** (0.3 g; 52%) as a white solid. mp 223-225 °C (methanol) (lit.,[24] 228 °C); ^{1}H NMR (CD_3OD + NaOH): 2.17 (dd, 1H, *J* = 8.1, *J* = 16.6), 2.34 (dd, 1H, *J* = 5.1, *J* = 16.6), 3.09 - 3.22 (m, 1H), 3.39 (dd, 1H, *J* = 6.7, *J* = 10.7), 3.54 (dd, 1H, *J* = 4.8, *J* = 10.7), 4.96 (br s, 3H, OH + NH_2); ^{13}C NMR (CD_3OD + NaOH): 43.3, 52.2, 67.7, 180.6; MS (EI): 120 (M^+ +1), 84. Anal. Calcd for $C_4H_9NO_3$: C, 40.33;

H, 7.62; N, 11.76. Found: C, 40.29; H, 7.59; N, 11.79.

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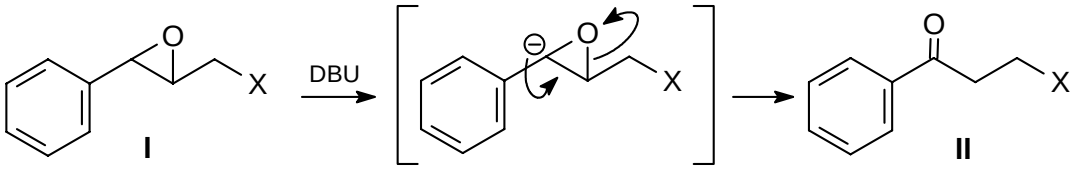
30. During the preparation of alkenols **(3)**, a base-induced rearrangement was observed (see: D. M. Hodgson, L. A. Robinson, and M. L. Jones, *Tetrahedron Lett.*, 1999, **40**, 8637, and references cited therein). In fact, when the epoxides **(Ia,b)** were treated with a catalytic amount of DBU, the corresponding hydroxy compounds were not observed at all, the 4-oxo derivatives **(IIa,b)** being the sole products, probably owing to the acidity of the benzylic hydrogen. **IIa**: IR ($CHCl_3$): 1745, 1697 cm^{-1}; ^1H NMR (200 MHz; $CDCl_3$): 2.74 (t, 2H, *J* = 6.5), 3.32 (t, 2H, *J* = 6.5), 3.71 (s, 3H), 7.41 - 7.62 (m, 3 ArH), 7.94 - 8.04 (m, 2 ArH); ^{13}C NMR (50 MHz; $CDCl_3$): 28.5, 33.9, 52.3, 128.5, 129.1, 133.7, 137.0, 173.8, 198.5. **IIb**: IR ($CHCl_3$): 1698 cm^{-1}. ^1H NMR (200 MHz; $CDCl_3$): 3.43 - 3.61 (m ,4H), 7.38 - 7.71 (m, 6 ArH), 7.74 - 7.99 (m, 4 ArH); ^{13}C NMR (50 MHz; $CDCl_3$): 31.9, 51.5, 128.4, 128.5, 129.0, 129.3, 129.6, 129.9, 134.3, 134.4, 136.3, 139.5, 195.9.



I II

a. X = COOMe, **b.** X = SO_2Ph

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