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NUCLEOPHILIC REACTIONS AT OPTICALLY ACTIVE *BIS*(4-METHYL-5-PHENYL-1,3-OXAZOLIDIN-3-YL)-METHANE

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Abstract – The reagents RMgCl, RLi, NaOMe and amines (R = Me or *t*-Bu) with *bis*(4-methyl-5-phenyl-1,3-oxazolidin-3-yl)methane (**1**) attack nucleophilically at its endo- or exocyclic methylenic groups (C-2 or C-6) giving: 3-ethyl-4-methyl-5-phenyl-1,3-oxazolidine (**3**), 3-*neo*pentyl-4-methyl-5-phenyl-1,3-oxazolidine (**4**), 2-[*neo*pentyl-(4-methyl-5-phenylethan-1,3-oxazolidin-3-ylmethyl)amino]-1-phenylpropan-1-ol (**6**), *N*-*neo*pentyl *nor*ephedrine (**7**), 3-methoxymethyl-4-methyl-5-phenyl-1,3-oxazolidine (**8**), *N*-benzyl-(4-methyl-5-phenyl-1,3-oxazolidin-3-yl)methane (**9**), 2-chloropropyl-(4-methyl-5-phenyl-1,3-oxazolidin-3-ylmethyl)amine (**10**), 2-[(benzylamino-methyl)amino]-1-phenylpropan-1-ol (**11**). A high yield synthesis of 3(*H*)-4-methyl-5-phenyl-1,3-oxazolidine (**5**) is also reported.

Chiral oxazolidines are very useful and widely used molecules in stereoselective organic syntheses. They have found applications as prodrugs,[1a] as chiral inductor reagents[1b] or as intermediates in stereocontroled

syntheses.[1c-e] Enormous research efforts have been recently dedicated to the preparation of new chiral oxazolidines and to the understanding of their chemistry,[1f-g] particularly with inorganic or organometallic reagents which afford a wide variety of new compounds with functional groups and of different structures.[1b,1e,2] N-H oxazolidines are important intermediates in the synthesis of structurally complex organic molecules.[2] The reactivity of chiral N-H group in these heterocycles allows the preparation of coordination compounds which have been used as catalysts.[3] In this context this paper aims an understanding of the chemistry of these complexes and versatile heterocycles derived there form.

We have found that condensation reactions of formaldehyde with ethanolamines did not give the expected 1,3,5-heterocyclohexanes[4,5] but the *bis*(1-hetero-3-azolidin-3-yl)methanes (heteroatom = O, S or N).[6] Therefore, we have prepared the optically active *bis*(4-methyl-5-phenyl-1,3-oxazolidin-3-yl)methane (**1**) *via* condensation of 1*S*,2*R*-(+)-*nor*ephedrine with formaldehyde and investigated its reactions with nucleophilic reagents such as RMgCl, RLi (R = CH_3 or *t*-Bu), NaOMe and benzylamine.

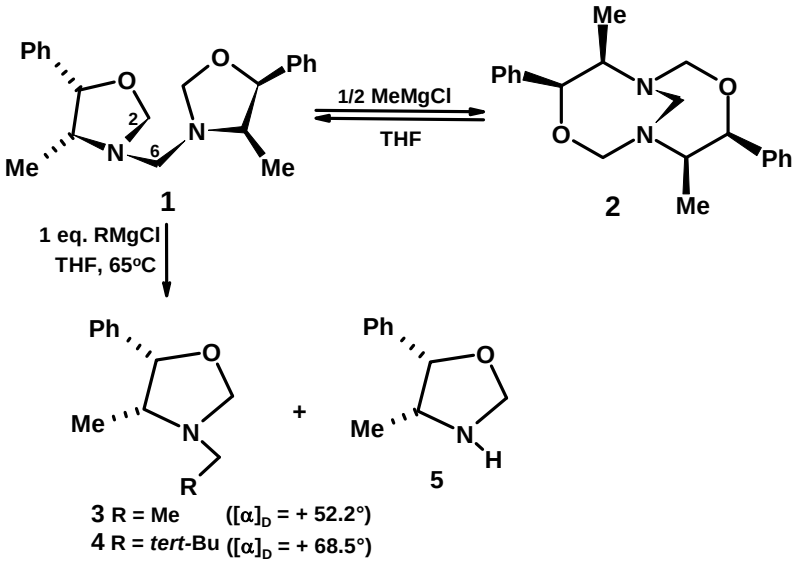
Results and Discussion

Reactions of *bis*(oxazolidine)methane (1) with nucleophilic reagents

a) with Grignard reagents

Compound (**1**) in the presence of 0.5 equivalents of MeMgCl, at 0 ^{o}C in THF, isomerizes to **2**, Scheme 1. On the other hand the reaction with methyl- or *tert*-butylmagnesium chloride in an equimolar ratio in boiling THF affords, by cleavage of one C-N bond, the oxazolidines (**3**) or (**4**) and one equivalent of N-H oxazolidine (**5**) respectively. Compound (**5**) is easily separated by distillation from the reaction mixture leaving behind pure **3** or **4**. Acidic treatment hydrolyzes compound (**4**) to *N*-*neo*pentyl*nor*ephedrine (**7**) hydrochloride which crystallizes in water. Its solid state structure presents an alternated conformation compound with the structure of the nitrogen atom *anti* to the phenyl group [N3-C2-C1-C7, 177.46^{o}],

Figure 1.



Scheme 1 Reactions of Grignard reagents with compound (**1**).

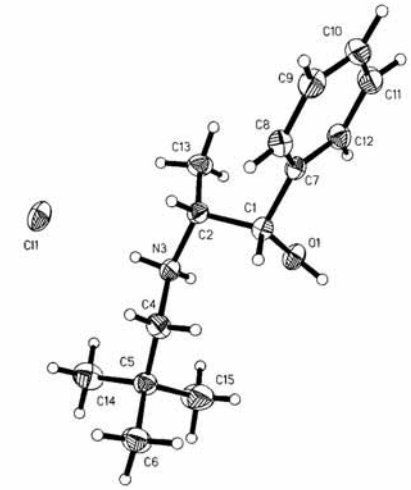
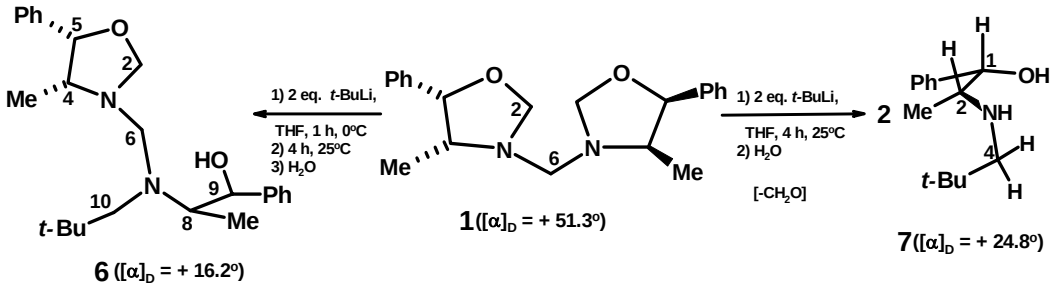


Figure 1 ORTEP description of *N-neo*pentyl*nor*ephedrine (**7**) hydrochloride. Selected interatomic distances (in Å) and angles (in degrees) are as follows: O1-C1 1.412(3), C1-C2 1.529(3), C2-N3 1.507(3), C2-C13 1.516(4), N3-C4 1.495(4), C4-C5 1.511(4), O1-C1-C2 106.1(2), C7-C1-C2 110.5(2), N3-C2-C13 107.0(2), C13-C2-C1 114.1(2), C4-N3-C2 117.1(2), N3-C4-C5 114.4(2)

b) with alkyllithium reagents

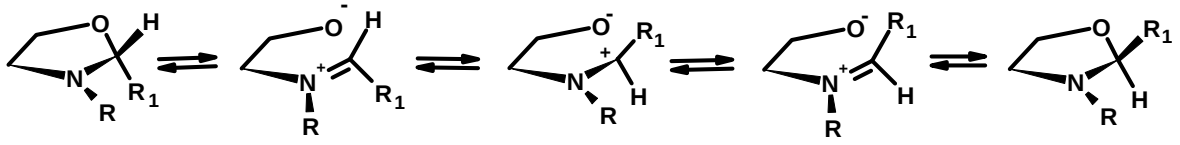
Reaction of compound (**1**) with two equivalents of *t*-BuLi in THF at 0 ^{o}C affords compound (**6**) by alkylation of C-2 and opening of one ring. Compound (**6**) is a yellow liquid. NMR spectra show two sets of signals for each ephedrine moiety. Both fragments remain bonded to the methylene group (C-6) which is observed in its ^{13}C NMR spectrum at 72.5 ppm. The methylene protons of the *neo*pentyl group give rise to an AB coupling pattern in the ^{1}H NMR spectrum at 2.51 and 2.36 ppm (^{2}J = 13.3 Hz).

At room temperature, the reaction of **1** with two equivalents of *t*-BuLi gives two molecules of *N*-*neo*pentyl*nor*ephedrine (**7**) with loss of the exocyclic methylene group, Scheme 2. A different result is obtained with one equivalent of MeLi in ether solution, the reaction affors oxazolidines (**3**) and (**5**), in analogy to the reaction with methylmagnesium shown in Scheme 1.



Scheme 2 Reactions of alkyllithium reagents with compound (**1**)

The behavior of compound (**1**) to ward the organometallic nucleophiles can be rationalized by an easy opening of oxazolidines as is known for the isomerization of 2-substituted oxazolidines and thiazolidines,[8] Scheme 3. It has been proposed that the equilibrium between an iminium structure intermediate and the oxazolidine can be shifted in the presence of Lewis acids and, if it is an alkylating agent, such as Grignard reagents, carbon C-2 is alkylated[1c] to give *N*-alkylated aminoalcohols.[1b,7]

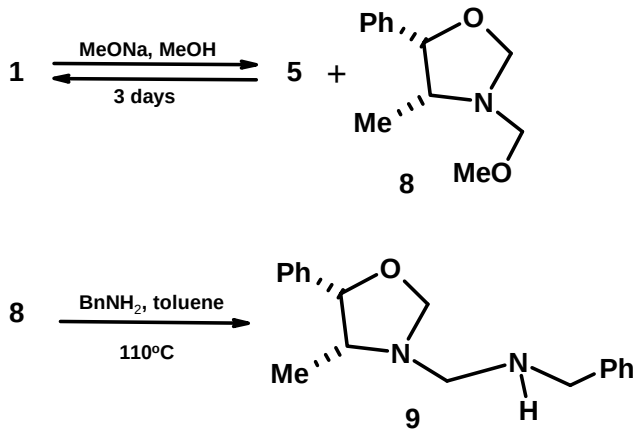


Scheme 3 C-2 Isomerization of 1,3-oxazolidines through a transient iminium

The different products found in the reaction of **1** with the RMgX and RLi compounds indicate a previous coordination these with one of the two basic sites of **1**, oxygen or nitrogen atoms, which depends on the nature of the organometallic compound and the steric effects in compound (**1**). Previous N→M coordination is deduced in all the reactions investigated based in the substitution products at methylene carbon N-C(6)-N, with exception of the *t*-BuLi, which reacts at methylene [O-C(2)-N] group.

c) with sodium methoxide

Sodium methoxide (3.5 equivalents) reacted in methanol with compound (**1**) at C-6 affording two oxazolidines (**5**) and (**8**) as observed in the reaction mixture after CH_2Cl_2 extractions, Scheme 4. When the mixture of **5** and **8** was set aside for 3 days compound (**1**) appears indicating that an equilibrium **1** ⇆ **5** + **8** is established. By evaporation in high vacuum, compound (**5**) can be separated from the reaction mixture. Compound (**8**) reacted with benzylamine at 110 °C to yield the new heterocycle benzyl-(4-methyl-5-phenyl-1,3-oxazolidin-3-yl)methylamine (**9**).

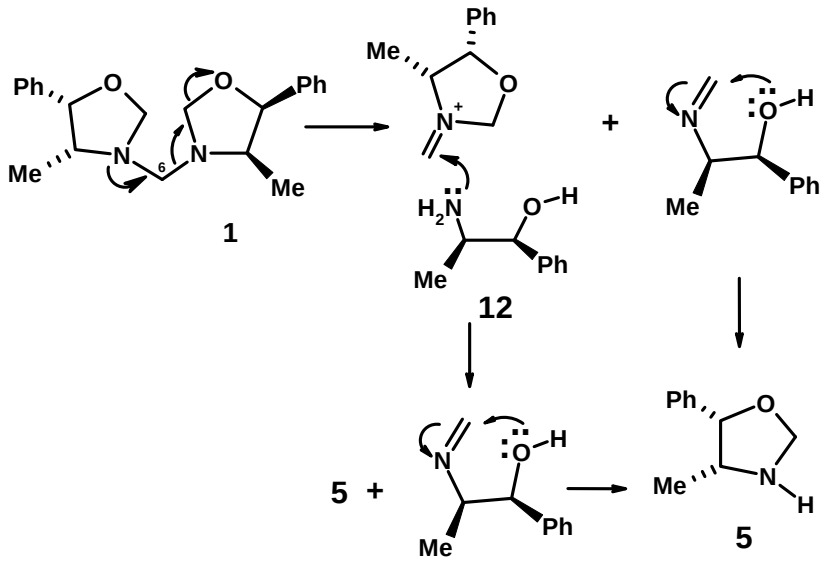


Scheme 4 Synthesis of *N*-substituted oxazolidines

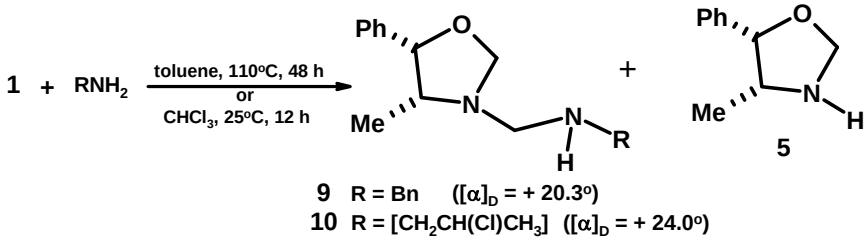
d) with primary amines

When compound (**1**) was heated at 110°C in deuterated toluene, the formation of traces of an imine were observed due to a signal at 164 ppm in the ^{13}C NMR spectrum. In order to trap this likely intermediate in the isomerization of oxazolidines, the *bis*(oxazoline)methane (**1**) was heated in toluene (110°C, 7 h) with one equivalent of *nor*ephedrine. The reaction afforded N-H oxazolidine (**5**) ($[\alpha]_D$ = + 7.0°) which was isolated in 90 % yield. This result is a good method to prepare compound (**5**), because N-H oxazolidines, which are very reactive compounds, cannot be directly prepared from ethanolamines and formaldehyde. Formation of three molecules of oxazolidine (**5**) starting from **1** and *nor*ephedrine are be explained by the mechanism depicted in Scheme 5. The structure of intermediate (**12**) can be deduced by comparison with reaction products described in Scheme 6.

The reaction of compound (**1**) with benzylamine and (±)-2-chloropropylamine at 110 ^{o}C gives **9** or **10** respectively, together with oxazolidine (**5**), Scheme 6. Compound (**10**) can be used as a synthon due its reactive N-H and C-Cl bonds. The same reaction with α-substituted primary amines, however, lead to a complex mixture of products.

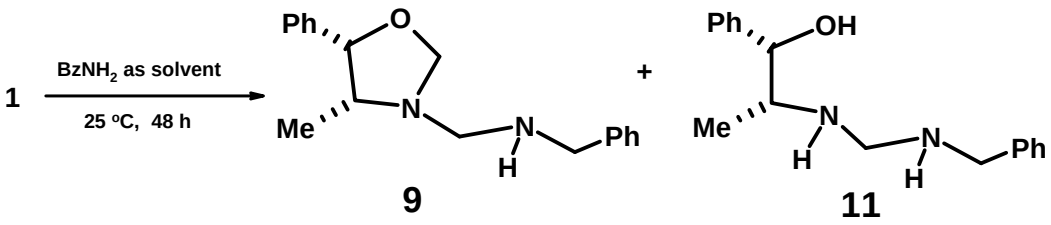


Scheme 5 Possible mechanism for oxazolidine (**5**) formation starting from **1** and *nor*ephedrine



Scheme 6 Reactions of amines with **1** produce compounds (**5**) and (**10**) by C-6 nucleophilic attack

In benzylamine as solvent, compound (**1**) produces a mixture of compounds (**9**) and (**11**). The explanation of this results may be that the reaction in a first step produces compounds (**9**) and (**5**). In a second step, **5** reacts with the excess of amine to give **11**, Scheme 7. This was confirmed by examining the reaction of compound (**5**) with one equivalent of benzylamine which affords exclusively compound (**11**) ($[\alpha]_D$ = + 16.3^{o}).



Scheme 7 Transformation of **1** using benzylamine as solvent

Conclusion

A preparation of a series of oxazolidines (**3**, **4**, **6**, **9** and **10**) bearing functionalized arms was achieved reacting *bis*(4-methyl-5-phenyl-1,3-oxazolidin-yl)methane (**1**) with nucleophiles. Compound (**10**) is attaked mainly at C-6 instead of the C-2 as observed for the other oxazolidines. A high yield synthesis of reactive 4-methyl-5-phenyl-1,3-oxazolidine (**5**) is reported which can be used as a starting material for the preparation of a series of optically active oxazolidines and ephedrines by substitution at the N-H group.

EXPERIMENTAL

All solvents were freshly distilled. The ^{1}H and ^{13}C NMR spectra were recorded with JEOL GXS-270 (^{1}H 270 MHz) or JEOL Eclipse (^{1}H 400 MHz). ^{1}H and ^{13}C δ are referenced to TMS. Melting points were measured on a Gallenkamp apparatus and are uncorrected. Elemental analyses were performed by Oneida Research Services, Whitesboro, New York. The MS spectra were obtained to 20 eV in a HP 5989 spectrometer. $[\alpha]_D$ values were obtained in a Perkin Elmer 241 polarimeter. Crystal data: compound (**4**) [$C_{15}H_{23}NOCl$], crystal system orthorhombic, space group $P2_12_12_1$, a 5.625(1) Å, b 12.167(1) Å, c 21.586(1) Å, V 1477.4(3) $Å^3$, Z 4, radiation MoKα, μ 0248 mm^{-1}, d calc 1.208 mg/m^3, 2θ range 5.04 to 51.94°, scan type ω, scan speed 16.1 to 60°/min in ω, reflection collected 3095, independent reflections 2885 (Rint = 0.0183), observed reflections 1636 ($F > 4\sigma(F)$), R1 = 0.0306, wR2 = 0.0936, data-to-parameter ratio 12.1:1 (6.9:1 [$F > 4\sigma(F)$], diffractometer used Enraf-Nonius. Computations for compound (**4**) were performed by using SHELXS-97 (Sheldrick 1997) and SHELXL-97 (Sheldrick 1997).[9] Atomic factors for neutral C, N, O and H were taken from [ref. 10]. Hydrogen atoms were found in the difference electron density maps. Crystallographic data (excluding structure factors) for the *N-neo*pentyl-*nor*ephedrine hydrochloride reported in this paper have been deposited with the Cambridge

Crystallographic Data as supplementary publications no. CCDC188510. Copies of the data can be obtained free of charge on application to 12 Union Road, Cambridge CB2 1EZ, UK [Fax: int. Code + 44(1223)336-033; E-mail: deposit@ccdc.cam.ac.uk).

***Bis((4R,5S)-4*-methy-5-phenyl-1,3-oxazolidin-3-yl)methane** (**1**).[6a,b] (+)-(1S,2R)-*Nor*-ephedrine (1 g, 6.6 mmol) was dissolved in methanol (30 mL) and cooled to 0 ^{o}C and a solution of aqueous formaldehyde (37 %, 1.43 mL, 16.5 mmol, at 0 ^{o}C) was added dropwise. The mixture was stirred for 24 h. Then, H_2O (15 mL) was added and the mixture extracted with $CHCl_3$ (4 x 30 mL). The *bis*-(oxazolidine)methane (**1**) was crystallized from methanol/water (80/20) (1.1 g, 98 %). mp 86-88 ^{o}C. $[\alpha]_D$ = + 51.3^{o} ($CHCl_3$, c = 0.1). ^{1}H NMR ($CDCl_3$): δ = 0.69 (d, ^{2}J = 6.0, 6H, CH_3), 3.48 (qd, ^{2}J = 6.0 and 6.6, 2H, H-4), 4.50 (dd, ^{2}J = 4.6, 2H, H-6), 4.90 (dd, ^{2}J = 5.2, 2H, H-2), 7.34 (m, 10H, Ar).^{13}C NMR ($CDCl_3$): δ = 15.35 (C-7), 60.10 (C-4), 72.56 (C-6), 80.10 (C-5), 85.12 (C-2), 126.40 (C_m), 127.16 (C_p), 128.06 (C_o), 139.61 (C_i). ^{15}N NMR ($CDCl_3$): δ = - 306.8. Anal. Calcd for $C_{21}H_{26}N_2O_2$: C, 74.53; H, 7.74; N, 8.28. Found: C, 74.48; H, 7.70; N, 7.98.

General procedure for Grignard reactions. To a rt solution of **1** (1.0 g, 3.0 mmol) in THF (100 mL), the Grignard reagent RMgCl (3.0 mmol, 1.8 M, R= *t*-Bu or Me) was added and the mixture refluxed for 1 h. Then, the reaction was quenched with 4.0 mL of H_2O and the solvent evaporated. To the pale yellow oil obtained brine (20 mL) was added and the mixture was extracted with $CHCl_3$ (20 mL). The organic phase was dried with Na_2SO_4 and the solvent evaporated. The residue was purified in a chromatographic silica gel column (hexane/$CHCl_3$, ratio 70:30) to give a colorless liquid (90%).

3-Ethyl-4-methyl-5-phenyl-1,3-oxazolidine (**3**). $[\alpha]_D$ = + 52.2^{o} ($CHCl_3$, 0.08). ^{1}H NMR ($CDCl_3$, 270 MHz): δ = 7.2-7.3 (m, 5H, Ar), 5.01 (d, ^{3}J = 6.93, 1H, H-5), 4.81 (d, ^{2}J = 3.46, 1H, H-2A), 4.11 (d, ^{2}J = 3.46, 1H, H-2B), 3.10 (dq, ^{3}J = 6.93 and 6.68, 1H, H-4), 2.75 (dq, ^{3}J = 7.17 and ^{2}J = 7.42, 1H, H-7A), 2.41 (dq, ^{3}J = 7.17 and ^{2}J = 7.42, 1H, H-7B), 1.13 (t, ^{3}J = 7.17, 3H, H-8), 0.59 (d, ^{3}J = 6.68, 3H, H-6). ^{13}C NMR ($CDCl_3$, 67.94 MHz): δ = 140.6 (C*i*), 128.1 (C*m*), 127.9 (C*p*), 126.8 (2C*o*), 86.1 (C-2), 81.1 (C-5), 61.9 (C-4), 46.5 (C-7), 15.1 (C-6), 13.8 (C-8). Anal. Calcd for $C_{12}H_{17}NO{\cdot}_{1/6}H_2O$: C, 74.19; H, 8.99; N, 7.21. Found: C, 73.70; H, 8.94; N, 6.99. This compound can also be obtained from the reaction of **1** with MeLi (0 °C for 4 h).

***Reactions with Alkyllithium Reagents.* 2-[(Neopentyl)-(4-methyl-5-phenyl-1,3-oxazolidin-3-ylmethyl)amino]-1-phenylpropan-1-ol** (**6**). To a solution of 1 (1 g, 2.9 mmol) in THF (10 mL) at 0 °C, tert-butyllitium in hexane 1.4 M (4.2 mL, 5.9 mmol) was slowly added. After stirring 1 h at 0 ^{o}C and 4 h at rt the reaction was quenched with 0.5 mL of H_2O and all volatile material evaporated. The residue was dissolved in $CHCl_3$ (10 mL) and the solution washed with brine (10 mL). The organic phase was dried over Na_2SO_4 and subsequently all volatile material evaporated. The oil obtained was purified on a chromatographic silica gel column using a mixture of hexane and $CHCl_3$ [45/55] as eluent. A yellow oil

was obtained (89 %, 1.0 g). $[\alpha]_D$ = + 16.2° ($CHCl_3$, c = 0.1). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.5-7.1 (m, 10H, Ar), 4.92 (d, ^{2}J = 6.5, 1H, H-5), 4.88 (d, ^{2}J = 6.5, 1H, H-9), 4.86 (d, ^{2}J = 6.7, 1H, H-6A), 4.46 (d, ^{2}J = 6.7, 1H, H-6B), 4.85 (d, ^{2}J = 4.0, 1H, H-2A), 4.24 (d, ^{2}J = 4.0, 1H, H-2B), 3.49 (dq, ^{3}J = 6.5 and 6.6, 1H, H-4), 3.15 (dq, ^{3}J = 6.5 and 6.7, 1H, H-8), 2.42 (d, ^{2}J = 13.6, 1H, H-10A), 2.31 (d, ^{2}J = 13.6, 1H, H-10B), 0,89 (s, 9H, 3CH_3), 0.73 (d, ^{3}J = 6.7, 3H, H-13), 0.63 (d, ^{3}J = 6.6, 3H, H-14). ^{13}C NMR ($CDCl_3$, 100.5 MHz): δ = 140.5 (Ci), 140.4 (Ci), 133.1 (1C), 128.8 (1C), 128.3 (2C), 128.2 (2C), 127.5 (1C), 127.2 (1C), 126.8 (2C), 126.5 (2C), 89.0 (C-2), 81.9 (C-6), 79.8 (C-9), 67.7 (C-13), 64.9 (C-4), 57.6 (C-8), 32.4 (C-10), 27.5 (3CH_3), 14.9 (C-13), 14.8 (C-14). Anal. Calcd for $C_{25}H_{36}N_2O_2$: C, 75.72; H, 9.15; N, 7.06. Found: C, 75.98, H, 8.94; N, 7.06.

***N-Neo*pentyl*nor*ephedrine** (**7**). To a solution of **1** (1.0 g, 2.9 mmol) in THF (10 mL) at 0 °C, *tert*-butyllithium in hexane 1.35 M (4.2 mL, 5.8 mmol) was slowly added. After 4 h of stirring, the reaction was quenched with 4.0 mL of H_2O and solvent evaporated. The residue was dissolved in $CHCl_3$ (20 mL) and washed with brine (20 mL). The organic phase was separated, dried over Na_2SO_4 and and the solvent subsequently evaporated. A yellow oil was obtained which was purified on a chromatographic silica gel column using a mixture of hexane and $CHCl_3$ [45/55] as eluent. Compound (**7**) was obtained as a yellow liquid (95%, 0.6 g). $[\alpha]_D$ = + 24.8° ($CHCl_3$, c = 0.07).^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.6-7.1 (m, 5H, Ar), 4.78 (d, ^{3}J = 4.0, 1H, H-1), 2.88 (qd, ^{2}J = 4.0, ^{3}J = 6.6, 1H, H-2), 2.54 (d, ^{2}J = 11.3, 1H, H-4A), 2.39 (d, ^{2}J = 11.3, 1H, H-4B), 0.93 (s, 9H, 3H-6, 3H-7, 3H-7), 0.80 (d, ^{3}J = 6.6, 3H, 3H-8). ^{13}C NMR ($CDCl_3$, 100.5 MHz): δ = 141.4 (C*i*), 128.0 (C*m*), 126.9 (C*p*), 126.0 (C*o*), 72.4 (C-1), 59.3 (C-5), 59.1 (C-2), 31.3 (C-5), 27.6 (3C-7), 14.5 (C-8). IR ($CHCl_3$, ν cm^{-1}): 4228, 3684, 3048, 3006, 2902,1520, 1246, 1188. Anal. Calcd. for $C_{14}H_{21}NO$: C, 75.97; H, 10.47; N, 6.32. Found: C, 75.88; H, 10.61; N, 5.96.

3-*Neo*pentyl-4-methyl-5-phenyl-1,3-oxazolidine (**4**). $[\alpha]_D$ = + 68.5° ($CHCl_3$, 0.04). ^{1}H NMR ($CDCl_3$, 270 MHz): δ = 7.2-7.3 (5H, Ar), 4.92 (d, J = 5.85, 1H, H-5), 4.83 (d, ^{2}J = 4.03, 1H, H-2A), 4.22 (d, ^{2}J = 4.03, 1H, H-2B), 3.19 (dq, ^{3}J = 5.85 and 6.59, 1H, H-4), 2.47 (d, ^{2}J = 13.5, 1H, H-6A), 2.34 (d, ^{2}J = 13.5, 1H, H-6B), 0.90 (s, 9H, H-8), 0.61 (d, ^{3}J = 6.59, 3H, H-9). ^{13}C NMR ($CDCl_3$, 67.94 MHz): δ = 140.4 (C*i*), 127.6 (2C*m*), 126.7 (C*p*), 126.4 (2C*o*), 88.7 (C-2), 79.4 (C-5), 67.9 (C-7), 65.0 (C-4), 32.4 (C-6), 27.3 (3C-8), 14.9 (C-9). Anal. Calcd for $C_{15}H_{23}NO \cdot 1/9H_2O$: C, 76.55; H, 9.95; N, 5.95. Found: C, 76.71; H, 9.76; N, 6.0.

Reaction of 1 with sodium methoxide. **3-Methoxymethyl-4-methyl-5-phenyl-1,3-oxazolidine** (**8**) . To a solution of **1** (0.50 g, 1.5 mmol) in MeOH (50 mL) metallic sodium (0.10 g, 4.3 mmol) was added. Initially the mixture was stirred at rt until the metal was dissolved, subsequently it was heated to reflux for 3 h. The solvent was evaporated and the white solid obtained dissolved in brine (50 mL) and extracted with $CHCl_3$. The organic solution was dried over Na_2SO_4. Compound (**8**) was obtained as a mixture with **5** in a [1:1] ratio (0.49 g, 92%). These compounds were not separated but directly identified by NMR

experiments. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.4-7.2 (m, 5H, Ph), 5.02 (d, ^{3}J = 6.42, 1H, H-5), 4.87 (d, ^{2}J = 4.08, 1H, H-2A), 4.59 (d, ^{2}J = 4.08, 1H, H-2B), 4.23 (s, 2H, H-6), 3.58 (dq, ^{3}J = 6.42 and 7.87, 1H, H-4), 3.31 (s, 3H, H-7), 0.65 (d, ^{3}J = 7.87, 3H, H-8). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 139.7 (Ci), 128.0 (2Cm), 127.4 (Cp), 126.6 (2Co), 85.4 (C-2), 81.7 (C-6), 80.5 (C-5), 58.1 (C-4), 54.3 (C-6), 14.7 (C-8).

General procedure for reactions of compound (1) with amines. 4-Methyl-5-phenyl-1,3-oxazolidine (5). To a solution of **1** (0.50 g, 1.46 mmol) in toluene (20 mL), norephedrine (0.22 g, 1.46 mmol) was added. The mixture was stirred and heated to reflux during 7 h. Thereafter, solvent was evaporated at reduced pressure at rt. Compound (**6**) was distilled at low pressure (70 ^{o}C, 0.25 mmHg) and was obtained as a yellow oil (90 %, 0.20 g). MS m/z 164 (3), 134 (2), 107 (7), 91 (6), 57 (100), 42 (4), 29 (7); $[\alpha]_D$ = + 7.0^{o} ($CHCl_3$, c = 0.1). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.2-7.1 (m, 5H, Ar), 4.83 (d, ^{2}J = 9.79, 1H, H-2A), 4.80 (d, ^{2}J = 9.79, 1H, H-2B), 4.40 (d, ^{3}J = 5.85, 1H, H-5), 3.38 (dq, ^{3}J = 5.85 and 6.75, 1H, H-4), 2.28 (s br, NH), 0.67 (d, ^{3}J = 6.75, 3H, H-5). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 140.3 (Ci), 128.1 (Cm), 127.4 (Cp), 126.3 (2Co), 82.0 (C-2), 79.8 (C-5), 57.9 (C-4), 15.4 (C-6). Anal. Calcd for $C_{10}H_{13}NO$: C, 73.59; H, 8.03; N, 8.58. Found: C, 73.38; H, 8.18; N, 8.46.

***N*-Benzyl-(4-methyl-5-phenyl-1,3-oxazolidin-3-yl)methylamine** (**9**). Compound (**9**) was obtained from an equimolecular mixture of **1** (0.54 g, 1.6 mmol) and benzylamine (0.18 mL, 1.6 mmol) heated in toluene (50 mL) at 110 ^{o}C for 48 h. The solvent was evaporated leaving behind an oil which was purified on a chromatographic silica gel column (hexane/$CHCl_3$, ratio 60:40) yellow oil (97 %, 0.74 g). $[\alpha]_D$ = + 20.3^{o} ($CHCl_3$, c = 0.1). MS *m*/*z* 194 ($[M - Bn]^+$ 82), 91(100), 65(5), 28(1). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.2-7.1 (m, 10H, Ar), 4.71 (s br, 1H, H-2A), 4.73 (s br, 1H, H-2B), 4.29 (d, ^{3}J = 6.0, 1H, H-5), 3.52 (s, 2H, H-6), 3.31 (dq, ^{3}J = 6.0 and 7.20, 1H, H-4), 3.21 (s, 2H, H-8), 3.20 (s br, NH), 0.60 (d, ^{3}J = 7.20, 3H, H-9). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 139.5 (C*i*), 138.0 (C*i*, Bn), 128.7 (2C*m*, Bn), 128.0 (2C*m*), 127.9 (C*p*, Bn), 127.8 (2C*o*, Bn), 127.2 (C*p*), 126.0 (2C*o*), 81.4 (C-2), 79.6 (C-5), 73.4 (C-6), 57.4 (C-8), 56.7 (C-4), 15.0 (C-9). Anal. Calcd for $C_{18}H_{22}N_2O$: C, 76.59; H, 7.80; N, 9.9. Found: C, 76.53; H, 7.70; N, 9.7.

2-Chloropropyl-(4-methyl-5-phenyl-1,3-oxazolidin-3-ylmethyl)amine (**10**). Compound (**10**) was obtained from a mixture of **1** (0.5 g, 1.47 mmol), 2-chloropropylamine hydrochloride (0.28 mL, 2.21 mmol) and Na_2CO_3 (0.47 g, 4.34 mmol) in $CHCl_3$ (50 mL). The reaction mixture was stirred 19 h at 25 ^{o}C and the solvent evaporated. Compound (**10**) was obtained as a yellow oil (0.37 g, 94 %). $[\alpha]_D$ = + 24.0^{o} ($CHCl_3$, c = 0.1). ^{1}H NMR ($CDCl_3$, 270 MHz): δ = 7.3-7.1 (m, 5H, Ar), 4.80 (d, ^{3}J = 6.2, 1H, H-5), 4.86 (d, ^{2}J = 7.5, 1H, H-2A), 4.46 (d, ^{2}J = 7.5, 1H, H-2B), 3.64 (qt, ^{3}J = 6.5 and 6.9, 1H, H-9), 3.45 (s, 2H, H-6), 3.48 (dq, ^{3}J = 6.2 and 6.7, 1H, H-4), 2.72 (dd, ^{3}J = 6.9 and ^{2}J= 6.8, 1H, H-8A), 2.70 (dd, ^{3}J = 6.9 and ^{2}J = 6.8, 1H, H-8B), 1.44 (d, ^{3}J = 6.7, 3H, H-10), 0.68 (d, ^{3}J = 6.7, 3H, H-11). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 140.2 (C*i*), 128.1 (C*o*), 127.3 (C*p*), 126.3 (C*m*), 81.9 (C-2), 79.8 (C-5), 74.7 (C-6), 60.5

(C-8), 57.8 (C-4), 56.1 (C-9), 23.2 (C-10), 15.4 (C-11). Anal. Calcd for $C_{14}H_{21}N_2OCl$: C, 62.56; H, 7.88; N, 10.42. Found: C, 62.78; H, 7.94; N, 10.46.

2-(Benzylaminomethyl)amino-1-phenylpropan-1-ol (**11**). To a solution of **5** (0.40 g, 2.44 mmol) in toluene (20 mL), benzylamine (0.27 mL, 2.44 mmol) was added. The mixture was stirred at rt during 7 h. Then the solvent was evaporated in vacuum at rt. Compound (**11**) was obtained pure as a yellow oil (90 %, 0.59 g). $[\alpha]_D$ = + 16.3^o ($CHCl_3$, c = 0.09). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.1-7.0 (m, 10H, Ph), 4.56 (d, ^{2}J = 4.4, 1H, H-1), 3.84 (s, 2H, 2H-5), 3.74 (s, 2H, 2H-7), 3.19 (dq, ^{3}J = 6.2 and 4.4, 1H, H-2), 1.11 (d, ^{3}J = 6.2, 3H, H-3). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 142.4 (C*i*), 138.7 (C*i*, Bn), 128.6 (2C*m*, Bn), 128.4 (C*m*), 127.8 (2C*o*, Bn), 127.4 (C*p*), 127.2 (C*p*, Bn), 127.0 (2C*o*), 77.5 (C-1), 73.9 (C-45), 57.2 (C-6), 52.5 (C-2), 18.3 (C-13). Anal. Calcd for $C_{17}H_{24}N_2O$: C, 75.50; H, 8.14; N, 10.37. Found: C, 75.84; H, 8.09; N, 9.94.

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