A Highly Efficient Chemoselective Cyclocondensation of *threo*-(1*S*,2*S*)-2-Amino-1-(4-nitrophenyl)-1,3-propanediol with Ketones and Isomerization of the Condensates

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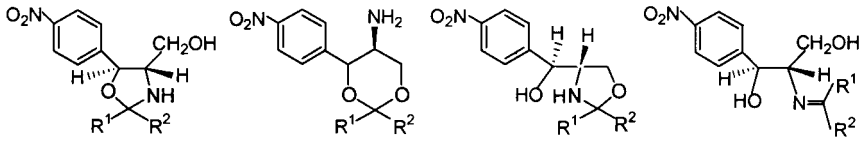
A convenient procedure for highly efficient chemoselective cyclization of *threo*-(1*S*,2*S*)-2-amino-1-(4-nitrophenyl)propane-1,3-diol with some ketones was described. The structures of the condensates were elucidated on the basis of the IR, ^{1}H- and ^{13}C-NMR, and mass spectra. Ring-ring tautomerism in 2-aminopropane-1,3-diol chemistry is reported for the first time.

1. Introduction. – *threo*-(1*S*,2*S*)-2-Amino-1-(4-nitrophenyl)propane-1,3-diol (*threo*-(1*S*,2*S*)-ANP), a 'chiral waste' in the production of chloromycetin, is one of the least expensive artificial chiral materials available. However, reports on the application of it and its derivatives to asymmetric reactions are quite limited up to now. When it reacts with a carbonyl compound, *e.g.*, acyl halide, its polyfunctional group structure can lead to formation of mixtures of several derivatives. While this polyfunctional reactivity can be viewed as an asset, the development of highly chemoselective preparations of derivatives of *threo*-(1*S*,2*S*-ANP) could be the key to improving application conditions. In the course of investigating the chemistry of *threo*-(1*S*,2*S*)-ANP, we once attempted to prepare the corresponding ketone condensates according to [1a]. We found that it was difficult to obtain a crystalline product, and the yield was low. To establish a convenient method to prepare the ketone condensates, we examined the reactions of *threo*-(1*S*,2*S*)-ANP with aliphatic, alicyclic, alkyl aryl, and diaryl ketones under different conditions, and elaborated a high-yield synthetic method for the condensates of *threo*-(1*S*,2*S*)-ANP with some aliphatic and alicyclic ketones [2]. In this paper, we wish to report a new procedure for highly efficient chemoselective cyclocondensation of *threo*-(1*S*,2*S*)-ANP with some aliphatic ketones, and ring-ring tautomerism in the chemistry of *threo*-(1*S*,2*S*)-ANP is reported for the first time.

2. Results and Discussion. – 2.1. *Preparation of Crystalline Ketone Condensates.* Condensates of racemic or (1*R*,2*R*)-ANP with ketones were previously prepared by azeotropic distillation of the components with benzene [3] and by catalysis with TsOH [4] or in the presence of P_2O_5 [5]. The condensation reactions of *threo*-(1*S*,2*S*)-ANP with the ketones investigated in [1a] were catalyzed by acetic acid, under which conditions usually a viscous residue was obtained after evaporating the excess ketone and solvent. From the residues, it was quite difficult to obtain a crystalline product in high yield. However, we discovered that crystalline condensates could be obtained in very high yields by azeotropic distillation when the reaction is performed in toluene or

xylene in the absence of catalyst. In certain cases, a good crystalline product could be directly isolated after cooling the reaction mixture to ambient temperature. For example, a 1:3 mixture of *threo*-(1*S*,2*S*)-ANP with acetone was allowed to dehydrate azeotropically in toluene under slightly higher than atmospheric pressure for 3 h to give a homogeneous solution. When the solution was cooled to room temperature, a colorless, transparent crystal was formed and isolated in more than 80% yield. Concentrating the mother liquor provided an additional crop, to increase the overall yield of the condensate to up to 90%. Similarly, cooling the solution resulting from the condensation of *threo*-(1*S*,2*S*)-ANP with cyclohexanone in a 1:1 molar ratio in xylene gave almost quantitatively the condensate as a xylene solvate of yellowish needles. However, for the condensations of *threo*-(1*S*,2*S*)-ANP with butanone, pentan-3-one, or cyclohexanone in toluene, no crystalline product could be isolated directly upon cooling the corresponding reaction solution. In these cases, the solvent was evaporated and the residue was extracted with Et_2O. After cooling or concentrating the extract or adding a seed crystal, the desired crystalline product was obtained. By this procedure, the products could be efficiently separated from the unchanged 2-amino 1,3-diol.

2.2. *Structures of the Ketone Condensates.* It is well known that *threo*-(1*R*,2*R*)-ANP, *threo*-(1*R*,2*R*)-ANP, or *threo*-(±)-ANP react with a given ketone under different experimental conditions to give condensates with different structures [1][3–5]. For example, *threo*-(±)-ANP was allowed to reflux with excess cyclohexanone in benzene with catalysis by TsOH for 24 h to furnish a mixture of a 2,2,4-trisubstituted 1,3-oxazolidine and a 2,2,4,5-tetrasubstituted 1,3-dioxane derivative, namely, (±)-2-[hydroxy(4-nitrophenyl)methyl]-1-oxa-2-azaspiro[5.4]decane and (±)-3-amino-2-(4-nitrophenyl)-1,5-dioxaspiro[5.5]undecane; however, the reaction of same reactants carried out in THF with P_2O_5 at 0–10° gave only a 1,3-dioxane derivative [5]. For a condensation of a trifunctional 2-aminopropane-1,3-diol and a ketone in a 1:1 molar ratio, it was expected that the reaction would form up to four structural isomers, namely, a 2,2,4,5-tetrasubstituted oxazolidine **1**, a 2,2,4,5-tetrasubstituted 1,3-dioxane **2**, a 2,2,4-trisubstituted oxazolidine **3** and a *Schiff* base **4** (*Fig. 1*). To solve the structures of the condensates formed as described in *Part 2.1.* by an azeotropic dehydration of *threo*-(1*S*,2*S*)-ANP and cyclohexanone (**a**), acetone (**b**), butanone (**c**) or pentan-3-one (**d**), we examined their IR, ^{1}H- and ^{13}C-NMR, and mass spectra.



1 **2** **3** **4**

a R^1–R^2 = –$(CH_2)_5$–
b R^1 = R^2 = Me
c R^1 = Me, R^2 = Et
d R^1 = R^2 = Et

Fig. 1. *Four possible structural isomers for a 1:1 condensate of* threo-*(1S,2S)-ANP with ketones cyclohexanone, acetone, butanone, and pentan-3-one*

IR Spectra of all the investigated condensates closely resemble each other. No band due to an asymmetric stretching vibration of a C=N bond was observed in the 1700–1600 cm^{-1} region. It is, thus, clear that the condensates are not *Schiff* bases of type **4**. On the other hand, there were two strong stretching-vibration bands (C–O or asymmetric C–O–C) in the 1060–1000 cm^{-1} region, and a deformation vibration for the NH_2 group at *ca.* 1570 cm^{-1} (a sharp absorption with medium intensity for *threo*-(1*S*,2*S*)-ANP) disappeared, indicating that the NH_2 and one OH group of *threo*-(1*S*,2*S*)-ANP participated in the condensation reaction. In the EI-MS of these condensates, the fragment-ion peaks 261 (6), 221 (15), 235 (11), and 249 (4), which correspond to the ions $[M-CH_2OH]^+$ for the oxazolidines **1a** ($R^1-R^2=-(Ch_2)_5-$), **1b** ($R^1=R^2=$ Me), **1c** ($R^1=$ Me, $R^2=$ Et), and **1d** ($R^1=R^2=$ Et), respectively, were observed. In the ^{1}H-NMR spectra ((D_6)DMSO), there was a *triplet* at 4.95 ± 0.05 ppm, which corresponds to the primary OH coupled to the CH_2; after adding D_2O, the signal disappeared. No resonance signals for a secondary OH group or an NH_2 group could be observed. The ^{13}C-NMR spectrum of the condensate of *threo*-(1*S*,2*S*)-ANP and cyclohexanone also exhibited only one isomer, one that corresponds to the structure **1a**. Based on these data, it can be established that the condensates are pure type-**1** compounds, *i.e.*, (4*S*,5*S*)-2,2-dialkyl-4-(hydroxymethyl)-5-(4-nitrophenyl)-1,3-oxazolidines. Therefore, the condensation reactions are highly chemoselective under these experimental conditions.

2.3. *Isomerization of the Ketone Condensates.* In the course of investigating the structures of the ketone condensates, we noted that the ^{1}H-NMR bands changed as a function of solvent. The spectra of the condensates in $CDCl_3$ are more complicated than in (D_6)DMSO, and the bands could be divided into two groups on the basis of their intensities, suggesting that isomerization occurred in $CDCl_3$. To estimate the molar ratio of the isomers, the H-atoms located in the 3.10–4.85 ppm region were chosen as 'reference protons'. This is because, in this range, the two resonance groups could be easily differentiated, and there was no resonance signal corresponding to protons bound to the O- or N-atom (see *Fig. 2*). The molar ratio of the isomers has been estimated to be *ca.* 4.0:1 (for the cyclohexanone condensate), 4.3:1 (for the acetone condensate), 6.5:1) (for the butanone condensate), and 4.2:1 (for the pentan-3-one condensate). As concerns the primary isomer, their chemical shifts are similar to that of type **1** oxazolidines. The resonance signals for H–C(2), C*H*$_2$OH, and H–C(3) appeared at 4.79 ± 0.02, 3.88 ± 0.02 and 3.69 ± 0.03 ppm, and 3.14 ± 0.03 ppm, respectively, for **1a**. As regards the secondary isomer, the chemical shifts for H–C(3), H–C(2), and C*H*OH of **3a** were at 3.47 ± 0.02, 3.78 ± 0.02, and 4.49 ± 0.04 ppm, respectively. When their ^{1}H-NMR spectra were compared with those of (+)- or (±)-*cis*-1,3-dioxanes and the *Schiff* bases [6] derived from ANP, a striking contrast was observed[1]). On the other hand, an absorption of the NH_2 group and the C=N bond

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[1]) According to [1b] and [5], the ^{1}H-NMR spectrum of (+)- or (±)-*cis*-5-amino-2,2-dimethyl-4-(4-nitrophenyl)-1,3-dioxane (and the corresponding spectrum of (±)-*cis*-3-amino-2-(4-nitrophenyl)-1,5-dioxaspiro-[5.5]undecane) showed that the signals for H_{ax}–C(4) at 5.13 ± 0.02 ppm and for H_{eq}–C(5) at 2.81 ± 0.01 ppm and the coupling constants to H_{ax}–C(6) and H_{eq}–C(6) were $2.0+0.22$ Hz and 1.2 ± 0.3 Hz, respectively. Two *q*s were found at 4.28 ± 0.01 and 3.80 ± 0.05 ppm ($J(6_{ax},6_{eq})=11.5\pm0.1$ Hz).

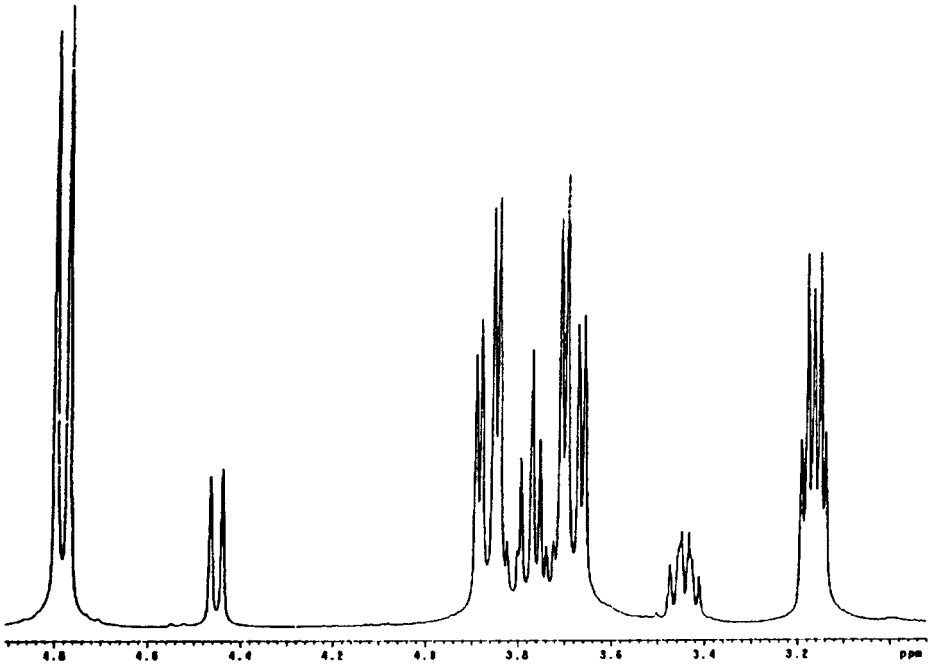

Fig. 2. *[1]H-NMR Chemical shifts of the condensate of* threo-*(1S,2S)-ANP with cyclohexanone in $CDCl_3$ in the range 4.85–3.10 ppm* (300 MHz, δ relative to Me_4Si)

were not observed in the IR spectra in $CDCl_3$[2]). The data indicate that the two isomers are not compounds of type **2** or **4**, and they can only be oxazolidines of types **1** and **3**. Because the coupling constants of the primary isomers and the secondary isomers are similar to those of oxazolidines of types **1** and **3**, it can be established that the primary isomers are the oxazolidines **1a**–**d**, and the secondary isomers are the oxazolidines **3a**–**d**. The chemical shifts of the condensates in the range of 4.85–3.10 ppm (in $CDCl_3$) in *Table 1*.

The $CDCl_3$-solution of the condensate of *threo*-(1*S*,2*S*)-ANP and cyclohexanone, after recording the ^{1}H-NMR spectrum, was evaporated under reduced pressure. To the residue was added (D_6)DMSO, and the ^{1}H-NMR spectrum was recorded again; it was identical to that of **1a**. It is obvious that two isomers in $CDCl_3$ are tautomers. Attempts to separate the two types of oxazolidines by fractional crystallization or column chromatography at ambient temperature did not succeed. It appears that interconversion between the two types of oxazolidines is quite rapid under these conditions.

2.4. *Theoretical Examination of the Isomerism. Darabantu et al.* previously found a chain-ring isomerism of some *Schiff* bases of *threo*-(1*S*,2*S*)-ANP in DMSO [6]; we observed a ring-ring tautomerism of the oxazolidines derived from *threo*-(1*S*,2*S*)-ANP in $CDCl_3$. To understand the tautomerisms, some theoretical calculations have been

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[2]) For example, the IR spectrum in $CDCl_3$ solution of the condensate of *threo*-(1*S*,2*S*)-ANP and cyclohexanone: 3348*m*, 3290*m*, 2935*s*, 2859*m*, 1602*m*, 1520v*s*, 1449*m*, 1347v*s*, 1279*mw*, 1156*mw*, 1110*m*, 1055*ms*, 927*m*, 847*m*, 752*mw*, 692*mw*.

Table 1. *^{1}H-NMR Chemical Shifts for* **1a–d** *and* **3a–d** (300 MHz, in $CDCl_3$, δ range 4.85–3.10 ppm relative to Me_4Si, J in Hz)

Condensate[a])	H–C(2) or H–C(5)[b])	H–C(3) or H–C(4)[c])	CH_2OH or $CHOH$[d])
1a	4.79 (*d*, *J*(5,4) = 8.4)	3.17 (*m*)	3.87, 3.69 (2*dd*, *J*(H_a,H_b) = 11.4, *J*(3,H_a) = *J*(3,H_b) = 3.6)
3a	3.77 (*m*)	3.45 (*m*)	4.45 (*d*, *J*(2,11) = 7.8)
1b	4.81 (*d*, *J*(5,4) = 8.1)	3.11 (*m*)	3.90 (*dd*, *J*(H_a,H_b) = 11.4, *J*(4,H_a) = 3.3, H_a); 3.72 (*dd*, *J*(H_a,H_b) = 11.4, *J*(4,H_b) = 3.6, H_b)
3b	3.81 (*m*)	3.49 (*m*)	4.53 (*d*, *J*(3,6) = 7.2)
1c	4.78 (*d*, *J*(5,4) = 8.1, (2*R*,4*S*,5*S*)); 4.73 (*d*, *J*(5,4) = 8.1, (2*S*4*S*,5*S*))	3.15 (*m*, both epimers)	3.88 (*m*, (2*R*,4*S*,5*S*)); 3.68 (*m*, (2*S*,4*S*,5*S*))
3c	3.76 (*m*, both epimers)	3.46 (*m*, both epimers)	4.50 (*d*, *J*(3,6) = 7.2, (3*R*,5*R*,6*S*)); 4.45 (*d*, *J*(3,6) = 7.2, (3*R*,5*S*,6*S*))
1d	4.77 (*d*, *J*(5,4) = 8.4)	3.11 (*m*)	3.89 (*dd*, H_a); 3.68 (*dd*, H_b); (*J*(H_a,H_b) = 11.1, *J*(4, H_a) = *J*(4,4 H_b) = 3.0)
3d	3.78 (*m*)	3.47 (*m*)	4.46 (*d*, *J*(3,6) = 7.5)

[a]) From condensation of *threo*-(1*S*,2*S*)-ANP with cyclohexanone (**a**), acetone (**b**), butanone (**c**), and pentan-3-one (**d**), as shown in *Fig. 1*. [b]) H–C(2) of **1a** and **3a** corresponds to H–C(5) of **1b–d** and **3b–d**. [c]) H–C(3) of **1a** and **3a** corresponds to H–C(4) of **1b–d** and **3b–d**. [d]) Corresponds to C(11) (3-(hydroxymethyl) of **1a** or 3-[hydroxy(4-nitrophenyl)methyl] of **3a**) or C(6) (4-(hydroxymethyl) of **1b–d** or 4-[hydroxy(4-nitrophenyl)-methyl] of **3b–d**).

performed. We obtained the heats of formation (ΔH_f) and total energy E for the four isomers **1–4a** by the extended HMO, AM1, and MNDO methods. The results (*Table 2*) that the energies are very similar, meaning that occurrence of a ring-ring or chain-ring tautomerism is quite possible for a condensate of *threo*-(1*S*,2*S*)-ANP and a carbonyl compound.

Table 2. *Calculated Heats of Formation* (ΔH_f) *and Total Energies* (E) *of* **1–4a**

	ΔH_f [kcal mol^{-1}]	E [kcal mol^{-1}]		
Method	HMO	HMO	MNDO	AM1
1a	17.9020	– 48561.51	– 4010.4751	– 4050.2284
2a	18.3027	– 48572.56	– 4075.6321	– 4107.9438
3a	20.2222	– 48558.51	– 3919.5306	– 3968.0462
4a	17.7894	– 48561.96	– 3917.2304	– 3966.2470

3. Conclusions. – Condensations of *threo*-(1*S*,2*S*)-ANP with cyclohexanone, acetone, butanone, and pentan-3-one in toluene or xylene by azeotropic distillation in the absence of catalyst afforded almost quantitatively 2,2,4,5-tetrasubstituted oxazolidine derivatives of type **1** *via* a highly efficient chemoselective cyclocondensation. The 2,2,4,5-tetrasubstituted oxazolidines partially isomerize to the 2,2,4-trisubstituted oxazolidines of type **3** in $CDCl_3$ at ambient temperature. This is the first report of ring-ring tautomerism in 2-aminopropane-1,3-diol chemistry.

Experimental Part

General. Cyclohexanone, acetone, butanone, and pentan-3-one were purchased and used directly without special treatment. M.p.: *VEB Wagetechnik Rapio PHMK05*; uncorrected. $[\alpha]_D$: *WZZ-1S* (Shanghai, China) polarimeter. IR Spectra: *Testscan Shimadzu FTIR 8000* and *Nicolet 170 SX* FT-IR spectrophotometers; in KBr; ν in cm^{-1}. ^1H- and ^{13}C-NMR Spectra: *Varian Mercury VS-300* and *JEOL FX-90Q* spectrometers; δ in (ppm) relative to Me_4Si. EI-MS: *VG ZAB-HF-3F* spectrometer (70 eV); *m/z* (rel. %). Elemental analysis: *Perkin-Elmer 240 B* analyzer.

threo-(1*S*,2*S*)-2-ANP was supplied by the *Wuhan Pharmaceutical Factory* and was purified by recrystallization: prior to use: m.p. 163°; $[\alpha]_D = +31.2$ ($c = 1$, 6N HCl).

Preparation of 2,2,4,5-Tetrasubstituted Oxazolidines. Method A: threo-*(4*S*,5*S*)-4-(Hydroxymethyl)-2,2-dimethyl-5-(4-nitrophenyl)-1,3-oxazolidine* (**1b**). To a 250 ml round-bottom flask, *threo*-(1*S*,2*S*)-2-ANP (4.24 g, 20 mmol) and acetone (4 ml) in toluene (35 ml) were added, and then fitted successively with an oil-water separator, a reflux condenser, and an oil bubbler with a stopcock. Under Ar, the mixture was refluxed with stirring for 3 h to form a homogeneous yellow soln. The soln. was cooled to r.t. to give 5.0 g of a solvate of the condensate **1b** with toluene as colorless needles (m.p. 40–42° (dec.)). The product was desolvated by treatment with Et_2O, crystallized, and dried under reduced pressure to give 4.7 g **1b**. Yield 93%. M.p. 76–78° (dec.). $[\alpha]_D^{15} = +45.02$ ($c = 2$, EtOH). IR: (3404*m*, 3261*m*, 3209 (sh, NH, OH); 2980*m*, 2920*m*, 2880*m*, 2860*m* (C–H); 1603*m* (C=C–C); 1522v*s*, 1350v*s* (NO_2), 1047*s* (asym. C–O–C), 854*s* (Ar–H). ^1H-NMR ((D_6)DMSO, 90 MHz): 8.15 (*d*, *J* = 8.7, H–C(3′), H–C(5′)); 7.57 (*d*, *J* = 8.7, H–C(2′), H–C(6′)); 4.96 (*t*, *J* = 5.4, CH_2OH); 4.65 (*d*, *J*(5,4) = 8.1, H–C(5)); 3.59 (br. *s*, CH_2OH; after adding D_2O: *d*, *J* = 3.6); 3.32 (br. *s*, NH; disappeared after adding D_2O); 3.00 (br. *s*, H–C(4); after adding D_2O: *m*); 1.42 (*s*, Me); 1.38 (*s*, Me). ^1H-NMR ((D_6)-DMSO, 300 MHz): 8.18 (*d*, *J* = 9.0, H–C(3′), H–C(5′)); 7.61 (*d*, *J* = 8.7, H–C(2′), H–C(6′)); 4.85 (*t*, *J* = 5.4, CH_2OH); 4.67 (*d*, *J*(5,4) = 7.8, H–C(5)); 3.60 (*m*, CH_2OH); 3.21 (*s*, NH); 3.04 (*m*, H–C(4)); 1.42 (*s*, Me); 1.38 (*s*, Me). MS: 237 (14, $[M - Me]^+$), 221 (15, $[M - CH_2OH]^+$), 195 (11), 177 (5), 165 (15), 146 (8), 136 (7), 131 (9), 117 (26), 101 (100), 100 (95), 89 (11), 84 (32), 83 (45), 77 (13), 68 (18), 59 (18), 58 (37), 51 (5), 43 (34). Anal. calc. for $C_{12}H_{16}N_2O_4$ (252.27): C 57.13, H 6.39, N 11.11; found: C 57.02, H 6.26, N 11.00.

threo-*(2*S*,3*S*)-3-(Hydroxymethyl)-2-(4-nitrophenyl)-1-oxa-4-azaspiro[4.5]decane* (**1a**). Similar to the above procedure: Condensation of *threo*-(1*S*,2*S*)-2-ANP (8.48 g, 40 mmol) and cyclohexanone (4.2 ml, *ca.* 3.98 g, 40.5 mmol) in xylene (70 ml) gave 13.8 g of the xylene solvate of **1a** as yellowish needles. Yield 92.5%. M.p. 54–56° (dec.). IR: 3404*m*, 3276*m* (sh, NH, OH); 2996*s*, 2858*ms* (C–H); 1601*m* (C=C–C); 1520v*s*, 1348v*s* (NO_2); 1056*s* (asym. C–O–C); 848*s* (Ar–H). MS: 292 (M^+), 263 ($[M - C_2H_5]^+$), 249 ($[M - C_3H_7]^+$), 195 ($[M - C_6H_{11}N]^+$), 177 ($[M - C_6H_{13}NO]^+$), 141 ($[M - C_7H_5NO_3]^+$), 140 ($[M - C_7H_6NO_3]^+$), 123 ($[M - C_8H_{13}N]^+$), 109 ($[M - C_8H_9NO_4]^+$), 106 ($M^{+\cdot}$ (xylene)), 91 ($[M(\text{xylene}) - Me]^+$), 77 ($C_6H_5^+$), 55 ($C_4H_7^+$). Anal. calc. for $C_{15}H_{20}N_2O_4 \cdot 0.5\ C_6H_4(CH_3)_2$ (345.41): C 66.06, H 7.30, N 8.11; found: C 65.62, H 7.26, N 7.81.

The **1a**–xylene solvate was treated with Et_2O, crystallized, to give pure **1a** (data reported under *Method B*).

Method B: Under Ar, a mixture of *threo*-(1*S*,2*S*)-2-ANP (16.96 g, 80 mmol) and cyclohexanone (8.4 ml, *ca.* 7.95 g, 81.0 mmol) in toluene (70 ml) was refluxed azeotropically for 3 h in a 250 ml round-bottomed flask to offer a homogeneous yellow soln. The soln. was evaporated to dryness. The residue was extracted with hot Et_2O (30 ml), and the extract was cooled to r.t., from which 19.30 g of yellowish crystals of **1a** were isolated. The mother liquor was concentrated to yield a further 2.3 g of crystals. Overall yield 92.5%. M.p. 78–80° (dec.). $[\alpha]_D^{15} = +51.50$ ($c = 2$, EtOH). IR: 3429*s*, 3288*s*, 3248 (sh, NH, OH); 1601*m* (C=C–C); 1516v*s*, 1350v*s* (NO_2); 1057v*s* (asym. C–O–C); 843*s* (Ar–H). ^1H-NMR ((D_6)DMSO, 300 MHz): 8.19 (*d*, *J* = 8.7, H–C(3′), H–C(5′)); 7.59 (*d*, *J* = 9.0, H–C(2′), H–C(6′)); 5.00 (*t*, *J* = 4.8, CH_2OH); 4.62 (*d*, *J*(5,4) = 6.6 H–C(2)); 3.50 (*m*, CH_2OH); 2.92 (*m*, 2 H, H–C(3), NH); 1.80–1.20 (*m*, C_6H_{10}). ^{13}C-NMR ((D_6)DMSO, 300 MHz): 150.807; 147.503; 127.804; 123.974; 97.323; 79.386; 68.133; 59.999; 41.315; 41.040; 40.765; 40.483; 40.208; 39.934; 39.651; 38.133; 37.874; 25.781; 24.247. MS: 292 (14, $M^{+\cdot}$), 263 (8), 261 (6, $[M - CH_2OH]^+$), 250 (16), 249 (100), 236 (4), 219 (4), 205 (3), 195 (9), 177 (9), 165 (4), 141 (30), 140 (42), 124 (10), 123 (10), 117 (8), 110 (9), 81 (8), 55 (24), 41 (15). Anal. calc. for $C_{15}H_{20}N_2O_4$ (292.33): C 61.63, H 6.90, N 9.59; found: C 61.67, H 7.98, N 9.66.

threo-*(2*RS*,4*S*,5*S*)-2-Ethyl-4-(hydroxymethyl)-2-methyl-5-(4-nitrophenyl)-1,3-oxazolidine* (**1c**). As described for **1a** under *Method B*. Mixture of epimers: yield, 88%. M.p. 62–64° (dec.). $[\alpha]_D^{15} = +52.56$ ($c = 2$, EtOH). IR: 3400*s*, 3291*m*, 3205*m* (NH, OH); 1603*m* (C=C–C); 1525v*s*, 1351v*s* (NO_2); 1052*s* (asym. C–O–C); 852*s* (Ar–H). ^1H-NMR ((D_6)DMSO, 300 MHz): 8.18 (*d*, *J* = 8.7, H–C(3′), H–C(5′), both epimers); 7.61 (*d*, *J* = 8.4, H–C(2′), H–C(6′), both epimers); 4.87 (*t*, *J* = 5.4, CH_2OH, (2*R*,4*S*,5*S*)); 4.84 (*t*, *J* = 5.7, CH_2OH, (2*S*,4*S*,5*S*)); 4.68 (*d*, *J*(5.4) = 8.1, H–C(5), (2*R*,4*S*,5*S*)); 4.64 (*d*, *J*(5,4) = 8.1, H–C(5), (2*S*,4*S*,5*S*)); 3.61 (*m*, CH_2OH, (2*R*,4*S*,5*S*)); 3.58 (*m*, CH_2OH, (2*S*,4*S*,5*S*)); 3.01 (*m*, H–C(4), NH, (2*R*,4*S*,5*S*)); 2.96 (*m*, H–C(4), NH,

(2*S*,4*S*,5*S*)); 1.71 (*q*, *J* = 3.6, C*H*$_2$Me, (2*R*4*S*,5*S*)); 1.67 (*q*, *J* = 3.6, C*H*$_2$Me, (2*S*,4*S*,5*S*)); 1.34 (*s*, Me, both epimers); 0.95 (*t*, *J* = 7.5, CH$_2$*Me*, (2*R*,4*S*,5*S*)); 0.94 (*t*, *J* = 7.5, CH$_2$*Me*, (2*S*,4*S*,5*S*)). MS: 251 (11, [*M* − Me]$^+$), 238 (10), 237 (78), 235 (10, [*M* − CH$_2$OH]$^+$), 219 (4), 195 (24), 177 (10), 165 (27), 150 (8), 136 (11), 131 (14), 117 (18), 115 (70), 114 (100), 98 (19), 97 (16), 84 (21), 77 (14), 72 (18), 68 (12), 60 (27), 58 (13), 57 (24), 55 (18), 43 (42). Anal. calc. for $C_{13}H_{18}N_2O_4$ (266.29): C 58.63, H 6.81, N 10.52; found: C 58.32, H 6.75, N 10.43.

threo-*(4*S*,5*S*)-2,2-Diethyl-4-hydroxymethyl-5-(4-nitrophenyl)-1,3-oxazolidine* (**1d**). As described for **1a** under *Method B*. Yield, 95%. M.p. 92–94° (dec.). $[\alpha]_D^{15} = +50.38$ (*c* = 2, EtOH). IR: 3422v*s*, 3335*m* (NH, OH), 1605*w* (C=C−C); 1518v*s*, 1350v*s* (NO_2); 1059*m*, 1028*m* (asym. C−O−C); 845*s* (Ar−H). ^{1}H-NMR ((D$_6$)DMSO, 300 MHz): 8.17 (*d*, *J* = 8.4, H−C(3′), H−C(5′)); 7.59 (*d*, *J* = 8.4, H−C(2′), H−C(6′)); 4.88 (*t*, *J* = 5.4, CH$_2$O*H*); 4.67 (*d*, *J*(5,4) = 8.4, H−C(5)); 3.60 (*m*, 1 H, C*H*$_2$OH); 2.98 (*m*, H−C(4), NH); 1.80 (*m*, 2 C*H*$_2$Me); 1.02 (*m*, CH$_2$*Me*). MS: 252 (15), 251 (100, [*M* − C$_2$H$_5$]$^+$), 249 (4, [*M* − CH$_2$OH]$^+$), 195 (7), 177 (4), 165 (6), 149 (3), 129 (10), 128 (15), 117 (3), 98 (5), 85 (4), 77 (4), 69 (3), 57 (36). Anal. calc. for $C_{14}H_{20}N_2O_4$ (280.32): C 59.98, H 7.19, N 10.00; found: C 59.71, H 6.95, N 9.83.

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