Tetrahedron 66 (2010) 6162–6166

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Highly stereoselective De-Novo synthesis of protected 2-amino-3-*C*-methyl-2,3-dideoxy-D-altrose

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ARTICLE INFO

Article history:
Received 5 May 2010
Accepted 27 May 2010
Available online 1 June 2010

Keywords:
Urethanes
Isocyanates
Branched carbohydrates
O,O-Migration

ABSTRACT

A new strategy for the stereoselective synthesis of 2-amino-2-deoxy-aldoses is described. Therefore epoxy carbamates are reacted with isocyanates to furnish urethanes, which will form the title compounds with high diastereoselectivities under basic conditions and O,O-migration of the carbamoyl group.

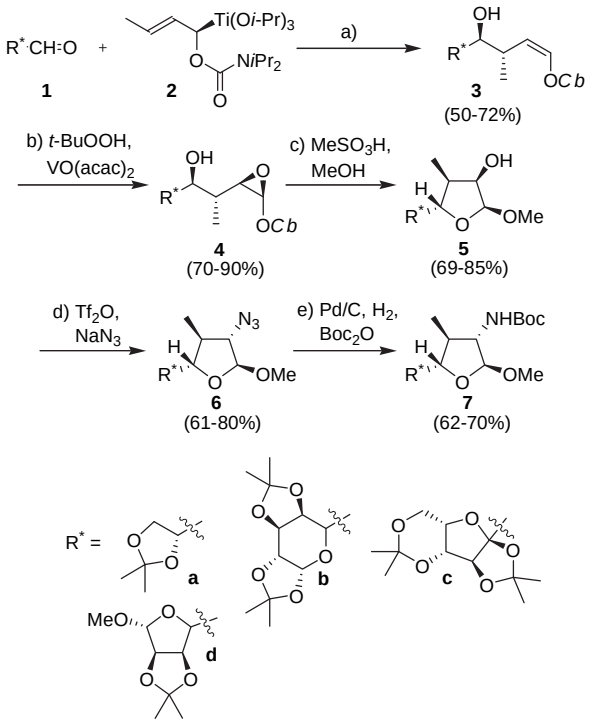
1. Introduction

Modified carbohydrates play an important role in the synthesis of antibodies,[1] enzymes,[2] and biologically active compounds.[3] Recently we published the highly stereoselective synthesis of methyl-branched 2-amino-2-deoxy-aldoses from protected sugar aldehydes **1** (Scheme 1).[4] Aldehydes **1** are elongated via introduction of the C-1–C-3 unit by homoaldol reaction of enantioenriched homoenolate reagent **2** to deliver enol carbamates **3**.[5] Diastereoselective epoxidation[6] provided epoxides **4** followed by aminolysis with sodium azide, reduction, and protection furnish target furanosides **7**.[4]

The synthesis of the framework turned out very straightforward but for the introduction of the amino group some improvement seemed to be possible since oxiranes are powerful alkylation moieties. Intramolecular delivery of the amino group might enhance the rate of its attack.

2. Results and discussion

Consequently, oxirane **4a** was refluxed with 4-bromophenyl isocyanate (**8a**) in dioxane.[7] The choice of the N-group was directed not by its protecting group-properties but by the expectation forming a crystalline product for facile structure elucidation (Scheme 2). In a couple of examples, *N*-bromophenyl groups led to crystallization of homoaldol products and their derivatives.[8]



Scheme 1. Synthesis of furanosides **7**. Reagents and conditions: (a) *n*-pentane/cyclohexane (6.7:1), −78 °C, 4 h; (b) *t*-BuOOH, $VO(acac)_2$, CH_2Cl_2, rt, 15 h; (c) $MeSO_3H$, MeOH, CH_2Cl_2, −78 °C, 15 h; (d) (i) $(CF_3SO_2)_2O$, pyridine, −15 °C→−5 °C, 3 h; (ii) NaN_3, DMSO, 50 °C, 5–15 h; (e) Boc_2O, Pd/C, H_2, THF, rt, 9 h.

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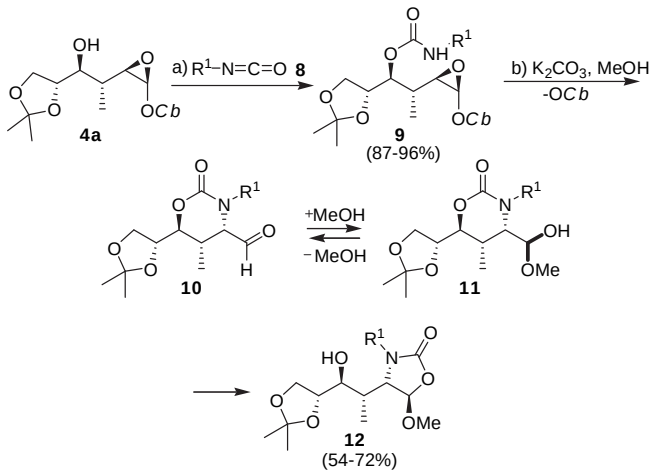
doi:10.1016/j.tet.2010.05.101

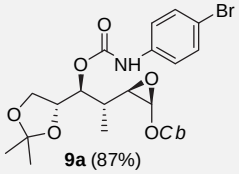
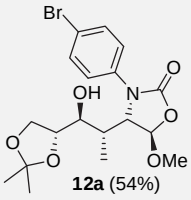
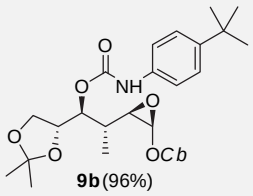
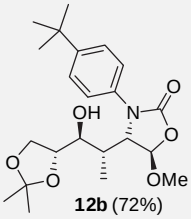
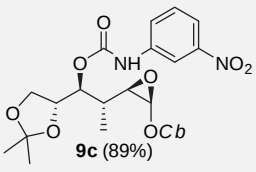
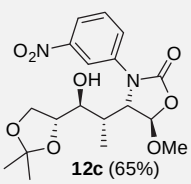


Scheme 2. Synthesis of 2-amino-3-*C*-methyl-2,3-dideoxy-D-altroses **12**. Reagents and conditions: (a) R–N=C=O, dioxane, reflux, 24 h; (b) K_2CO_3, MeOH, reflux, 3 h.

After heating for 24 h at 100 °C, the carbamate ester **9a** was obtained with 87% yield. Similarly, the urethanes **9b** and **9c**, were prepared from 4-*tert*-butylphenyl (**8b**) and 3-nitrophenyl (**8c**) isocyanate (Table 1). Only the 3-nitrobenzoate **9c** provided suitable crystals for an X-ray analysis, which showed the epoxide group being still present (Fig. 1).

By refluxing epoxy carbamates **9** with a suspension of solid potassium carbonate in methanol, the intramolecular opening of the epoxide moiety **9** took place at C-2 with inversion of the configuration. We expected the formation of amino aldehydes **10** or the corresponding hemiacetals **11**. Fortunately, the product obtained

Table 1
Results of the reaction of **4a** with various isocyanates

Isocyanate	Urethane[a] (yield)	Oxazolidin-2-one[a] (yield)
4-Br–C_6H_4–N=C=O (**8a**)	 **9a** (87%)	 **12a** (54%)
4-*t*-Bu–C_6H_4–N=C=O (**8b**)	 **9b** (96%)	 **12b** (72%)
3-NO_2–C_6H_4–N=C=O (**8c**)	 **9c** (89%)	 **12c** (65%)

[a] For all compounds: *dr*>98:2, determined by ^{1}H NMR analysis of the crude product.

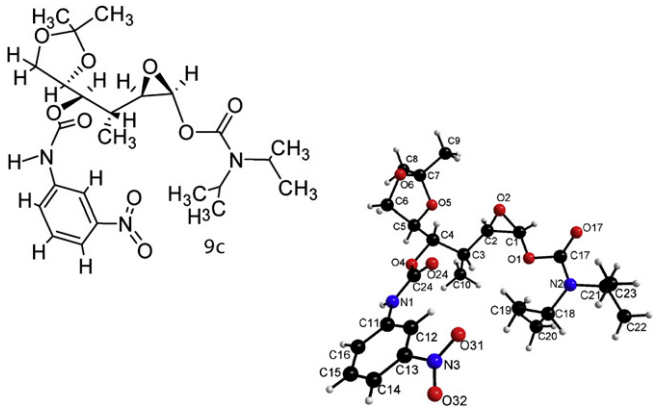


Figure 1. X-ray crystal structure of epoxy carbamate **9c**.[9,10]

from epoxide **9b** turned out to be crystalline after O-benzoylation, and we learned that oxazolidin-2-one **12** is the product (Fig. 2). We assume that the hemiacetal anion formed from intermediate **11** undergoes an O-1–O-3 migration of the carbamoyl group under the basic reaction conditions.

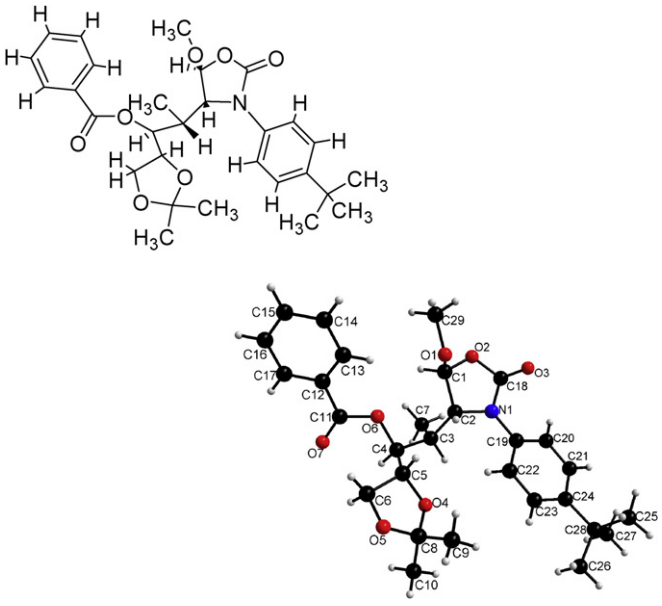


Figure 2. X-ray crystal structure of oxazolidin-2-one **13b**.[10,11]

We have not yet explored the synthetic advantages of the unique protecting group pattern of compounds **12**, which bridges N-2 and O-1 by a urethane moiety, combined with a free OH group at C-4. Liberation of the aldehyde group appears possible under acidic and under basic conditions via attack at the carbonyl group.

3. Conclusion

A new and surprisingly simple method for the synthesis of stereochemically pure 2-amino-2-deoxy-aldoses has been discovered. Although demonstrated only for one type, a wide scope of applicability is expected. By selection of the starting aldehyde and the homoenolate reagent, a large variation in the structure seems to be possible. In addition, the choice of the isocyanate should allow for the introduction of optimal N-protecting groups.

4. Experimental

4.1. General

All moisture-sensitive reactions were carried out under an atmosphere of argon in flame-dried glassware sealed by rubber septa. Unless otherwise specified, materials were obtained from commercial sources and used without purification. All solvents were dried according to standard procedures and purified by distillation prior to use. Addition of chemicals was performed by using disposable plastic syringes. Flash chromatography was performed using Merck silica gel 60 (230–400 mesh) at a pressure of about 1.5 bar and monitored by TLC. Solvents for chromatography (cyclohexane, EtOAc) were distilled prior to use. For analytic thin layer chromatography, Merck plastic sheets (60 F_{254} silica gel) were used. Visualization was accomplished with permanganate solution and vanilline solution. ^1H and ^{13}C NMR spectra were recorded on a Bruker ARX 400 or a Varian Inova 500 spectrometer. Chemical shifts are given in parts per million (δ), with tetramethylsilane (^1H) and $CDCl_3$ (^{13}C) as internal standard. The multiplicities are indicated by s (singlet), br s (broad singlet), d (doublet), t (triplet), and m (multiplet). The numbering of the compounds may differ from the IUPAC nomenclature. Optical rotations were measured at 20 °C with a Perkin-Elmer 341 at the sodium D line, the IR spectra were recorded using a Varian 3100 Excalibur series spectrometer. Elemental analysis was performed at the Chemistry Department of the University of Münster. ESI (Exact Mass Determination) was carried out with a Quattro LCZ (Waters-Micromass, Manchester, UK) with nanospray inlet.

4.2. General procedure for the synthesis of compounds 9 (GPA)

1,2-Epoxy-4-hydroxyalkylcarbamate **4a** (1.0 equiv) and 1.5 equiv isocyanate **8a**, **8b** or **8c** were dissolved in dioxane (10 mL/mmol), and the solution was stirred for 24 h under reflux. The reaction was stopped by addition of water (10 mL/mmol) and the aqueous layer was separated and extracted with Et_2O (3×10 mL/mmol). The combined organic phases were dried over $MgSO_4$, the solvent was evaporated, and the residue was purified by column chromatography (EtOAc/*c*-hexane=1:2→1:1).

*4.2.1. [1S,2R,3R,4S,5R]-4-O-(4-Bromophenylcarbamoyl)-1,2-epoxy-4,5,6-trihydroxy-5,6-O-isopropylidene-3-methyl-hexyl N,N-diisopropylcarbamate (**9a**).* According to GPA, carbamate **4a** (69 mg, 0.2 mmol) was reacted with 4-bromophenyl isocyanate (57.9 mg, 0.3 mmol) in 4 mL dioxane to afford **9a** (94.3 mg, 87%) as yellow solid. R_f 0.59 (EtOAc/*c*-hexane=1:1); t_R 8.46 min (HP 5); mp 135.5 °C (EtOAc); $[\alpha]_D^{20}$ +7.1 (*c* 0.59, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ/ppm=1.11 (d, $^3J_{3,3\text{-}CH3}$=7.3 Hz, 3H, 3-CH_3); 1.22 (d, $^3J_{1',2'}$=6.8 Hz, 12H, 2′-CH_3); 1.32, 1.37 (each s, 6H, C(CH_3)$_2$); 2.12 (m, 1H, 3-H_1); 2.99 (dd, $^3J_{1,2}$=2.8 Hz, $^3J_{2,3}$=9.2 Hz, 1H, 2-H_1); 3.72, 4.09 (each br s, 2H, 1′-H_1); 3.94 (dd, $^3J_{5,6A}$=8.7 Hz, $^3J_{6A,6B}$=5.7 Hz, 1H, 6-H_A); 4.07–4.11 (m, 1H, 6-H_B); 4.38 (m, 1H, 5-H_1); 5.13 (dd, $^3J_{3,4}$=4.2 Hz, $^3J_{4,5}$=6.0 Hz, 1H, 4-H_1); 5.61 (d, 1H, 1-H_1); 6.96 (s, 1H, N*H*); 7.31–7.41 (m, 4H, Ar–*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm=13.4 (3-*C*H_3); 20.3, 21.4 (C-2′); 25.1, 26.5 (C(*C*H_3)$_2$); 34.5 (C-3); 45.7, 47.0 (C-1′); 56.3 (C-2); 65.9 (C-6); 74.8 (C-1); 75.8 (C-5); 77.2 (C-4); 109.3 (*C*(CH$_3$)$_2$); 120.2 (CH, C_{Ar}); 132.0, 136.9 (C_q, C_{Ar}); 152.8 (O*C*=O); 154.1 (N*C*=O). IR (ATR): $\tilde{\nu}$/cm^{-1}=3306, 3061, 2975, 2935, 2878, 1687, 1595, 1531, 1371, 1305, 1211, 1046, 825, 1135. ESI-MS (*m*/*z*): 565.15 [(M+Na)$^+$].

*4.2.2. [1S,2R,3R,4S,5R]-4-O-4-tert-(Butylphenylcarbamoyl)-1,2-epoxy-4,5,6-trihydroxy-5,6-O-isopropylidene-3-methylhexyl N,N-diisopropylcarbamate (**9b**).* According to the GPA, carbamate **4a** (0.10 mg, 0.3 mmol) was reacted with 4-*tert*-butylphenyl isocyanate (72.9 mg, 0.45 mmol) in 5 mL dioxane to afford **9b** (150 mg, 96%) as yellow solid. R_f 0.64 (EtOAc/*c*-hexane=1:1); t_R 9.37 min (HP 5); mp 113.6 °C (EtOAc); $[\alpha]_D^{20}$ +3.4 (*c* 0.90, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ/ppm=1.11 (d, $^3J_{3,3\text{-}CH3}$=7.2 Hz, 3H, 3-CH_3); 1.23 (d, $^3J_{1',2'}$=6.8 Hz, 12H, 2′-CH_3); 1.30 (s, 9H, C(CH_3)$_3$); 1.33, 1.38 (each s, 6H, C(CH_3)$_2$); 2.14 (m, 1H, 3-H_1); 3.01 (dd, $^3J_{1,2}$=2.8 Hz, $^3J_{2,3}$=9.3 Hz, 1H, 2-H_1); 3.73, 4.09 (each br s, 2H, 1′-H_1); 3.95 (dd, $^3J_{5,6A}$=5.7 Hz, $^3J_{6A,6B}$=8.5 Hz, 1H, 6-H_A); 4.10 (m, 1H, 6-H_B); 4.39 (m, 1H, 5-H_1); 5.13 (dd, $^3J_{3,4}$=3.6 Hz, $^3J_{4,5}$=6.1 Hz, 1H, 4-H_1); 5.63 (d, 1H, 1-H_1); 6.74 (s, 1H, N*H*); 7.24–7.35 (m, 4H, Ar–*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm=13.5 (3-*C*H_3); 20.3, 21.4 (C-2′); 25.2, 26.6 (C(*C*H_3)$_2$); 31.3 (C(CH_3)$_3$); 34.3 (*C*(CH$_3$)$_3$); 34.5 (C-3); 45.3, 45.8 (C-1′); 56.2 (C-2); 66.1 (C-6); 74.8 (C-4); 75.8 (C-1); 77.2 (C-5); 109.3 (*C*(CH$_3$)$_2$); 120.9, 125.7, 126.0 (*C*H, C_{Ar}); 135.5, 147.0 (C_q, C_{Ar}); 153.6 (O*C*=O); 154.1 (N*C*=O). IR (ATR): $\tilde{\nu}$/cm^{-1}=3307, 3055, 2965, 2904, 2873, 1705, 1598, 1529, 1434, 1296, 1214, 1050, 834, 1135. Anal. Calcd for $C_{28}H_{44}N_2O_7$: C, 64.59; H, 8.52; N, 5.38. Found: C, 64.77; H, 8.53; N, 5.12.

*4.2.3. [1S,2R,3R,4S,5R]-1,2-Epoxy-4,5,6-trihydroxy-5,6-O-isopropylidene-3-methyl-4-O-(3-nitrophenylcarbamoyl)-hexyl N,N-diisopropylcarbamate (**9c**).* According to GPA, carbamate **4a** (158 mg, 0.30 mmol) was reacted with 3-nitrophenyl isocyanate (0.35 g, 1.0 mmol) in 15 mL dioxane to afford **9c** (450 mg, 89%) as yellow crystals. R_f 0.55 (EtOAc/*c*-hexane=1:1); t_R 11.73 min (HP 5); mp 130.8 °C (EtOAc); $[\alpha]_D^{20}$ +6.4 (*c* 0.61, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ/ppm=1.14 (d, $^3J_{3,3\text{-}CH3}$=7.2 Hz, 3H, 3-CH_3); 1.23 (d, $^3J_{1',2'}$=6.8 Hz, 12H, 2′-CH_3); 1.34, 1.39 (each s, 6H, C(CH_3)$_2$); 2.13 (m, 1H, 3-H_1); 3.01 (dd, $^3J_{1,2}$=2.9 Hz, $^3J_{2,3}$=9.4 Hz, 1H, 2-H_1); 3.73, 4.11 (each br s, 2H, 1′-H_1); 3.96 (dd, $^3J_{5,6A}$=5.7 Hz, $^3J_{6A,6B}$=8.6 Hz, 1H, 6-H_A); 4.08–4.14 (m, 1H, 6-H_B); 4.41 (m, 1H, 5-H_1); 5.18 (dd, $^3J_{3,4}$=4.4 Hz, $^3J_{4,5}$=5.7 Hz, 1H, 4-H_1); 5.62 (d, 1H, 1-H_1); 7.18 (s, 1H, N*H*); 7.38–8.40 (m, 4H, Ar–*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm=13.4 (3-*C*H_3); 20.3, 21.5 (C-2′); 25.1, 26.6 (C(*C*H_3)$_2$); 34.6 (C-3); 45.8, 47.0 (C-1′); 56.3 (C-2); 65.8 (C-6); 74.8 (C-4); 75.7 (C-1); 77.2 (C-5); 109.4 (*C*(CH$_3$)$_2$); 118.2, 129.9 (CH, C_{Ar}); 139.0, 148.8 (C_q, C_{Ar}); 152.7 (O*C*=O); 154.1 (N*C*=O). IR (ATR): $\tilde{\nu}$/cm^{-1}=3291, 3096, 2975, 2938, 2880, 1686, 1600, 1530, 1350, 1296, 1214, 1051, 753, 1135; ESI-MS (*m*/*z*): 532.23 [(M+Na)$^+$].

4.3. General procedure for the synthesis of compounds 12 (GPB)

Urethane **9** (1.0 equiv) was dissolved in MeOH (5 mL/mmol) and the solution was treated with 1.0 equiv finely grind K_2CO_3, and stirred for 3–6 h under reflux. The reaction was stopped by addition of satd NH_4Cl (10 mL/mmol), the aqueous layer was separated and extracted with Et_2O (3×10 mL/mmol). The combined organic phases were dried over $MgSO_4$, the solvent was evaporated, and the residue was purified by column chromatography (EtOAc/*c*-hexane 1:2→1:1).

*4.3.1. [4S,5S,5(1R,2S,2(4R))]-3-(4-Bromophenyl)-4-[2-hydroxy-1-methyl-2-(2,2-dimethyl-[1,3]dioxolan-4-yl)-ethyl]-5-methoxy-oxazolidin-2-one (**12a**).* According to GPB urethane **9a** (0.11 g, 0.20 mmol) was dissolved in 7.0 mL of dry MeOH and treated with K_2CO_3 (28 mg, 0.2 mmol). Work-up and purification of the crude product by flash chromatography (EtOAc/*c*-hexane=1:1) yielded 47 mg (54%) oxazolidin-2-one **12a** as yellow crystals. R_f 0.21 (EtOAc/*c*-hexane=1:1); t_R 23.62 min (HP 5); mp 98.7 °C (EtOAc); $[\alpha]_D^{20}$ +47.6 (*c* 0.54, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ/ppm=0.86 (d, $^3J_{3,3\text{-}CH3}$=7.3 Hz, 3H, 3-CH_3); 1.38, 1.41 (each s, 6H, C(CH_3)$_2$); 1.99–2.08 (m, 1H, 3-H_1); 2.42 (br s, 1H, 4-OH); 3.56 (s, 3H, OCH_3); 3.71–3.79 (m, 1H, 4-H_1); 3.85 (dd, $^3J_{5,6A}$=6.4 Hz, $^3J_{6A,6B}$=8.3 Hz, 1H, 6-H_A); 3.99 (dd, $^3J_{5,6B}$=6.5 Hz, 1H, 6-H_B); 4.19 (m, 1H, 5-H_1); 4.68 (dd, $^3J_{1,2}$=1.8 Hz, $^3J_{2,3}$=2.9 Hz, 1H, 2-H_1); 5.38 (d, 1H, 1-H_1);

7.40–7.50 (m, 4H, Ar–*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm=9.65 (3-*C*H$_3$); 25.1, 26.5 (C(*C*H$_3$)$_2$); 33.3 (C-3); 56.4 (O–*C*H$_3$); 62.2 (C-2); 64.9 (C-6); 72.1 (C-4); 76.3 (C-5); 98.9 (C-1); 109.3 (*C*(CH$_3$)$_2$); 122.3, 132.1 (CH, C_{Ar}); 135.2 (C_q, C_{Ar}); 153.9 (O*C*=O). IR (ATR): $\tilde{\nu}$/cm^{-1}=3483, 3075, 2985, 2936, 2885, 2360, 1726, 1494, 1425, 1382, 1208, 1070, 993, 827, 1109, 753. ESI-MS (*m*/*z*): 452.07 [(M+Na)$^+$]; 883.14 [(2M+Na)$^+$].

*4.3.2. [4S,5S,5(1R,2S,2(4R))]-3-(4-tert-Butylphenyl)-4-[2-hydroxy-1-methyl-2-(2,2-dimethyl-[1,3]dioxolan-4-yl)-ethyl]-5-methoxy-oxazolidin-2-one (**12b**).* According to GPB urethane **9b** (0.47 g, 0.90 mmol) was dissolved in 20.0 mL of dry MeOH and treated with K_2CO_3 (0.13 g, 0.90 mmol). Work-up and purification of the crude product by flash chromatography (EtOAc/*c*-hexane=1:2→1:1) yielded 26 mg (72%) oxazolidin-2-one **12b** as colorless solid. R_f 0.48 (EtOAc/*c*-hexane=1:1); t_R 23.63 min (HP 5); mp 79.5 °C (EtOAc); $[\alpha]_D^{20}$ +38.8 (*c* 0.64, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm=0.87 (d, $^3J_{3,3\text{-}CH3}$=7.0 Hz, 3H, 3-C*H*$_3$); 1.31 (s, 9H, C(C*H*$_3$)$_3$); 1.38, 1.42 (each s, 6H, C(C*H*$_3$)$_2$); 2.00 (m, 1H, 3-H$_1$); 2.32 (d, $^3J_{4,4\text{-}OH}$=2.8 Hz, 1H, 4-OH); 3.56 (s, 3H, OC*H*$_3$); 3.75–3.80 (m, 1H, 4-H$_1$); 3.87 (dd, $^3J_{5,6A}$=6.8 Hz, $^3J_{6A,6B}$=8.3 Hz, 1H, 6-H$_A$); 3.96 (dd, $^3J_{5,6B}$=6.5 Hz, 1H, 6-H$_B$); 4.20 (ddd, $^3J_{4,5}$=4.3 Hz, 1H, 5-H$_1$); 4.70 (dd, $^3J_{1,2}$=1.9 Hz, $^3J_{2,3}$=2.8 Hz, 1H, 2-H$_1$); 5.33 (d, 1H, 1-H$_1$); 7.35–7.48 (m, 4H, Ph–*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm=9.55 (3-*C*H$_3$); 25.1, 26.5 (C(*C*H$_3$)$_2$); 31.3 (C(*C*H$_3$)$_3$); 33.8 (*C*(CH$_3$)$_3$); 34.3 (C-3); 56.3 (O–*C*H$_3$); 62.5 (C-2); 64.3 (C-6); 71.5 (C-4); 76.5 (C-5); 98.9 (C-1); 109.3 (*C*(CH$_3$)$_2$); 120.9, 126.1 (CH, C_{Ar}); 133.3, 148.0 (C_q, C_{Ar}); 154.3 (O*C*=O). IR (ATR): $\tilde{\nu}$/cm^{-1}=3476, 3078, 2935, 2890, 2888, 2844, 1739, 1531, 1385, 1348, 1205, 1068, 751, 1094. ESI-MS (*m*/*z*): 430.22 [(M+Na)$^+$].

*4.3.3. [4S,5S,5(1R,2S,2(4R))]-4-[2-Hydroxy-1-methyl-2-(2,2-dimethyl-[1,3]dioxolan-4-yl)-ethyl]-5-methoxy-3-(3-nitrophenyl)-oxazolidin-2-one (**12c**).* According to GPB urethane **9a** (0.15 g, 0.30 mmol) was dissolved in 10.0 mL of dry MeOH and treated with K_2CO_3 (42 mg, 0.30 mmol). Work-up and purification of the crude product by flash chromatography (EtOAc/*c*-hexane=1:2→1:1) yielded 770 mg (65%) oxazolidin-2-one **12c** as colorless solid. R_f 0.44 (EtOAc/*c*-hexane=1:1); t_R 22.89 min (HP 5); mp 67.7 °C (EtOAc); $[\alpha]_D^{20}$ +18.5 (*c* 1.07, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm=0.92 (d, $^3J_{3,3\text{-}CH3}$=7.2 Hz, 3H, 3-C*H*$_3$); 1.41, 1.43 (each s, 6H, C(C*H*$_3$)$_2$); 2.18 (m, 1H, 3-H$_1$); 3.58 (s, 3H, OC*H*$_3$); 3.75 (t, $^3J_{3,4}$=6.5 Hz, 1H, 4-H$_1$); 3.88 (dd, $^3J_{5,6A}$=5.7 Hz, $^3J_{6A,6B}$=8.4 Hz, 1H, 6-H$_A$); 4.08 (dd, $^3J_{5,6B}$=6.2 Hz, 1H, 6-H$_B$); 4.22 (m, 1H, 5-H$_1$); 4.78 (dd, $^3J_{1,2}$=1.7 Hz, $^3J_{2,3}$=2.8 Hz, 1H, 2-H$_1$); 5.53 (d, 1H, 1-H$_1$); 7.56–8.42 (m, 4H, Ar–*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm=9.8 (3-*C*H$_3$); 25.0, 26.6 (C(*C*H$_3$)$_2$); 32.9 (C-3); 56.6 (O*C*H$_3$); 62.1 (C-2); 65.9 (C-6); 73.2 (C-4); 76.1 (C-5); 99.3 (C-1); 109.8 (*C*(CH$_3$)$_2$); 114.7, 119.1, 125.9, 130.0 (CH, C_{Ar}); 137.6, 148.8 (C_q, C_{Ar}); 153.9 (O*C*=O). IR (ATR): $\tilde{\nu}$/cm^{-1}=3446, 3005, 2964, 2906, 2884, 2360, 1734, 1520, 1427, 1384, 1214, 1066, 992, 836, 1101. ESI-MS (*m*/*z*): 419.14 [(M+Na)$^+$]; 815.30 [(2M+Na)$^+$].

4.4. Synthesis of benzoyl-substituted oxazolidin-2-one 13b

*4.4.1. [1S,2R,2(4S,5S),1(4R)]-3-(4-tert-Butylphenyl)-4-[2-benzoyloxy-1-methyl-2-(2,2-dimethyl-[1,3]dioxolan-4-yl)-ethyl]-5-methoxy-oxazolidin-2-one (**13b**).* Oxazolidin-2-one **12b** (79.7 mg, 0.18 mmol) and DMAP (16 mg, 0.009 mmol) were dissolved in CH_2Cl_2 cooled to 0 °C, and treated with benzoic anhydride (71 mg, 0.31 mmol). After 1 h stirring at room temperature, aqueous work-up and purification by flash chromatography on silica gel (EtOAc/*c*-hexane=1:1) benzoyl-substituted oxazolidin-2-one **13b** was isolated as colorless solid (76.7 mg, 86%). R_f 0.29 (EtOAc/*c*-hexane=1:1); mp 66.6 °C (EtOAc); $[\alpha]_D^{20}$ +45.4 (*c* 1.12, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm=0.98 (d, $^3J_{3,3\text{-}CH3}$=7.1 Hz, 3H, 3-C*H*$_3$); 1.32 (s, 9H, C(C*H*$_3$)$_3$); 1.32, 1.40 (each s, 6H, C(C*H*$_3$)$_2$); 2.50 (m, 1H, 3-H$_1$); 3.53 (s, 3H, OC*H*$_3$); 3.86 (dd, $^3J_{5,6A}$=5.9 Hz, $^3J_{6A,6B}$=8.5 Hz, 1H, 6-H$_A$); 4.08 (dd, $^3J_{5,6B}$=6.2 Hz, 1H, 6-H$_B$); 4.38 (ddd, $^3J_{4,5}$=7.5 Hz, 1H, 5-H$_1$); 4.62 (dd, $^3J_{1,2}$=1.7 Hz, $^3J_{2,3}$=2.8 Hz, 1H, 2-H$_1$); 5.34 (dd, 1H, 4-H$_1$); 5.40 (d, 1H, 1-H$_1$); 7.37–7.67, 8.02–8.06 (m, 9H, Ph–*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm=10.3 (3-*C*H$_3$); 25.4, 26.5 (C(*C*H$_3$)$_2$); 31.3 (C(*C*H$_3$)$_3$); 32.9 (*C*(CH$_3$)$_3$); 34.4 (C-3); 56.1 (O–*C*H$_3$); 62.5 (C-2); 67.2 (C-6); 74.9 (C-5); 75.4 (C-4); 98.9 (C-1); 109.9 (*C*(CH$_3$)$_2$); 121.2, 126.0, 128.7, 129.6 (CH, C_{Ar}); 133.0, 133.7, 148.2 (C_q, C_{Ar}); 154.1 (O(*C*=O)N); 165.5 (O*C*=O). IR (ATR): $\tilde{\nu}$/cm^{-1}=3036, 2963, 2876, 2360, 1761, 1724, 1520, 1388, 1347, 1213, 1070, 992, 837, 1099, 711. Anal. Calcd for $C_{29}H_{37}NO_7$: C, 68.08; H, 7.29; N, 2.74. Found: C, 67.86; H, 7.26; N, 2.69.

Acknowledgements

This work was supported by the Deutsche Forschungsgemeinschaft (SFB 424).

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2010.05.101. These data include MOL files and InChIKeys of the most important compounds described in this article.

References and notes

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9. Crystal data for $C_{24}H_{35}N_3O_9$ (**9c**), *M*=509.55, orthorhombic, space group $P2_12_12_1$ (No. 19), *a*=7.1888(3), *b*=9.1608(3), *c*=40.0831(17) Å, *V*=2639.68(18) Å^3, D_c=1.282 g cm^{-3}, μ=0.824 mm^{-1}, *Z*=4, λ=1.54178 Å, *T*=223(2) K, 12,208 reflections collected ($\pm h$, $\pm k$, $\pm l$), [(sinθ)/λ]=0.60 Å^{-1}, 4015 independent (R_{int}=0.066), and 3147 observed reflections [$I \geq 2\sigma(I)$], 335 refined parameters, *R*=0.047, wR_2=0.112, Flack −0.3(3).
10. Data sets were collected with a Nonius KappaCCD diffractometer. Programs used: data collection COLLECT (Nonius B.V., 1998), data reduction Denzo-SMN (Z. Otwinowski, W. Minor, *Methods in Enzymology*, 1997, **276**, 307–326), absorption correction Denzo (Z. Otwinowski, D. Borek, W. Majewski, W. Minor, *Acta Cryst.* 2003, **A59**, 228–234), structure solution SHELXS-97 (G.M.

Sheldrick, *Acta Cryst*. 1990, **A46**, 467–473), structure refinement SHELXL-97 (G.M. Sheldrick, *Acta Cryst.* 2008, **A64**, 112–122), graphics DIAMOND (G. Bergerhoff, M. Berndt, K. Brandenburg, *J. Res. Natl. Inst. Stand. Technol.* 1996, **101**, 221–225). *R*-Value is given for the observed, wR^2-value for all reflections. Linderman, R.J.; Siedlecki, J.M. *J. Org. Chem.* **1996**, *61*, 6492–6492. CCDC 773262 and 773263 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at <www.ccdc.cam.ac.uk/conts/retrieving.html> [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (internet.) +44(1223)336 033, E-mail: deposit@ccdc.cam.ac.uk].

11. Crystal data for $C_{29}H_{37}NO_7$ (**13b**), M=511.60, monoclinic, space group $P2_1$ (No. 4), a=12.0080(2), b=8.9588(1), c=12.9416(2) Å, β=92.568(2)°, V=1390.82(4) Å^3, D_c=1.222 g cm^{-3}, μ=0.709 mm^{-1}, Z=2, λ=1.54178 Á, T=223(2) K, 17,451 reflections collected ($\pm h$, $\pm k$, $\pm l$), [(sinθ)/λ]=0.60 Å^{-1}, 4773 independent (R_{int}=0.042), and 4550 observed reflections [$I \geq 2\sigma(I)$], 342 refined parameters, R=0.040, wR^2=0.103.