Synthesis of β-Hydroxy *O*-Alkyl Hydroxylamines from Epoxides Using a Convenient and Versatile Two-Step Procedure

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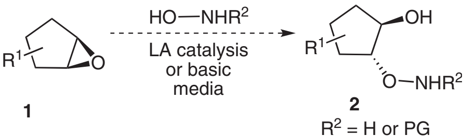
Received: 25.09.2012; Accepted after revision: 06.11.2012

Abstract: A simple and convenient synthetic method was developed to prepare β-hydroxy O-alkyl hydroxylamines in which base-mediated ring opening of epoxides with acetophenone oxime followed by cleavage of the oxime with 2,4-dinitrophenylhydrazine in acidic media furnished the hydroxylamine, which can be protected in situ with various N-protecting groups.

Key words: hydroxylamines, epoxides, ring opening, oxime cleavage, protecting groups

O-Alkyl hydroxylamines (or aminooxy compounds), which are non-basic substitutes for amines,[1] are found in various natural products such as L-canaline[2] and in various synthetic products displaying interesting biological activities.[2,3] Along with their β-hydroxy congeners,[4] these compounds predominantly show enzyme inhibition activities whereby the aminooxy moiety forms a stable oxime with an aldehyde group present on the cofactor. In preparative chemistry these reactive species usually serve as starting material for the preparation of functionalized *O*-alkyl oximes by simple condensation with aldehydes or ketones, often with quantitative yields and with almost complete functional group compatibility. This classical reaction has undergone a renaissance as a chemoselective ligation strategy and has emerged as a powerful means for the assembly of bioconjugates.[5]

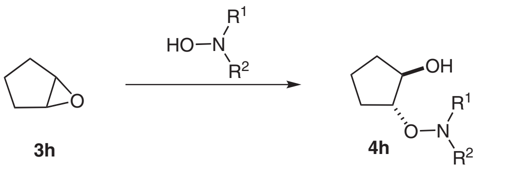
In connection with ongoing projects in our laboratory,[6] we required a variety of β-hydroxy *O*-alkyl hydroxylamines **2** and conceived that these might be accessed by the opening of epoxides **1** by N-protected hydroxylamines followed by deprotection of the nitrogen atom (Scheme 1). Toward this end, the most efficient approach leading to **2** seemed to be a direct opening of epoxide **1** with an N-protected hydroxylamine (i.e., *N*-Fmoc-hydroxylamine[7] or commercially available *N*-Boc-hydroxylamine). Surprisingly, such protocols are scarcely documented in the literature. In most reports, *N*-Boc-hydroxylamine is used under basic conditions, which leads to the expected β-hydroxy *O*-alkyl hydroxylamines in low to modest yields.[4b,c,8] The successful employment of *N*-hydroxyphthalimide in this context was also described by Porco and co-workers[9] with promotion by a Co-oligosalen catalyst.[10] In pursuit of our goal, we initially looked for viable conditions on commercially available cyclopentene oxide (**3h**; see Table 1). Because the use of potassium carbonate with *N*-Fmoc-hydroxylamine under Plenkiewicz's conditions[8b] showed no discernible conversion (Table 1, entry 1), we decided to leave basic conditions aside and investigate the ring opening of epoxide **3h** under Lewis acid catalysis conditions (Table 1, entries 2–15), which is a method usually used for the insertion of alcohols and/or amines but not yet employed with hydroxylamines as the nucleophile component. The ring opening of epoxide **3h** with *N*-Fmoc-hydroxylamine was first investigated with $BF_3{\cdot}Et_2O$ in dichloromethane (Table 1, entry 2), conditions that are known to be efficient for the reaction of benzyl alcohol with a similar epoxide,[6a] but this approach was unsuccessful in this case. The use of lanthanide-based Lewis acids [i.e., $Sc(OTf)_3$ and $Yb(OTf)_3$] also failed (Table 1, entries 3–6). Changing the nucleophile to *N*-Boc hydroxylamine or *N*-hydroxypiperidine, presumably more nucleophilic species, was also unproductive with numerous types of Lewis acid [LiBr, $InCl_3$, $ZrCl_4$, $Cu(OTf)_2$, or $Ti(OiPr)_4$; Table 1, entries 7–15]. Finally, we envisaged an alternative two-step procedure based on the intermediate introduction of an oxime under basic conditions as a hydroxylamine precursor, followed by its acid-mediated cleavage to give the expected β-hydroxy *O*-alkyl hydroxylamine. Oximes are more nucleophilic than hydroxylamines under basic conditions and their high-yield ring-opening of epoxides has been described.[11] Thus, the group of Soltani Rad recently described the aqueous-mediated ring opening of various epoxides with a range of oximes.[11a] Their protocol involved the use of a slight excess of potassium hydroxide (1.3 equiv) to deprotonate the oxime (1 equiv) in a mixture of water–dimethyl sulfoxide (DMSO) (7:3) at room temperature, followed by the addition of an excess of epoxide (1.5 equiv). Similar conditions were evaluated on cyclopentene oxide (**3h**) but with a slight excess of acetophenone oxime, as it would ultimately represent the least precious component in reactions employing more complex epoxides (Table 1, entry

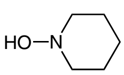
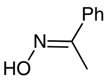


Scheme 1

SYNTHESIS 2013, 45, 0065–0074
Advanced online publication: 26.11.2012
DOI: 10.1055/s-0032-1317699; Art ID: SS-2012-M0756-OP

Table 1 Ring Opening of Cyclopentene Oxide with Hydroxylamine-Derived Nucleophiles



Entry	Nucleophile	LA (cat.) or base	Solvent	Temp (°C)	Yield (%)[a,b]
1	HONHFmoc	K_2CO_3	EtOH	60	NR
2	HONHFmoc	BF_3Et_2O	CH_2Cl_2	r.t.	NR
3		$Sc(OTf)_3$	CH_2Cl_2	r.t.	NR
4		$Sc(OTf)_3$	MeCN	r.t.	NR
5		$Sc(OTf)_3$	THF	r.t.	NR
6		$Yb(OTf)_3$	THF	r.t.	NR
7	HONHBoc	$Sc(OTf)_3$	CH_2Cl_2	r.t.	NR
8		$Yb(OTf)_3$	CH_2Cl_2	r.t.	NR
9		$Sc(OTf)_3$	CH_2Cl_2	r.t.	NR
10		$Yb(OTf)_3$	CH_2Cl_2	r.t.	NR
11		LiBr	CH_2Cl_2	r.t.	NR
12		$InCl_3$	CH_2Cl_2	r.t.	NR
13		$Ti(OiPr)_4$	CH_2Cl_2	r.t.	NR
14		$Cu(OTf)_2$	CH_2Cl_2	r.t.	NR
15		$ZrCl_4$	CH_2Cl_2	r.t.	NR
16		KOH	H_2O–DMSO[c]	r.t.	trace
17		KOH	H_2O–DMSO[c]	90	23
18		KOH	DMF	r.t.	trace
19		KOH	DMF	90	73

[a] Isolated yield.
[b] NR = no reaction.
[c] In a 7:3 ratio.

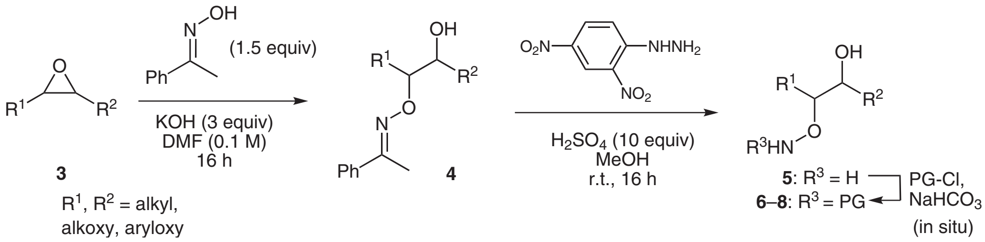
16). Surprisingly, the solvent system used by Soltani Rad et al. was not efficient for our model epoxide and only traces of the expected compound were obtained. Heating to 90 °C led to formation of the desired oxime **4h** in low yield (23%; Table 1, entry 17). Switching from DMSO to *N*,*N*-dimethylformamide (DMF) did not increase the yield at room temperature (Table 1, entry 18) but compound **4h** was obtained in a good yield at 90 °C (73%; Table 1, entry 19).

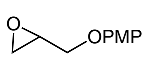
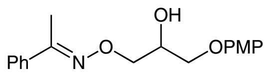
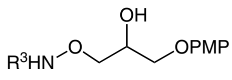
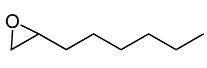
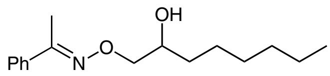
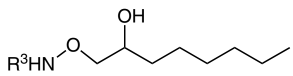
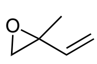
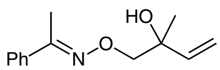
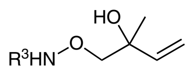
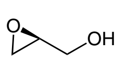
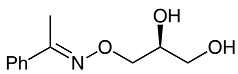
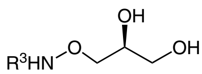
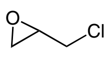
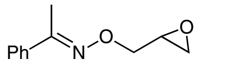
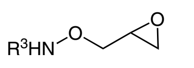
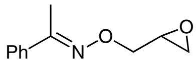
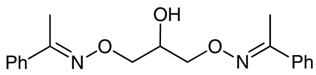
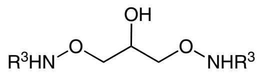
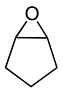
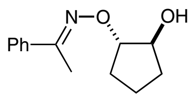
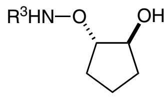
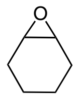
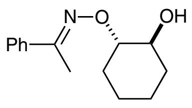
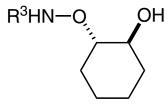
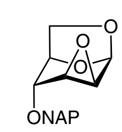
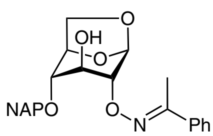
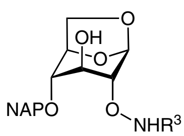
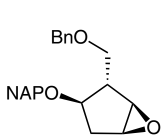
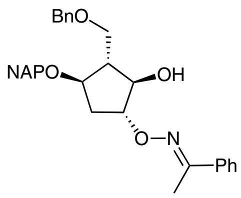
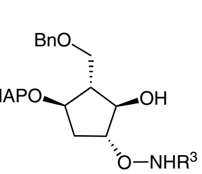
With conditions established for the ring-opening of cyclopentene oxide by acetophenone oxime, we next focused on the cleavage of the oxime functionality to liberate the *O*-alkyl hydroxylamine. After many unfruitful assays under acidic conditions, we found that 2,4-dinitrophenylhydrazine was efficient for the liberation of *O*-alkyl hydroxylamine from oximes with generation of 2,4-dinitrophenylhydrazone as a by-product. We also established that protection of the hydroxylamine product in situ was possible by reaction with FmocCl, CbzCl, or AllocCl, which provides a means to isolate the target compound in the form of a carbamate, cleavable under basic, acidic, or metal-catalyzed conditions. To evaluate the scope of the process, we tested its versatility towards various epoxides **3**, so as to obtain the corresponding β-hydroxy *O*-alkyl hydroxylamines **5**. The results, presented in Table 2, show regioselective ring-opening of terminal epoxides with preferential attack at the less hindered position (Table 2, entries 1–6). The presence of a double bond or an aromatic core did not affect the yield (Table 2, entries 1 and 3). The PMP-protected glycidol epoxide furnished α-hydroxyoxime **4a** in 83% yield. Hydrolysis of the oxime furnished free hydroxylamine **5a** in 77% yield or **6a**–**8a** in a range of 80–89%, depending on the carbamate used (Table 2, entry 1). A free hydroxyl group was found to be compatible with the ring opening but decreased the yield to 46% (Table 2, entry 4). In the case of epichlorohydrin (Table 2, entry 5), the epoxide, which is known to be the more reactive site,[12] was opened smoothly to afford **4e** with acetophenone oxime in 73% yield. Unfortunately, the presence of an epoxide was not compatible with 2,4-dinitrophenylhydrazine-mediated cleavage of the oxime (Table 2, entry 5). Thus, epoxide **4e** was opened with a second equivalent of acetophenone oxime to give **4f** in good yield (Table 2, entry 6). Highly functionalized Cerny's epoxide **3j** was converted into its β-hydroxy *O*-alkyl hydroxylamine derivative **5j** in 76% over two steps (Table 2, entry 9). Protection as carbamates in situ was also successful, and **5**–**8j** were obtained in high yields (Table 2, entry 9). Finally, the cyclopentene-derived epoxide **1a** was opened with acetophenone oxime at 90 °C and converted into the Fmoc-protected targeted skeleton **2a** in good yield (73%) over two steps (Table 2, entry 10).

In conclusion, we have established a convenient two-step procedure for the synthesis of β-hydroxy *O*-alkyl hydroxylamines by oxime-mediated regioselective opening of epoxides under basic conditions, followed by cleavage of the resulting oxime by 2,4-dinitrophenylhydrazine. We showed that various protecting groups could be introduced for protection of the highly polar resulting *O*-alkyl hydroxylamines in situ. The scope of the reaction revealed its good tolerance for alkenes, halogens, and alcohols.

Reactions were performed under an atmosphere of argon and monitored by thin-layer chromatography on Merck silica gel plates (60 F_{254} aluminum sheets). All separations were carried out under flash-chromatographic conditions on silica gel (Redi Sep prepacked column, 230–400 mesh) with the use of a CombiFlash Companion. *N*,*N*-Dimethylformamide (DMF) was purified by filtration through an activated alumina column under argon. MeOH was purchased from Acros Organics at the highest commercial quality and used without further purification. Reagent-grade chemicals were ob-

Table 2 Scope of the Two-Step Procedure; Synthesis of β-Hydroxy *O*-Alkyl Hydroxylamines



Entry	Epoxide **3**	*O*-Alkyl oxime **4**	Product	Yield (%)[a]	*O*-Alkyl hydroxylamine **5–8**	R^3	Product	Yield (%)[a]
1			**4a**[b]	83		H Fmoc Cbz Alloc	**5a** **6a** **7a** **8a**	77 81[c] 80 89
2			**4b**	74[d]		Fmoc	**6b**	95
3			**4c**	84[d]		Fmoc	**6c**	69
4			**4d**	46[e]		Fmoc	**6d**	93
5			**4e**	73		H Fmoc	**5e** **6e**	0[f] 0[f]
6			**4f**	86		Fmoc Alloc	**6f** **8f**	–[h] 61
7			**4h**	73[e]		H Fmoc	**5h** **6h**	–[g] 99
8			**4i**	89[e]		Fmoc Alloc	**6i** **8i**	–[h] 81
9			**4j**	89[e]		H Fmoc Cbz Alloc	**5j** **6j** **7j** **8j**	76 76 88 74
10	 **1a**		**4k**	84[e]		Fmoc	**2a**	87

[a] Isolated yield.
[b] PMP = *p*-methoxyphenyl.
[c] The yield dropped to 54% when only 2 equiv of H_2SO_4 were used.
[d] Reaction performed at 50 °C.
[e] Reaction performed at 90 °C
[f] Formation of the expected product was not observed.
[g] Formation of the expected product was observed by ^{1}H NMR spectroscopic analysis, but its isolation was troublesome.
[h] The expected product was obtained as an inseparable mixture with Fmoc-protected 2,4-dinitrophenylhydrazine.

tained from Sigma–Aldrich or Acros Organics chemical companies and were used as received. Optical rotations were measured with an Anton Paar MCP 300 polarimeter at 589 nm and are expressed in $deg·cm^3·g^{-1}·dm^{-1}$ and *c* is expressed in g/100 cm^3. IR spectra were recorded with a Perkin–Elmer FT-IR system using a diamond window Dura SamplIR II and the data are reported in reciprocal centimeters (cm^{-1}). ^{1}H (500 or 300 MHz) and ^{13}C (125 or 75 MHz) NMR spectra were recorded with Brüker Avance spectrometers. Chemical shifts are given in ppm (δ) and are referenced to the internal solvent signal or to TMS used as an internal standard. High-resolution mass spectra (HRMS) were recorded with a Micromass LCT Premier XE instrument (Waters) and were determined by electrospray ionization (ESI).

Epoxide Opening; General Procedure A

Acetophenone oxime (1.5 equiv) and KOH (3 equiv) were dissolved in anhydrous DMF (0.15 M in epoxide) and the solution was stirred at r.t. for 30 min. A solution of epoxide (1 equiv) in anhydrous DMF (0.3 M in epoxide) was then added and the mixture was stirred at the indicated temperature for 16 h. After addition of H_2O, aq HCl (1 M) was added dropwise until pH 1–2. The mixture was extracted with MTBE (3×) and the combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. Purification by column chromatography with the indicated eluent afforded β-hydroxy oxime O-ethers.

(*E*)-Acetophenone *O*-[2-Hydroxy-3-(4-methoxyphenoxy)propyl]oxime (4a)

The reaction was carried out according to General Procedure A with glycidyl 4-methoxyphenyl ether (90 mg, 0.5 mmol), acetophenone oxime (101 mg, 0.75 mmol) and KOH (84 mg, 1.5 mmol) in DMF (5 mL). The mixture was stirred at r.t. for 16 h and worked up as described. The crude product was purified by column chromatography (heptane–EtOAc, 95:5→9:1) to give **4a**.

Yield: 131 mg (0.415 mmol, 83%); colorless oil; R_f = 0.19 (heptane–EtOAc, 4:1).

IR (neat): 3461, 2953, 2926, 1739, 1507, 1228, 1113, 1034, 826, 766, 742, 696 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.25 (s, 3 H, Me), 3.75 (s, 3 H, OMe), 3.98–4.06 (m, 2 H, H-3), 4.31–4.44 (m, 3 H, H-1, H-2), 6.82 (d, *J* = 8.9 Hz, 2 H, ArH), 6.87 (d, *J* = 8.9 Hz, 2 H, ArH), 7.32–7.39 (m, 3 H, Ph-H), 7.58–7.64 (m, 2 H, Ph-H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.7 (CH_3), 55.6 (OCH_3), 69.5 (C-3), 70.0 (C-2), 74.6 (C-1), 114.6 (CH-Ar), 115.5 (CH-Ar), 126.0 (CH-Ph), 128.4 (CH-Ph), 129.3 (CH-Ph), 136.0 (C_q-Ph), 152.7 (C_q-O), 154.0 (C_q=N), 155.8 (C_q-OMe).

HRMS (ESI-TOF): *m/z* $[M + H]^+$ calcd for $C_{18}H_{22}NO_4$: 316.1549; found: 316.1556.

(*E*)-Acetophenone *O*-(2-Hydroxyoctyl) Oxime (4b)

The reaction was carried out according to General Procedure A with 1,2-epoxyoctane (128 mg, 1 mmol), acetophenone oxime (203 mg, 1.5 mmol), and KOH (168 mg, 3 mmol) in DMF (10 mL). The mixture was stirred at 50 °C for 16 h and worked up as described. The crude product was purified by preparative HPLC (NW50 column, Merck; heptane–EtOAc, 10:0→7:3 over 35 min; 100 mL/min; UV detection at 254 nm) to give **4b**.

Yield: 97 mg (0.368 mmol, 74%); colorless oil; R_f = 0.39 (heptane–EtOAc, 4:1).

IR (neat): 3411, 2954, 2927, 2857, 1444, 1369, 1313, 1036, 927, 912, 901, 758, 691 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.85–0.93 (m, 3 H, H-8), 1.24–1.56 (m, 10 H, H3–H7), 2.26 (s, 3 H, Me), 2.93 (br s, 1 H, OH), 3.94–4.04 (m, 1 H, H-2), 4.08 and 4.22 (ABX, J_{AB} = 11.6 Hz, J_{AX} = 1.2 Hz, J_{BX} = 8.0 Hz, 2 H, H-1), 7.33–7.40 (m, 3 H, Ph-H), 7.58–7.66 (m, 2 H, Ph-H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.7 (CH_3), 14.1 (C-8), 22.6 (C-7), 25.4 (C-4 or C-5), 29.3 (C-4 or C-5), 31.8 (C-6), 33.2 (C-3), 71.4 (C-2), 77.9 (C-1), 126.0 (CH-Ph), 128.4 (CH-Ph), 129.3 (CH-Ph), 136.2 (C_q-Ph), 155.6 (C_q=N).

HRMS (ESI-TOF): *m/z* $[M + H]^+$ calcd for $C_{16}H_{26}NO_2$: 264.1964; found: 264.1965.

(*E*)-Acetophenone *O*-(2-Hydroxy-2-methylbut-3-en-1-yl) Oxime (4c)

The reaction was carried out according to General Procedure A with 2-methyl-2-vinyloxirane (84 mg, 1 mmol), acetophenone oxime (203 mg, 1.5 mmol) and KOH (168 mg, 3 mmol) in DMF (10 mL). The mixture was stirred at 50 °C for 16 h and worked up as described. The crude product was purified by preparative HPLC (NW50 column, Merck; heptane–EtOAc, 10:0→8:2 over 35 min; 100 mL/min; UV detection at 254 nm) to give **4c**.

Yield: 92 mg (0.420 mmol, 84%); colorless oil; R_f = 0.24 (heptane–MTBE, 4:1).

IR (neat): 3425, 2976, 2930, 2873, 1445, 1370, 1307, 1044, 994, 914, 758, 691 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.31 (s, 3 H, H-5), 2.25 (s, 3 H, Me), 3.41 (br s, 1 H, OH), 4.14 (s, 2 H, H-1), 5.14 (dd, *J* = 1.5, 10.7 Hz, 1 H, H-4), 5.37 (dd, *J* = 1.5, 17.1 Hz, 1 H, H-4), 5.96 (dd, *J* = 10.7, 17.1 Hz, 1 H, H-3), 7.32–7.39 (m, 3 H, Ph-H), 7.57–7.65 (m, 2 H, Ph-H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.8 (CH_3), 72.5 (C-2), 77.2 (C-1), 116.3 (C-4), 115.5 (CH-Ar), 126.0 (CH-Ph), 128.4 (CH-Ph), 129.4 (CH-Ph), 136.1 (C_q-Ph), 136.4 (C-3), 155.9 (C_q=N).

HRMS (ESI-TOF): *m/z* $[M + H]^+$ calcd for $C_{13}H_{18}NO_2$: 220.1338; found: 220.1336.

(*S*,*E*)-Acetophenone *O*-(2,3-Dihydroxypropyl) Oxime (4d)

The reaction was carried out according to General Procedure A with (*S*)-glycidol (74 mg, 1 mmol), acetophenone oxime (203 mg, 1.5 mmol) and KOH (168 mg, 3 mmol) in DMF (10 mL). The mixture was stirred at 90 °C for 16 h and worked up as described. The crude product was purified by column chromatography (heptane–EtOAc, 1:1) to give **4d**.

Yield: 97 mg (0.464 mmol, 46%); pale-yellow oil; $[\alpha]_D^{24}$ –12.6 (*c* 0.89, $CHCl_3$); R_f = 0.22 (heptane–EtOAc, 3:7).

IR (neat): 3277, 2927, 2872, 1467, 1441, 1058, 1046, 914, 754, 690 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.24 (s, 3 H, Me), 3.26 (br s, 2 H, 2 × OH), 3.66 and 3.74 (ABX, J_{AB} = 11.6 Hz, J_{AX} = 3.9 Hz, J_{BX} = 5.9 Hz, 2 H, H-3), 4.01–4.12 (m, 1 H, H-2), 4.25 (d, *J* = 5.3 Hz, 2 H, H-1), 7.32–7.39 (m, 3 H, Ph-H), 7.55–7.63 (m, 2 H, Ph-H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.8 (CH_3), 63.6 (C-3), 71.6 (C-2), 74.6 (C-1), 126.0 (CH-Ph), 128.4 (CH-Ph), 129.3 (CH-Ph), 136.0 (C_q-Ph), 156.0 (C_q=N).

HRMS (ESI-TOF): *m/z* $[M + H]^+$ calcd for $C_{11}H_{16}NO_3$: 210.1130; found: 210.1133.

(*E*)-Acetophenone *O*-Oxiran-2-ylmethyl Oxime (4e)

The reaction was carried out according to General Procedure A with epichlorohydrin (234 μL, 3 mmol), acetophenone oxime (405 mg, 3 mmol) and KOH (336 mg, 6 mmol) in DMF (20 mL). The mixture was stirred at r.t. for 16 h and worked up as described. The crude product was purified by column chromatography (heptane–EtOAc, 4:1) to give **4e**.

Yield: 420 mg (2.2 mmol, 73%); colorless oil; R_f = 0.48 (heptane–EtOAc, 7:3).

IR (neat): 3056, 3001, 2926, 2876, 1497, 1445, 1370, 1311, 1038, 992, 909, 885, 759, 693 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.28 (s, 3 H, Me), 2.69 (dd, J = 2.8, 5.1 Hz, 1 H, H-3), 2.87 (d, J = 4.5 Hz, 1 H, H-3), 3.30–3.37 (m, 1 H, H-2), 4.16 and 4.42 (ABX, J_{AB} = 12.2 Hz, J_{AX} = 3.4 Hz, J_{BX} = 6.0 Hz, 2 H, H-1), 7.33–7.41 (m, 3 H, Ph-H), 7.61–7.69 (m, 2 H, Ph-H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.7 (CH_3), 44.8 (C-3), 50.2 (C-2), 74.8 (C-1), 126.0 (CH-Ph), 128.3 (CH-Ph), 129.1 (CH-Ph), 136.3 (C_q-Ph), 155.3 (C_q=N).

HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{11}H_{14}NO_2$: 192.1025; found: 192.1034.

(1*E*,1′*E*)-Acetophenone *O*-(2-Hydroxy-3-{[(*E*)-(1-phenylethylidene)amino]oxy}propyl) Oxime (4f)

The reaction was carried out according to General Procedure A with **4e** (100 mg, 0.52 mmol), acetophenone oxime (106.1 mg, 0.78 mmol) and KOH (88 mg, 1.6 mmol) in DMF (5 mL). The mixture was stirred at r.t. for 16 h and worked up as described. The crude product was purified by column chromatography (heptane–EtOAc, 7:3) to give **4f**.

Yield: 147.5 mg (0.45 mmol, 86%); colorless oil; R_f = 0.63 (heptane–EtOAc, 3:2).

IR (neat): 3423, 3059, 2931, 2877, 1497, 1444, 1369, 1311, 1042, 998, 935, 919, 889, 759 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.28 (s, 6 H, Me), 4.26–4.42 (m, 5 H, H-1, H-2), 7.32–7.41 (m, 6 H, Ph-H), 7.59–7.69 (m, 4 H, Ph-H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.8 (CH_3), 70.8 (C-2), 74.8 (C-1), 126.0 (CH-Ph), 128.4 (CH-Ph), 129.3 (CH-Ph), 136.2 (C_q-Ph), 155.6 (C_q=N).

HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{19}H_{23}N_2O_3$: 327.1709; found: 327.1714.

(*E*)-Acetophenone *O*-[(*trans*)-2-Hydroxycyclopentyl] Oxime (4h)

The reaction was carried out according to General Procedure A with cyclopentene oxide (50 mg, 0.6 mmol), acetophenone oxime (121 mg, 0.9 mmol) and KOH (100 mg, 1.8 mmol) in DMF (6 mL). The mixture was stirred at 90 °C for 16 h and worked up as described. The crude product was purified by column chromatography (heptane–EtOAc, 80:20) to give **4h**.

Yield: 96 mg (0.44 mmol, 73%); colorless oil; R_f = 0.31 (heptane–EtOAc, 4:1).

IR (neat): 3358, 3056, 2961, 1496, 1445, 1369, 1316, 1083, 1037, 995, 973, 914, 760, 693 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.56–1.83 (m, 4 H, H-3, H-4, H-5), 1.93–2.18 (m, 2 H, H-3, H-5), 2.21 (s, 3 H, Me), 2.87 (br s, 1 H, OH), 4.28 (td, J = 4.1, 6.2 Hz, 1 H, H-2), 4.53 (ddd, J = 3.8, 4.8, 7.3 Hz, 1 H, H-1), 7.31–7.38 (m, 3 H, Ph-H), 7.57–7.65 (m, 2 H, Ph-H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.7 (CH_3), 20.8 (C-4), 28.5 (C-5), 31.6 (C-3), 77.8 (C-2), 89.7 (C-1), 126.0 (CH-Ph), 128.3 (CH-Ph), 129.1 (CH-Ph), 136.5 (C_q-Ph), 155.1 (C_q=N).

HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{13}H_{18}NO_2$: 220.1338; found: 220.1339.

(*E*)-Acetophenone *O*-[(*trans*)-2-Hydroxycyclohexyl] Oxime (4i)

The reaction was carried out according to General Procedure A with cyclohexene oxide (46.1 mg, 0.5 mmol), acetophenone oxime (101.3 mg, 0.75 mmol) and KOH (84 mg, 1.5 mmol) in DMF (5 mL). The mixture was stirred at r.t. for 16 h and worked up as described. The crude product was purified by preparative HPLC (Eurospher 100–5 Si column, Knauer; 250 × 20 mm; heptane–EtOAc, 10:0→7:3 over 40 min; 12 mL/min; UV detection at 254 nm) to give **4i**.

Yield: 104.4 mg (0.45 mmol, 89%); colorless oil; R_f = 0.32 (heptane–EtOAc, 7:3).

IR (neat): 3429, 2933, 2862, 1497, 1447, 1371, 1074, 1039, 1007, 998, 936, 920, 760, 693 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.22–1.43 (m, 4 H, H-3, H-4, H-5, H-6), 1.68–1.80 (m, 2 H, H-3, H-4), 2.02–2.15 (m, 2 H, H-6, H-5), 2.27 (s, 3 H, Me), 3.69–3.76 (m, 1 H, H-2), 3.97–4.07 (m, 1 H, H-1), 7.32–7.41 (m, 3 H, Ph-H), 7.58–7.66 (m, 2 H, Ph-H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.7 (CH_3), 23.7 (C-3 or C-4), 24.2 (C-3 or C-4), 29.6 (C-5), 32.6 (C-6), 74.6 (C-2), 85.8 (C-1), 126.0 (CH-Ph), 128.4 (CH-Ph), 129.2 (CH-Ph), 136.2 (C_q-Ph), 155.2 (C_q=N).

HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{14}H_{20}NO_2$: 234.1494; found: 234.1487.

Compound 4j

The reaction was carried out according to General Procedure A with NAP-protected Cerny's epoxide[6a] (142 mg, 0.5 mmol), acetophenone oxime (101 mg, 0.75 mmol) and KOH (84 mg, 1.5 mmol) in DMF (5 mL). The mixture was stirred at 90 °C for 16 h and worked up as described. The crude product was purified by column chromatography (heptane–EtOAc, 8:2→7:3) to give **4j**.

Yield: 187 mg (0.446 mmol, 89%); pale-yellow foam; $[\alpha]_D^{24}$ –7.6 (c 1.09, $CHCl_3$); R_f = 0.47 (heptane–EtOAc, 1:1).

IR (neat): 3411, 2925, 2905, 1445, 1359, 1318, 1304, 1039, 972, 918, 905, 886, 760, 690 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.23 (s, 3 H, Me), 3.23 (br s, 1 H, OH), 3.43 (s, 1 H, H-2), 3.64 (dd, J = 6.4 Hz, 1 H, H-6), 3.84 (d, J = 7.3 Hz, 1 H, H-6), 4.07–4.14 (m, 2 H, H-3, H-4), 4.60 (d, J = 4.9 Hz, 1 H, H-5), 4.77 and 4.84 (AB, J_{AB} = 12.2 Hz, 2 H, CH_2-NAP), 5.63 (s, 1 H, H-1), 7.28–7.36 (m, 3 H, ArH), 7.39–7.51 (m, 3 H, ArH), 7.56–7.63 (m, 2 H, ArH), 7.73–7.82 (m, 4 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.0 (CH_3), 66.5 (C-6), 71.0 (C-3), 71.8 (CH_2-NAP), 75.6 (C-5), 79.9 (C-2), 83.3 (C-4), 100.6 (C-1), 125.7 (CH-Ar), 125.9 (CH-Ar), 126.1 (CH-Ar), 126.1 (CH-Ar), 126.5 (CH-Ar), 127.6 (CH-Ar), 127.8 (CH-Ar), 128.2 (CH-Ar), 128.4 (CH-Ar), 129.4 (CH-Ar), 132.9 (C_q-NAP), 133.1 (C_q-NAP), 135.3 (C_q-NAP), 136.0 (C_q-Ph), 156.8 (C_q=N).

HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{25}H_{25}NNaO_5$: 442.1630; found: 442.1631.

(1*R*,2*S*,3*R*,5*S*)-2-[(Benzyloxy)methyl]-3-(naphthalen-2-ylmethoxy)-6-oxabicyclo[3.1.0]hexane (1a)

To a solution of (1*R*,2*S*,3*R*,5*S*)-2-[(benzyloxy)methyl]-6-oxabicyclo[3.1.0]hexan-3-ol[6a] (205 mg, 0.931 mmol, 1 equiv) in anhydrous DMF (10 mL) were added NaH (60% in mineral oil, 67 mg, 1.68 mmol, 1.8 equiv) and 2-bromomethylnaphthalene (309 mg, 1.40 mmol, 1.5 equiv) and the mixture was stirred at r.t. for 4 h. After addition of crushed ice, the mixture was extracted with MTBE (3 × 10 mL). The combined organic layers were washed with brine (20 mL), dried over Na_2SO_4, and concentrated in vacuo. Purification by column chromatography (heptane–EtOAc, 7:3) gave **1a**.

Yield: 322 mg (0.893 mmol, 96%); pale-yellow oil; $[\alpha]_D^{24}$ –48.0 (c 0.89, $CHCl_3$); R_f = 0.43 (heptane–EtOAc, 3:2).

IR (neat): 2925, 2856, 1362, 1121, 1084, 1027, 839, 815, 737, 697 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.04 (ddd, J = 0.9, 7.6, 15.3 Hz, 1 H, H-5), 2.18 (d, J = 15.3 Hz, 1 H, H-5), 2.65 (t, J = 5.8 Hz, 1 H, H-2), 3.37 and 3.40 (ABX, J_{AB} = 9.5 Hz, J_{AX} = 6.1 Hz, J_{BX} = 6.1 Hz, 2 H, CH_2-OBn), 3.46 (d, J = 2.1 Hz, 1 H, H-4), 3.54 (br s, 1 H, H-3), 3.93 (d, J = 7.6 Hz, 1 H, H-1), 4.45 (s, 2 H, CH_2-Bn), 4.61 and 4.68 (AB, J_{AB} = 12.8 Hz, 2 H, CH_2-NAP), 7.20–7.33 (m, 5 H, ArH), 7.40–7.50 (m, 3 H, ArH), 7.69–7.84 (m, 4 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 34.8 (C-5), 47.4 (C-2), 57.9 (C-3), 59.7 (C-4), 69.2 (CH_2-OBn), 70.9 (CH_2-NAP), 73.2 (CH_2-Bn), 80.9

(C-1), 125.7 (CH-Ar), 125.9 (CH-Ar), 126.0 (CH-Ar), 126.4 (CH-Ar), 127.4 (CH-Ar), 127.6 (CH-Ar), 127.8 (CH-Ar), 128.0 (CH-Ar), 128.3 (CH-Ar), 132.9 (C_q-NAP), 133.2 (C_q-NAP), 135.9 (C_q-NAP), 138.0 (C_q-Bn).

HRMS (ESI-TOF): *m/z* [M + NH_4]$^+$ calcd for $C_{24}H_{28}NO_3$: 378.2069; found: 378.2070.

(*E*)-Acetophenone *O*-{(1*R*,2*R*,3*R*,4*R*)-3-[(Benzyloxy)methyl]-2-hydroxy-4-(naphthalen-2-ylmethoxy)cyclopentyl} Oxime (4k)

The reaction was carried out according to General Procedure A with **1a** (23 mg, 0.064 mmol), acetophenone oxime (13 mg, 0.096 mmol) and KOH (11 mg, 0.192 mmol) in DMF (850 μL). The mixture was stirred at 90 °C for 16 h and worked up as described. The crude product was purified by column chromatography (heptane–MTBE, 4:1) to give **4k**.

Yield: 27 mg (0.054 mmol, 84%); colorless oil; $[\alpha]_D^{24}$ +3.6 (*c* 0.72, $CHCl_3$); R_f = 0.41 (heptane–MTBE, 1:1).

IR (neat): 3441, 3058, 3027, 2924, 2858, 1366, 1065, 1028, 995, 913, 855, 815, 756, 736, 693 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.03–2.15 (m, 1 H, H-5), 2.20 (s, 3 H, Me), 2.23–2.39 (m, 2 H, H-2, H-5), 3.63 and 3.67 (ABX, J_{AB} = 9.3 Hz, J_{AX} = 5.3 Hz, J_{BX} = 5.7 Hz, 2 H, CH_2-OBn), 3.95–4.03 (m, 1 H, H-1), 4.11 (dd, *J* = 6.2, 8.3 Hz, 1 H, H-3), 4.49 and 4.53 (AB, J_{AB} = 12.0 Hz, 2 H, CH_2-Bn), 4.62 and 4.70 (AB, J_{AB} = 12.1 Hz, 2 H, CH_2-NAP), 4.71–4.85 (m, 1 H, H-4), 7.20–7.50 (m, 11 H, ArH), 7.55–7.64 (m, 2 H, ArH), 7.72–7.86 (m, 4 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.8 (CH_3), 34.7 (C-5), 51.7 (C-2), 69.4 (CH_2-OBn), 71.2 (CH_2-NAP), 73.2 (CH_2-Bn), 77.1 (C-1), 78.1 (C-3), 86.9 (C-4), 125.8 (CH-Ar), 126.0 (CH-Ar), 126.0 (CH-Ar), 126.3 (CH-Ar), 127.5 (CH-Ar), 127.6 (CH-Ar), 127.7 (CH-Ar), 127.9 (CH-Ar), 128.1 (CH-Ar), 128.3 (CH-Ar), 128.4 (CH-Ar), 128.4 (CH-Ar), 129.2 (CH-Ar), 132.9 (C_q-NAP), 133.3 (C_q-NAP), 135.9 (C_q-Ph), 136.4 (C_q-NAP), 138.3 (C_q-Bn), 155.4 (C_q=N).

HRMS (ESI-TOF): *m/z* [M + Na]$^+$ calcd for $C_{32}H_{33}NNaO_4$: 518.2307; found: 518.2313.

Synthesis of N-Protected *O*-Alkyl Hydroxylamine; General Procedure B

To a solution of β-hydroxy oxime *O*-ether (1 equiv) in anhydrous MeOH (0.13 M) were added H_2SO_4 (10 equiv) and 2,4-dinitrophenylhydrazine (2 equiv) and the mixture was stirred at r.t. for 16 h. After dilution with MeOH (4 × initial volume), powdered $NaHCO_3$ (20 equiv) was added slowly at 0 °C, followed by protecting reagent (5 equiv). The reaction mixture was stirred for 3 h at r.t. and diluted with EtOAc (2 × volume of MeOH). The organic layer was washed with H_2O (×2), brine, dried over Na_2SO_4 and concentrated in vacuo. Purification by column chromatography with the indicated eluent gave the expected N-protected β-hydroxy *O*-alkyl hydroxylamine.

1-(Aminooxy)-3-(4-methoxyphenoxy)propan-2-ol (5a)

To a solution of **4a** (79 mg, 0.25 mmol, 1 equiv) in anhydrous MeOH (2 mL) were added H_2SO_4 (135 μL, 2.5 mmol, 10 equiv) and 2,4-dinitrophenylhydrazine (99 mg, 0.5 mmol, 2 equiv) and the mixture was stirred at r.t. for 16 h. Powdered $NaHCO_3$ (420 mg, 5 mmol, 20 equiv) was then added slowly and the reaction mixture was diluted with H_2O (20 mL). The aqueous layer was extracted with EtOAc (3 × 15 mL) and the combined organic layers were washed with H_2O (20 mL), brine (20 mL), dried over Na_2SO_4 and concentrated in vacuo. Purification by column chromatography (heptane–EtOAc, 1:1→3:7) gave **5a**.

Yield: 41 mg (0.192 mmol, 77%); pale-yellow amorphous solid; R_f = 0.10 (heptane–EtOAc, 1:4).

IR (neat): 3301, 3249, 2935, 1513, 1240, 1046, 1033, 825 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.76 (s, 3 H, OMe), 3.83 and 3.90 (ABX, J_{AB} = 11.7 Hz, J_{AX} = 3.1 Hz, J_{BX} = 6.5 Hz, 2 H, H-1), 3.96 (d, *J* = 5.6 Hz, 2 H, H-3), 4.22–4.30 (m, 1 H, H-2), 6.79–6.89 (m, 4 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.7 (OCH_3), 69.5 (C-3), 70.0 (C-2), 75.8 (C-1), 114.6 (CH-Ar), 115.5 (CH-Ar), 152.7 (C_q-O), 154.0 (C_q-OMe).

HRMS (ESI-TOF): *m/z* [M + H]$^+$ calcd for $C_{10}H_{16}NO_4$: 214.1079; found: 214.1076.

(9*H*-Fluoren-9-yl)methyl 2-Hydroxy-3-(4-methoxyphenoxy)propoxycarbamate (6a)

The reaction was carried out according to General Procedure B with **4a** (79 mg, 0.25 mmol), 2,4-dinitrophenylhydrazine (99 mg, 0.5 mmol), H_2SO_4 (135 μL, 2.5 mmol) in MeOH (2 mL), and then with $NaHCO_3$ (420 mg, 5 mmol) and FmocCl (323 mg, 1.25 mmol) in MeOH (10 mL). The mixture was worked up as described and the crude product was purified by column chromatography (heptane–EtOAc, 8:2→7:3) to give **6a**.

Yield: 88 mg (0.202 mmol, 81%); pale-yellow amorphous solid; R_f = 0.22 (heptane–EtOAc, 3:2).

IR (neat): 3238, 1707, 1508, 1269, 1230, 1124, 1107, 1042, 822, 755, 737 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.76 (s, 3 H, OMe), 3.91–4.07 (m, 4 H, H-1, H-3), 4.16–4.21 (m, 1 H, H-2), 4.23 (t, *J* = 7.0 Hz, 1 H, CH-Fmoc), 4.52 and 4.56 (ABX, J_{AB} = 10.7 Hz, J_{AX} = 6.7 Hz, J_{BX} = 6.7 Hz, 2 H, CH_2-Fmoc), 6.79–6.87 (m, 4 H, ArH), 7.31 (t, *J* = 7.6 Hz, 2 H, ArH), 7.40 (t, *J* = 7.3 Hz, 2 H, ArH), 7.56 (d, *J* = 7.6 Hz, 2 H, ArH), 7.64 (s, 1 H, NH), 7.76 (d, *J* = 7.3 Hz, 2 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 47.0 (CH-Fmoc), 55.7 (OCH_3), 67.5 (C-2), 67.7 (CH_2-Fmoc), 69.1 (C-3), 78.9 (C-1), 114.7 (CH-Ar), 115.5 (CH-Ar), 120.1 (CH-Ar), 124.9 (CH-Ar), 124.9 (CH-Ar), 127.2 (CH-Ar), 127.9 (CH-Ar), 141.3 (C_q-Fmoc), 143.2 (C_q-Fmoc), 143.3 (C_q-Fmoc), 152.6 (C_q-O), 154.1 (C_q-OMe), 158.6 (C=O).

HRMS (ESI-TOF): *m/z* [M + Na]$^+$ calcd for $C_{25}H_{25}NNaO_6$: 458.1580; found: 458.1573.

Benzyl 2-Hydroxy-3-(4-methoxyphenoxy)propoxycarbamate (7a)

The reaction was carried out according to General Procedure B with **4a** (79 mg, 0.25 mmol), 2,4-dinitrophenylhydrazine (99 mg, 0.5 mmol), H_2SO_4 (135 μL, 2.5 mmol) in MeOH (2 mL), and then with $NaHCO_3$ (420 mg, 5 mmol) and CbzCl (188 μL, 1.25 mmol) in MeOH (10 mL). The mixture was worked up as described and the crude product was purified by column chromatography (heptane–EtOAc, 8:2→7:3) to give **7a**.

Yield: 69 mg (0.199 mmol, 80%); yellow amorphous solid; R_f = 0.24 (heptane–EtOAc, 3:2).

IR (neat): 3406, 3160, 2954, 1724, 1506, 1266, 1232, 1129, 1109, 1041, 823, 739, 696 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.76 (s, 3 H, OMe), 3.92–4.12 (m, 4 H, H-1, H-3), 4.20–4.29 (m, 1 H, H-2), 5.19 (s, 2 H, CH_2-Bn), 6.78–6.87 (m, 4 H, ArH), 7.33–7.40 (m, 5 H, H-Bn), 7.63 (s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.7 (OCH_3), 67.5 (C-2), 68.1 (CH_2-Bn), 69.1 (C-3), 79.0 (C-1), 114.7 (CH-Ar), 115.5 (CH-Ar), 128.4 (CH-Ar), 128.7 (CH-Ar), 135.1 (C_q-Bn), 152.6 (C_q-O), 154.1 (C_q-OMe), 158.7 (C=O).

HRMS (ESI-TOF): *m/z* [M – H]$^-$ calcd for $C_{18}H_{20}NO_6$: 346.1291; found: 346.1306.

Allyl 2-Hydroxy-3-(4-methoxyphenoxy)propoxycarbamate (8a)

The reaction was carried out according to General Procedure B with **4a** (79 mg, 0.25 mmol), 2,4-dinitrophenylhydrazine (99 mg, 0.5 mmol), H_2SO_4 (135 μL, 2.5 mmol) in MeOH (2 mL), and then with $NaHCO_3$ (420 mg, 5 mmol) and AllocCl (133 μL, 1.25 mmol) in

MeOH (10 mL). The mixture was worked up as described and the crude product was purified by column chromatography (heptane–EtOAc, 8:2→7:3) to give **8a**.

Yield: 66 mg (0.222 mmol, 89%); yellow amorphous solid; R_f = 0.18 (heptane–EtOAc, 3:2).

IR (neat): 3351, 3177, 2933, 2913, 1708, 1507, 1267, 1220, 1104, 994, 827, 756 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.76 (s, 3 H, OMe), 3.92–4.12 (m, 4 H, H-1, H-3), 4.21–4.29 (m, 1 H, H-2), 4.64 (t, *J* = 1.3 Hz, 1 H, C*H*$_2$-CH=CH$_2$), 4.66 (t, *J* = 1.3 Hz, 1 H, C*H*$_2$-CH=CH$_2$), 5.23–5.38 (m, 2 H, CH$_2$-CH=C*H*$_2$), 5.83–5.98 (m, 1 H, CH$_2$-C*H*=CH$_2$), 6.78–6.87 (m, 4 H, ArH), 7.89 (s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.7 (OCH_3), 66.8 (*C*H$_2$-CH=CH$_2$), 67.5 (C-2), 69.1 (C-3), 78.8 (C-1), 114.6 (CH-Ar), 115.5 (CH-Ar), 119.0 (CH$_2$-CH=*C*H$_2$), 131.5 (CH$_2$-*C*H=CH$_2$), 152.6 (C$_q$-O), 154.0 (C$_q$-OMe), 158.5 (C=O).

HRMS (ESI-TOF): *m/z* [M + Na]$^+$ calcd for $C_{14}H_{19}NNaO_6$: 320.1110; found: 320.1106.

(9*H*-Fluoren-9-yl)methyl (2-Hydroxyoctyl)oxycarbamate (6b)

The reaction was carried out according to General Procedure B with **4b** (70 mg, 0.266 mmol), 2,4-dinitrophenylhydrazine (105 mg, 0.532 mmol), and H_2SO_4 (143 μL, 2.66 mmol) in MeOH (2 mL), and then with $NaHCO_3$ (447 mg, 5.32 mmol) and FmocCl (344 mg, 1.33 mmol) in MeOH (10 mL). The mixture was worked up as described and the crude product was purified by column chromatography (heptane–EtOAc, 8:2→7:3) to give **6b**.

Yield: 97 mg (0.253 mmol, 95%); pale-rose crystals; R_f = 0.27 (heptane–EtOAc, 7:3).

IR (neat): 3319, 3271, 2954, 2925, 2855, 1698, 1495, 1479, 1465, 1447, 1268, 1127, 755, 736, 725 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.78–0.94 (m, 3 H, H-8), 1.18–1.54 (m, 10 H, H3–H7), 3.62 (dd, *J* = 9.8, 11.3 Hz, 1 H, H-1), 3.75 (br s, 1 H, OH), 3.78–3.85 (m, 2 H, H-1, H-2), 4.22 (t, *J* = 6.7 Hz, 1 H, CH-Fmoc), 4.50 and 4.54 (ABX, J_{AB} = 10.5 Hz, J_{AX} = 6.4 Hz, J_{BX} = 7.1 Hz, 2 H, CH$_2$-Fmoc), 7.30 (t, *J* = 7.3 Hz, 2 H, ArH), 7.40 (t, *J* = 7.3 Hz, 2 H, ArH), 7.55 (d, *J* = 7.3 Hz, 2 H, ArH), 7.67 (s, 1 H, NH), 7.75 (d, *J* = 7.3 Hz, 2 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1 (C-8), 22.6 (C-7), 25.5 (C-4 or C-5), 29.3 (C-4 or C-5), 31.7 (C-6), 32.1 (C-3), 46.9 (CH-Fmoc), 67.6 (CH$_2$-Fmoc), 68.1 (C-2), 81.8 (C-1), 120.0 (CH-Ar), 124.9 (CH-Ar), 124.9 (CH-Ar), 127.1 (CH-Ar), 127.8 (CH-Ar), 141.3 (C$_q$-Fmoc), 143.3 (C$_q$-Fmoc), 143.3 (C$_q$-Fmoc), 158.7 (C=O).

HRMS (ESI-TOF): *m/z* [M + Na]$^+$ calcd for $C_{23}H_{29}NNaO_4$: 406.1994; found: 406.1999.

(9*H*-Fluoren-9-yl)methyl (2-Hydroxy-2-methylbut-3-en-1-yl)oxycarbamate (6c)

The reaction was carried out according to General Procedure B with **4c** (96 mg, 0.438 mmol), 2,4-dinitrophenylhydrazine (173 mg, 0.876 mmol), and H_2SO_4 (235 μL, 4.38 mmol) in MeOH (3 mL), and then with $NaHCO_3$ (736 mg, 8.76 mmol) and FmocCl (567 mg, 2.19 mmol) in MeOH (12 mL). The mixture was worked up as described and the crude product was purified by column chromatography (heptane–EtOAc, 8:2→7:3) to give a mixture of **6c** and Fmoc-protected 2,4-dinitrophenylhydrazine (304 mg) as an orange solid. This mixture was purified by preparative HPLC (NW50 column, Merck; heptane–EtOAc, 10:0→6:4 over 35 min; 100 mL/min; UV detection at 254 nm) to give **6c**.

Yield: 102 mg (0.301 mmol, 69%); pale-yellow oil; R_f = 0.31 (heptane–EtOAc, 3:2).

IR (neat): 3262, 2975, 1716, 1449, 1252, 1115, 757, 737 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.25 (s, 3 H, H-5), 3.10 (br s, 1 H, OH), 3.77 and 3.83 (AB, J_{AB} = 10.5 Hz, 2 H, H-1), 4.21 (t, *J* = 6.6 Hz, 1 H, CH-Fmoc), 4.49 (d, *J* = 6.6 Hz, 2 H, CH$_2$-Fmoc), 5.12 (d, *J* = 10.7 Hz, 1 H, H-4), 5.36 (dd, *J* = 1.1, 17.1 Hz, 1 H, H-4), 5.87 (dd, *J* = 10.7, 17.3 Hz, 1 H, H-3), 7.30 (t, *J* = 7.3 Hz, 2 H, ArH), 7.39 (t, *J* = 7.3 Hz, 2 H, ArH), 7.55 (d, *J* = 7.3 Hz, 2 H, ArH), 7.75 (d, *J* = 7.3 Hz, 2 H, ArH), 7.85 (br s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.4 (C-5), 46.9 (CH-Fmoc), 67.6 (CH$_2$-Fmoc), 72.6 (C-2), 84.4 (C-1), 113.8 (C-4), 120.0 (CH-Ar), 124.9 (CH-Ar), 127.1 (CH-Ar), 127.8 (CH-Ar), 141.3 (C$_q$-Fmoc), 141.6 (C-3), 143.3 (C$_q$-Fmoc), 143.3 (C$_q$-Fmoc), 158.0 (C=O).

HRMS (ESI-TOF): *m/z* [M + Na]$^+$ calcd for $C_{20}H_{21}NNaO_4$: 362.1368; found: 362.1371.

(*S*)-(9*H*-Fluoren-9-yl)methyl 2,3-Dihydroxypropoxycarbamate (6d)

The reaction was carried out according to General Procedure B with **4d** (80 mg, 0.382 mmol), 2,4-dinitrophenylhydrazine (152 mg, 0.765 mmol), and H_2SO_4 (205 μL, 3.82 mmol) in MeOH (3 mL), and then with $NaHCO_3$ (642 mg, 7.64 mmol) and FmocCl (494 mg, 1.91 mmol) in MeOH (15 mL). The mixture was worked up as described and the crude product was purified by column chromatography (heptane–EtOAc, 1:1→0:1) to give **6d**.

Yield: 117 mg (0.355 mmol, 93%); pale-yellow amorphous solid; $[\alpha]_D^{24}$ +7.9 (*c* 1.11, MeOH); R_f = 0.13 (heptane–EtOAc, 3:7).

IR (neat): 3496, 3336, 3149, 2959, 2934, 2905, 2874, 1699, 1510, 1447, 1261, 1118, 1103, 1071, 755, 733 cm^{-1}.

^{1}H NMR (300 MHz, CD_3OD): δ = 3.49–3.63 (m, 2 H, H-3), 3.73–3.91 (m, 3 H, H-1, H-2), 4.14 (t, *J* = 6.6 Hz, 1 H, CH-Fmoc), 4.40 (d, *J* = 6.6 Hz, 2 H, CH$_2$-Fmoc), 7.27 (dt, *J* = 1.1, 7.3 Hz, 2 H, ArH), 7.35 (t, *J* = 7.3 Hz, 2 H, ArH), 7.58 (d, *J* = 7.3 Hz, 2 H, ArH), 7.73 (d, *J* = 7.3 Hz, 2 H, ArH).

^{13}C NMR (75 MHz, CD_3OD): δ = 48.2 (CH-Fmoc), 64.1 (C-3), 68.2 (CH$_2$-Fmoc), 70.6 (C-2), 79.2 (C-1), 120.9 (CH-Ar), 126.0 (CH-Ar), 128.1 (CH-Ar), 128.8 (CH-Ar), 142.5 (C$_q$-Fmoc), 144.9 (C$_q$-Fmoc), 159.8 (C=O).

HRMS (ESI-TOF): *m/z* [M + Na]$^+$ calcd for $C_{18}H_{19}NNaO_5$: 352.1161; found: 352.1157.

Diallyl [(2-Hydroxypropane-1,3-diyl)bis(oxy)]dicarbamate (8f)

The reaction was carried out according to General Procedure B with **4f** (74 mg, 0.227 mmol), 2,4-dinitrophenylhydrazine (90 mg, 0.453 mmol), and H_2SO_4 (122 μL, 2.27 mmol) in MeOH (1.75 mL), and then with $NaHCO_3$ (381 mg, 4.54 mmol) and AllocCl (120 μL, 1.14 mmol) in MeOH (7 mL). The mixture was worked up as described and the crude product was purified by column chromatography (heptane–EtOAc, 4:1→1:1) to give **8f**.

Yield: 40 mg (0.138 mmol, 61%); pale-yellow oil; R_f = 0.19 (heptane–EtOAc, 1:1).

IR (neat): 3262, 2924, 2851, 1714, 1249, 1109, 1042, 992, 930, 768 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.92 and 3.98 (ABX, J_{AB} = 11.3 Hz, J_{AX} = 2.9 Hz, J_{BX} = 7.8 Hz, 4 H, H-1), 4.14–4.20 (m, 1 H, H-2), 4.65 (d, *J* = 5.2 Hz, 4 H, C*H*$_2$-CH=CH$_2$), 5.26 (d, *J* = 10.7 Hz, 2 H, CH$_2$-CH=C*H*$_2$), 5.34 (d, *J* = 17.4 Hz, 2 H, CH$_2$-CH=C*H*$_2$), 5.86–5.97 (m, 2 H, CH$_2$-C*H*=CH$_2$), 7.99 (br s, 2 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 66.7 (*C*H$_2$-CH=CH$_2$), 67.0 (C-2), 77.7 (C-1), 118.9 (CH$_2$-CH=*C*H$_2$), 131.7 (CH$_2$-*C*H=CH$_2$), 158.1 (C=O).

HRMS (ESI-TOF): *m/z* [M + H]$^+$ calcd for $C_{11}H_{18}N_2NaO_7$: 313.1012; found: 313.1004.

(9*H*-Fluoren-9-yl)methyl (2-Hydroxycyclopentyl) Oxycarbamate (6h)

The reaction was carried out according to General Procedure B with **4h** (100 mg, 0.457 mmol), 2,4-dinitrophenylhydrazine (175 mg, 0.914 mmol), and H_2SO_4 (244 μL, 4.57 mmol) in MeOH (3 mL), and then with $NaHCO_3$ (1.47 g, 18.28 mmol) and FmocCl (1.13 g, 5.48 mmol) in MeOH (15 mL). The mixture was worked up as described and the crude product was purified by column chromatography (heptane–EtOAc, 9:1→8:2) to give **6h**.

Yield: 152.8 mg (0.451 mmol, 99%); pale-yellow oil; R_f = 0.13 (heptane–EtOAc, 7:3).

IR (neat): 3270, 2957, 1723, 1450, 1251, 1115, 908, 758, 728 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.49–1.58 (m, 1 H, H-3), 1.59–1.73 (m, 3 H, H-4, H-5), 1.89–2.00 (m, 2 H, H-3, H-5), 2.36 (br s, 1 H, OH), 4.04–4.09 (m, 1 H, H-1), 4.13–4.18 (m, 1 H, H-2), 4.20 (t, *J* = 6.7 Hz, 1 H, CH-Fmoc), 4.50 (d, *J* = 6.7 Hz, 2 H, CH_2-Fmoc), 7.29 (td, *J* = 0.9, 7.6 Hz, 2 H, ArH), 7.38 (t, *J* = 7.3 Hz, 2 H, ArH), 7.55 (br s, 1 H, NH), 7.56 (d, *J* = 7.3 Hz, 2 H, ArH), 7.74 (d, *J* = 7.6 Hz, 2 H, ArH).

^{13}C NMR (75 MHz, CD_3OD): δ = 20.5 (C-4), 27.9 (C-5), 31.7 (C-3), 47.3 (CH-Fmoc), 67.6 (CH_2-Fmoc), 75.8 (C-2), 93.5 (C-1), 120.2 (CH-Ar), 125.1 (CH-Ar), 127.3 (CH-Ar), 128.0 (CH-Ar), 141.5 (C_q-Fmoc), 143.6 (C_q-Fmoc), 158.3 (C=O).

HRMS (ESI-TOF): *m/z* $[M + H]^+$ calcd for $C_{20}H_{22}NO_4$: 340.1549; found: 340.1561.

Allyl [(1*S*,2*S*)-2-Hydroxycyclohexyl]oxycarbamate (8i)

The reaction was carried out according to General Procedure B with **4i** (63 mg, 0.27 mmol), 2,4-dinitrophenylhydrazine (107 mg, 0.54 mmol), and H_2SO_4 (145 μL, 2.70 mmol) in MeOH (2 mL), and then with $NaHCO_3$ (454 mg, 5.40 mmol) and AllocCl (145 μL, 1.35 mmol) in MeOH (8 mL). The mixture was worked up as described and the crude product was purified by column chromatography (heptane–EtOAc, 8:2→6:4) to give an inseparable mixture of **8i** and Alloc-protected 2,4-dinitrophenylhydrazine (117 mg) as an orange solid. This mixture was purified by preparative HPLC (NW50 column, Merck; heptane–EtOAc, 10:0→6:4 over 40 min; 100 mL/min; UV detection at 254 nm) to give **8i**.

Yield: 47 mg (0.218 mmol, 81%); pale-yellow oil; R_f = 0.44 (heptane–EtOAc, 1:1; visualized by $KMnO_4$ only).

IR (neat): 3223, 2938, 2863, 1718, 1453, 1256, 1111, 1084, 993, 920, 770 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.13–1.51 (m, 4 H, CH_2-cyclohexane), 1.64–1.84 (m, 2 H, CH_2-cyclohexane), 1.92–2.13 (m, 2 H, CH_2-cyclohexane), 3.47–3.62 (m, 2 H, H-1, H-2), 4.50 (br s, 1 H, OH), 4.65 (d, *J* = 5.5 Hz, 2 H, CH_2-CH=CH_2), 5.27 (d, *J* = 10.4 Hz, 1 H, CH_2-CH=C*H*$_2$), 5.34 (d, *J* = 17.1 Hz, 1 H, CH_2-CH=C*H*$_2$), 5.87–5.97 (m, 1 H, CH_2-C*H*=CH_2), 7.86 (br s, 2 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.7, 24.3 (C-4, C-5), 28.8, 32.3 (C-3, C-6), 66.7 (*C*H$_2$-CH=CH_2), 71.0 (C-2), 90.4 (C-1), 118.8 (CH_2-CH=*C*H$_2$), 131.6 (CH_2-*C*H=CH_2), 158.8 (C=O).

HRMS (ESI-TOF): *m/z* $[M + H]^+$ calcd for $C_{10}H_{18}NO_4$: 216.1236; found: 216.1219.

(1*R*,2*R*,3*S*,4*R*,5*R*)-4-(Aminooxy)-2-(naphthalen-2-ylmethoxy)-6,8-dioxabicyclo[3.2.1]octan-3-ol (5j)

To a solution of **4j** (100 mg, 0.238 mmol, 1 equiv) in anhydrous MeOH (2 mL) and THF (100 μL) were added H_2SO_4 (128 μL, 2.38 mmol, 10 equiv) and 2,4-dinitrophenylhydrazine (94 mg, 0.477 mmol, 2 equiv) and the mixture was stirred at r.t. for 16 h. 2,4-Dinitrophenylhydrazine (47 mg, 0.238 mmol, 1 equiv) was then added to complete the reaction and the mixture was stirred for 1 h before being neutralized with powdered $NaHCO_3$ (400 mg, 4.76 mmol, 20 equiv). After addition of H_2O (20 mL), the aqueous layer was extracted with EtOAc (3 × 15 mL) and the combined organic layers were washed with H_2O (20 mL), brine (20 mL), dried over Na_2SO_4, and concentrated in vacuo. Purification by column chromatography (heptane–EtOAc, 1:1→3:7) gave **5j**.

Yield: 57 mg (0.180 mmol, 76%); pale-yellow oil; $[\alpha]_D^{24}$ –22.4 (*c* 0.86, MeOH); R_f = 0.15 (heptane–EtOAc, 3:7).

IR (neat): 3524, 3327, 2912, 1102, 1029, 1016, 896, 860, 813 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.39 (d, *J* = 3.4 Hz, 1 H, H-4), 3.49 (d, *J* = 3.4 Hz, 1 H, H-2), 3.64 (dd, *J* = 5.5, 7.0 Hz, 1 H, H-6), 3.80 (d, *J* = 7.0 Hz, 1 H, H-6), 3.95 (t, *J* = 3.7 Hz, 1 H, H-3), 4.57 (d, *J* = 5.5 Hz, 1 H, H-5), 4.83 and 4.91 (AB, J_{AB} = 12.2 Hz, 2 H, CH_2-NAP), 5.52 (s, 1 H, H-1), 7.44–7.55 (m, 3 H, ArH), 7.79–7.88 (m, 4 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 66.5 (C-6), 70.7 (C-3), 72.0 (CH_2-NAP), 75.5 (C-5), 79.6 (C-4), 84.0 (C-2), 100.1 (C-1), 125.8 (CH-Ar), 126.0 (CH-Ar), 126.2 (CH-Ar), 126.8 (CH-Ar), 127.7 (CH-Ar), 127.9 (CH-Ar), 128.4 (CH-Ar), 133.0 (C_q-NAP), 133.2 (C_q-NAP), 135.3 (C_q-NAP).

HRMS (ESI-TOF): *m/z* $[M + H]^+$ calcd for $C_{17}H_{20}NO_5$: 318.1341; found: 318.1350.

Fluorenylmethyl {(1*R*,2*R*,3*S*,4*R*,5*R*)-3-Hydroxy-2-(naphthalen-2-ylmethoxy)-6,8-dioxabicyclo[3.2.1]octan-4-yl}oxycarbamate (6j)

The reaction was carried out according to General Procedure B with **4j** (100 mg, 0.238 mmol), 2,4-dinitrophenylhydrazine (94 mg, 0.477 mmol), and H_2SO_4 (128 μL, 2.38 mmol) in MeOH (2 mL). THF (100 μL) was added to improve the solubility of the starting material. After 16 h at r.t., 2,4-dinitrophenylhydrazine (47 mg, 0.238 mmol, 1 equiv) was added to complete the reaction and the mixture was stirred for 2 h before being diluted with MeOH (8 mL). $NaHCO_3$ (400 mg, 4.76 mmol) and FmocCl (308 mg, 1.19 mmol) were added and the reaction mixture was stirred at r.t. for 4 h. Addition of $NaHCO_3$ (200 mg, 2.38 mmol) and FmocCl (154 mg, 0.595 mmol) were necessary to complete the reaction. The mixture was then stirred overnight and worked up as described. Purification by column chromatography (heptane–EtOAc, 4:1→3:2) afforded **6j**.

Yield: 98 mg (0.182 mmol, 76%); pale-yellow amorphous solid; $[\alpha]_D^{24}$ –2.6 (*c* 0.94, $CHCl_3$); R_f = 0.21 (heptane–EtOAc, 1:1).

IR (neat): 3264, 1725, 1450, 1249, 1102, 1073, 1009, 757, 739 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.36 (dd, *J* = 0.8, 4.5 Hz, 1 H, H-4), 3.56–3.63 (m, 2 H, H-2, H-6), 3.74 (d, *J* = 7.5 Hz, 1 H, H-6), 3.95 (t, *J* = 4.5 Hz, 1 H, H-3), 4.18 (t, *J* = 6.6 Hz, 1 H, CH-Fmoc), 4.42–4.56 (m, 3 H, H-5, CH_2-Fmoc), 4.76 and 4.87 (AB, J_{AB} = 12.4 Hz, 2 H, CH_2-NAP), 5.55 (s, 1 H, H-1), 7.22–7.57 (m, 9 H, ArH), 7.68–7.84 (m, 6 H, ArH), 7.91 (s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 46.9 (CH-Fmoc), 66.5 (C-6), 67.7 (CH_2-Fmoc), 69.4 (C-3), 72.0 (CH_2-NAP), 75.7 (C-5), 79.4 (C-4), 86.4 (C-2), 100.1 (C-1), 120.0 (CH-Ar), 124.9 (CH-Ar), 125.8 (CH-Ar), 126.0 (CH-Ar), 126.2 (CH-Ar), 126.8 (CH-Ar), 127.2 (CH-Ar), 127.7 (CH-Ar), 127.9 (CH-Ar), 128.3 (CH-Ar), 133.0 (C_q-NAP), 133.2 (C_q-NAP), 135.1 (C_q-NAP), 141.3 (C_q-Fmoc), 143.2 (C_q-Fmoc), 143.3 (C_q-Fmoc), 158.3 (C=O).

HRMS (ESI-TOF): *m/z* $[M+NH_4]^+$ calcd for $C_{32}H_{33}N_2O_7$: 557.2288; found: 557.2264.

Benzyl {(1*R*,2*R*,3*S*,4*R*,5*R*)-3-Hydroxy-2-(naphthalen-2-ylmethoxy)-6,8-dioxabicyclo[3.2.1]octan-4-yl}oxycarbamate (7j)

The reaction was carried out according to General Procedure B with **4j** (100 mg, 0.238 mmol), 2,4-dinitrophenylhydrazine (141 mg, 0.714 mmol, 3 equiv), and H_2SO_4 (128 μL, 2.38 mmol) in MeOH (2 mL) and THF (100 μL, added to improve the solubility of the starting material) and then with $NaHCO_3$ (400 mg, 4.76 mmol) and CbzCl (179 μL, 1.19 mmol) in MeOH (8 mL). The mixture was worked up as described and the crude product was purified by column chromatography (heptane–EtOAc, 8:2→6:4) to give **7j**.

Yield: 95 mg (0.210 mmol, 88%); pale-yellow oil; $[\alpha]_D^{24}$ –0.3 (*c* 1.02, $CHCl_3$); R_f = 0.15 (heptane–EtOAc, 3:2).

IR (neat): 3384, 3209, 1721, 1511, 1269, 1116, 1101, 1076, 1011, 993, 973, 877, 826, 751, 735 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.36 (dd, J = 0.8, 4.5 Hz, 1 H, H-4), 3.57 (dd, J = 5.7, 7.5 Hz, 1 H, H-6), 3.66–3.75 (m, 2 H, H-2, H-6), 3.99 (d, J = 4.7 Hz, 1 H, H-3), 4.51 (d, J = 5.3 Hz, 1 H, H-5), 4.75 and 4.87 (AB, J_{AB} = 12.3 Hz, 2 H, CH_2-NAP), 5.10 and 5.11 (AB, J_{AB} = 12.2 Hz, 2 H, CH_2-Cbz), 5.60 (s, 1 H, H-1), 7.26–7.31 (m, 5 H, ArH), 7.41–7.49 (m, 3 H, ArH), 7.74–7.82 (m, 6 H, ArH), 8.13 (s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 66.4 (C-6), 67.9 (CH_2-Cbz), 69.4 (C-3), 71.9 (CH_2-NAP), 75.6 (C-5), 79.5 (C-4), 86.6 (C-2), 100.1 (C-1), 125.7 (CH-Ar), 126.0 (CH-Ar), 126.1 (CH-Ar), 126.7 (CH-Ar), 127.6 (CH-Ar), 127.8 (CH-Ar), 128.2 (CH-Ar), 128.5 (CH-Ar), 128.5 (CH-Ar), 133.0 (C_q-NAP), 133.1 (C_q-NAP), 135.1 (C_q-NAP), 135.2 (C_q-Cbz), 158.3 (C=O).

HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{25}H_{25}NNaO_7$: 474.1529; found: 474.1534.

Allyl {(1*R*,2*R*,3*S*,4*R*,5*R*)-3-Hydroxy-2-(naphthalen-2-ylmethoxy)-6,8-dioxabicyclo[3.2.1]octan-4-yl}oxycarbamate (8j)

The reaction was carried out according to General Procedure B with **4j** (100 mg, 0.238 mmol), 2,4-dinitrophenylhydrazine (141 mg, 0.714 mmol, 3 equiv), and H_2SO_4 (128 μL, 2.38 mmol) in MeOH (2 mL) and THF (100 μL, added to improve the solubility of the starting material) and then, with $NaHCO_3$ (400 mg, 4.76 mmol) and AllocCl (126 μL, 1.19 mmol) in MeOH (8 mL). The mixture was worked up as described and the crude product was purified by column chromatography (heptane–EtOAc, 8:2→6:4) to give **8j**.

Yield: 71 mg (0.177 mmol, 74%); pale-yellow solid; $[\alpha]_D^{24}$ –1.1 (c 0.92, $CHCl_3$); R_f = 0.15 (heptane–EtOAc, 3:2).

IR (neat): 3381, 3217, 1714, 1507, 1258, 1099, 1076, 996, 819, 749 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.38 (d, J = 4.5 Hz, 1 H, H-4), 3.60 (dd, J = 5.7, 7.5 Hz, 1 H, H-6), 3.67–3.77 (m, 2 H, H-2, H-6), 4.00 (t, J = 4.7 Hz, 1 H, H-3), 4.54 (d, J = 5.3 Hz, 1 H, H-5), 4.59 (d, J = 5.7 Hz, 2 H, CH_2-CH=CH_2), 4.78 and 4.90 (AB, J_{AB} = 12.4 Hz, 2 H, CH_2-NAP), 5.18–5.34 (m, 2 H, CH_2-CH=CH_2), 5.63 (s, 1 H, H-1), 5.79–5.94 (m, 1 H, CH_2-CH=CH_2), 7.42–7.51 (m, 3 H, ArH), 7.75–7.84 (m, 4 H, ArH), 8.18 (s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 66.5 (C-6), 66.7 (CH_2-CH=CH_2), 69.4 (C-3), 71.9 (CH_2-NAP), 75.7 (C-5), 79.5 (C-4), 86.6 (C-2), 100.1 (C-1), 118.8 (CH_2-CH=CH_2), 125.8 (CH-Ar), 126.0 (CH-Ar), 126.1 (CH-Ar), 126.7 (CH-Ar), 127.6 (CH-Ar), 127.8 (CH-Ar), 128.3 (CH-Ar), 131.5 (CH_2-CH=CH_2), 133.0 (C_q-NAP), 133.1 (C_q-NAP), 135.2 (C_q-NAP), 158.2 (C=O).

HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{21}H_{23}NNaO_7$: 424.1372; found: 424.1355.

(9*H*-Fluoren-9-yl)methyl {(1*R*,2*R*,3*R*,4*R*)-3-[(Benzyloxy)methyl]-2-hydroxy-4-(naphthalen-2-ylmethoxy)cyclopentyl}oxycarbamate (2a)

The reaction was carried out according to General Procedure B with **4k** (37 mg, 0.075 mmol), 2,4-dinitrophenylhydrazine (30 mg, 0.150 mmol), and H_2SO_4 (40 μL, 0.750 mmol) in MeOH (600 μL), and then with $NaHCO_3$ (126 mg, 1.5 mmol) and FmocCl (97 mg, 0.375 mmol) in MeOH (2.5 mL). The mixture was worked up as described and the crude product was purified by column chromatography (heptane–EtOAc, 8:2→6:4) to give **2a**.

Yield: 40 mg (0.065 mmol, 87%); pale-yellow foam; $[\alpha]_D^{24}$ –36.6 (c 1.63, $CHCl_3$); R_f = 0.12 (heptane–EtOAc, 3:2).

IR (neat): 3256, 3061, 2887, 2863, 1723, 1451, 1250, 1114, 1096, 1074, 755, 741 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.90–2.04 (m, 1 H, H-5), 2.07–2.30 (m, 2 H, H-2, H-5), 3.18 (br s, 1 H, OH), 3.56 and 3.63 (ABX, J_{AB} = 9.3 Hz, J_{AX} = 5.2 Hz, J_{BX} = 6.2 Hz, 2 H, CH_2-OBn), 3.80–3.88 (m, 1 H, H-1), 3.97 (dd, J = 6.4, 8.3 Hz, 1 H, H-3), 4.20 (t, J = 6.8 Hz, 1 H, CH-Fmoc), 4.34 (dt, J = 6.3, 7.8 Hz, 1 H, H-4), 4.46 and 4.50 (AB, J_{AB} = 11.9 Hz, 2 H, CH_2-Bn), 4.47 (s, 2 H, CH_2-Fmoc), 4.56 and 4.63 (AB, J_{AB} = 12.1 Hz, 2 H, CH_2-NAP), 7.20–7.50 (m, 12 H, ArH), 7.52–7.58 (m, 2 H, ArH), 7.59 (s, 1 H, NH), 7.69–7.84 (m, 4 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 33.6 (C-5), 46.9 (CH-Fmoc), 51.1 (C-2), 67.5 (CH_2-Fmoc), 69.7 (CH_2-OBn), 71.2 (CH_2-NAP), 73.2 (C-3), 76.3 (CH_2-Bn), 76.5 (C-1), 90.4 (C-4), 120.0 (CH-Ar), 125.0 (CH-Ar), 125.7 (CH-Ar), 125.8 (CH-Ar), 126.1 (CH-Ar), 126.4 (CH-Ar), 127.1 (CH-Ar), 127.6 (CH-Ar), 127.6 (CH-Ar), 127.6 (CH-Ar), 127.8 (CH-Ar), 128.1 (CH-Ar), 128.4 (CH-Ar), 132.9 (C_q-NAP), 133.2 (C_q-NAP), 135.6 (C_q-NAP), 138.1 (C_q-Bn), 141.3 (C_q-Fmoc), 143.3 (C_q-Fmoc), 143.4 (C_q-Fmoc), 158.1 (C=O).

HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{39}H_{37}NNaO_6$: 638.2519; found: 638.2529.

Acknowledgment

A.F. and G.M. thank the ICSN for financial support.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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