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3- and 4-Uloses Derived from *N*-Acetyl-D-glucosamine: A Unique Pair of Complementary Organocatalysts for Asymmetric Epoxidation of Alkenes

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Dedicated to Professor Waldemar Adam on the occasion of his 75th birthday.

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Abstract: The 4-ulose and the 3-ulose, both derived in two steps from the α-methyl glycoside of *N*-acetyl-D-glucosamine (GlcNAc), act as organocatalysts in the asymmetric epoxidation of alkenes, with unprecedented complementary enantioselectivity. The best results are found with α,β-unsaturated esters as substrates, with enantiomeric ratios up to 90:10 and 11:89, respectively.

Keywords: asymmetric epoxidation; complementary enantioselection; *N*-acetyl-glucosamine; organocatalysis; uloses

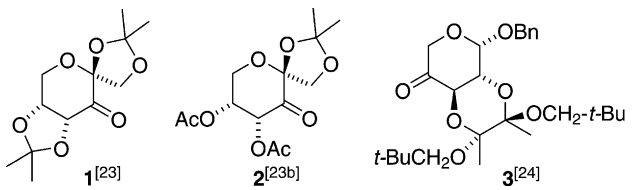
Chiral epoxides are important building blocks for the synthesis of enantiomerically pure complex structures, in particular biologically active compounds. Catalytic enantioselective epoxidation, based on transition metal complexes, is well known.[1] Thus, allylic alcohols can be epoxidized in excellent enantioselectivity and yield with the titanium complexes introduced by Sharpless et al.,[2] Katsuki et al.,[3] and Jacobsen et al.[4] found very efficient catalysts for the epoxidation of unfunctionalized *cis*-alkenes using manganese salen systems.[5a,6]

Highly reactive oxo-metal (M=O) intermediates based on chiral, catalytically active metalloporphyrins like those of Fe, Ru, Mn etc. are also good agents for the asymmetric epoxidation of styrene derivatives and non-conjugated terminal alkenes.[7] For α,β-unsaturated ketones lanthanum- or ytterbium-BINOL systems with hydroperoxides as oxidants gave excellent results, as shown by Shibasaki[7] and others.[8,9b–d] This is paralleled by Enders' stoichiometric zinc-mediated asymmetric epoxidations of enones.[9a]

As for the metal-free nucleophilic oxygen transfer to electron-deficient alkenes like α,β-unsaturated esters, amides, or ketones, the Weitz–Scheffer epoxidation with alkaline hydrogen peroxide[10] has seen formidable extensions to catalytic asymmetric versions. The Julia–Colonna epoxidation employs optically active polyleucine derivatives as catalysts in a bi- or tri-phasic medium with urea-hydrogen peroxide or hydrogen peroxide under basic conditions, each leading to excellent yields (and *ee*s).[11,12]

A recent organocatalytic method to epoxidize α,β-unsaturated aldehydes using chiral amines such as proline derivatives was published by Jørgensen et al.[13] Also, iminium salts have been used as organocatalysts for asymmetric epoxidation.[14,15,16]

Concerning the metal-free, organocatalytic epoxidations of alkenes and α,β-unsaturated carbonyl compounds, *in situ* generated dioxiranes from optically active ketones have become most important.[15] Pioneering work in this field came from Curci's and Adam's groups[17,18] causing a rush for new optically active ketone catalysts, mostly with C_2 symmetry.[19–22] The most impressive catalysts, however, are the fructose-derived ketones **1** and **2** developed by Shi[16,23] (Scheme 1) and the arabinose-borne complement **3** advanced by Shing et al. (Scheme 1).[24] During the progress of our work described here,[25] Davis et al.



1[23] **2**[23b] **3**[24]

Scheme 1. Organocatalysts from Shi et al. (**1**, **2**) and Shing et al. (**3**) for asymmetric epoxidation of alkenes.

published results on a variety of 3-uloses based on glucosamine for the epoxidation of some arylalkenes.[26]

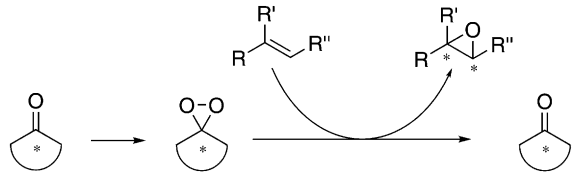
Our entry to this field derived from studies on the synthesis of glycosidase inhibitors.[27] In one of these projects uloses were required as building blocks for pseudo-disaccharides.[28] Some of these uloses were tested concerning potential activity as catalysts for asymmetric epoxidation of alkenes. Actually, the first ketone tested, the readily available GlcNAc derivative **5**, showed surprisingly high enantioselectivity and good yield with regard to cinnamyl acetate.[25] Consequently, we have prepared and tested a series of hexose-derived ketones.[26]

In view of potential applications we have paid particular attention to the short and efficient access of these presumed organocatalysts. The preparation of the 4-ulose **5** was done in 2 steps from the methyl *N*-acetyl-α-D-glucosaminide **4**.[29] Another ketone available from GlcNAc in only 2 steps on a multigram scale is the 3-ulose **6** (Scheme 2). A variety of related uloses has been prepared likewise, but **5** and **6** proved the best candidate of the respective series.

With respect to the temperature, oxidant-buffer system, solvent system, and concentration of substrate, the standard conditions given in Scheme 3 were established, based on Shi's[23b] and Shing's[24] reports. For simple olefins 15 mole percent of ulose and for the less reactive α,β-unsaturated esters 25 mole percent of ulose was used. The reactions were carried out until no more substrate or no change in TLC analyses was observed. In the case of incomplete reaction, the remaining substrate was re-isolated. Using a dioxirane/$EDTA_{aq}$ solvent system the stereoselectivities and yields were slightly higher than those for acetonitrile/$EDTA_{aq}$, but the latter system was chosen for better comparability of the results with Shi's[23b] and Shing's[24] catalysts.

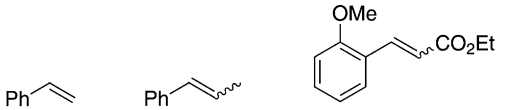
First, the effect of the double bond geometry of alkene substrates was evaluated with the 4-ulose **5** as catalyst. The terminal (Table 1, entry 1) and *Z*-alkenes used (Table 1, entries 3 and 5) showed lower enantioselectivity as compared to *E*-alkenes (Table 1, entries 2 and 4).

Guided by the results given in Table 1, more di- and tri-substituted alkenes and α,β-unsaturated esters with *E*-geometry were screened (Table 2). In order to specify the electronic influence of the substrate, some *para*-substituted stilbene derivatives **12**–**14** were included. Earlier studies had shown the electrophilic character of the oxygen addition to the C=C double bond.[30] Now, for the first time, the electronic influence of the substrate was demonstrated with stilbene derivatives, using the ulose **5** as catalyst. As expected, on going from the *p*-methoxy- to *p*-nitrostilbene a decrease of the reaction rate and/or conversion was found, correlating with the increasing electron withdrawal, as illustrated by the yields (Table 2, entries 1–3). This was also substantiated in a competition ex-



Scheme 3. Asymmetric epoxidation with uloses. *Standard reaction conditions*: 0.15–0.25 equiv. ulose, Bu_4NHSO_4 (0.09 equiv.), oxone/$NaHCO_3$ (5 equiv./15 equiv.), CH_3CN/$EDTA_{aq}$, pH 7–8, 28 °C.

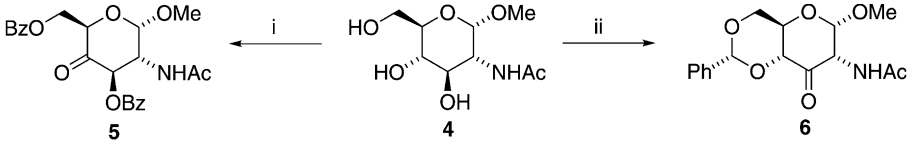
Table 1. Asymmetric epoxidation of terminal and (*Z*/*E*) pairs of olefins catalyzed by the 4-ulose **5**.[a]



7 | *E* = **8**, *Z* = **9** | *E* = **10**, *Z* = **11**

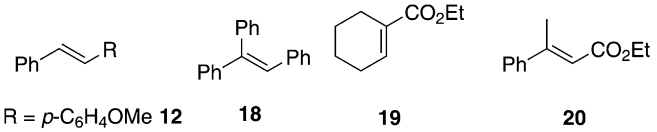
Entry	Substrate	Yield [%]	*er*[b]	Major Enantiomer
1	**7**	73[c]	57:43	(+)-(*S*)
2	**8**	91[c]	75:25	(−)-(*S,S*)
3	**9**	48[c,e]	59:41	(+)-(*1S,2R*)
4	**10**	32[d,e]	84:16	(−)
5	**11**	35[d,e]	56:44	(−)

[a] Reaction performed in CH_3CN/$EDTA_{aq}$, oxone/$NaHCO_3$ (5 equiv./15 equiv.), Bu_4NHSO_4 (0.09 equiv.), 28 °C, 2-26 h. Yields refer to isolated, spectroscopically pure products after chromatographic separation.
[b] Determined by GC on chiral stationary phase.
[c] 15 mol% ulose **5**.
[d] 25 mol% ulose **5**.
[e] Reaction incomplete, remaining substrate re-isolated.



Scheme 2. Synthesis of GlcNAc-derived uloses **5** and **6**. Reaction conditions: i) 1. 2.1 equiv. BzCl, pyridine/CH_2Cl_2, 69% (Lit.[29] 82%); 2. PCC, CH_2Cl_2, 73%; ii) 1. $PhCH(OMe)_2$, *p*TosOH (cat.), DMF, 99%; 2. Dess–Martin periodinane, CH_2Cl_2, 95%.

Table 2. Asymmetric epoxidation of di- and tri-substituted olefins and α,β-unsaturated esters with *E*-geometry catalyzed by the 4-ulose **5**.[a]



R = *p*-C_6H_4OMe **12**; Ph **13**; *p*-$C_6H_4NO_2$ **14**; CH_2OAc **15**; CO_2Et **16**; $CO_2{}^tBu$ **17**

18 **19** **20**

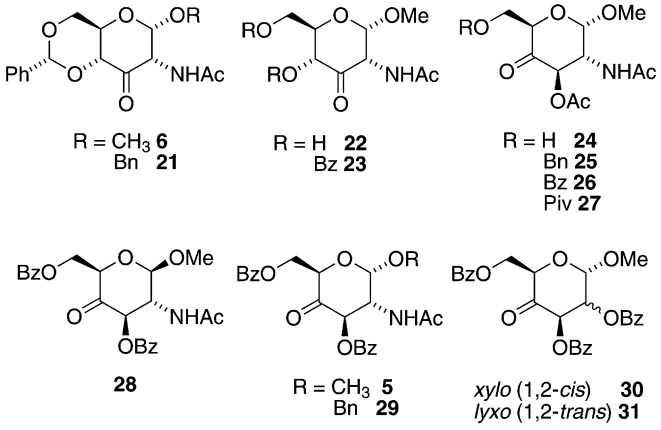
Entry	Substrate	Yield [%]	*er*	Major Enantiomer
1	**12**	92[c]	71:29[b]	(−)-(*S*,*S*)
2	**13**	78[c]	81:19[b]	(−)-(*S*,*S*)
3	**14**	59[c,e]	87:13[b]	(−)-(*S*,*S*)
4	**15**	85[c]	81:19[b]	(−)-(*S*,*S*)
5	**16**	62[d,e]	90:10[f]	(−)-(2*R*,3*S*)
6	**17**	38[d,e]	88:12[f]	(−)-(2*R*,3*S*)
7	**18**	47[c,e]	78:22[b]	(+)-(*S*)
8	**19**	72[d,e]	78:22[f]	(−)
9	**20**	61[d,e]	90:10[f]	(−)-(2*R*,3*S*)

[a] *Reaction conditions:* see Scheme 3, 4–48 h. Yields refer to isolated, spectroscopically pure products after chromatographic separation.
[b] Determined by HPLC on a chiral stationary phase.
[c] 15 mol% ulose **5**.
[d] 25 mol% ulose **5**.
[e] Reaction incomplete, remaining substrate re-isolated.
[f] Determined by GC on a chiral stationary phase.

periment: The epoxidation of a mixture of the electronically "neutral" stilbene **13** and the deactivated *p*-nitrostilbene **14** was carried out under standard conditions. After 2 h the crude reaction product included the starting materials **13** and **14** and the epoxides of *trans*-stilbene **13** and *trans*-*p*-nitrostilbene **14** in a ratio of 89:11 (^{1}H NMR). The stereoselectivity, however, showed the opposite trend to the reaction rate: epoxidation of the deactivated *p*-nitrostilbene **14** was more enantioselective than that of stilbene **13** or that of the activated *p*-methoxy derivative **12** (Table 2, entries 1–3).

In line with this, α,β-unsaturated esters (Table 2, entries 5, 6, 8, and 9) were transformed with distinctly higher selectivity than simple olefins (Table 1, entry 2; Table 2, entries 1, 2, and 4). The lower reactivity of α,β-unsaturated esters was in part compensated for by using a higher proportion (0.25 equiv.) of the ulose catalyst **5**. A steric effect of the substrate's ester group affected mainly the reaction rate (yield), but not the stereoselectivitiy (Table 2, entries 5 and 6). Adding a smaller third substituent like methyl to the C=C double bond as in 3-methylcinnamate **20** practically had no influence on the epoxidation result (*cf.* Table 2, entries 5 and 9).

Table 3. Epoxidation of cinnamyl acetate **15** with different uloses.[a]



R = CH_3 **6**, Bn **21**; R = H **22**, Bz **23**; R = H **24**, Bn **25**, Bz **26**, Piv **27**

28; R = CH_3 **5**, Bn **29**; *xylo* (1,2-*cis*) **30**, *lyxo* (1,2-*trans*) **31**

Entry	Catalyst	Yield [%]	*er*[b]	Major Enantiomer
1	**6**	47[c]	17:83	(+)-(*R*,*R*)
2	**21**	39[c]	40:60	(+)-(*R*,*R*)
3	**22**	70[c]	31:69	(+)-(*R*,*R*)
4	**23**	68[c]	46:54	(+)-(*R*,*R*)
5	**5**	85	81:19	(−)-(*S*,*S*)
6	**24**	41[c]	59:41	(−)-(*S*,*S*)
7	**25**	48[c]	70:30	(−)-(*S*,*S*)
8	**26**	92	76:24	(−)-(*S*,*S*)
9	**27**	69	78:22	(−)-(*S*,*S*)
10	**28**	73[c]	63:37	(−)-(*S*,*S*)
11	**29**	46[c]	70:30	(−)-(*S*,*S*)
12	**30**	48[c]	77:23	(−)-(*S*,*S*)
13	**31**	31[c,d]	59:41	(−)-(*S*,*S*)

[a] *Reaction conditions:* see Scheme 3; 15 mol% catalyst, 2–36 h. Yields refer to isolated, spectroscopically pure products after chromatographic separation.
[b] Determined by GC on a chiral stationary phase.
[c] Reaction incomplete, remaining substrate re-isolated.
[d] A decomposition product of the catalyst **31** was isolated: 75% of methyl 3,6-di-*O*-benzoyl-2-deoxy-α-D-glycero-2-hexene-4-ulose.[25b]

Inspired by the initial results with the 4-ulose **5**,[25a] a variety of related ketones also in the 3-ulose series was prepared from GlcNAc. For the screening of these uloses, cinnamyl acetate **15** was chosen as the substrate; the results of these epoxidations are depicted in Table 3. The highest stereoselectivity (*er* 17:83) was found using the bicyclic 4,6-di-*O*-benzylidene-3-ulose **6** (Table 3, entry 1), in a relatively slow, incomplete reaction with moderate yield (47% after 36 h, 46% of substrate **15** re-isolated).

Surprisingly, the monocyclic *ribo*-3-uloses **22** and **23** showed low or negligible enantioselectivity (Table 3, entries 3 and 4). Unexpectedly, when changing the α-substituent at the anomeric centre from methoxy (**5**) to benzyloxy (**21**), both yield and enantioselectivity decreased (Table 3, entries 1 and 2). A noteworthy feature of the results with the 3-uloses **6**, **21**–**23**, is

that the major enantiomer of the epoxides formed was shown to have the (+)-(*R,R*) configuration (*trans*-epoxides).

As shown above, with the *xylo*-4-ulose **5** tested first,[25a] the opposite enantiomer, the (−)-(*S,S*)-epoxide, was mainly formed. This proved valid throughout with all the other 4-uloses tested, but the best results were recorded with the 4-ulose **5** (Table 3, entries 5–13). Changing the substituents at 3-*O* or 6-*O* did not show a fundamental change in selectivity, but the activity of the catalyst remained superior with *O*-acyl groups (Table 3, entries 5–11). Replacing the amide group in the 2-position of **5** by another benzyloxy group, as in the glucose- or mannose-derived 4-uloses **30** and **31**, had some influence on the enantio-selectivity (*cf.* Table 3, entries 5, 12, and 13): While the *xylo* compound **30** (stereoanalogue to **5**) exhibited still good, albeit slightly lower selectivity, the *lyxo*-epimer **31** was clearly less selective. Anyway, the moderate enantioselectivity of the simple glucose-offsprings is remarkable. The inducing effect of the anomeric configuration was checked also, but could not be determined clearly (cf. Table 3, entries 5, 10, and 11). It was found throughout that the anomers with an α-methoxy group gave better results. It is in general difficult to compare our results with those in the literature because of frequent differences concerning the reaction parameters. In the case of the epoxidation of cinnamyl acetate **15**, however, it is possible to relate our results with those of Shing et al.,[24] since nearly identical reaction conditions were used there. For cinnamyl acetate **15** the best catalyst from Shing's group, the arabinose-derived bicyclic acetal **3**, showed higher enantioselectivity (91:9)[24] than the 4-ulose **5** [(81:19), *cf.* Table 3, entry 5]. Thus, both 4-uloses **3** and **5** as epoxidation catalysts follow the same stereochemical pathway.

Several ulose catalysts were also screened with regard to the epoxidation of α,β-unsaturated esters like ethyl cinnamate **16** (Table 4). We observed that the uloses **5**, **6**, **24** and **26** showed similar effects in the epoxidation as seen above. Generally with the ester **16** higher enantioselectivities and lower yields were found as compared to the results with cinnamyl acetate **15** (Table 3). The excellent properties of Shi's catalyst **2**[23b] under the standard epoxidation conditions used were confirmed (Table 4, entry 5).

Concerning mechanistic and stereochemical rationalizations, detailed discussions of possible transition states of the oxygen atom transfer from the *in situ* generated dioxirane to the C=C double bond have been given in the literature.[16,23,24,30] A stabilizing secondary orbital interaction should be possible only in a spiro, but not in a planar, arrangement. Therefore, in the discussion of epoxidations of the present work, only spiro transition states were considered.

Table 4. Epoxidation of ethyl cinnamate **16** with different uloses and Shi's catalyst **2**.[a]

Entry	Catalyst	Yield [%]	*er*[b]	Major Enantiomer
1	**5**	62[c]	90:10	(−)-(2*R*,3*S*)
2	**6**	30[c]	11:89	(+)-(2*S*,3*R*)
3	**24**	11[c]	75:25	(−)-(2*R*,3*S*)
4	**26**	40[c]	86:14	(−)-(2*R*,3*S*)
5	**2**[23b]	87[c]	3:97	(+)-(2*S*,3*R*)

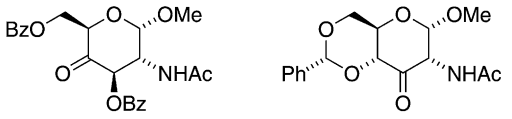
[a] *Reaction conditions:* see Scheme 3; 25 mol% catalyst, 1–2 d. Yields refer to isolated, spectroscopically pure products after chromatographic separation.
[b] Determined by GC on chiral stationary phase.
[c] Reaction incomplete, remaining substrate re-isolated.

On the basis of the enantiomeric ratios, the transition states in the literature were confirmed in principle. In the literature reports,[16,23,24] there always was an axial substituent present near the reactive ketone centre. Because of this fact and based on the enantiomeric ratios found, these authors postulated a preferred transition state due to minimal steric interactions.[16,23,24] In contrast to this, it is much more difficult to derive favoured transition states for the uloses used in this work. Usually all substituents close to the reactive centre of the 3- and 4-uloses are in the sterically less hindered equatorial position. Thus, no obvious steric interaction of the *in situ* generated dioxirane with the substrate is discernible, although differences of free activation enthalpy up to 1.32 kcal mol^{-1} are stated.[31] Comparison of the *in situ* generated dioxiranes from the *xylo*-4-ulose **30** and the *lyxo*-4-ulose **31**, however, suggests that the transfer of the quasi-axial oxygen should dominate. If the quasi-equatorial oxygen atom would be transferred, an effect by the substituents at the remote stereocentre C-2 would seem unlikely.

Furthermore, in this work no significant steric interactions become evident which would suggest a preferred transition state for the enantioselective oxygen atom transfer from the *ribo*-3-uloses such as **6** to an olefin.

The advantages and disadvantages of the uloses developed in this work, as compared to the known organocatalysts, based on monosaccharides, are obvious:[16,23,24,26] The main asset of the most stereoselective uloses from this work (**5** and **6**) is the simple and efficient synthesis in only two steps each (Scheme 4). Furthermore, both are also available on a large scale, with excellent overall yields, and are produced from inexpensive, amply available natural monosaccharides.

On the other hand, the uloses advanced here exhibit lower enantioselectivity and often reactivity, in comparison to the best ketone catalysts disclosed by the groups of Shi[16,23] and Shing.[24] In order to close



5
Σ 49%
2 steps from
α-Me-GlcNAc

6
Σ 92%
2 steps from
α-Me-GlcNAc
(22–48 % 5 steps)[26]

Scheme 4. Overall yields of the catalysts **5** and **6**.

this gap, modifications and optimizations of the uloses presented here seem worthwhile.

Notwithstanding this, the 4-ulose **5** and the 3-ulose **6** described represent a unique pair of complementary asymmetric organocatalysts for the epoxidation of olefins,[32] both being most readily accessible from the same monosaccharide **4**, i.e., *N*-acetyl-D-glucosamine (GlcNAc), in two steps only. In particular, the reactivity of both uloses **5** and **6** is high enough to allow for epoxidation of α,β-unsaturated esters in an enantioselective way.

Experimental Section

Melting points were determined using a Fisher–Johns (type 4017) apparatus and are uncorrected. NMR spectra were recorded using Bruker AC 300 (^{1}H: 300.1 MHz; ^{13}C: 75.5 MHz) and Bruker AC 500 (^{1}H: 500.2 MHz; ^{13}C: 125.8 MHz) spectrometers. The chemical shifts (δ) are given in parts per million (ppm) and coupling constants are given in Hertz. Spectra splitting patterns are designated as singlet (s), doublet (d) and triplet (t). Optical rotations were measured using Perkin–Elmer polarimeter (type 241 MC). IR spectra were recorded using a Bruker IFS 28 spectrometer and intensities of the signals were given as strong (s), medium (m), weak (w) or broad (b). Analytical TLCs were carried out using Merck Kieselgel 60 F_{254} plates and the spots were visualized by heating the plates after treatment with $KMnO_4$ or $Ce(SO_4)_2$ solution or using UV lamp. Preparative column chromatography was performed using silica gel from Macherey–Nagel (size: 40–63 μm).

Methyl 2-Acetamido-3,6-di-*O*-benzoyl-2-deoxy-α-D-*xylo*-hexapyranosid-4-ulose (5)

Methyl 2-acetamido-3,6-di-*O*-benzoyl-2-deoxy-α-D-glucopyranoside (11.150 g; 25.10 mmol) was dissolved in CH_2Cl_2 (200 mL, p.a.) under nitrogen. Then molecular sieves (10 g, 40 pm) and pyridinium chlorochromate (10.00 g, 46.4 mmol) were added at room temperature. After 1 day the mixture was filtered, washed with CH_2Cl_2 (100 mL, p.a.), and evaporated nearly to dryness. The resulting syrupy liquid was first purified by flash column chromatography over silica gel (350 g, column 7 cm × 20 cm; eluent CH_2Cl_2:EtOH 96:4). The crude product was co-evaporated with silica gel (23 g) and purified by column chromatography over silica gel (220 g, column 7 cm × 13 cm; eluent CH_2Cl_2:EtOH 96:4) to afford the ulose **5** as a colourless, analytically pure foam; yield: 8.080 g (18.30 mmol, 73%); $[\alpha]_D^{20}$: 115 (*c* 1.00, CH_2Cl_2); elemental analysis: calcd.: C 62.58, H 5.25, N 3.17; found: C 62.54, H 5.42, N 3.06; IR: ν = 3279, 3073, 1719, 1659, 1583, 1531, 1451, 1267, 1128, 1109, 1090, 1066, 1024, 907, 707, 687 cm^{-1}; ^{1}H NMR (500.2 MHz, $CDCl_3$): δ = 1.95 (s, 3H, $COCH_3$), 3.55 (s, 3H, OCH_3), 4.60 (dd, $J_{5,6a}$ = 2.8, $J_{6a,6b}$ = 11.4 Hz, 1H, 6-H$_a$), 4.66 (dd, $J_{5,6a}$ = 2.8, $J_{5,6b}$ = 6.2 Hz, 1H, 5-H), 4.82 (dd, $J_{5,6b}$ = 6.2, $J_{6a,6b}$ = 11.4 Hz, 1H, 6-H$_b$), 4.95 (ddd, $J_{1,2}$ = 3.4, $J_{2,3}$ = 11.4, $J_{2,NH}$ = 9.6 Hz, 1H, 2-H), 5.00 (d, $J_{1,2}$ = 3.4 Hz, 1H, 1-H), 5.76 (d, $J_{2,3}$ = 11.4 Hz, 1H, 3-H), 5.95 (d, $J_{2,NH}$ = 9.5 Hz, 1H, NH), 7.35–7.60 (m, 6H, *p*-H and *m*-H of 2 C_6H_5), 8.00–8.15 (m, 4H, *o*-H of 2 C_6H_5); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 23.2 (q, $CO\mathit{C}H_3$), 53.6 (d, C-2), 56.2 (q, OCH_3), 61.8 (t, C-6), 71.5 (d, C-5), 74.8 (d, C-3), 98.5 (d, C-1), 128.5, 128.6 (2d, *m*-C of 2 C_6H_5), 128.7, 129.6 (2 d, *i*-C of 2 C_6H_5), 129.7, 130.2 (2 d, *o*-C of 2 C_6H_5), 133.2, 133.7 (2d, *p*-C of 2 C_6H_5), 166.1, 166.2 (2s, 2 $\mathit{C}OC_6H_5$), 169.7 (s, 2 $\mathit{C}OCH_3$), 195.4 (s, C-4).

Methyl 2-Acetamido-4,6-di-*O*-benzylidene-2-deoxy-α-D-*ribo*-hexapyranosid-3-ulose (6)

Methyl 2-acetamido-4,6-di-*O*-benzylidene-2-deoxy-α-D-glucopyranoside (250 mg, 0.77 mmol) was suspended in CH_2Cl_2 (10 mL, p.a.). Then Dess–Martin periodinane (424 mg, 1.00 mmol) and $NaHCO_3$ (30 mg) were added with vigorous stirring. After 15 h additional Dess–Martin periodinane (212 mg, 0.50 mmol) was added and after 2 h (TLC control) the mixture was worked up. First saturated $Na_2S_2O_3$ (5 mL) and saturated $NaHCO_3$ solutions (5 mL) were added; after 1 h the mixture was diluted with water (10 mL) and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were dried ($MgSO_4$) and the filtrate was evaporated to give the 3-ulose **6** as a colourless, analytically pure solid; yield: 233 mg (0.73 mmol; 95%); mp 254 °C; $[\alpha]_D^{20}$: 105 (*c* 0.56, CH_2Cl_2); elemental analysis: calcd. C 59.81, H 5.96, N 4.36; found: C 59.65, H 5.92, N 4.22; IR: ν = 3288, 2996, 2836, 1739, 1638, 1542, 1373, 1272, 1220, 1184, 1157, 1109, 1074, 1038, 992, 953, 756, 697 cm^{-1}; ^{1}H NMR (500.2 MHz, $CDCl_3$): δ = 2.08 (s, 3H, $NCOCH_3$), 3.39 (s, 3H, OCH_3), 3.96 ("t", $J_{5,6a}$ = $J_{6a,6b}$ = 10.1, Hz, 1H, 6-H$_a$), 4.09 (ddd, $J_{4,5}$ = 9.5, $J_{5,6a}$ = 10.1, $J_{5,6b}$ = 4.2 Hz, 1H, 5-H), 4.39 (dd, $^4J_{2,4}$ = 1.3, $J_{4,5}$ = 9.5 Hz, 1-H) and 4.41 (dd, $J_{5,6b}$ = 4.2, $J_{6a,6b}$ = 10.1 Hz, 6-H$_b$) together 2H, 4.97 (ddd, $J_{1,2}$ = 4.2, $^4J_{2,4}$ = 1.3, $J_{2,NH}$ = 7.8 Hz, 1H, 2-H), 5.22 (d, $J_{1,2}$ = 4.2 Hz, 1H, 1-H), 5.59 (s, 1H, HCPh), 6.27 (d, $J_{2,NH}$ = 7.8 Hz, 1H, NH), 7.34–7.40 (m, 3H, *m*-H, *p*-H of C_6H_5), 7.47–7.53 (m, 2H, *o*-H of C_6H_5); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 23.4 (q, $NCO\mathit{C}H_3$), 56.0 (q, OCH_3), 59.3 (d, C-2), 66.3 (d, C-5), 69.8 (t, C-6), 82.9 (d, C-4), 102.3 (d, C-1), 102.4 (d, H*C*Ph), 126.7 (d, *o*-C of C_6H_5), 128.7 (d, *m*-C of C_6H_5), 129.8 (d, *p*-C of C_6H_5), 136.6 (s, *i*-C of C_6H_5), 170.5 (s, N*C*OCH$_3$), 195.4 (s, C-3).

Typical Epoxidation Protocol, *trans*-1-Acetoxy-2,3-epoxy-3-phenylpropane (Table 2, entry 5)

Cinnamyl acetate (88.1 mg, 0.50 mmol) was dissolved in acetonitrile and aqueous Na_2EDTA solution (10^{-4} M, 2 mL each) and Bu_4NHSO_4 (15 mg) were added with vigorous stirring at 28 °C. A small portion of a mixture of oxone (1.537 g, 2.5 mmol) and $NaHCO_3$ (0.651 g, 7.75 mmol) was added to the mixture to bring the pH to >7. Then the 4-

ulose **5** (33.0 mg, 0.07 mmol, 15 mol%) was added. The rest of the oxone buffer was added in small portions over 5 h. The mixture was stirred until cinnamyl acetate was consumed or no further change in TLC was seen. The resulting mixture was diluted with half-saturated brine (15 mL) and extracted with ethyl acetate (4×20 mL). The combined organic phases were dried ($MgSO_4$) and the filtrate was evaporated. The crude product was purified over silica gel (4 g, column 0.5 cm×12 cm; eluent petrol ether:ethyl acetate 90:10) to afford the epoxide as a colourless liquid; yield: 81.0 mg (0.42 mmol, 85%); $[\alpha]_D^{20}$: −47 (*c* 1.00, CH_2Cl_2; *er* 81:19), lit.:[33] $[\alpha]_D^{22}$: −50 (*c* 0.5, $CHCl_3$; 89% *ee*); GC (bondex α, 0.4 bar H_2, 40 °C for 1 min, then 2.5 °C min^{-1} up to 200 °C): t_R = 38.33 min (major enantiomer), t_R = 39.18 min (minor enantiomer); NMR and IR data, see lit.[24]

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