104. Brominations of Cyclic Acetals from α-Amino Acids and α- or β-Hydroxy Acids with *N*-Bromosuccinimide

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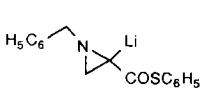
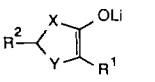
The preparation of novel electrophilic building blocks for the synthesis of enantiomerically pure compounds (EPC) is described. Thus, the 2-(*tert*-butyl)dioxolanones, -oxazolidinones, -imidazolidinones, and -dioxanones obtained by acetalization of pivalaldehyde with 2-hydroxy-, 3-hydroxy-, or 2-amino-carboxylic acids are treated with *N*-bromosuccinimide under typical radical-chain reaction conditions (azoisobutyronitril/CCl_4/reflux). Products of bromination in the α-position of the carbonyl group of the five-membered-ring acetals are isolated or identified (**2**, **5**, and **8**; *Scheme 1*). The dioxanones are converted to 2*H*,4*H*-dioxinones under these conditions (**12**, **14**, **15**, **21**, and **22**; *Schemes 2* and *3*). The products can be converted to chiral derivatives of pyruvic acid (methylidene derivatives **3** and **6**) or of 3-oxo-butanoic and -pentanoic acid **16** and **23**). The mechanism of the brominations is interpreted. The conversion of serine to enantiomerically pure dioxanones **26–28** *(Scheme 4)* is also discussed.

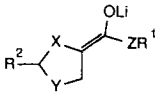
A) Introduction. – In the course of our investigations on the preparation of useful chiral building blocks for the synthesis of enantiomerically pure compounds (EPC) from simple amino and hydroxy acids, we have so far focused our attention on the nucleophilic reactivity (see for instance the heterocyclic enolates **A**–**F**). Most of this work was reviewed in [1] [2].



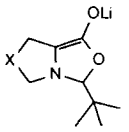
A (from serine [3])



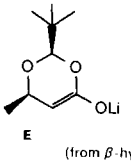
B (from α-amino- and α-hydroxy acids)



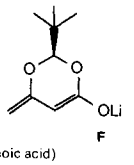
C (from glyceric acid or from serine)



D (from proline, hydroxyproline, or cystein)



E



F

(from β-hydroxybutanoic acid)

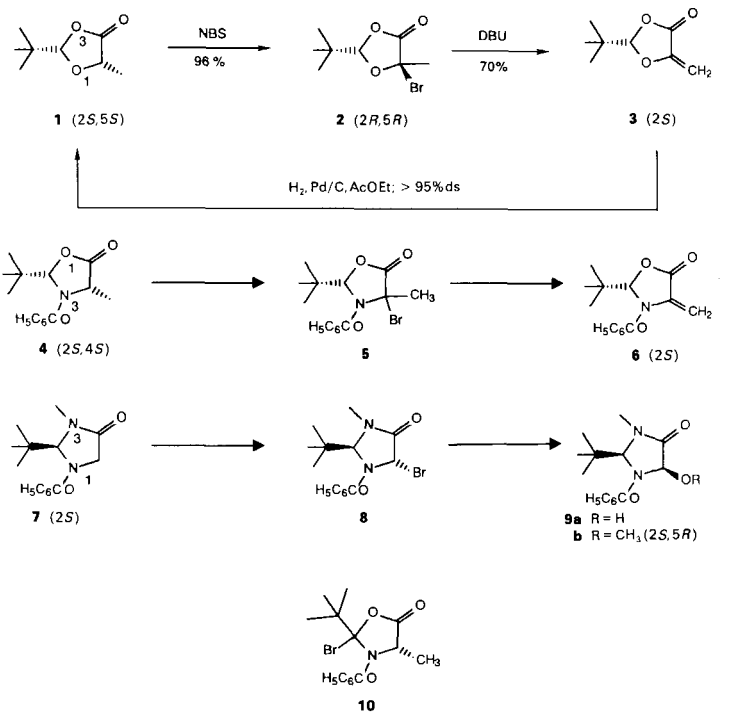
To test radical and electrophilic reactivity of the cyclic acetals at hand, we now studied their reactions with *N*-bromosuccinimide (NBS), hoping that we would obtain intermediates suitable for reactions with nucleophiles. The results, some of which are very surprizing to us, are described herein.

[1]) Part of the projected dissertation of *J. Z.*, ETH Zürich.

The brominations with NBS were all carried out under typical radical-chain conditions, *i.e.* in the presence of a chain initiator (azoisobutyronitrile, AIBN) in refluxing CCl_4, as originally described by *Wohl* [4] and *Ziegler et al.* [5][2]). The reaction times ranged from 1 to 5 h.

B) Bromination of Dioxolanones, Oxazolidinones, and Imidazolidinones. – The results observed with the five-membered heterocycles are collected in *Scheme 1*. The dioxolanone **1** from (*S*)-lactic acid [7] was brominated in essentially quantitative yield to give a single product **2**, the constitution and configuration of which was proved by NMR measurements. HBr elimination with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) gave the 5-methylidene derivative **3**, formally an enol acetal from pyruvic acid[3]) and pivalaldehyde. Catalytic hydrogenation of the C=C bond in **3** gives the starting material **1** in high yield and with a diastereoselectivity greater than 95%. This not only proves that the enantiomeric excess is preserved *en route* from the lactic-acid derivative **1** to the pyruvic-acid derivative **3**, but also demonstrates that the 2-*t*-Bu group on the dioxolanone ring directs the hydrogenation of the 5-methylidene group to the opposite face of the ring, as it does in the case of enolate alkylations [1] (both processes occur with rel. topicity *ul*-1,3 [9]).

Scheme 1



1 (2*S*,5*S*) **2** (2*R*,5*R*) **3** (2*S*)

4 (2*S*,4*S*) **5** **6** (2*S*)

7 (2*S*) **8** **9a** R = H **b** R = CH_3 (2*S*,5*R*)

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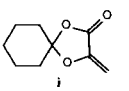
[2]) For a recent review, see [6].

[3]) For the preparation and reactions of achiral pyruvic-acid enol acetals such as **i**, see the work by *Ramage et al.* [8].



i

The oxazolidinone **4** from (*S*)-alanine [10] was brominated by NBS under the standard conditions (see above) to give the 4-bromo compound **5**, and subsequent dehydrohalogenation with DBU led to the methylidene derivative **6** (45% overall from **4**). The two α,β-unsaturated carbonyl derivatives **3** and **6** thus available[4]), formally derivatives of 2-alkoxy- and 2-(acylamino)acrylate, respectively, should be amenable to nucleophilic and radical [16] conjugate additions. Finally, the glycine-derived imidazolidinone **7** [17], most readily prepared by a resolution route [18], gave a bromide **8** which was so reactive that it could hardly be isolated: attempted chromatography led to the rather stable hydroxy compound **9a**, and reaction with MeOH gave the methoxy analogue **9b** (53% overall from **7**). The configuration of **9b** is *cis* according to measurements of difference nuclear *Overhauser* effects (NOE) in the ^{1}H-NMR spectrum, suggesting that the bromide **8** has *trans*-configuration, with an S_N2-type substitution taking place. The ease with which this reaction occurred is promising with respect to substitutions by other nucleophiles which are now being studied in our laboratory[5]).

In the case of the dioxolanone **1**, we detected no other bromination product besides **2**. In contrast, the crude bromination mixture from the oxazolidinone **4** and from the imidazolidinone **7** contained considerable amounts of other Br-containing compounds of which **10** with a brominated acetal center was clearly identified by ^{1}H-NMR (*ca.* 30%)[6]). By-products of this type do, however, not interfere with the isolation of the desired products **6** and **9**.

C) Bromination of Dioxanones. – The NBS-brominations of the 1,3-dioxan-4-ones **11**, **13**, and **20** from (*R*)-3-hydroxybutanoic and -pentanoic acid are shown in *Scheme 2* and *3*. The parent hydroxy acids are readily available from the biopolymers [2] PHB (polyhydroxybutyrate) [21] and PHB/PHV (polyhydroxyvalerate) [22]. Acetalization of aldehydes with these acids was achieved either directly (H^+-catalyzed, azeotropic removal of H_2O) or through the corresponding silyl silyloxy esters [23–25]. In all cases studied, the reaction with NBS led to the α,β-unsaturated lactones (2*H*,4*H*-dioxinones). Thus, the *cis*-dimethyldioxanone **11** gave a 45% yield of the bromodimethyldioxinone **12** when treated with slightly more than 2 equiv. of NBS under the standard conditions[7]). Likewise, up to 70% of the monobromo- and up to 50% of the dibromodioxinone **14** and **15**, respectively, could be isolated after reaction of the *cis*(*tert*-butyl)methyldioxanone **13** with NBS; both or mixtures of the two were hydrogenated[8]) catalytically to the chiral

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4) Compounds with similar functionality pattern have been isolated in our previous work on cystein- [11–13] and methionine-derived heterocycles [14] [15]. The reactions of these derivatives have not been studied as yet. The access described here is shorter and more simple than the former routes.

5) A chiral, non-racemic 2-bromoglycine derivative was obtained by NBS bromination of a morpholin-3-one and turned out to be also extremely reactive towards nucleophiles [19]. For another glycine a^2-reagent, see [20].

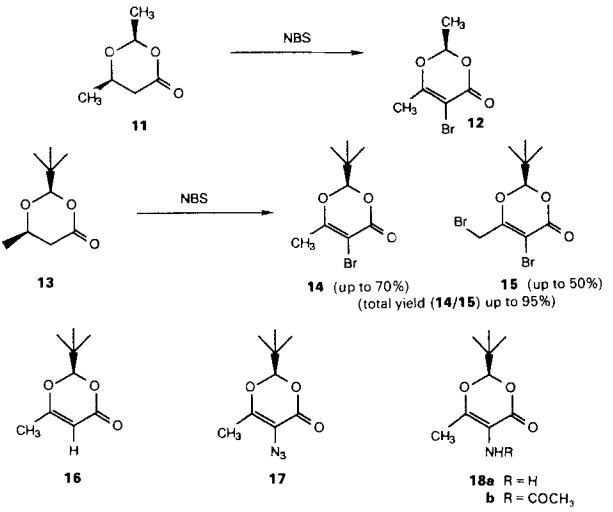
6) In the case of **7**, the major by-product was a dibromide of which we do not know the constitution (either a 5,5- or a 2,5-dibromoimidazolidinone). Bromination of the methyl oxazolidincarboxylates **ii** and **iii** (H instead of Br) gave the *cis*/*trans*-mixture of **ii** and **iii** predominantly.

ii R^1 = H, R^2 = *t*-Bu
iii R^1 = OCH_3, R^2 = *sec*-Pr

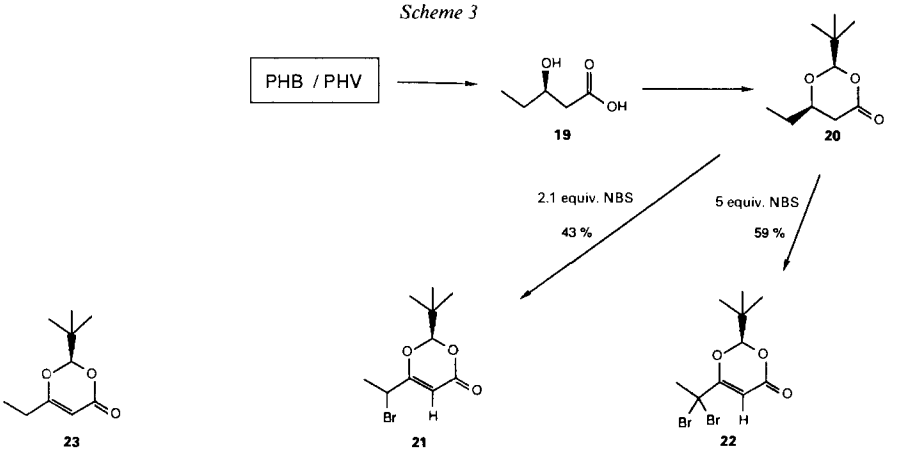
7) Derived from the bromination at the acetal center, AcOH was isolated as by-product.

8) The hydrogenative debromination is possible (H_2, 1 atm., Pd, Et_3N) without competing hydrogenation of the C=C bond. This latter process requires more drastic conditions (H_2, 30 atm. PtO_2) and gives exclusively the starting material, the *cis*-disubstituted dioxanone **13** (hydrogenation from the face opposite to the *t*-Bu group) [26].

Scheme 2



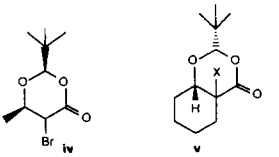
Scheme 3



acetoacetic-acid derivative **16**, a most versatile synthetic building block [26]. Thus, **16** is now available on large scale by the bromination procedure, while the previously used lithium-enolate selenation/oxidation/elimination route [26], when scaled up, failed completely[9]).

The reactivity of the bromide **14** is demonstrated by its conversion with NaN_3 in DMF to the 5-azido derivative **17** (55%) which is readily reduced to the amino (**18a**) or to the acetamido compound (**18b**) (H_2, 1 atm., Pd).

[9]) Bromination of the enolate from **13** gave a mixture of diastereoisomeric bromodioxanones **iv**[1]). The pivalaldehyde acetal obtained with *cis*-2-hydroxycyclohexanecarboxylic acid yielded products of type **v** [27] by reactions of the enolate with heteroelectrophiles.



The two brominated products obtained from the ethyl-substituted dioxanone **20** (prepared from **19**) were the allylic bromide **21** (1:1 mixture of diastereoisomers) and dibromide **22** *(Scheme 3)*. The surprising difference between the NBS brominations of the methyl and ethyl analogues **13** and **20**, respectively, is discussed below. The crude mixture **21**/**22** was hydrogenated (Pd, AcOEt, H_2, 1 atm.) to give the chiral non-racemic β-oxopentanoic-acid derivative **23**. As in the other two cases (**11**→**12** and **13**→**14**/**15**; *Scheme 2*), the overall result is an introduction of a double bond into the dioxanone ring, with removal of the original PHB/PHV-derived chirality center to give products which are enantiomerically pure due only to the presence of the stereogenic acetal center in these molecules.

D) Discussion of the Results. – We have done only a few experiments to elucidate the mechanism of the brominations described here. It is important to state first, that the reactions work better in the presence of AIBN than in its absence[10]).

The increasing amount of bromination at the acetal center in going from the O,O- (**1**, **13**, and **20**) to the N,O- and N,N-acetals (**4**, **ii**, and **iii** and **7**, respectively) is not compatible with the fact [30] that the reaction of NBS with *p*-substituted benzyl methyl ether follows a *Hammet* relationship[11]), with a ρ-value of -0.35[12]). It is remarkable that the diastereotopic faces of the trigonal centers at the α-carbonyl (ring) position of the intermediates from the five-membered ring acetals **1**, **4**, and **7** exhibit the same high reactivity differences as those of the corresponding enolates (see **A**–**F** and [1]), although the brominations are carried out in refluxing CCl_4 and the enolate alkylations at $-75°$ in THF.

The influence of steric hindrance is evident from the different reactivity of the dioxanones **11** (2-methyl) and **13** (2-(*tert*-butyl)): **11** also underwent acetal bromination, while no reaction at the acetal center of **13** was detected[13]).

In the case of the dioxanones **13** (6-methyl) and **20** (6-ethyl), we have done some experiments in order to gain information about the reasons for their different reactivity. The following observations appear to be relevant: *a*) bromination (NBS, AIBN) of the 6-methyldioxinone **16** gave the products **vi**[14]) and **15** of allylic attack[15]) *and* the vinylic bromide[14]) **14** which must result from addition/elimination; *b*) bromination of the dioxanone **13** with 0.2 equiv. NBS in the presence of AIBN gave the dioxinone **16** in *ca.* 10% yield; *c*) treatment of the 6-ethyldioxinone **23** with NBS/AIBN/CCl_4 under the same conditions employed with the methyl analogue **16** gave *only* rise to bromination in the allylic position (→**21** and **22**). These results are in agreement with the following assumptions about the mechanism: a) The 2-(*tert*-butyl)dioxanones **13** and **20** react preferentially[10]) by abstraction of H^6, see

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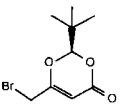
[10]) For a discussion of the mechanism of NBS bromination of acyl chlorides, see [28]. Bromination of butyl acetate occurs only in the alcohol-derived chain [29].

[11]) For the values of σ_p^+, see [31].

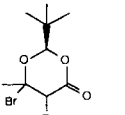
[12]) The crystal structure of an *N*-benzoyloxazolidin-5-one [14] shows a pyramidalization of the amide N-atom. If the N-atom of the imidazolidinone **7** and of the oxazolidinones **4**, **ii**, and **iii**, see *Footnote*[6]), could be considered as an amine rather than an amide N-atom, our results would be less surprising (σ_p^+: amino < alkoxy < acylamino). For a discussion of stereoelectronic effects in the stabilization of radicals at an acetal center, see [32].

[13]) For an example of steric hindrance in a radical chlorination, see [33].

[14]) Treatment of the dioxinone **16** with Br_2 in CCl_4 in an NMR tube gave exclusively the 5-bromodioxinone **14**. An intermediate, for example **vii**, was not detected.



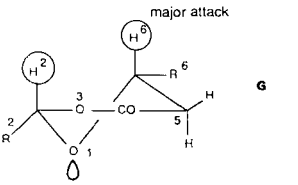
vi



vii

[15]) For the allylic bromination of the enol acetonide of acetoacetic acid with NBS/AIBN, see [34].

[16]) The half-chair conformation **G** of *cis*-2,6-disubstituted 1,3-dioxan-4-ones was deduced from the NMR spectra [23]. In this connection, it is interesting to note that a 3:1 mixture of *trans*- and *cis*-dioxanone **13** yields, after NBS bromination, the same mixture of bromodioxinone **14**/**15** as the pure *cis*-isomer **13**, but in *ca.* 5% ee. The *cis*/*trans*-mixture equilibrates under acidic conditions [23], and this is in competition with the bromination. Fortunately, the bromination of the *cis*-dioxanone **13** is faster than its epimerization! Luckily, the dioxinones do not racemize under the conditions of their preparation (see, however, *Footnote 21* in the *Exper. Part*).

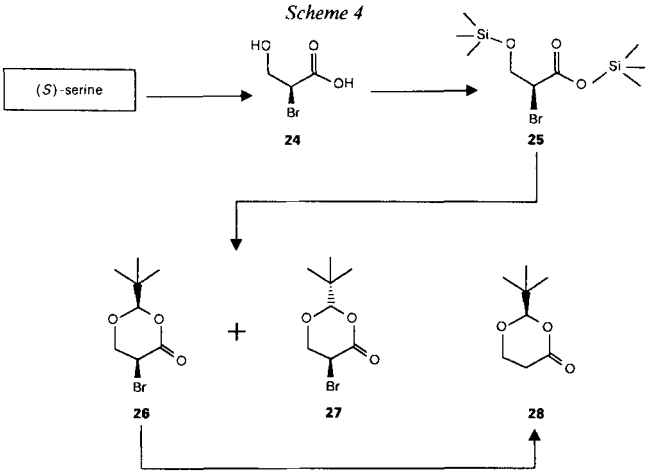


G

G[16]). *b*) The less bulky substituent in the 2-position of **11** allows for competing H^2 abstraction. *c*) The resulting 6-bromodioxanones readily loose HBr to give dioxinones[17]). *d*) These, in turn, undergo competing bromination at the allylic position[18]) and the double bond.

E) Appendix. A Chiral β-Hydroxypropanoic-Acid Derivative from Serine. – Although not obtained by halogenation with NBS, the bromo acetals **26** and **27** with dioxanone structure should also be mentioned here *(Scheme 4)*. They were available from the amino acid serine which was converted to 2-bromo-3-hydroxypropanoic acid **24** by the known retentive nucleophilic substitution ($NaNO_2$, KBr, H_2SO_4) [36], followed by silylation (→**25**) and silyltriflate-catalyzed [37] acetalization of pivalaldehyde. The mixture of the two diastereoisomers **26** and **27** which were formed in essentially equal amounts could be separated chromatographically. Catalytic hydrogenative debromination of the *cis*-isomer **26** gave (*R*)-2-(*tert*-butyl)-1,3-dioxan-4-one (**28**), an enantiomerically pure derivative of 3-hydroxypropanoic acid[19]).

Scheme 4



We gratefully acknowledge the staff of the analytical department of the ETH Organic Chemistry Laboratory for obtaining the analytical data, Mr. *Ch. Gerber* and Mr. *H.-J. Gründler* for measuring the ^{13}C-NMR spectra, Miss *B. Suter* and Mr. *D. Manser* for carrying out the microanalyses, Mr. *K. Job*, Mr. *P. Kälin* (both Kilolabor ETH), Mr. *G. Krummenacher* for the preparation of starting material, and Mr. *A.K. Beck* and Dr. *Y. Noda* for helpful discussions. The *BASF AG* (D–Ludwigshafen), *Degussa AG* (D–Hanau-Wolfgang), and *ICI* (GB–Billingham) generously supplied pivalaldehyde, amino acids, and PHB/PHV biopolymer, respectively. We thank the *Sandoz AG* (CH–Basel) for continuing financial support of our work.

[17]) In fact, the 5-bromodioxanone **iv** shown in *Footnote 9* is quite resistent to HBr elimination.

[18]) The benzylic position of ethylbenzene reacts 25 times faster with NBS than that of toluene [35].

[19]) With respect to the mechanism of bromination of 1,3-dioxan-4-ones, as discussed in *Chap. D*, it is interesting to note that **28** does not react with NBS, neither at the sterically hindered acetal center nor at C(6) which is devoid of substitution rendering the corresponding radical less stable.

Experimental Part

General. All solvents for reactions were of *purissimum* quality. Unless otherwise stated, org. extracts were dried with $MgSO_4$ and evaporated by using a rotary evaporator. Buffer soln. of pH 7 was prepared by dissolving $Na_2H_2PO_4$ (85 g) and NaOH (14.5 g) in H_2O (950 ml). Bulb-to-bulb distillations: air bath temp. Flash chromatography (FC): *Merck* silica gel (mesh size 0.040–0.063). Specific rotations: *Perkin-Elmer 241* polarimeter; $CHCl_3$ solns. at 25°; *c* in g/100 ml. M.p.: *Büchi/Tottoli* melting point apparatus; uncorrected. IR spectra: *Perkin-Elmer 297* spectrometer; KBr discs or $CHCl_3$ soln. ^1H- and ^{13}C-NMR spectra: *Varian EM-390* (90 MHz) or *Bruker WM 300* (300 MHz) instrument and *Varian CFT-20* instrument, resp.; TMS as internal standard, $CDCl_3$ solns. MS: 70 eV; *Hitachi-Perkin-Elmer RMV 6M* instrument.

*(2R,5R)-5-Bromo-2-(*tert*-butyl)-5-methyl-1,3-dioxolan-4-one* (**2**). The mixture of dioxolane **1** [7] (5 g, 31.6 mmol), NBS (8.9 g, 50 mmol) and AIBN (120 mg) in CCl_4 was refluxed for 4.5 h, then cooled to 0°, filtered, and evaporated. The crude product (10 g), which was purified by bulb-to-bulb distillation: pure **2** (7.2 g, 96%). M.p. 36–38°. B.p. 82–85°/18 Torr. $[\alpha]_D^{25} = +229.8°$ (*c* = 0.99). IR (KBr): 3560–3300*m* (br.), 2970*m*, 2940*m*, 2870*m*, 1820*s*, 1220*s*, 1140*s*, 1070*s*, 630*m*, 595*m*. ^1H-NMR (300 MHz): 1.01 (*s*, *t*-Bu); 2.23 (*s*, CH_3); 5.22 (*s*, CH). ^{13}C-NMR (20 MHz): 23.30; 27.02; 33.51; 89.04; 107.30; 166.96. MS: 238 (0.3, $M^{+\cdot}$), 236 (0.3, $M^{+\cdot}$), 157 (5), 149 (31), 99 (33), 85 (30), 57 (100), 56 (32), 43 (52), 41 (43), 28 (69). Anal. calc. for $C_8H_{13}BrO_3$: C 40.53, H 5.53; found: C 40.54, H 5.63.

*(2S)-2-(*tert*-Butyl)-5-methylidene-1,3-dioxolan-4-one* (**3**). To a soln. of **2** (4 g, 16.8 mmol) in benzene (35 ml), DBU (2.6 ml, 17.5 mmol) was added. The mixture was stirred for 50 min, filtered, and evaporated. The residue was purified by FC (hexane/Et_2O 4:1): **3** (1.8 g, 71%) as an oil. $[\alpha]_D^{25} = -1.9°$ (*c* = 1.16). IR ($CHCl_3$): 3020*m*, 2970*m*, 2940*m*, 2880*m*, 1795*s*, 1670*s*, 1480*s*, 1310*s*, 1130*s*, 990*s*. ^1H-NMR (300 MHz): 0.98 (*s*, *t*-Bu); 4.85 (*d*, *J* = 2.64, =CH); 5.13 (*d*, *J* = 2.64, =CH); 5.43 (*s*, H–C(2)). ^{13}C-NMR (75 MHz): 22.82; 35.87; 90.83; 109.38; 144.19; 162.48. MS: 156 (11, $M^{+\cdot}$), 87 (14), 86 (14), 57 (100), 43 (20), 42 (16), 41 (24), 29 (16). Anal. calc. for $C_8H_{12}O_3$: C 61.52, H 7.74; found: C 61.43, H 7.96.

*(2S,5S)-2-(*tert*-Butyl)-5-methyl-1,3-dioxolan-4-one* (**1**) *by Hydrogenation of* **3**. To the soln. of **3** (50 mg, 0.32 mmol) in AcOEt (5 ml), 10% Pd (10 mg, 10% on charcoal) was added. The mixture was stirred under H_2 for 16 h, filtered, and evaporated. The residue was filtered through flash silica gel (3 cm) in a *Pasteur* pipette using hexane/Et_2O 3:1. The filtrate was evaporated: **1** (48 mg, 95%), identical with the material prepared according [7]. $[\alpha]_D^{25} = +44.4$ (*c* = 1.39; [7]: $[\alpha]_D^{25} = +44.8°$ (*c* = 1.83)).

*(2S)-3-Benzoyl-2-(*tert*-butyl)-4-methylidene-1,3-oxazolidin-5-one* (**6**). The oxazolidinone **4**[20]) (2 g, 7.6 mmol), NBS (1.42 g, 8 mmol), and AIBN (80 mg) were refluxed in CCl_4 (40 ml) for 1 h. The suspension was cooled to 0°, filtered, and evaporated to give the crude bromooxazolidinone **5** which was dissolved in benzene (100 ml). DBU (1.8 ml, 11.7 mmol) was added and the mixture stirred for 30 min. The brown suspension was filtered, evaporated, and the residue was purified by FC (hexane/Et_2O 4:1): **6** (900 mg, 45.5%) as an oil. $[\alpha]_D^{25} = -148.6°$ (*c* = 0.68). IR ($CHCl_3$): 3020*m*, 2970*m*, 2880*w*, 1790*s*, 1680*s*, 1640*m*, 1370*s*, 1345*s*, 1280*s*, 1145*s*. ^1H-NMR (300 MHz): 0.99 (*s*, *t*-Bu); 4.57 (br. *s*, =CH); 5.42 (*d*, *J* = 1.8, =CH); 6.16 (*s*, H–C(2)); 7,65 (*m*, 5 arom. H). ^{13}C-NMR (20 MHz): 24.17; 38.75; 93.16; 101.72; 127.58; 128.66; 131.07; 131.56; 134.40; 164.40; 169.87. MS: 259 (2, $M^{+\cdot}$), 106 (12), 105 (100), 77 (31), 57 (3), 51 (6). Anal. calc. for $C_{15}H_{27}NO_3$: C 69.48, H 6.61, N 5.40; found: C 69.23, H 6.64, N 5.09.

*(2S,5R)-1-Benzoyl-2-(*tert*-butyl)-5-methoxy-3-methylimidazolidin-4-one* (**9b**). Imidazolidinone **7** [18] (1 g, 3.85 mmol), NBS (685 mg, 3.85 mmol), and AIBN (10 mg) were suspended in CCl_4 (40 ml) and refluxed for 40 min, cooled to 0°, filtered, and evaporated: **8** (1.3 g). MeOH (30 ml) was added, the soln. was stirred for 5.5 h, and evaporated to give an oil which was chromatographed (hexane/Et_2O 1:4) to give **9b** (580 mg, 52.3%). M.p. 130–131°. $[\alpha]_D^{25} = -88.95°$ (*c* = 1.14). IR (KBr): 2980*m*, 2960*m*, 2940*m*, 2830*w*, 1710*s*, 1670*s*, 1365*s*, 1300*s*, 1080*s*. ^1H-NMR (300 MHz): 1.11 (*s*, *t*-Bu); 3.02 (*s*, CH_3N); 3.48 (*s*, CH_3O); 4.48 (*s*, H–C(5)); 5.53 (*s*, H–C(2)); 7.48 (*m*, 3 arom. H); 7.75 (*m*, 2 arom. H). ^{13}C-NMR (75 MHz): 26.27; 30.96; 37.23; 56.11; 79.77; 85.57; 128.37; 128.43; 131.76; 134.19; 167.59; 172.53. MS: 289 (0.1, $M^{+\cdot} - 1$), 234 (11), 233 (76), 106 (11), 105 (100), 77 (35), 51 (5), 42 (13), 41 (5), 29 (3). Anal. calc. for $C_{16}H_{22}N_2O_3$: C 66.18, H 7.64, N 9.65; found: C 65.94, H 7.70, N 9.63.

*(2R)-5-Bromo-2,6-dimethyl-2*H*,4*H*-1,3-dioxin-4-one* (**12**). Dioxanone **11** [23] (0.5 g, 3.8 mmol; 9:1 mixture of *cis*/*trans*-isomer) was dissolved in CCl_4 (30 ml), NBS (1.44 g, 8 mmol), and AIBN (50 mg) were added. The mixture

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[20]) We changed the original workup procedure [10] as follows: the org. layer was stirred with conc. $NaHCO_3$ soln., dried, and evaporated. The residue was dissolved in Et_2O, hexane was added until the soln. became cloudy, and after standing at r.t. and at −20°, the product had crystallized.

was refluxed for 1.5 h, cooled to 0°, and evaporated. The residue was purified by FC (hexane/Et_2O 2:1): **12** (340 mg, 45%) as an oil. $[\alpha]_D^{25} = -185.9°$ ($c = 2.52$, max. 80% ee). IR ($CHCl_3$): 3040*m*, 2920*w*, 1740*s*, 1620*s*, 1390*s*, 1330*s*, 1110*m*, 1020*s*. ^{1}H-NMR (90 MHz): 1.68 (*d*, $J = 5$, CH_3–C(2)); 2.25 (*s*, CH_3–C(6)); 5.62 (*q*, $J = 5$, H–C(2)). ^{13}C-NMR (20 MHz): 18.83; 24.79; 91.79; 98.19; 158.31; 169.51. MS: 208 (16, $M^{+\cdot}$), 206 (17, $M^{+\cdot}$), 165 (8), 164 (49), 162 (50), 122 (30), 120 (32), 55 (11), 43 (100). Anal. calc. for $C_6H_7BrO_3$: C 34.81, H 3.41, Br 38.60; found: C 34.83, H 3.45, Br 38.34.

*(2*R*)-5-Bromo-2-(*tert*-butyl)-6-methyl-2*H*,4*H*-1,3-dioxin-4-one* (**14**). Dioxanone **13** [24] (17.2 g, 0.1 mol), NBS (37.8 g, 0.21 mol), and AIBN (860 mg) were refluxed for 4.6 h in CCl_4 (140 ml). The mixture was cooled to 0°, filtered, evaporated, and distilled to give 4:1 mixture **14**/**15** (26 g). The yellow oil was purified by FC (hexane/Et_2O 3:1): **14** (17.8 g, 71%[21])) as an oil. $[\alpha]_D^{25} = -183.9°$ ($c = 1.17$). IR (KBr): 2970*m*, 2940*m*, 2920*m*, 2880*m*, 1740*s*, 1600*s*, 1330*s*, 1170*s*, 1090*s*, 980*s*, 750*m*. ^{1}H-NMR (90 MHz): 1.08 (*s*, *t*-Bu); 2.28 (*s*, CH_3); 5.15 (*s*, H–C(2)). ^{13}C-NMR (75 MHz): 19.79; 23.86; 34.31; 91.77; 105.77; 158.95; 169.64. MS: 250 (16, $M^{+\cdot}$), 248 (16, $M^{+\cdot}$), 165 (60), 164 (63), 163 (63), 162 (61), 122 (26), 120 (28), 86 (28), 85 (15), 71 (18), 69 (11), 57 (99), 55 (18), 43 (100). Anal. calc. for $C_9H_{13}BrO_3$: C 43.40, H 5.26, Br 32.08; found: C 43.35, H 5.28, Br 32.53.

*(2*R*)-5-Bromo-6-(bromomethyl)-2-(*tert*-butyl)-2*H*,4*H*-1,3-dioxin-4-one* (**15**). The dioxanone **13** [24] (1.0 g, 5.8 mmol), NBS (3.9 g, 22 mmol), and AIBN (30 mg) were refluxed in CCl_4 (20 ml) for 4.5 h. The mixture was cooled to 0°, filtered, and evaporated. The residue was purified by FC (CH_2Cl_2/hexane 3:1): **15** (907 mg, 48%). B.p. 85°/0.01 Torr. $[\alpha]_D^{25} = -131.6°$ ($c = 1.21$). IR ($CHCl_3$): 3040*w*, 2980*m*, 2970*m*, 1745*s*, 1605*m*, 1350*s*, 1180*m*, 1080*s*. ^{1}H-NMR (300 MHz): 1.09 (*s*, *t*-Bu); 4.09, 4.30 (*AB*, $J = 11.0$, CH_2Br); 5.16 (*s*, H–C(2)). ^{13}C-NMR (75 MHz): 23.81; 25.36; 34.48; 93.66; 107.23; 158.43; 165.70. MS: 330 (2, $M^{+\cdot} + 1$), 328 (4, $M^{+\cdot} \pm 1$), 326 (2, $M^{+\cdot} - 1$), 244 (11), 243 (18), 242 (22), 240 (11), 149 (11), 147 (12), 107 (12), 105 (12), 86 (19), 57 (100), 43 (13), 41 (40), 39 (15), 29 (20), 27 (13). Anal. calc. for $C_9H_{12}Br_2O_3$: C 32.96, H 3.69; found: C 33.06, H 3.44.

*(2*R*)-2-(*tert*-Butyl)-6-methyl-2*H*,4*H*-1,3-dioxin-4-one* (**16**). Dioxanone **13** [24] (5 g, 29.1 mmol), NBS (10.9 g, 61 mmol), and AIBN (100 mg) were refluxed in CCl_4 (100 ml) for 3 h. The mixture was cooled to 0°, filtered, and evaporated to give a yellow oil (7.4 g), which was dissolved in EtOH (100 ml), 10% Pd (1 g), and Et_3N (7.8 ml, 56 mmol) were added, and the mixture was stirred under H_2 for 6 h (TLC hexane/Et_2O 3:1). Filtration and evaporation gave a yellow solid which was purified by recrystallization (hexane/Et_2O) to give **16** (2.95 g, 60%), which was identical with the material prepared according [26]. M.p. 48.5°. $[\alpha]_D^{25} = -217.7°$ ($c = 1.00$). IR (KBr): 3120*w*, 2980*m*, 2970*m*, 2920*m*, 2880*w*, 1740*s*, 1710*m*, 1640*m*, 1390*m*, 1350*m*, 1240*m*, 1220*m*, 1080*m*. ^{1}H-NMR (90 MHz): 1.05 (*s*, *t*-Bu); 2.05 (*s*, CH_3); 5.00 (*s*, H–C(2)); 5.35 (*s*, =CH). ^{13}C-NMR (75 MHz): 19.46; 24.11; 34.44; 95.88; 106.15; 163.13; 172.18. MS: 169 (2, $M^{+\cdot} - 1$), 168 (13), 153 (12), 125 (6), 86 (25), 85 (17), 84 (16), 69 (21), 57 (100), 43 (40), 41 (87), 39 (31), 29 (56), 27 (25). Anal. calc. for $C_9H_{14}O_3$: C 63.51, H 8.29; found: C 63.35, H 8.49.

*(2*R*)-5-Azido-2-(*tert*-butyl)-6-methyl-2*H*,4*H*-1,3-dioxin-4-one* (**17**). Dioxinone **14** (5 g, 20.1 mmol), AcOH (0.2 ml), and NaN_3 (6.5 g, 0.1 mol) were stirred in DMF (100 ml) at 25° for 3 d. H_2O (400 ml) was added and the mixture extracted with hexane (3 × 150 ml), dried, and evaporated. The residue was purified by FC (hexane/Et_2O 8:1): **17** (2.2 g, 52%) as an oil. $[\alpha]_D^{25} = -218.6°$ ($c = 1.34$). IR ($CHCl_3$): 2980*m*, 2960*m*, 2910*w*, 2880*w*, 2120*s*, 1730*s*, 1640*s*, 1410*s*, 1400*s*, 1300*s*, 1180*m*, 1110*s*. ^{1}H-NMR (90 MHz): 1.10 (*s*, *t*-Bu); 2.05 (*s*, CH_3): 5.08 (*s*, CH). ^{13}C-NMR (75 MHz): 15.61; 23.89; 34.26; 105.47; 108.99; 159.21; 160.47. MS: 211 (2, $M^{+\cdot}$), 140 (16), 87 (19), 86 (7), 71 (8), 70 (12), 69 (49), 57 (58), 55 (15), 43 (100), 41 (46), 29 (19), 28 (18). Anal. calc. for $C_9H_{13}O_3N_3$: C 51.18, H 6.20, N 19.89; found: C 50.94, H 6.24, N 19.64.

*(2*R*)-5-Amino-2-(*tert*-butyl)-6-methyl-2*H*,4*H*-1,3-dioxin-4-one* (**18a**). Azide **17** (200 mg, 0.95 mmol) was dissolved in AcOEt (10 ml), 10% Pd (50 mg) was added, and the mixture was stirred under H_2 for 16 h, filtered, and evaporated: **18a** (168 mg, 96%; pure according to the ^{1}H-NMR). ^{1}H-NMR (90 MHz): 1.01 (*s*, *t*-Bu); 2.01 (*s*, CH_3); 2.85 (br., NH_2); 4.91 (*s*, O–CH–O). The neat **18a** was unstable and can best be characterized as the acetamido derivative **18b**.

*(2*R*)-5-Acetamido-2-(*tert*-butyl)-6-methyl-2*H*,4*H*-1,3-dioxin-4-one* (**18b**). Azide **17** (0.2 g, 0.95 mmol) was dissolved in AcOH/Ac_2O (10 ml, 1:1), 10% Pd (50 mg) was added, and the mixture was stirred under H_2 for 16 h, filtered, and evaporated. The residue was purified by FC (Et_2O/hexane 3:1): **18b** (207 mg, 96%) as a foam. $[\alpha]_D^{25} = -177.2°$ ($c = 0.45$). IR (KBr): 3540*m*, 3420*m*, 3310*s*, 2980*s*, 2970*m*, 2880*m*, 1745*s*, 1720*s*, 1670*s*, 1640*s*, 1535*s*, 1400*s*, 1370*s*, 1350*s*, 1240*s*, 1225*s*, 1165*s*, 1090*s*. ^{1}H-NMR (90 MHz): 1.08 (*s*, *t*-Bu); 2.02 (*s*, CH_3); 2.13 (*s*, CH_3); 5.12 (*s*, H–C(2)); 6.85 (br., NH). ^{13}C-NMR: 17.24; 23.25; 24.02; 34.27; 105.53; 105.91; 162.36; 167.58;

[21]) Upon standing at r.t. for several days, a sample of crude **14** racemized and crystallized (m.p. of the racemic mixture, 85.5–86.5°).

168.62. MS 228 (2, $M^{+\cdot}$ + 1), 227 (7, $M^{+\cdot}$), 185 (3), 149 (4), 146 (16), 141 (100), 123 (83), 113 (18), 100 (11), 99 (88), 71 (53), 43 (97), 18 (7). Anal. calc. for $C_{11}H_{17}NO_4$: C 58.14, H 7.54, N 6.16; found: C 57.85, H 7.60, N 6.04.

(3R)-3-Hydroxypentanoic Acid (**19**). KOH (1280 ml, 1N, 1.28 mol) was added dropwise to (*R*)-ethyl 3-hydroxypentanoate (from PHB/PHV, [22]; 80.5 g, 0.55 mol) at 0°. The mixture was left at 4° for 20 d. HCl (1280 ml, 1N, 1.28 mol) was added dropwise at 0°. The mixture was extracted with Et_2O (2000 ml; *Kutscher-Steudel* apparatus), dried, and evaporated. The residue was purified by distillation: **19** (61 g, 94%) as an oil which solidfied on standing in the refrigerator. B.p. 85–90°/0.08 Torr. M.p. 30–31°. $[\alpha]_D^{25} = -37.6°$ (*c* = 1.25; [38]: −35°). IR ($CHCl_3$): 3500*w* (br., 3000*m*, 2970*s*, 2940*m*, 2880*m*, 1710*s*, 1410*m*, 1060*m*, 1030*m*. ^{1}H-NMR (300 MHz): 0.97 (*t*, *J* = 7.4, CH_3); 1.54 (*m*, 2H–C(4)); 2.46 (*dd*, *J* = 3.41, 16.43, H_A–C(2)); 2.56 (*dd*, *J* = 3.41, 16.43, H_B–C(2)); 3.98 (*m*, H–C(3)); 6.64 (br., OH, COOH). ^{13}C-NMR (75 MHz): 9.78; 29.26; 40.66; 69.47; 177.07. MS: 118 (0,8, $M^{+\cdot}$), 117 (11), 100 (13), 71 (100), 70 (26), 57 (14), 56 (50), 45 (20), 42 (24), 18 (28). Anal. calc. for $C_5H_{10}O_3$: C 50.84, H 8.53; found: C 50.61, H 8.54.

*(2R,6R)-2-(*tert*-Butyl)-6-ethyl-1,3-dioxan-4-one* (**20**). (3*R*)-3-Hydroxyvaleric acid (10 g, 84.7 mmol), pivalaldehyde (20 ml, 181.2 mmol), and *Dowex 50W* (1 g) were refluxed in CH_2Cl_2 (120 ml) for 17 h using an inverse H_2O trap. The mixture was filtered, extracted with 10% Na_2CO_3 (3 × 100 ml), dried, and evaporated: **20** (11.8 g, 75%) as a 7.5:1 mixture of *cis*/*trans*-isomers. This was fractionally distilled through a *Spaltrohrkolonne* (*Fischer*; 60 theoretical plats, reflux ratio 50:1) to give **20** (> 98% *cis*). B.p. 55°/0.08 Torr. $[\alpha]_D^{25} = -37.2°$ (*c* = 1.28). IR ($CHCl_3$): 3050*m*, 2965*s*, 2940*m*, 2880*m*, 1740*s*, 1485*m*, 1370*m*, 1350*m*, 1270*m*, 1250*s*, 1090*m*. ^{1}H-NMR (300 MHz): 0.97 (*t*, *J* = 7.5, CH_3CH_2); 0.98 (*s*, *t*-Bu); 1.62 (*m*, CH_3CH_2); 2.36 (*dd*, *J* = 10.5, 17.5, H_A–C(5)); 2.66 (*dd*, *J* = 4.5, 17.5, H_B–C(5)); 3.78 (*m*, H–C(6)); 4.90 (*s*, H–C(2)). ^{13}C-NMR (75 MHz): 9.16; 23.88; 28.44; 35.21; 35.95; 75.15; 108.30; 168.16. MS: 185 (0.3, $M^{+\cdot}$ −1), 149 (2), 129 (23), 87 (32), 83 (100), 57 (60), 56 (34), 43 (6), 41 (14), 29 (7), 18 (9). Anal. calc. for $C_{10}H_{18}O_3$: C 64.49, H 9.74; found: C 64.44, H 10.19.

*(2R)-6-(1-Bromoethyl)-2-(*tert*-butyl)-2H,4H-1,3-dioxin-4-one* (**21**). Dioxanone **20** (1 g, 5.4 mmol), NBS (2 g, 11.9 mmol), and AIBN (100 mg) were refluxed in CCl_4 for 1.5 h. The mixture was cooled to 0°, filtered, and evaporated to give a yellow oil. The residue was purified by FC (hexane/Et_2O 4:1): **21** (610 mg, 43%) as an oily 1:1 mixture of diastereoisomers. $[\alpha]_D^{25} = -98.1°$ (*c* = 2.6). IR ($CHCl_3$): 3020*m*, 2980*m*, 2965*m*, 1735*s*, 1630*s*, 1485*m*, 1395*s*, 1360*s*, 1295*m*, 1090*s*. ^{1}H-NMR (300 MHz): 1.09, 1.10 (*s*, *t*-Bu); 1.84, 1.85 (2*d*, *J* = 6.9, CH_3CHBr); 5.54, 5.55 (2*q*, *J* = 6.9, CH_3CHBr); 5.08, 5.09 (2*s*, H–C(2)); 5.51, 5.56 (2*s*, H–C(5)). ^{13}C-NMR (75 MHz): 21.52; 21.69; 23.83; 34.48; 40.34; 41.41; 94.79; 106.91; 162.19; 171.08; 171.76. MS: 264 (1, $M^{+\cdot}$), 262 (1, $M^{+\cdot}$), 179 (98), 177 (100), 126 (26), 98 (58), 97 (9), 87 (37), 71 (13), 69 (75), 57 (66), 43 (13), 41 (41), 39 (16), 29 (19), 27 (19). Anal. calc. for $C_{10}H_{15}BrO_3$: C 45.65, H 5.75, Br 30.37; found: C 45.48, H 5.68, Br 30.41.

*(2R)-2-(*tert*-Butyl)-6-(1,1-dibromoethyl)-2H,4H-1,3-dioxin-4-one* (**22**). Dioxanone **20** (1 g, 5.37 mmol), NBS (4.7 g, 26.4 mmol), and AIBN (100 mg) were refluxed in CCl_4 (94 ml) for 135 min. The mixture was cooled to 0°, filtered, and evaporated to give a yellow oil, which was purified by FC (hexane/Et_2O 4:1): **22** (1.08 g, 58.6%). M.p. 61°. $[\alpha]_D^{25} = -92.9°$ (*c* = 0.86). IR ($CHCl_3$): 3010*w*, 2980*m*, 2970*m*, 1740*s*, 1620*m*, 1490*w*, 1350*s*, 1100*m*. ^{1}H-NMR (90 MHz): 1.12 (*s*, *t*-Bu); 2.65 (*s*, CH_3); 5.15 (*s*, H–C(2)); 5.80 (*s*, H–C(5)). ^{13}C-NMR (75 MHz): 23.98; 34.72; 36.76; 51.14; 93.61; 107.56; 161.97; 170.02. MS: 344 (0.2, $M^{+\cdot}$), 342 (0.3, $M^{+\cdot}$), 340 (0.2, $M^{+\cdot}$), 258 (4), 256 (7), 254 (4), 149 (4), 147 (3), 86 (15), 69 (100), 57 (58), 43 (24), 41 (48), 39 (29), 32 (23), 29 (26), 28 (83), 27 (21). Anal. calc. for $C_{16}H_{14}Br_2O_3$: C 35.12, H 4.13, Br 46.72; found: C 35.04, H 4.11, Br 46.61.

*(2R)-2-(*tert*-Butyl)-6-ethyl-2H,4H-1,3-dioxin-4-one* (**23**). Dioxanone **20** (5 g, 26.9 mmol), NBS (10.05 g, 56.4 mmol), and AIBN (100 mg) were refluxed in CCl_4 (100 ml) for 6 h. The mixture was cooled to 0°, filtered, and evaporated to give a yellow oil (7.8 g), which was dissolved in AcOEt (100 ml). 10% Pd (1 g) and Et_3N (7.8 ml, 56 mmol) were added, and the mixture was stirred under H_2 for 6.5 h. The suspension was filtered, extracted with H_2O (50 ml), evaporated, and the residue was purified by FC (hexane/Et_2O 3:1): **23** (2.5 g, 50.5%) as an oil. $[\alpha]_D^{25} = -170.8°$ (*c* = 1.39). IR ($CHCl_3$): 3010*w*, 2990*m*, 2970*m*, 2880*m*, 1730*s*, 1630*s*, 1400*s*, 1370*s*, 1360*s*, 1300*m*, 1090*s*. ^{1}H-NMR (300 MHz): 1.06 (*s*, *t*-Bu); 1.14 (*t*, *J* = 7.5, CH_3CH_2); 2.35 (*qd*, *J* = 7.5, 0.8, CH_3CH_2); 5.03 (*s*, H–C(2)); 5.29 (*t*, *J* = 0.8, H–C(5)). ^{13}C-NMR (75 MHz): 9.90; 23.83; 26.21; 34.21; 93.98; 105.87; 163.22; 176.53. MS: 185 (3, $M^{+\cdot}$ +1), 184 (4, $M^{+\cdot}$), 127 (30), 99 (100), 69 (45), 57 (42), 43 (19), 41 (43), 39 (30), 29 (36), 27 (35), 15 (10). Anal. calc. for $C_{10}H_{16}O_3$: C 65.19, H 8.75; found: C 65.23, H 9.02.

(2S)-2-Bromo-3-hydroxypropanoic Acid (**24**). We followed the procedure described in [36]. $[\alpha]_D^{25} = -7.8°$ (*c* = 1.3). IR (KBr): 3400*s* (br.), 2950*m*, 2650*m*, 1730*s*, 1460*m*, 1400*m*, 1250*m*, 1190*m*, 1070*m*, 1030*m*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 3.66 (*'dd'*, *J* = 5.9, 11.7, H_A–C(3)); 3.80 (*'dd'*, *J* = 7.8, 11.5, H_B–C(3)); 4.25 (*'dd'*, *J* = 6.0, 7.8, H–C(2)); 5.20 (br., OH); 12.50 (br., COOH). ^{13}C-NMR (25 MHz, (D_6)DMSO): 48.62; 64.74; 171.64. MS: 171 (1, $M^{+\cdot}$ + 1), 169 (1, $M^{+\cdot}$ + 1), 153 (7), 151 (7), 140 (12), 138 (12), 123 (10), 122 (18), 120 (18), 81 (12), 79 (12), 71 (38), 55 (32), 45 (77), 43 (77), 42 (46), 31 (88), 29 (80), 27 (100), 26 (42). Anal. calc. for $C_3H_5BrO_3$: C 21.32, H 2.98; found: C 21.52, H 3.13.

(2S)-(Trimethylsilyl) 2-Bromo-3-(trimethylsilyloxy)propanoate (**25**). Hexamethyldisilazane (27.2 ml, 130 mmol) was added within 20 min at − 20° to a suspension of **24** (20 g, 118 mmol) in CH_2Cl_2 (100 ml). The mixture was stirred at − 20° for 14 h and at 25° for 6 h, and evaporated. The residue was distilled: **25** (36.5 g, 98.8%) as a colourless liquid. B.p. 58°/0.2 Torr. $[\alpha]_D^{25}$ = + 4.51 (*c* = 2.25). IR ($CHCl_3$): 3020*w*, 2960*m*, 1720*s*, 1290*m*, 1255*s*, 1110*s*, 1070*m*, 850*s*. ^{1}H-NMR (300 MHz): 0.12 (*s*, $(CH_3)_3Si$); 0.32 (*s*, $(CH_3)_3Si$); 3.86 (*'dd'*, *J* = 5.6, 10.3, H_A–C(3)); 4.00 (*'dd'*, *J* = 8.5, 10.3, H_B–C(3)); 4.18 (*'dd'*, *J* = 5.6, 8.5, H–C(2)). ^{13}C-NMR (25 MHz): 45.89; 63.21; 168.54. MS: 299 (11), 297 (11), 232 (2), 177 (8), 147 (62), 139 (6), 137 (6), 103 (8), 101 (16), 73 (70), 59 (11), 55 (10), 45 (14), 32 (24), 28 (100). Anal. calc. for $C_9H_{21}BrO_3Si_2$: C 34.50, H 6.71; found: C 34.34, H 6.75.

*(2R,5S)- and (2S,5S)-5-Bromo-2-(*tert*-butyl)-1,3-dioxan-4-one* (**26** and **27**). Pivalaldehyde (1.8 ml, 16.4 mmol) was added dropwise to a stirred soln. of **25** (4.0 g, 12.7 mmol) and trimethylsilyl trifluoromethanesulfonate (0.23 ml, 1.27 mmol) in CH_2Cl_2 (40 ml) at − 78°. The mixture was stirred at − 78° for 7 h, quenched with phosphate buffer (pH 7; 20 ml), extracted with CH_2Cl_2 (3 × 40 ml), and evaporated: **26/27** as a 1:1 mixture. The mixture was recrystallized (hexane/Et_2O): **26** (600 mg, 20%) as a solid. The filtrate was evaporated and the residue purified by FC (hexane/Et_2O 2:1): **27** (730 mg, 24.5%).

26: m.p. 96–100°. $[\alpha]_D^{25}$ = + 10.25 (*c* = 1.3). IR (KBr): 2980*m*, 2940*w*, 2910*m*, 1730*s*, 1485*w*, 1405*m*, 1370*s*, 1250*m*, 1115*m*, 1025*m*, 965*m*, 945*m*. ^{1}H-NMR (300 MHz): 1.04 (*s*, *t*-Bu); 4.26 (*'dd'*, *J* = 3.2, 13.1, H_A–C(6)); 4.38 (*'dd'*, *J* = 1.6, 13.1, H_B–C(6)); 4.44 (*'dd'*, *J* = 1.6, 3.2, H–C(5)); 5.0 (*s*, H–C(2)). ^{13}C-NMR (75 MHz): 23.74; 35.43; 37.76; 69.99; 110.16; 164.49. MS: 239 (0.4, $M^{+\cdot}$ + 1), 237 (0.4, $M^{+\cdot}$ + 1), 181 (6), 179 (6), 140 (9), 138 (8), 135 (9), 133 (9), 71 (10), 57 (100), 55 (16), 43 (22), 41 (35), 29 (32), 27 (31). Anal. calc. for $C_8H_{13}BrO_3$: C 40.53, H 5.53, Br 33.70; found: C 40.40, H 5.48, Br 34.36.

27: m.p. 55–58°. $[\alpha]_D^{25}$ = + 53.0 (*c* = 1.1). IR (KBr): 2980*m*, 2970*m*, 2940*m*, 2910*m*, 2880*w*, 1745*s*, 1480*w*, 1410*m*, 1370*m*, 1320*m*, 1050*m*, 1030*m*, 970*m*. ^{1}H-NMR (300 MHz): 0.99 (*s*, *t*-Bu); 4.02 (*'dd'*, *J* = 9.4, 10.3, H_A–C(6)); 4.50 (*'dd'*, *J* = 7.5, 10.4, H_B–C(6)); 4.54 (*'dd'*, *J* = 7.5, 9.4, H–C(5)); 5.05 (*s*, H–C(2)). ^{13}C-NMR (75 MHz): 23.76; 35.35; 37.16; 70.22; 110.10; 163.99. MS: 239 (1, $M^{+\cdot}$ + 1), 237 (1, $M^{+\cdot}$ + 1), 181 (5), 179 (5), 140 (6), 138 (7), 135 (7), 133 (8), 57 (100), 55 (10), 43 (13), 41 (21), 29 (14), 27 (16). Anal. calc. for $C_8H_{13}BrO_3$: C 40.53, H 5.53, Br 33.70; found: C 40.26, H 5.52, Br 34.13.

*(2R)-2-(*tert*-Butyl)dioxan-4-one* (**28**). A mixture of **26** (711.3 mg, 3 mmol), 10% Pd (150 mg), and Et_3N (0.63 ml, 4.5 mmol) was stirred under H_2 in AcOEt (100 ml) for 16 h. The mixture was filtered and washed with AcOEt (2 × 15 ml). The filtrate was extracted with H_2O (0°, 1 × 40 ml), dried, and evaporated. The crude acetal was recrystallized from hexane/Et_2O: **28** (410 mg, 86.5%). M.p. 71–72°. $[\alpha]_D^{25}$ = − 39.3° (*c* = 1.49). IR (KBr): 2980*m*, 2960*m*, 2940*w*, 2920*m*, 1750*s*, 1720*s*, 1380*m*, 1270*m*, 1250*m*, 990*s*. ^{1}H-NMR (300 MHz): 0.98 (*s*, *t*-Bu); 2.61 (*'ddd'*, *J* = 2.4, 5.5, 17.8, H_A–C(5)); 2.80 (*'ddd'*, *J* = 8.1, 10.6, 17.8, H_B–C(5)); 3.92 (*'ddd'*, *J* = 5.5, 10.6, 11.2, H_A–C(6)); 4.24 (*'ddd'*, *J* = 2.4, 8.1, 11.2, H_B–C(6)); 4.88 (*s*, H–C(2)). ^{13}C-NMR (75 MHz): 24.02; 30.39; 35.32; 63.31; 108.92; 167.98. MS: 159 (5, $M^{+\cdot}$ +1), 114 (9), 101 (26), 86 (28), 73 (35), 71 (11), 57 (100), 55 (69), 43 (25), 41 (26), 29 (23), 27 (13). Anal. calc. for $C_8H_{14}O_3$: C 60.74, H 8.92; found: C 60.51, H 9.17.

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