Pergamon

Tetrahedron 58 (2002) 10485–10500

TETRAHEDRON

Optically active nitroalkenes—synthesis, addition reactions and transformation into amino acids

Jan Hübner, Jürgen Liebscher and Michael Pätzel*

Institut für Chemie, Humboldt-Universität Berlin, Brook-Taylor-Strasse 2, D-12489 Berlin, Germany

Dedicated to Professor Dr Dr h. c. Ekkehard Winterfeldt on the occasion of his 70th birthday

Received 12 June 2002; revised 19 September 2002; accepted 24 October 2002

Abstract—Optically active nitroalkenes **4** were synthesized via Henry reaction. Conjugate addition of vinylmagnesium bromide to **4** gave nitroalkane *syn*-**5** while cyclopropanation with sulfur ylides or dibromocarbene afforded nitrocyclopropanes **8**, **10** and **11** in a diastereoselective manner. These products were used to synthesize optically active β-amino acids **7** and **16** as well as cyclopropane γ-amino acids **19** and **20** by reduction of the nitro group and oxidative cleavage of the dioxolane substituent.

Nitroalkenes have found wide application in organic synthesis.[1] Their character as electron deficient alkenes allows easy 1,4-addition reactions or cycloadditions to the C–C-double bond. Such additions can be diastereoselective if chiral substituents are attached to the C–C-double bond.[2] Recently the stereoselective 1,3-dipolar cycloaddition of diazomethane to nitroalkenes derived from glyceraldehyde was reported.[3] Elimination of nitrogen from the resulting pyrazolines gave access to chiral nitrocyclopropanes. Following our strategy to use optically active nitroalkenes as precursors for amino acids, we described first results of the conjugate addition of organometallics and cyclopropanation at nitroalkenes **4** (R*=dioxolanyl) derived from glyceraldehyde, to nitroalkanes and nitrocyclopropanes, respectively.[4] We now report attempts to convert these products into optically active β-amino and γ-amino acids mainly in the cyclopropane series. Such amino acids are incorporated in a series of biologically active[1] natural products, e.g. bestatin, pepstatin and cryptophycin A.[5a,b] Furthermore, they are of interest in the synthesis of unnatural peptides and β-lactams. γ-Amino acids have gained considerable attention as analogues of γ-amino butyric acid, which acts a neurotransmitter in the brain.[6]

Nitroalkenes **4** (Table 1) were obtained starting from (*R*)-glyceraldehyde, (L)-serine and the Garner aldehyde adopting known procedures, i.e. by Henry reaction and dehydration of the resulting nitroaldols **3**.[7] The chiral substituents R* will later serve as precursors for a carboxylic acid moiety by glycol cleavage. The nitroalkenes **4** appeared as *E*/*Z*-mixtures, which could be separated by flash chromatography (Scheme 1). Nitroalkenes **4f**–**4h** were prepared by protective group manipulation at the (*E*)-isomer of nitroalkenes **4b** and **4e**.

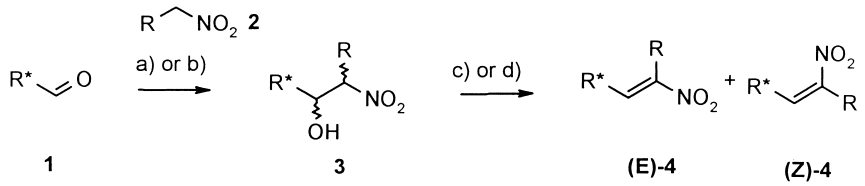
Investigations of conjugate additions of organometallic reagents to nitroolefines **4** by Cossio et al. and our group[2e,4] revealed that the *anti*-adduct predominated the *syn*-isomer in most cases. We chose the vinylated adduct *syn*-**5**, obtained by Grignard addition of vinylmagnesium bromide to nitroolefin (*E*)-**4a**, as precursor for an enantiopure β-amino acid by reduction of the nitro group and glycol cleavage (Scheme 2). After reduction of the nitro group and Boc-protection the resulting homoallyl amine was hydrogenated and O-deprotected affording the aminoalcohol **6**. The latter gave the envisaged β-amino acid **7** upon glycol cleavage with $NaIO_4/RuCl_3$. This method is known to maintain chirality in the synthesis of other β-amino acids.[8] The optical purity and the configuration of the final product **7** could be proved by comparison with literature data of the corresponding methyl derivative,[8] which served as building block in the total synthesis of cryptophycin-derivatives.[8]

As shown in the previous short communication,[4] sulphur ylides are useful reagents for the cyclopropanation of nitroalkenes (*Z*)-**4** and (*E*)-**4** to nitrocyclopropanes **8b** and **10** or **11** (Table 2), respectively (Schemes 3 and 4, respectively). Polymerisation of the nitroalkene and formation of a 1,2-oxazoline-*N*-oxide **12** (v.i.) were occasionally observed as side reactions. Further investigations (Scheme 3) using dibromocarbene allowed cyclopropanation of (*Z*)-**4b** to **8a** but in comparatively low yield.

Keywords: cyclopropanation; nitroolefines; conjugate addition; amino acids.

* Corresponding author. Fax: +49-3020936940;
e-mail: michael.paetzel@rz.hu-berlin.de

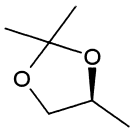
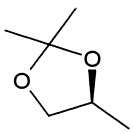
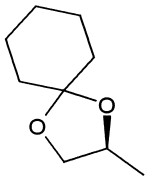
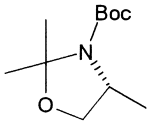
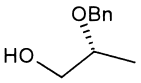
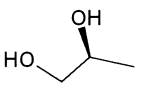
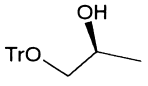
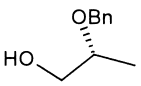
0040–4020/02/$ - see front matter
PII: S0040-4020(02)01406-0



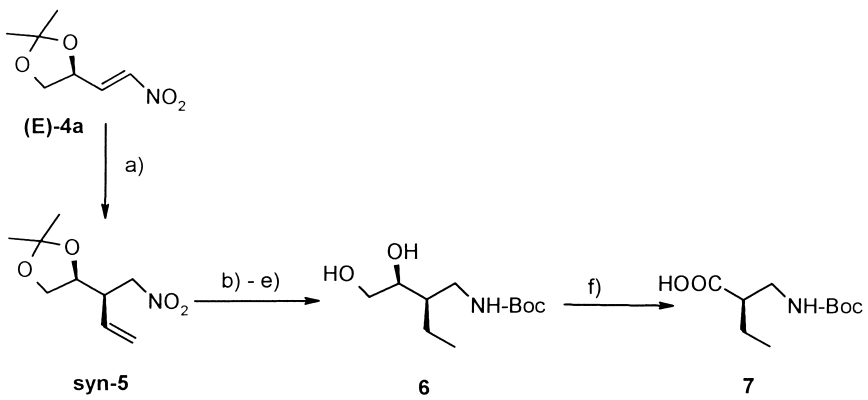
Scheme 1. (a) KF (cat.), neat, room temperature, 18 h; or (b) KF (cat.), *i*PrOH, benzene (10:1), room temperature, 18 h; 62–95%; (c) DCC (1.2 equiv.), CuCl (cat.), Et_2O, room temperature, 24–100 h; 14–70%; (d) MsCl (1.2 equiv.), Hünig's base (2.5 equiv.), CH_2Cl_2, −78°C to room temperature, 2 h; 60–70%.

In contrast to the other cases **10/11** (Table 2) no diastereoselectivity could be achieved in the cyclopropanation of the nitroalkene (*E*)-**4d** to **10f/11f** with sulphur ylides. In this sterically congested case, relatively high reaction temperature was necessary thus preventing a stereoselective reaction. Unfortunately neither the diastereomers **10f** and **11f** nor diastereomeric mixtures of their derivatives, such as the corresponding aminocyclopropanes could be separated. In the other cases, cyclopropanation of (*Z*)-**4** and (*E*)-**4** gave preferentially *syn*/*cis* **8** and *syn*/*trans* **10**, respectively. This stereochemical outcome can be explained by the anti-periplanar effect,[9] where negatively charged nucleophiles add *anti* with respect to an α-heteroatom-substituted group attached to the reactive site. This situation is shown for the dioxolane-substituted nitroalkene **4b** in Scheme 5a and b. According to Houks, outside crowded model,[10] the transition state b leading to the *syn*-product is preferred because it keeps the small hydrogen atom in the crowded outside position. Density functional calculations of related nitroalkenes and their transition states in 1,3-dipolar cycloaddition with diazomethane show the same preferred conformations and diastereofacilities.[3] Since the relative orientation of the substituents at the alkene moiety of **4** was maintained, i.e. (*Z*)-**4** gave *cis*-**8** (Scheme 3) and **4** gave *trans*-**10/11** (Scheme 4), the second step of the cyclopropanation must be fast. Thus there is not enough time for a

Table 1. Nitroalkenes **4**

4	R*	R	Starting material	Method	Isolated yield (%) of **4**	(*E*)-**4**/(*Z*)-**4**
a		H	**1**	B	60	90:10
b		Me	**1**	B	70	70:30
c		Me	**1**	A (Et_2O) A (THF)	35 26	92:8 20:80
d		Me	**1**	B	61	76:24
e		Me	**1**	A (Et_2O)	14[a]	95:5
f		Me	**4b**		72	Pure *E*
g		Me	**4f**		25	Pure *E*
h		Me	**4e**		100	Pure *E*

[a] 80% starting material recovered.



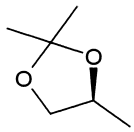
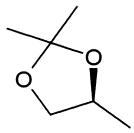
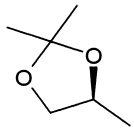
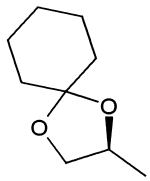
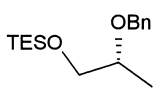
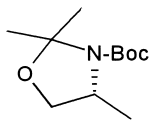
Scheme 2. (a) HC≡CH–MgBr, THF, −78°C; (b) $LiAlH_4$ (4.0 equiv.), Et_2O, room temperature, 1 h; 96%; (c) Boc_2O (3.2 equiv.), $NaHCO_3$ (excess), dioxane, H_2O (1:1), room temperature, 18 h; 90%; (d) H_2 (1 bar), Pd–C (cat.), MeOH, room temperature, 2 h; (e) TsOH (cat.), MeOH, room temperature 2 h, 78% (over the two steps); (f) $NaIO_4$ (2.5 equiv.), $RuCl_3 \times 7H_2O$ (cat.), H_2O, MeCN, CCl_4 (1:1:1), room temperature, 2 h; 73%.

rotation around the C–C-bond derived from the starting C–C-double bond in the intermediate **9** (Scheme 4).[11] The formation of the 1,2-oxazoline-*N*-oxide **12** as by-product in some cyclopropanations (see also footnote Table 2) can be explained via the same intermediate **9**, by nucleophilic intramolecular displacement of the diphenylsulfide group by the nitro oxygen atom rather than by the carbon atom (Scheme 4). Similar 1,2-oxazoline-*N*-oxides were observed before in cyclopropanation reactions of other nitroalkenes with dimethyloxosulfoniummethylide.[12]

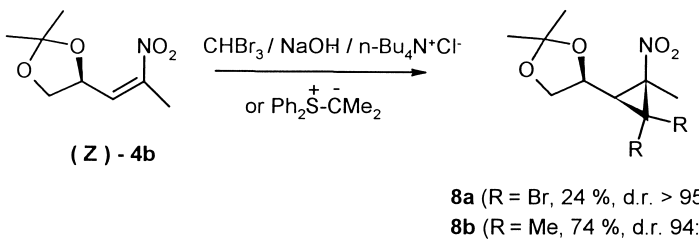
The structure of products **10**–**12** was elucidated by NMR-data and X-ray crystal analyses of **10c** and **8b**.[4]

In order to synthesize 2-aminocyclopropane-1-carboxylic acids such as **16** from nitroalkenes **10** the nitro group had to

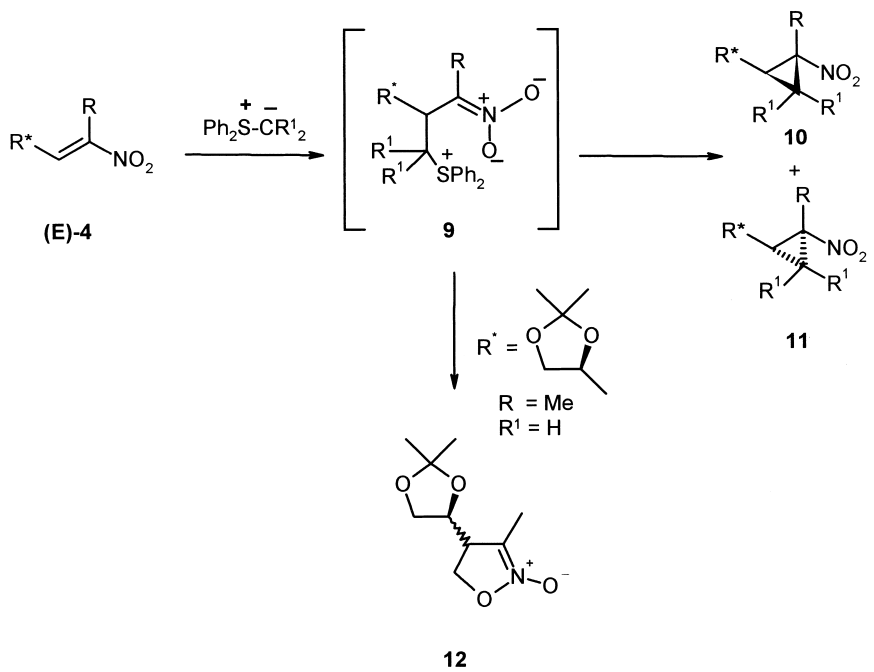
Table 2. Nitrocyclopropanes **10** and **11**

10	**11**	R*	R	R^1	Yield	**10/11**
a	**a**		H	CH_3	60	70:30[a]
b	**b**		CH_3	H	25[b]	60:40
c			CH_3	CH_3	90	97:3
d			CH_3	CH_3	74	95:5
	e		CH_3	CH_3	37	3:97
f	**f**		CH_3	CH_3	54[a,c]	50:50

[a] Not separable.
[b] By-product **12** in 15% yield, d.v. 60:40.
[c] 84% conversion.

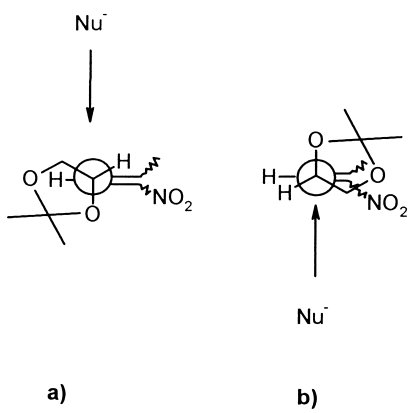


Scheme 3. (a) $CHBr_3$ (1.05 equiv.), NaOH (50% in H_2O), benzene, room temperature, 17 h; 24%, d.r. >95:5; (b) $PhS^{+-}CMe$ (1.2 equiv.), DME, −70°C to room temperature, 18 h; 74%, d.r. 94:6.

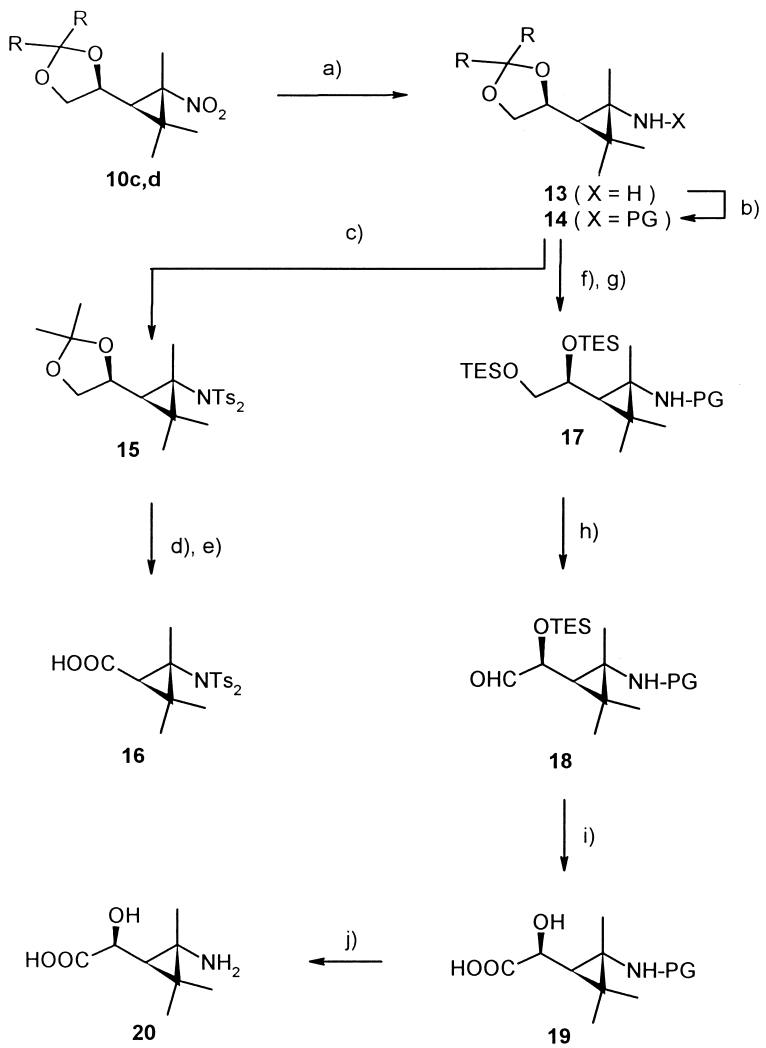


Scheme 4.

be reduced and the glycol moiety had to be oxidized. It was advantageous to reduce the nitro group first. Catalytic hydrogenation at 15 or 25 atm, respectively, gave high yields of the corresponding aminocyclopropanes **13a** and **13b** under optimised conditions (Scheme 6, Table 3). Higher pressures caused unfavourable ring opening reactions. In order to lower the nucleophilicity of the amino groups and thus stabilizing the expected amino acids one or two electron-withdrawing protective groups were introduced affording *N*-protected aminocyclopropanes **14** (Table 3) and **15**, respectively. The *O*-deprotected aminocyclopropylglycols, obtained after acid hydrolysis of **13** or **14** were submitted to glycol cleavage. However, *N*-monoprotected aminocyclopropanes gave only complex reaction mixtures under different conditions such as with $Pb(OAc)_4$ in dichloromethane at −78°C, with $NaIO_4$ in methanol or with $NaIO_4/RuCl_3$, without the possibility of isolating definite products. Presumably, the amino cyclopropane carbaldehydes formed by glycol cleavage from the amines **13** or **14** were sensitive to opening of the cyclopropane ring. Such cleavages are well known, if donor and acceptor substituents are attached to adjacent positions of the cyclopropane ring. This assumption is supported by the fact that the *N*,*N*-ditosylated aminocyclopropane **15**, which has no nucleophilicity at the nitrogen atom could successfully converted to the anticipated 2-aminocyclopropane-1-carboxylic acid **16** upon treatment with $NaIO_4/RuCl_3$. Product **16** is the first example of an optically active β-alkylsubstituted β-aminocyclopropane carboxylic acid. The total yield of **16** over six steps starting from the nitroalkene (*E*)-**4b** was 14%. Hitherto racemic β-aminocyclopropane carboxylic acids or derivatives have been known with a hydrogen atom or an ester or acid moiety attached to the β-position or in the bicyclic series. They were synthesized via Curtius or Hoffmann rearrangement, by cyclopropanation of *N*,*N*-disubstituted vinylamines with



Scheme 5.



Scheme 6. (a) H_2 (10–15bar), Pd–C (cat.), MeOH, room temperature, 48 h; 74%; (b) N-protection yields, see Table 3; (c) NaH (1.07 equiv.), TsCl (1.0 equiv.), DMF, room temperature, 15 h; 74%; (d) *p*-TsOH×1H_2O (cat.) MeOH, H_2O (10:1), room temperature, 18 h; 86%; (e) $NaIO_4$ (8.0 equiv.), $RuCl_3$×7H_2O (cat.), MeCN, $CHCl_3$, H_2O (1:1:1.5), room temperature, 5 h; 56%; (f) *p*-TsOH×1H_2O (cat.) MeOH, H_2O (10:1), room temperature, 18 h; R=Me: PG=Boc, 72%, PG=Cbz, 80%; PG=Bz, 83%; PG=CF_3CO, 92%; PG=Ts, 89%; PG=N-Cbz-Gly, 67%; R=–(CH)–: PG=Boc, 93%, PG=Bz, 80%; (g) Et_3SiCl (3.0 equiv.), Net_3 (4.0 equiv.), CH_2Cl_2, DMAP (cat.), −18°C to room temperature, 18 h; PG=Bz, 76%; PG=N-Cbz-Gly, 85%; PG=CF_3CO, 97%; (h) Swern oxidation; PG=Bz, 68%; PG=N-Cbz-Gly, 77%; PG=CF_3CO, 77%; (i) $NaOCl_2$ (1.4 equiv.), H_2O (1.05 equiv.), NaH_2PO_4 (cat.), MeCN, H_2O (2:1), 0°C to room temperature, 1 h; PG=Bz, 99%; PG=N-Cbz-Gly, 82%; PG=CF_3CO, 42%; (j) $Ba(OH)_2$×8H_2O (4.8 equiv.), MeOH, room temperature/reflux, 24 and 2 h, respectively; 96%.

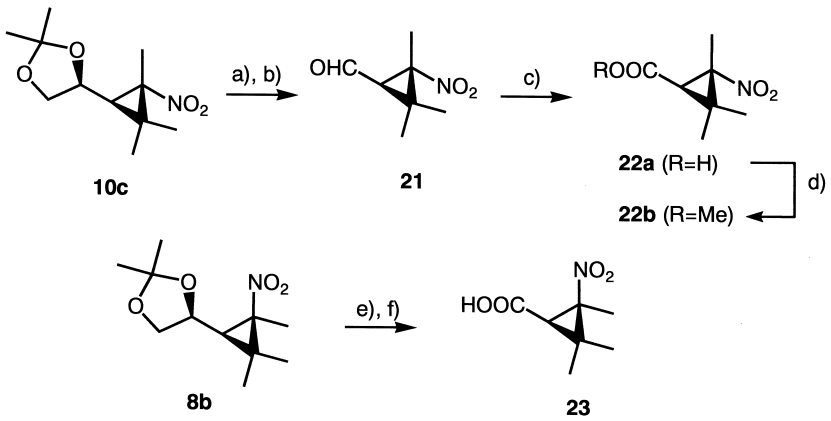
diazoacetate,[13,14] by addition of amines to cyclopropene carboxylates[15] or by carboxylation of lithiated cyclopropylamines.[16] Some of those investigations also revealed that *N*-unprotected β-aminocyclopropane carboxylic acids show a tendency towards ring opening reactions affording derivatives of β-formyl or β-acylcarboxylic acids.[13]

Since the sensitivity of 2-aminocyclopropane-1-carboxylic

Table 3. Aminocyclopropanes **13**, **14**, **17**, **18** and aminocyclopropane carboxylic acids **19**, **20**

PG	R′	Product (yield (%))					
		13	**14**	**17**	**18**	**19**	**20**
H	Me	**a** (74)					
H	$(CH_2)_3$	**b** (47)					
Boc	Me_2		**a** (80)				
Z	Me_2		**b** (99)				
CFCO	Me_2		**c** (99)	**c** (97)	**c**[a]	**c** (42)[b]	(96)
N-Z-Gly	Me_2		**d** (70)	**d** (85)	**d** (77)	**d** (82)	
Ts	Me_2		**e** (57)				
Boc	$(CH_2)_5$		**f** (63)				
Bz	$(CH_2)_f$		**g** (88)	**g** (76)	**g** (68)	**g** (99)	

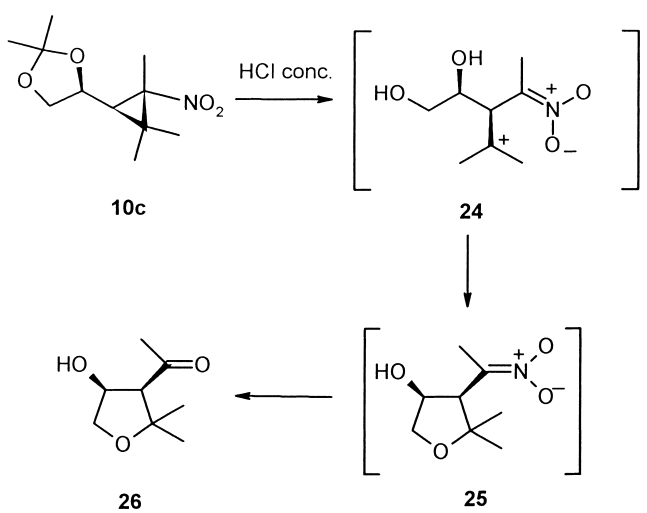
[a] Used as crude product in the oxidation to **19c**.
[b] Yield over two steps starting from **17c**.



Scheme 7. (a) *p*-TsOH×1H_2O (cat.) MeOH, H_2O (10:1), room temperature, 18 h; 100%; (b) $NaIO_4$ (1.1 equiv.), MeOH, phosphate buffer (pH 7) (4:1), room temperature, 2 h; 77%; (c) air, $CHCl_3$, 48 h; 90% or $NaIO_4$ (1.0 equiv.), $RuCl_3$×7H_2O (cat.), MeCN, CCl_4, H_2O (1:1:1.5), room temperature, 2.5 h; 79%; (d) CH_2N_2 (3.0 equiv.), Et_2O, 0°C, 1 h; 100%; (e) *p*-TsOH×1H_2O (cat.) MeOH, H_2O (10:1), room temperature, 18 h; 100%; (f) $NaIO_4$ (2.2 equiv.), $RuCl_3$×7H_2O (cat.), MeCN, CCl_4, H_2O (1:1:1.5), room temperature, 2.5 h; 70%.

acids against ring opening reactions is caused by the presence of an electron-withdrawing and an electron-donating substituent at the cyclopropane ring, higher homologues, i.e. 2-(2-aminocyclopropyl)-2-hydroxycarboxylic acids such as **20**, with the electron acceptor not directly being attached to the ring, can be expected to be more stable.[17] The synthesis of the γ-amino acid **20** was straightforward. The glycols, obtained from the *N*-monoprotected amines **14** were *O*,*O*-deprotected with triethylsilyl chloride (formation of **17**) and submitted to Swern oxidation affording aldehydes **18** (Scheme 6, Table 3). Upon further oxidation of the aldehyde with sodium chlorite/H_2O_2 the remaining TES-group was also lost and thus the corresponding β-hydroxy carboxylic acids **19** were directly obtained (Table 3). The target molecule **20** could be generated by deprotection of the trifluoroacetyl derivative **19c** and was found to be stable, as expected. The successful synthesis of the glycine derivative **19d** further demonstrated that nitroalkenes **4** can also serve as precursors for interesting dipeptides of an α-amino and a γ-amino acid.

In order to synthesize 2-amino-cyclopropane-carboxylic acids similar to **16** starting from nitrocyclopropane **10c** we approached a reversed reaction sequence (Scheme 7), i.e. first glycol cleavage of the dioxolane moiety and final reduction of the nitro group. Thus *trans*-**10c** was deprotected and oxidized with $NaIO_4$ in methanol affording the cyclopropane carbaldehyde **21**, which could be transformed into the corresponding acid **22a** in high yield by air-oxidation or with $NaIO_4$/$RuCl_3$. A one-pot procedure, i.e. direct conversion of **10c** into **22a** with $NaIO_4$/$RuCl_3$ was less efficient. The aldehyde **21** turned out to be reluctant to oxidation by other oxidizing reagents such as NaOCl, $KMnO_4$, H_2O_2 or pyridinium dichromate probably due to sterical hindrance. The synthesis of the *cis*-2-nitro-cyclopropane-1-carboxylic acid **23** could be achieved in a similar sequence starting from the *cis*-nitrocyclopropane **8b**. The cyclopropane carboxylic acid **22a** was converted into the corresponding methyl ester **22b** with diazomethane. Unfortunately, the final reduction of the nitro groups of **22** and **23** which would have led to the anticipated amino acids, was unsuccessful, because the envisaged cyclopropanes face the problem of donor and acceptor substituents at adjacent positions again. Thus opening of the cyclopropane ring occurred under catalytic hydrogenation or with Ni_2B leading to the oximes of the corresponding γ-ketoacid or ester. $NaBH_4$ reduction of **22b** effected the ester moiety rather than the nitro group affording the corresponding alcohol.



Scheme 8.

If the hydrolytic acetal cleavage of the dioxolane in compound **10c** was exerted under too strongly acid conditions, i.e. with concentrated aqueous HCl, the *cis*-tetrahydrofurane **26** was obtained in up to 38% yield. This product could be formed via carbenium ion **24**, which gave intramolecular ether formation and final Neef reaction (Scheme 8). 3-Acyl-4-hydroxytetrahydrofuranes are rare compounds. Besides some sugar derivatives with hetero-substituents in position 5, racemic 3-aroyl-4-hydroxy-tetrahydrofuranes were reported by ring opening of isoxazolines[18] and optically active compounds were obtained by kinetic resolution of the products or precursors using lipase.[19]

In summary, it could be demonstrated that nitroalkenes are versatile precursors for the synthesis of interesting optically active β-amino and γ-amino acids either via conjugate addition of organometallics or via cylopropanation with

sulphur ylides. The nitro group served as a precursor for the amino functionality and a dioxolanyl side chain as precursor for the carboxylic acid moiety. Amino acids where the amino group and the carboxylate group are attached to adjacent positions of a cyclopropane ring are instable and have to be protected by two strong electron withdrawing *N*-protective groups.

1. Experimental

^{1}H NMR spectra were recorded on Bruker AC-300 (300 MHz) spectrometer, ^{13}C NMR spectra on Bruker AC-300 (75 MHz) spectrometer. If not otherwise mentioned the samples were dissolved in $CDCl_3$ with tetramethylsilane (TMS) as internal standard. The following abbreviations are used: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad singlet. Elemental analyses were performed in a Leco CHNS-932 apparatus. Optical rotations were measured on a Perkin–Elmer 241 polarimeter using a 2 mL cell (c=1.0 in $CHCl_3$). Solvents were dried and purified according to standard procedures. Silica (0.040–0.063 mm) was used for column chromatography. Dimethoxyethane (DME) was distilled from $LiAlH_4$ before use.

1.1. General procedure for the synthesis of nitroalkenes 4

Formation of nitroaldols.

To a solution of enantiomerically pure aldehyde **1** (10 mmol, 1.0 equiv.) in *i*-PrOH (20 mL) and benzene (2 mL) nitroalkane **2** (50 mmol, 5.0 equiv.) and KF (cat., 100 mg) were added. The mixture was stirred at room temperature for 24 h. CH_2Cl_2 (20 mL) was added and the solution was filtered through a pad of celite. After evaporation of the solvents under reduced pressure the residue was dissolved in CH_2Cl_2, washed with saturated NaCl-solution and dried with $MgSO_4$. Evaporation of the solvent under reduced pressure gave crude nitroaldols, as diastereomeric mixtures, which were used in the dehydration step without further purification.

Dehydration of nitroaldols.

Method A. The crude nitroaldol (10 mmol, 1.0 equiv.) was dissolved in dry Et_2O or THF (20 mL). DCC (2.48 g, 12 mmol, 1.2 equiv.) and CuCl (cat., 25 mg) were added. The mixture was stirred at room temperature for 3–5 days while the progress of the reaction was monitored by TLC. After completion of the reaction pentane (20 mL) was added and the dicyclohexylurea was filtered off. Evaporation of the solvent and purification by chromatography (**4a**–**4d**: hexane/AcOEt, 9:1→7:3, **4e**: hexane/AcOEt, 8:2→1:1) afforded pure nitroolefines **4**.

Method B. Methanesulfonyl chloride (0.445 g, 3.89 mmol, 1.2 equiv.) was added to a solution of crude nitroaldol (3.25 mmol, 1.0 equiv.) in 20 mL of dry CH_2Cl_2 in one portion at −78°C (−18°C for **4e**) within 10 min followed by *i*-Pr_2NEt (1.05 g, 8.12 mmol, 2.5 equiv.). The reaction mixture was allowed to warm to room temperature and was washed with water, 2N HCl and sat. NH_4Cl-solution. After drying with $MgSO_4$ the solvent was evaporated under reduced pressure and the remaining residue was purified by chromatography as described above.

1.1.1. (4*S*)-(*E*)-2,2-Dimethyl-4-(2-nitro-vinyl)-[1.3]dioxolane [(*E*)-4a].[2d] Yellow oil. $[\alpha]_{546}^{20}$=+39.6 (c 1.3, CH_2Cl_2). r_f=0.55 (hexane/AcOEt, 7:3). ^{13}C NMR δ 140.2 (C_q–NO_2), 139.0 (CH=), 110.8 (C), 72.0 (CH), 68.3 (CH_2), 26.3 (CH_3), 25.4 (CH_3). ^{1}H NMR δ 7.14 (s, 2H), 4.73 (t, J=6.7 Hz, 1H), 4.21 (dd, J=7.5, 7.9 Hz, 1H), 3.70 (dd, J=7.1, 8.1 Hz, 1H), 1.40 (s, 3H), 1.35 (s, 3H).

1.1.2. (4*S*)-(*E*)-2,2-Dimethyl-4-(2-nitro-propenyl)-[1.3]-dioxolane [(*E*)-4b]. Yellow oil. $[\alpha]_{546}^{20}$=+6.8 (c 1.0, $CHCl_3$). r_f=0.42 (hexane/AcOEt, 8:2), ^{13}C NMR δ 149.5 (C_q–NO_2), 132.4 (CH=), 110.6 (C_q), 71.8 (CH), 68.6 (CH_2), 26.5 (CH_3), 25.6 (CH_3), 12.7 (CH). ^{1}H NMR δ 6.99 (dd, J=0.9, 8.1 Hz, 1H), 4.75 (m, 1H), 4.17 (dd, J=6.3, 8.4 Hz, 1H), 3.71 (dd, J=6.7, 8.4 Hz, 1H), 2.19 (s, 3H), 1.41 (s, 3H), 1.37 (s, 3H).

1.1.3. (4*S*)-(*Z*)-2,2-Dimethyl-4-(2-nitro-propenyl)-[1.3]-dioxolane [(*Z*)-4b]. Yellow oil. $[\alpha]_{546}^{20}$=+7.5 (c 1.0, $CHCl_3$). r_f=0.53 (hexane/AcOEt, 8:2). ^{13}C NMR δ 147.3 (C_q–NO_2), 136.9 (CH=), 110.5 (C_q), 73.6 (CH), 69.7 (CH_2), 26.8 (CH_3), 25.5 (CH_3), 18.8 (CH_3). ^{1}H NMR δ 6.09 (d, J=5.8 Hz, 1H), 5.12 (m, 1H), 4.37 (dd, J=7.1, 8.5 Hz, 1H), 3.66 (dd, J=6.4, 8.5 Hz, 1H), 2.15 (t, J=1.1 Hz, 3H), 1.39 (s, 3H), 1.31 (s, 3H).

1.1.4. (2*S*)-(*E*)-2-(2-Nitro-propenyl)-1,4-dioxa-spiro[4,5]-decane [(*E*)-4c]. Yellow oil. $[\alpha]_{546}^{20}$=+6.5 (c 1.01, $CHCl_3$). r_f=0.48 (hexane/AcOEt, 7:3). ^{13}C NMR δ 148.4 (C_q–NO_2), 131.7 (CH=), 110.2 (C_q), 70.5 (CH), 67.3 (CH_2), 35.1 (CH_2), 34.1 (CH_2), 24.0 (CH_2), 22.8 (2×CH_2), 12.0 (CH_3). ^{1}H NMR δ 6.95 (dd, J=0.7, 8.1 Hz, 1H), 4.72 (dd, J=7.0, 14.1 Hz, 1H), 4.13 (dd, J=6.9, 14.1 Hz, 1H), 3.66 (m, 1H), 1.55 (m, 10H), 1.38 (s, 3H). Anal. calcd for $C_{11}H_{17}NO_4$: C 58.14; H 7.54; N 6.16. Found: C 58.28; H 7.68; N 6.18.

1.1.5. (2*S*)-(*Z*)-2-(2-Nitro-propenyl)-1,4-dioxa-spiro[4,5]-decane [(*Z*)-4c]. Yellowish solid (melting at room temperature). $[\alpha]_{546}^{20}$=−14.2 (c 1.06, $CHCl_3$). r_f=0.54 (hexane/AcOEt, 7:3). ^{13}C NMR δ 147.1 (C_q–NO_2), 137.3 (CH=), 111.2 (C_q), 73.3 (CH), 69.3 (CH_2), 36.4 (CH_2), 35.0 (CH_2), 25.4 (CH_2), 24.2 (CH_2), 24.1 (CH_2) 18.8 (CH_3). ^{1}H NMR δ 6.10 (d, J=6.0 Hz, 1H), 5.11 (m, 1H), 4.36 (dd, J=7.0, 8.4 Hz, 1H), 3.35 (dd, J=6.4, 8.4 Hz, 1H), 1.58, 1.53 and 1.35 (3 broad m, 10H), 1.41(s, 3H).

1.1.6. (4*R*)-(*E*)-3-*N*-*t*-Butyloxycarbonyl-2,2-dimethyl-4-(2-nitro-propenyl)-oxazolidine [(*E*)-4d]. Yellow oil. $[\alpha]_{546}^{20}$=−42.2 (c 1.0, $CHCl_3$). r_f=0.43 (hexane/AcOEt, 7:3). ^{13}C NMR δ 152.2 (C), 144.3 (C_q–NO_2), 134.6/133.5 (CH), 133.5 (CH), 95.0/94.4 (C), 81.3/81.0 (C), 67.7/67.5 (CH), 64.0/63.5 (CH), 28.7 (CH_3), 27.8/26.7 (CH_3), 25.1/24.3 (CH_3), 13.1 (CH_3). ^{1}H NMR δ 6.92 (dd, J=0.7, 9.8 Hz, 1H), 4.57 (m, 2H), 4.46 (m, 1H), 4.09 (m, 1H), 1.58/1.53 (s, 3H), 1.48/1.45 (s, 3H), 1.40 (s, 9H), 1.34 (s, 3H). Due to the appearance of rotamers some signals are doubled. Anal. calcd for $C_{13}H_{22}N_2O_5$: C,54.53; H 7.74; N

9.78. Found: C 54.26; H 7.70; N 9.69. HRMS: calcd for (M^+) $C_{13}H_{22}N_2O_5$: 271.1293, found 271.1294.

1.1.7. (4*R*)-(*Z*)-3-*N*-*t*-Butyloxycarbonyl-2,2-dimethyl-4-(2-nitro-propenyl)-oxazolidine [(*Z*)-4d]. Yellowish solid (melting at room temperature). $[\alpha]_{546}^{20}=+106.2$ (*c* 1.0, $CHCl_3$). r_f=0.51 (hexane/AcOEt, 7:3). ^{13}C NMR δ 152.0 (C), 146.6 (C_q-NO_2), 139.7/137.0 (CH=), 95.0/94.5 (C_q), 81.2/80.7 ($C_q-{}^t$Bu), 69.1/68.7 (CH_2), 56.9/55.9 (CH), 28.7 ($CH_3-{}^t$Bu), 27.7/26.9 (CH_3), 24.9/23.9 (CH_3), 18.9 (CH_3). ^{1}H NMR δ 6.04 (d, *J*=6.0 Hz, 1H), 5.06 (m, 1H), 4.92 (m, 1H), 4.25 (m, 1H), 2.15 (s, 3H), 1.57/1.54 (s, 3H), 1.44/1.41 (s, 3H), 1.31 (s, 9H). Due to the appearance of rotamers some signals are doubled. Anal. calcd for $C_{13}H_{22}N_2O_5$: C 54.53; H 7.74; N 9.78. Found: C 54.25; H 7.82; N 9.49.

1.1.8. (2*R*)-(*E*)-2-Benzyloxy-4-nitro-pent-3-en-1-ol [(*E*)-4e]. Yellow oil. $[\alpha]_{546}^{20}=-57.7$ (*c* 1.0, $CHCl_3$). r_f=0.45 (hexane/AcOEt, 1:1). ^{13}C NMR δ 151.3 (C_q-NO_2), 138.2 (C), 133.4 (CH=), 129.8 (CH), 129.4 (CH), 129.2 (CH), 77.0 (CH), 72.9 (CH_2), 65.3 (CH_2), 14.4 (CH_3). ^{1}H NMR δ 7.23 (m, 5H), 6.89 (d, *J*=8.8 Hz, 1H), 4.53 (d, *J*=11.6 Hz, 1H), 4.35 (d, *J*=11.6 Hz, 1H), 4.15 (m, 1H), 3.60 (dd, *J*=6.6, 11.7 Hz, 1H), 3.53 (dd, *J*=4.3, 11.7 Hz, 1H), 2.07 (s, 3H).

1.1.9. (2*S*)-(*E*)-4-Nitro-pent-3-en-1,2-diol [(*E*)-4f]. Nitroalkene (*E*)-**4b** (1.0 g, 5.3 mmol, 1.0 equiv.) was dissolved in a mixture of water (5 mL), 1 M HCl (5 mL) and THF (20 mL). After stirring at room temperature for 4 days Na_2CO_3 was added until the pH was 8–9. The organic layer was separated and the aqueous phase was extracted with CH_2Cl_2 3 times. The combined organic layers were dried and the solvent was evaporated under reduced pressure. The residue was purified by chromatography (hexane/AcOEt, 1:1) to give diol (*E*)-**4f**. Yellow oil. $[\alpha]_{546}^{20}=-25.4$ (*c* 1.0, $CHCl_3$). r_f=0.07 (hexane/AcOEt, 1:1). ^{13}C NMR (CD_3OD) δ 150.3 (C_q-NO_2), 135.2 (CH=), 69.7 (CH), 66.0 (CH_2), 13.2 (CH_3). ^{1}H NMR (CD_3OD) δ 6.96 (dd, *J*=1.0, 8.5 Hz, 1H), 4.43 (m, 1H), 3.61 (dd, *J*=5.9, 11.2 Hz, 1H), 3.54 (dd, *J*=5.5, 11.2 Hz, 1H), 2.22 (d, *J*=1.0 Hz, 3H).

1.1.10. (2*S*)-(*E*)-4-Nitro-1-trityloxy-pent-3-en-2-ol [(*E*)-4g]. Diol (*E*)-**4f** (204 mg, 1.64 mmol, 1.0 equiv.) was dissolved in dry pyridine (5 mL). To the solution, trityl chloride (503 mg, 1.80 mmol, 1.1 equiv.) was added in one portion. After stirring at room temperature for 3 days, MeOH (2 mL) was added. After 2 h pyridine was azeotropically removed from the mixture with MeOH under reduced pressure. The residue was dissolved in CH_2Cl_2 and washed with saturated NH_4Cl-solution (25 mL) and with water (25 mL). After drying with $MgSO_4$ the solvent was evaporated under reduced pressure and the residue was purified by chromatography (hexane/AcOEt, 9:1→8:2) to afford (*E*)-**4g**. Yellow oil. r_f=0.46 (hexane/AcOEt, 7:3). ^{13}C NMR δ 150.0 (C_q-NO_2), 143.7 (C), 133.5 (CH=), 128.9 (CH), 128.4 (CH), 127.8 (CH), 87.5 (C_q), 68.3 (CH), 66.6 (CH_2), 13.5 (CH_3). ^{1}H NMR ($CDCl_3$) δ 7.35 and 7.23 (m, 15H), 6.86 (d, *J*=8.0 Hz, 1H), 4.35 (m, 1H), 3.23 (s, 1H), 3.21 (s, 1H), 2.02 (s, 3H).

1.1.11. (2*R*)-(*E*)-2-Benzyloxy-1-trimethylsilyloxy-4-nitro-pent-3-ene [(*E*)-4h]. Nitroalkene (*E*)-**4e** (711 mg, 3 mmol, 1.0 equiv.) was dissolved in a solution of DMAP (37 mg, 0.3 mmol, 0.1 equiv.) and NEt_3 (0.84 mL, 6 mmol, 2.0 equiv.) in dry CH_2Cl_2 (60 mL). After cooling to −78°C TES-Cl (0.75 mL, 4.5 mmol, 1.5 equiv.) was added dropwise over 10 min. The solution was allowed to warm up to room temperature overnight and was quenched with concentrated aqueous $NaHCO_3$ (40 mL). The organic layer was dried with $MgSO_4$ and the solvent was removed under reduced pressure. Chromatography (hexane/AcOEt, 9:1→7:3) afforded pure product (*E*)-**4h**. Yellowish oil. r_f=0.56 (hexane/AcOEt, 7:3). ^{13}C NMR δ 149.1 (C_q-NO_2), 136.3 (C), 132.6 (CH=), 127.4 (C), 126.9 (C), 126.8 (C), 74.7 (CH), 70.6 (CH_2), 63.9 (CH_2), 12.3 (CH_3), 5.6 (CH_3), 3.2 (CH_2). ^{1}H NMR δ 7.24 (m, 5H), 6.91 (dd, *J*=0.8, 8.8 Hz, 1H), 4.55 (d, *J*=11.9 Hz, 1H), 4.39 (d, *J*=11.9 Hz, 1H), 4.13 (m, 1H), 3.78 (dd, *J*=5.6, 10.3 Hz, 1H), 3.58 (dd, *J*=6.4, 10.2 Hz, 1H), 2.06 (d, *J*=0.8 Hz, 3H), 0.84 (t, *J*=7.8 Hz, 9H), 0.50 (q, *J*=7.8 Hz, 6H).

1.2. Addition of vinylmagnesiumbromide to nitroolefin (*E*)-4a

A solution of vinylmagnesium bromide (1 M in THF, 1.6 mL, 1.6 mmol, 1.3 equiv.) was diluted with THF (3 mL) and cooled to −78°C. A solution of nitroolefin (*E*)-**4a** (198 mg, 1.2 mmol, 1.0 equiv.) in THF (2 mL) was added and the reaction mixture was kept at this temperature for 2 h. The reaction was quenched by adding acetic acid (10 drops) in 0.5 mL water and the mixture was allowed to warm to room temperature. After the addition of saturated aqueous NH_4Cl (25 mL), the aqueous layer was extracted with CH_2Cl_2 (3×25 mL). The combined organic layers were washed with $NaHCO_3$, dried with Na_2SO_4 and the solvent was removed under reduced pressure. The residue was purified by chromatography (hexane/AcOEt, 7:3) to afford 156 mg (68%) of the major diastereomer *syn*-**5** and 12 mg (5%) of the minor diastereomer *anti*-**5**.

1.2.1. (4*S*)-2,2-Dimethyl-4-(1*R*)-1-nitromethyl-allyl-[1,3]-dioxolane (*syn*-5). Major diastereomer. Colourless oil. r_f=0.8 (hexane/AcOEt, 7:3). $[\alpha]_{546}^{20}=+41.2$ (*c* 0.9, CH_2Cl_2). ^{13}C NMR δ 132.8 (CH), 121.3 (CH_2), 109.8 (C), 76.8 (CH_2), 75.0 (CH_2), 66.3 (CH), 45.2 (C), 26.1 (CH_3), 24.9 (CH_3). ^{1}H NMR δ 5.91 (ddd, *J*=8.9, 10.2, 19.2 Hz, 1H), 5.47 (d, *J*=10.0 Hz, 1H), 5.40 (d, *J*=17.2 Hz, 1H), 4.74 (dd, *J*=5.8, 12.4 Hz, 1H), 4.61 (dd, *J*=9.1, 12.4 Hz, 1H), 4.40 (dt, *J*=3.4, 6.1 Hz, 1H), 4.20 (dd, *J*=6.7, 8.4 Hz, 1H), 3.87 (dd, *J*=6.5, 8.4 Hz, 1H), 2.97 (ddt, *J*=3.4, 5.8, 9.0 Hz, 1H), 1.58 (s, 3H), 1.50 (s, 3H).

1.2.2. (4*S*)-2,2-Dimethyl-4-(1*R*)-1-nitromethyl-allyl-[1,3]-dioxolane (*anti*-5). Minor diastereomer. Colourless oil. r_f=0.85 (hexane/AcOEt, 7:3). $[\alpha]_{546}^{20}=+13.1$ (*c* 0.8, CH_2Cl_2). ^{13}C NMR δ 132.7 (CH), 120.8 (CH_2), 110.1 (C), 76.2 (CH_2), 75.4 (CH), 67.9 (CH), 47.7 (C), 26.7 (CH_3), 25.3 (CH_3). ^{1}H NMR δ 5.61 (ddd, *J*=8.9, 10.2, 19.1 Hz, 1H), 5.25 (d, *J*=17.0 Hz, 1H), 5.25 (d, *J*=10.6 Hz, 1H), 4.72 (dd, *J*=4.4, 12.2 Hz, 1H), 4.39 (dd, *J*=9.7, 12.2 Hz, 1H), 4.03 (dd, *J*=6.1, 11.7 Hz, 1H), 3.99 (dd, *J*=6.1, 9.0 Hz, 1H), 3.76 (dt, *J*=11.7, 9.2 Hz, 1H), 2.97 (qd, *J*=9.2, 4.2 Hz, 1H), 1.43 (s, 3H), 1.33 (s, 3H).

1.2.3. (2*S*,3*R*)-3-(*t*-Butyloxycarbonyl-aminomethyl)-pentane-1,2-diol (6). *Reduction of the nitro group*. $LiAlH_4$ (228 mg, 6 mmol, 4.0 equiv.) was added to a solution of *syn*-**5** (322 mg, 1.6 mmol, 1.0 equiv.) in Et_2O (10 mL) at 0°C. After stirring at room temperature for 1 h, water (5 drops) was added, followed by 15% aq. NaOH (5 drops). After 15 min of stirring the mixture was filtrated through a pad of celite and $MgSO_4$. After removal of the solvent under reduced pressure 263 mg (96%) of the crude (2*R*)-2-((4*S*)-2,2-dimethyl-[1,3]dioxolan-4-yl)-but-3-enyl-amine were obtained, which was used in the next step without further purification. Colourless liquid. $[\alpha]_{546}^{20}$=+28.0 (*c* 1.1, CH_2Cl_2). r_f=0.2 ($CHCl_3$/MeOH, 8:2). ^{13}C NMR δ 135.8, 118.7, 108.7, 76.4, 67.0 (CH_2), 50.4 (C), 43.0 (C), 26.3 (CH_3), 25.4 (CH_3). ^1H NMR δ 5.48–5.61 (m, 1H), 5.07 (dd, *J*=10.4, 1.4 Hz, 1H), 4.98 (dd, *J*=16.6, 0.6 Hz, 1H), 3.98 (qd, *J*=6.2, 1.5 Hz, 1H), 3.82 (tt, *J*=7.9, 1.5 Hz, 1H), 3.49 (tt, *J*=7.9, 1.5 Hz, 1H), 2.61 (ddt, *J*=12.6, 4.9, 1.4 Hz, 1H), 2.52 (tdd, *J*=12.4, 7.2, 1.4 Hz, 1H), 1.97–2.06 (m, 1H), 1.75 (br, 2H), 1.22 (s, 3H, CH_3).

Introduction of N-Boc. Boc_2O (960 mg, 4.8 mmol, 3.2 equiv.) and a suspension of $NaHCO_3$ (2.65 g) in water (10 mL) were added to a solution of the unprotected amine (256 mg, 1.5 mmol, 1.0 equiv.) in dioxane (10 mL). The mixture was stirred overnight and the solvents were removed under reduced pressure. The residue was dissolved in Et_2O (20 mL) and washed with brine. After re-extraction of the aqueous layer with Et_2O, the combined organic layers were dried with Na_2SO_4. Removal of the solvent under reduced pressure afforded crude (2*R*)-*N*-*t*-butyloxycarbonyl-2-((4*S*)-2,2-dimethyl-[1,3]dioxolan-4-yl)-but-3-enyl-amine (366 mg, 90%), which was used in the next step without further purification. Colourless liquid. r_f=0.7 (hexane/AcOEt, 7:3). ^{13}C NMR δ 156.0 (C), 135.5 (C), 119.5 (C), 109.4 (C), 79.0 (C), 76.6 (CH), 67.4 (CH_2), 47.1 (C), 42.4 (C), 28.8 (CH_3), 26.7 (CH_3), 25.7 (CH_3). ^1H NMR δ 5.67–5.79 (m, 1H), 5.24 (dd, *J*=10.3, 1.6 Hz, 1H), 5.15 (dd, *J*=17.3, 0.9 Hz, 1H), 4.12–4.18 (m, 1H), 4.01 (dd, *J*=6.5, 8.0 Hz, 1H), 3.69 (t, *J*=7.5 Hz, 2H), 3.28–3.30 (m, 1H), 3.12 (ddd, *J*=13.6, 5.3, 2.9 Hz, 1H), 2.36–2.40 (m, 1H), 1.44 (s, 9H), 1.40 (s, 3H), 1.35 (s, 3H).

Hydrogenation of C–C double bond to **6**. 10% Pd–C (cat., 30 mg) was added to a solution of the preceding N-Boc-protected amine (325 mg, 1.2 mmol, 1.0 equiv.) in MeOH (4 mL). The mixture was hydrogenated at 1 bar H_2 for 2 h. The reaction mixture is filtered through celite to remove the catalyst. *p*-TosOH (20 mg) was added and the mixture was stirred at room temperature for 2 h. After removing the solvent under reduced pressure, the residue was dissolved in CH_2Cl_2. The organic phase was washed with saturated aqueous $NaHCO_3$ and dried over $MgSO_4$. Removal of the solvent and column chromatography (hexane/AcOEt, 1:1) afforded 218 mg (78%) of **6**, which was used in the subsequent step (transformation into **7**) without further purification and full analytical characterisation.

1.2.4. (2*S*,3*R*)-3-(*t*-Butyloxycarbonyl-aminomethyl)-pentan-1,2-diol (6). Colourless oil. $[\alpha]_{546}^{20}$=+11.2 (*c* 1.0, CH_2Cl_2). r_f=0.2 (hexane/AcOEt, 1:1). ^{13}C NMR δ 156.9 (C), 79.4 (C), 72.6, 64.4, 43.0, 40.8 (CH_2), 28.3 (CH_3), 12.7, 11.9. ^1H NMR δ 3.60–3.72 (m, 1H), 3.51–3.56 (m, 2H), 3.11–3.18 (m, 2H), 1.40–1.45 (m, 3H), 1.39 (s, 9H), 0.89 (t, *J*=7.3 Hz, 3H).

1.2.5. (2*R*)-2-(*tert*-Butyloxycarbonyl-aminomethyl)-butyric acid (7). A solution of $NaIO_4$ (190 mg, 0.88 mol, 2.5 equiv.) in water (1.5 mL) and $RuCl_3$ (cat., 8 mg) were added to the diol **6** (82 mg, 0.35 mol, 1.0 equiv.) in MeCN/CCl_4 (3 mL, 1:1). After stirring at room temperature for 2 h, the mixture was diluted with Et_2O (15 mL). After 5 min of stirring, $MgSO_4$ was added at 0°C. The mixture was filtered through celite and the celite was washed with Et_2O. The combined organic layers were evaporated under reduced pressure. Purification of the residue by chromatography (hexane/AcOEt, 1:1) afforded the protected amino acid **7** (55 mg, 73%). HPLC analysis (0.5N $HClO_4$ in NaClO-solution/MeCN=60:40), column Chiralcel ODR. rate 0.8 mL/min. detection: UV (220 nm) and polarimeter (Chiralyser): t_R=4.73 min. e.e. >95%. Colourless oil. $[\alpha]_{546}^{20}$=−22.2, $[\alpha]_D^{20}$=−18.2 (*c* 1.0, CH_2Cl_2). r_f=0.25 (hexane/AcOEt, 1:1). ^{13}C NMR δ 179.5 (C), 156.0 (C), 79.3 (C), 47.0 (C), 41.1 (CH_2), 28.3 (CH_3), 22.7 (C), 11.5 (C). ^1H NMR δ 8.40 (b, 1H), 3.18–3.30 (m, 2H), 2.30–2.45 (m, 1H), 1.43–1.65 (m, 2H), 1.38 (s, 9H), 0.92 (t, *J*=7.5 Hz, 3H). Anal. calcd for $C_{10}H_{19}NO_4 \times H_2O$: C 51.04; H 8.99; N 5.95. Found: C 51.29; H 8.94; N 5.97.

1.2.6. (4*S*,1*R*,3*R*)-*cis*-4-(2,2-Dibromo-3-methyl-3-nitro-cyclopropyl)-2,2-dimethyl-[1,3]-dioxo-lane (8a). A mixture of 50%-aqueous NaOH (5 mL), benzene (5 mL) and triethylbenzylammonium chloride (cat., 10 mg) was cooled to 0°C. A solution of $CHBr_3$ (0.2 mL, 2.1 mmol, 1.05 equiv.) and nitroolefin (*Z*)-**4b** (375 mg, 2.0 mmol, 1.0 equiv.) in benzene (5 mL) was added dropwise. The colour of the reaction mixture turned brown. After stirring at room temperature for 17 h, the reaction was quenched with water (10 mL) and extracted three times with benzene. After drying of the combined organic layers (Na_2SO_4) the solvent was removed under reduced pressure. Chromatography afforded 172 mg (24%) of the dibromocyclopropane **8a**. Colourless crystals. Mp 60–65°C. $[\alpha]_{546}^{20}$=−98.0 (*c* 1.0, $CHCl_3$). r_f=0.33 (hexane/AcOEt, 8:2). ^{13}C NMR δ 110.5 (C), 74.5 (CH), 73.6 (C), 68.1 (CH_2), 40.8 (CH), 28.0 (C), 26.9 (CH_3) 25.4 (CH_3), 16.0 (CH_3). ^1H NMR δ 4.17 (dd, *J*=5.7, 8.7 Hz, 1H), 4.00 (dd, *J*=3.9, 8.7 Hz, 1H), 3.79 (m, 1H), 2.99 (d, *J*=9.1 Hz, 1H), 1.92 (s, 3H), 1.41 (s, 3H), 1.28 (s, 3H). HRMS: calcd for (M^+−Me) $C_8H_{10}Br_2NO_4$: 341.8976, found 341.8981.

1.3. General procedure for cyclopropanation with diphenylsulfoniumisopropylylide—synthesis of 8, 10, 11 (except 10b/11b; see Table 2 and Scheme 3, respectively)

Diphenylsulfoniumisopropylylide. A freshly prepared solution of LDA [18 mmol, prepared from 1.6 M BuLi solution in hexane (11.25 mL) and diisopropylamine (2.6 mL) in dry DME (20 mL) at −70°C] was added to a solution of diphenylethylsulfonium tetrafluoroborate[20] (5.5 g, 18.3 mmol) in dry DME (200 mL) under argon at-70°C. The resulting yellow-green solution became turbid after 10–15 min. After stirring at −70°C for further 30 min, methyl iodide (1.13 mL, 18 mmol) was added dropwise. The solution was stirred at this temperature for 3 h. Further LDA

(18 mmol) was added at −70°C while the mixture turned deeply orange fast. After 1 h stirring the resulting solution contained about 18 mmol of diphenylsulfoniumisopropylylide.

Cyclopropanation. A solution of the nitroalkene **4** (15 mmol) in dry DME (20 mL) was added to a solution of diphenylsulfoniumisopropylylide (v.s.) at −70°C during 30 min (in case of (*E*)-**4d** 1 h) while the reaction mixture became colourless. The resulting turbid solution was allowed to warm up to room temperature under stirring overnight. After the addition of half saturated aqueous NH_4Cl (100 mL) and extraction with Et_2O/pentane (3:1, 3 times 100 mL) the combined organic layers were washed with saturated brine (200 mL) and dried with $MgSO_4$. After evaporation of the solvent nitrocyclopropanes were purified by column chromatography (gradient eluation with hexane/AcOEt, 9:1→7:3 for **8b**, **10** and **11** but hexane/Et_2O, 9.9:0.1→9:1 for **11e**). For yields and diastereomeric ratios, see Table 2.

1.3.1. (4*S*,1*R*,3*S*)-*cis*-2,2-Dimethyl-4-(2,3,3-trimethyl-2-nitro-cyclopropyl)-[1,3]dioxolane (8b). Colourless crystals. Mp 66–67°C (pentane). $[\alpha]_{546}^{20}=-50.8$ (*c* 1.0, $CHCl_3$). r_f=0.25 (hexane/AcOEt, 8:2). ^{13}C NMR δ 109.1 (C), 73.4 (C), 73.2 (CH), 69.4 (CH_2), 40.3 (CH), 27.2 (C), 27.0 (CH_3), 25.3 (CH_3), 22.5 (CH_3), 19.8 (CH_3), 16.2 (CH_3). ^{1}H NMR δ 4.24 (m, 2H), 3.73 (m, 1H), 1.68 (s, 3H), 1.38 (s, 3H), 1.29(s, 3H), 1.20 (s, 3H), 1.13 (s, 3H), 1.00 (d, *J*=9.0 Hz, 1H). Anal. calcd for $C_{11}H_{19}NO_4$: C 57.62; H 8.35; N 6.11. Found C, 57.41; H 8.31; N 6.08.

1.3.2. (4*S*)-*trans*-4-(2,2-Dimethyl-3-nitro-cyclopropyl)-2,2-dimethyl-[1,3]dioxolane (10a/11a). Diastereomers not separated by column chromatography.

Major diastereomer. ^{13}C NMR δ 109.9 (C), 73.4 (CH), 69.6 (CH), 69.3 (CH_2), 37.0 (CH), 30.4 (C), 27.0 (CH_3) 26.0 (CH_3), 20.7 (CH_3), 20.0 (CH_3).

Minor diastereomer. ^{13}C NMR δ 110.1 (C), 74.1 (CH), 69.5 (CH), 69.1 (CH_2), 37.0 (CH), 31.0 (C), 27.2 (CH_3), 25.9 (CH_3), 20.6 (CH_3), 20.0 (CH_3).

1.3.3. (4*S*)-2,2-Dimethyl-4-(2-methyl-2-nitro-cyclopropyl)-[1,3]dioxolane (10b/11b). A solution of diphenylmethylsulfonium tetrafluoroborate[20] (3.1 g, 10.0 mmol) and dry CH_2Cl_2 (0.64 mL, 10.0 mmol) in freshly distilled absolute DME (100 mL) under argon was cooled to −70°C and combined with a cold solution of LDA [10 mmol, freshly prepared from 1.6 M BuLi in hexane (6.25 mL) and diisopropylamine (1.4 mL) in 10 mL of dry DME (10 mL) at −70°C]. The resulting yellow-greenish solution turned brown. After 10 min of intensive stirring nitroalkene (*E*)-**4b** (1.3 g, 7 mmol) dissolved in dry DME (5 mL) was added fast, while the colour of the mixture turned to greenish brown and a solid precipitated. The mixture was allowed to warm up to room temperature overnight. It was combined with half-saturated aqueous NH_4Cl and extracted with Et_2O/pentane (3:1, 4 times 40 mL). The combined organic layers were washed with brine (100 mL) and dried with $MgSO_4$. After stripping off the solvent the nitrocyclopropane **10b/11b** and isoxazoline-*N*-oxide **12** (R=Me) were separated by column chromatography (gradient eluation with hexane/AcOEt, 9:1→1:2).

First diastereomer (faster on TLC). Yellow oil. $[\alpha]_{546}^{20}=-111.7$ (*c* 1.0, $CHCl_3$). r_f=0.23 (hexane/AcOEt, 8:2). ^{13}C NMR δ 110.1 (C), 73.8 (CH), 69.7 (CH_2), 63.4 (C), 32.2 (CH_3), 26.8 (CH_3), 26.1 (CH_2), 21.7 (CH_3), 15.3 (CH). ^{1}H NMR δ 4.09 (dd, *J*=6.1, 8.1 Hz, 1H), 3.90 (m, 1H), 3.67 (dd→t, *J*=7.5 Hz, 1H), 2.15 (m, 1H), 1.97 (dd, *J*=5.5, 10.6 Hz, 1H), 1.70 (s, 3H), 1.35 (s, 3H), 1.28 (s, 3H), 1.19 (dd, *J*=5.5, 7.5 Hz, 1H). Anal. calcd for $C_9H_{15}NO_4$: C 53.72; H 7.51; N 6.96. Found C, 54.22; H 7.52; N 6.78.

Second diastereomer (slower on TLC). Yellow oil. $[\alpha]_{546}^{20}=+66.3$ (*c* 1.0, $CHCl_3$). r_f=0.13 (hexane/AcOEt, 8:2). ^{13}C NMR δ 110.3 (C), 76.3 (CH), 69.2 (CH_2), 64.1 (C), 32.5 (CH), 27.1 (CH_3), 26.2 (CH_3), 22.2 (CH_3), 15.5 (CH_3). ^{1}H NMR δ 4.06 (dd, *J*=6.1, 8.1 Hz, 1H), 3.76 (dd, *J*=6.5, 8.1 Hz, 1H), 3.57 (m, 1H), 2.19 (m, 1H), 1.92 (dd, *J*=5.7, 10.5 Hz, 1H), 1.76 (s, 3H), 1.35 (s, 3H), 1.26 (s, 3H), 0.87 (dd, *J*=5.8, 7.5 Hz, 1H). Anal. calcd for $C_9H_{15}NO_4$: C 53.72; H 7.51; N 6.96. Found C, 53.93; H 7.74; N 6.91.

1.3.4. 2,2-Dimethyl-4-(2,3,3-trimethyl-2-nitro-cyclopropyl)-[1,3]dioxolane(10c/11c). *Major diastereomer*: (4*S*, 1*R*, 3*R*)-*trans*-2,2-dimethyl-4-(2,3,3-trimethyl-2-nitro-cyclopropyl)-[1,3]dioxolane (**10c**). Colourless crystals. Mp 85–87°C (pentane). $[\alpha]_{546}^{20}=+50.3$ (*c* 1.0 $CHCl_3$). r_f=0.28 (hexane/AcOEt, 8:2). ^{13}C NMR (DMSO-d_6) δ 108.5 (C_q), 72.7 (C), 71.8 (CH), 68.2 (CH_2), 35.8 (CH), 29.1 (C), 26.8 (CH_3), 25.6 (CH_3), 21.1 (CH_3), 16.0 (CH_3), 13.3 (CH_3). ^{13}C NMR ($CDCl_3$) δ 109.4 (C), 72.5 (CH), 68.8 (CH_2), 35.5 (CH), 29.3 (C), 26.7 (CH_3) 25.7 (CH_3), 21.4 (CH_3), 16.2 (CH_3), 13.7 (CH_3). ^{1}H NMR (DMSO-d_6) δ 3.99 (dd, *J*=6.2, 7.4 Hz, 1H), 3.92 (m, 1H), 3.62 (dd, *J*=5.9, 7.5 Hz, 1H), 2.05 (d, *J*=9.3 Hz, 1H), 1.61 (s, 3H), 1.36 (s, CH_3), 1.26 (s, 3H), 1.15 (s, 3H), 1.06 (s, 3H). Anal. calcd for $C_{11}H_{19}NO_4$: C 57.62; H 8.35; N 6.11. Found C, 57.65; H 8.12; N 6.14.

Minor diastereomer. Colourless oil. r_f=0.20 (hexane/AcOEt, 8:2). ^{13}C NMR δ 109.1 (C), 73.2 (CH), 69.4 (CH_2), 35.9 (CH), 28.9 (C), 26.8(CH_3), 25.3 (CH_3), 21.1 (CH_3), 16.6 (CH_3), 13.4 (CH_3).

1.3.5. 2-(2,3,3-Trimethyl-2-nitro-cyclopropyl)-1,4-dioxa-spiro[4,5]decane (10d/11d). *Major diastereomer*: (2*S*,1*R*,2*R*)-*trans*-2-(2,3,3-trimethyl-2-nitro-cyclopropyl)-1,4-di-oxa-spiro[4,5]decane (**10d**). Colourless waxy solid. $[\alpha]_{546}^{20}=+47.0$ (*c* 1.0, $CHCl_3$). r_f=0.56 (hexane/AcOEt, 7:3). ^{13}C NMR δ 108.9 (C), 71.8 (C), 71.1 (CH), 67.6 (CH_2), 35.4 (CH_2), 34.7 (CH), 34.3 (CH_2), 28.3 (C), 24.0 (CH_2), 22.9 (CH_2), 22.8 (CH_2), 20.4 (CH_3), 15.3 (CH_3), 12.7 (CH_3). ^{1}H NMR δ 3.97 (dd, *J*=5.4, 7.6 Hz, 1H), 3.70 (m, 2H), 2.15 (d, *J*=9.2 Hz, 1H), 1.58 and 1.49 (br, 13H), 1.16 (s, 3H), 1.11 (s, 3H). Anal. calcd for $C_{14}H_{23}NO_4$: C 62.43; H 8.60; N 5.20. Found C, 62.51; H 8.61; N 5.34. MS (FAB) *m/z* 270.2 $(M+1)^+$.

Minor diastereomer. Light yellow oil. r_f=0.47 (hexane/AcOEt, 7:3). ^{13}C NMR δ 108.8 (C), 71.8 (C), 71.7 (CH), 68.1 (CH_2), 35.7 (CH_2), 34.9 (CH), 33.8 (CH_2), 28.3 (C), 24.0, 22.9 (CH_2), 22.8 (CH_2), 22.7 (CH_3), 15.3 (CH_3) 12.7 (CH_3).

1.3.6. 2-Benzyloxy-1-triethylsilyloxy-(2,3,3-trimethyl-2-nitro-cyclopropyl)-ethane (10e/11e). *Major diastereomer*: (2*R*,1*S*,2*S*)-*trans*-2-benzyloxy-1-triethylsilyloxy-(2,3,3-trimethyl-2-nitro-cyclopropyl)-ethane (**11e**). Colourless oil. r_f=0.26 (hexane/Et_2O, 95:5). ^{13}C NMR δ 137.3 (C), 127.3 (CH), 126.7 (CH), 126.6 (CH), 75.5 (CH), 72.0 (C), 70.9 (CH_2), 64.6 (CH_2), 34.3 (CH), 28.0 (C), 20.3 (CH_3), 16.0 (CH_3), 13.3 (CH_3), 5.7 (CH_3), 3.2 (CH_2). ^1H NMR δ 7.25 (m, 5H), 4.60 (d, *J*=11.5 Hz, 1H), 4.48 (d, *J*=11.5 Hz, 1H), 3.75 (dd, *J*=6.2, 10.5 Hz, 1H), 3.60 (dd, *J*=4.5, 10.5 Hz, 1H), 3.20 (m, 1H), 2.21 (d, *J*=10.0 Hz, 1H), 1.56 (s, 3H), 1.07 (s, 3H), 1.01 (s, 3H), 0.87 (t, *J*=8.0 Hz, 9H), 0.51 (q, *J*=8.0 Hz, 6H). Anal. calcd for $C_{21}H_{35}NO_4Si$: C 64.08; H 8.96; N 3.56. Found C, 63.55; H 9.60; N 3.59.

Minor diastereomer (**10e**). Colourless oil. r_f=0.23 (hexane/AcOEt, 95:5). ^{13}C NMR δ 137.3 (C), 126.8 (CH), 126.7 (CH), 126.6 (CH), 75.5 (CH), 72.0 (C), 70.6 (CH_2), 64.4 (CH_2), 34.6 (CH), 28.2 (C), 20.3 (CH_3), 16.3 (CH_3), 12.9 (CH_3), 5.5 (CH_3), 3.2 (CH_2).

1.3.7. (4*R*)-3-*N*-*tert*-Butyloxycarbonyl-2,2-dimethyl-4-(2,3,3-trimethyl-2-nitro-cyclopropyl)-oxazolidine (10f/11f). *First diastereomer* (faster on TLC). Light yellow oil. r_f=0.27 (hexane/AcOEt, 9:1). ^{13}C NMR δ 152.2 (C), 94.5 (C), 80.6 (C), 72.5 (C), 68.3 (CH_2), 58.2 (CH), 54.1 (CH), 38.6 (CH_3), 32.0 (C_q), 28.7 (CH_3), 27.7 (CH_3), 21.8 (CH_3), 17.4(CH_3), 14.3 (CH_3). ^1H NMR δ 3.95 (m, 1H), 3.65 (m, 2H), 2.25 (d, *J*=9.7 Hz, 1H) 1.55 (s, 3H), 1.54 (s, 3H), 1.42 (s, 3H), 1.42 (s, 9H), 1.20 (s, 3H) 1.08 (s, 3H).

Second diastereomer (slower on TLC). Light yellow oil. r_f=0.24 (hexane/AcOEt, 9:1). ^{13}C NMR δ 152.2 (C), 94.7 (C), 80.7 (C), 74.8 (C), 68.4 (CH_2), 54.3 (CH), 37.9 (CH), 28.6 (CH_3), 28.4 (CH_3), 27.9 (C), 25.8 (CH_3), 21.9 (CH_3), 17.0 (CH_3), 14.7 (CH_3). ^1H NMR δ 3.94 (m, 1H), 3.66 (m, 2H), 2.30 (d, *J*=11.7 Hz, 1H), 1.75 (s, 3H), 1.56 (s, 3H), 1.43 (s, 3H), 1.38 (s, 9H), 1.06 (s, 3H), 1.00 (s, 3H).

1.3.8. (4*S*)-4-(2,2-Dimethyl-[1,3]dioxolane-4-yl)-3-methyl-4,5-dihydro-isoxazole-2-oxide (12) (R=Me). *First diastereomer* (faster on TLC). Yellow oil. r_f=0.15 (hexane/AcOEt, 1:1). ^{13}C NMR δ 111.8 (C), 108.9 (C), 73.2 (CH), 66.0 (CH_2), 64.1 (CH_2), 48.5 (CH), 25.5 (CH_3), 24.1 (CH_3), 10.5 (CH_3). ^1H NMR δ 4.38 (m, 3H), 4.13 (dd, *J*=6.5, 8.4 Hz, 1H), 3.64 (dd, *J*=6.4, 8.5 Hz, 1H), 3.48 (m, 1H), 2.00 (d, *J*=1.5 Hz, 3H), 1.43 (s, 3H), 1.35 (s, 3H).

Second diastereomer (slower on TLC). Yellow oil. r_f=0.08 (hexane/AcOEt, 1:1). ^{13}C NMR δ 113.6 (C), 110.2 (C), 75.4 (CH), 66.6 (CH_2), 64.7 (CH_2), 49.7 (CH), 26.6 (CH_3), 24.8 (CH_3), 11.9 (CH_3). ^1H NMR δ 4.42 (dd, *J*=8.1, 9.4 Hz 1H), 4.30 (m, 1H), 4.16 (dd, *J*=5.1, 8.1 Hz, 1H), 4.08 (dd, *J*=6.4, 8.7 Hz, 1H), 3.74 (dd, *J*=5.4, 8.7 Hz, 1H), 3.43 (m, 1H), 2.05 (d, *J*=1.4 Hz, 3H), 1.45 (s, CH_3), 1.34 (s, 3H).

1.4. Reduction of nitrocyclopropanes 10c,d—synthesis of aminocyclopropanes 13a,b

Nitrocyclopropane **10c** or **10d** (600 mg) was dissolved in 15 mL of dry MeOH and 10% Pd/C (20 mg) was added. The reaction mixture was hydrogenated at 15 bar (for **10c**) or 25 bar (for **10d**) under vigorous stirring for 48 h. The catalyst was filtered through celite and the solvent was removed carefully at reduced pressure. The remainder was purified by column chromatography ($CHCl_3$/MeOH, 90:10) to give **13a** (74%) or **13b** (47%).

1.4.1. (4*S*,1*R*,3*R*)-*trans*-3-(2,2-Dimethyl-[1,3]dioxolane-4-yl)-1,2,2-trimethyl-cyclopropylamine (13a). Colourless wax. $[\alpha]_{546}^{20}=-6.6$ (*c* 0.5, $CHCl_3$). r_f=0.33 ($CHCl_3$/MeOH, 8:2). ^{13}C NMR δ 108.3 (C), 74.6 (CH), 69.2 (CH_2), 39.5 (C), 36.5 (CH), 26.8 (CH_3), 25.9 (CH_3), 24.1 (C), 22.1 (CH_3), 19.1 (CH_3), 16.8 (CH_3). ^1H NMR δ 3.79 (dd, *J*=5.6, 7.6 Hz, 1H), 3.53 (m, 1H), 3.41 (dd→t, *J*=7.7 Hz, 1H), 1.92 (s, 2H), 1.20 (s, 3H), 1.12 (s, 3H). 1.02 (s, 3H), 0.98 (s, 3H), 0.88 (s, 3H), 0.37 (d, *J*=9.6 Hz, 1H).

1.4.2. (2*S*,1*R*,3*R*)-*trans*-3-(1,4-Dioxa-spiro-[4,5]dec-2-yl)-1,2,2-trimethyl-cyclopropylamine (13b). Colourless wax. r_f=0.17 ($CHCl_3$/MeOH, 9:1). ^{13}C NMR δ 109.2 (C), 74.7 (CH), 69.5 (CH_2), 40.0 (C), 37.4 (CH), 36.9 (CH_2), 35.9 (CH_2), 25.5 (CH_2), 24.7 (C), 24.3 (CH_2), 24.2 (CH_2), 22.7 (CH_3), 19.9 (CH_3), 17.4 (CH_3). ^1H NMR δ 3.97 (dd, *J*=5.6, 7.9 Hz, 1H), 3.70 (m, 1H), 3.55 (dd→t, *J*=7.5 Hz, 1H), 1.92 (s, 2H), 1.62–1.54 (broad, 10H), 1.19 (s, 3H), 1.14 (s, 3H), 1.08 (s, 3H), 0.50 (d, *J*=9.4 Hz, 1H).

1.5. Introduction of protecting groups into aminocyclopropanes 13—synthesis of 14

1.5.1. Boc-protection—general procedure (Table 3). The corresponding amine **13** (0.42 mmol, 1.0 equiv.) was dissolved in water/dioxane (1:1, 5 mL) and cooled to 0°C under stirring. $NaHCO_3$ (352 mg, 4.2 mmol, 10 equiv.) and Boc_2O (0.45 mL, 2.09 mmol, 5.0 equiv.) were added. After stirring overnight the solvent was evaporated under reduced pressure. The residue was diluted with aqueous NH_4Cl (10 mL) and extracted three times with CH_2Cl_2 (20 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was stripped off under reduced pressure. Chromatography on silica gel (hexane/AcOEt, 8:2) afforded the *N*-Boc-aminocyclopropanes **14a** and **14f**.

1.5.1.1. (4*S*,1*R*,3*R*)-*trans*-*N*-*t*-Butoxycarbonyl-3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-1,2,2-trimethyl-cyclopropylamine (14a). Colourless wax. r_f=0.27 (hexane/AcOEt, 8:2). ^{13}C NMR δ 155.4 (C), 108.4 (C), 78.8 (C), 74.2 (CH), 69.2 (CH_2), 38.3 (C), 36.4 (CH), 28.3 (CH_3), 26.9 (CH_3), 25.8 (CH_3), 24.5 (C), 22.6 (CH_3), 16.4 (CH_3), 15.6 (CH_3). ^1H NMR δ 4.83 (s, 1H), 4.02 (m, 1H), 3.82 (m, 1H), 3.67 (m, 1H), 1.42 (s, 3H), 1.35 (s, 9H), 1.28 (s, 3H), 1.16 (s, 3H), 1.14 (s, 3H), 1.06 (s, 3H), 0.69 (d, *J*=9.6 Hz, 1H).

1.5.1.2. (2*S*,1*R*,3*R*)-*trans*-*N*-*t*-Butoxycarbonyl-3-(1,4-dioxa-spiro-[4,5]dec-2-yl)-1,2,2-trimethyl-cyclopropylamine (14f). Colourless wax. r_f=0.63 (hexane/AcOEt, 1:1). ^{13}C NMR δ 156.0 (C), 109.3 (C), 79.0 (C), 74.1 (CH), 69.4 (CH_2), 39.2 (C), 36.9 (CH), 36.9 (CH_2), 35.8 (CH_2), 38.7 (CH_3), 25.5 (CH_2), 25.0 (C), 24.3 (CH_2), 24.2 (CH_2), 23.0 (CH_3), 16.9 (CH_3), 15.9 (CH_3). ^1H NMR δ 4.78 (s, 1H), 3.98 (m, 1H), 3.75 (m, 1H), 3.67 (m, 1H), 1.50–1.34 (m, 19H), 1.15 (s, 3H), 1.13 (s, 3H), 1.06 (s, 3H), 0.67 (d, *J*=9.4 Hz, 1H).

1.5.2. Benzoylation

1.5.2.1. (2*S*,1*R*,3*R*)-*trans*-*N*-Benzoyl-3-(1,4-dioxa-spiro-[4,5]dec-2-yl)-1,2,2-trimethyl-cyclopropyl-amine (14g). A solution of benzoyl cyanide (120 mg, 0.92 mmol,

1.1 equiv.) in dry CH_2Cl_2 (1 mL) was dropped into a solution of amine **13b** (0.84 mmol, 1.0 equiv.) in dry CH_2Cl_2 (5 mL) at −18°C during 10 min, while the evolving HCN was stripped off by a gentle stream of argon and absorbed in 10% aqueous NaOH. The mixture was allowed to warm up to room temperature overnight. After stripping off the solvent, the remainder was purified by column chromatography (hexane/AcOEt, 8:2) affording **14g**. Colourless wax. r_f=0.45 (hexane/AcOEt 1:1). ^{13}C NMR δ 168.0 (N–C=O), 135.2 (C), 131.8 (CH), 128.9 (CH), 127.1 (CH), 109.4 (C), 74.2 (CH), 69.4 (CH_2), 39.0 (C), 37.1 (CH), 36.8 (CH_2), 36.0 (CH_2), 25.5 (CH_2), 24.8 (C), 24.3 (CH_2), 24.2 (CH_2), 23.2 (CH_3), 16.8 (CH_3), 15.7 (CH_3). ^{1}H NMR δ 7.61 (d, J=6.9 Hz, 2H), 7.36 (m, 3H), 6.51 (s, 1H), 4.08 (dd, J=5.9, 8.2 Hz, 1H), 3.95 (dd→t, J=8.0 Hz, 1H), 3.75 (m, 1H), 1.53 (b, 10H), 1.25 (s, 3H), 1.20 (s, 3H), 1.13 (s, 3H), 0.84 (d, J=9.7 Hz, 1H). MS (CI) m/z: 344 (M^++1, 40), 246 (95), 228 (90), 202 (100), 160 (8), 141 (10).

1.5.3. Introduction of Z-group

1.5.3.1. (4*S*,1*R*,3*R*)-*trans*-*N*-Benzyloxycarbonyl-3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-1,2,2-trimethyl-cyclopropyl-amine (14b). Na_2CO_3 (660 mg, 6.23 mmol, 5.0 equiv.) and Z-Cl (0.2 mL, 1.38 mmol, 1.1 equiv.) were added to a solution of aminocyclopropane **13a** (248 mg, 1.25 mmol, 1.0 equiv.) in 1:1 water/dioxane (20 mL) at 0°C under vigorous stirring. After stirring at 0° for 1 h the temperature was increased to room temperature over a period of another 1 h. Water (10 mL) was added and the mixture was extracted with CH_2Cl_2 (4 times 25 mL). After drying of the combined organic layers ($MgSO_4$) the solvent was removed by rotatory evaporator and the remainder was purified by chromatography (silica, hexane/AcOEt, 9:1) to give **14b**. Waxy solid. $[\alpha]_{546}^{20}$=+134 (c 1.0, $CHCl_3$). r_f=0.60 (hexane/AcOEt, 1:1). ^{13}C NMR δ 156.4 (C), 136.8 (C), 128.9 (CH), 128.5 (CH), 127.3 (CH), 108.9 (C), 74.5 (CH), 69.5 (CH_2), 66.8 (CH_2), 38.8 (C), 36.9 (CH), 27.3 (CH_3), 26.4 (CH_3), 24.8 (C), 23.0 (CH_3), 16.7 (CH_3), 16.0 (CH_3). ^{1}H NMR δ 7.24 (m, 5H), 5.12 (s, 1H), 5.00 (d, J=12.1 Hz, 1H), 4.93 (d, J=12.1 Hz, 1H), 4.02 (m, 1H), 3.89 (dd→t, J=7.7 Hz, 1H), 3.67 (m, 1H), 1.34 (s, 3H), 1.27 (s, 3H), 1.15 (s, 3H), 1.11 (s, 3H), 1.05 (s, 3H), 0.77 (d, J=9.8 Hz, 1H). Anal. calcd for $C_{19}H_{27}NO_4$: C 68.44; H 8.16; N 4.20. Found: C 68.12; H 8.16; N 4.14.

1.5.4. Introduction of trifluoroacetyl group

1.5.4.1. (4*S*,1*R*,3*R*)-*trans*-*N*-(Trifluoroacetyl)-3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-1,2,2-tri-methyl-cyclopropylamin (14c). Trifluoroacetic anhydride (0.52 mL, 3.76 mmol, 3.0 equiv.) was added to a solution of aminocyclopropane **13a** (250 mg, 1.25 mmol, 1.0 equiv.) and NEt_3 (1.05 mL, 7.54 mmol, 6.0 equiv.) in dry Et_2O (20 mL) at −18°C under stirring over a period of 10 min. After 1 h stirring at −18°C, the reaction mixture was washed with saturated aqueous $NaHCO_3$ (3 times 5 mL) and with brine (once, 5 mL). The organic layer was dried (Na_2SO_4) and the solvent was stripped off by a rotatory evaporator. The residue was purified by column chromatography (hexane/AcOEt, 7:3) affording the product **14c**. Light yellowish oil. r_f=0.48 (hexane/AcOEt, 1:1). ^{13}C NMR δ 157.9 (C, J_{CF}=36.4 Hz), 116.1 (C, J_{CF}=288.6 Hz), 109.1 (C), 74.0 (CH), 69.4 (CH_2), 38.9 (C), 36.5 (CH), 27.2 (CH_3), 26.2 (CH_3), 24.8 (C), 22.8 (CH_3), 16.4 (CH_3), 14.9 (CH_3). ^{1}H NMR δ 6.82 (s, 1H), 4.05 (dd, J=5.9 Hz, 8.3 Hz, 1H), 3.88 (dd→t, J=7.7 Hz), 3.71 (m, 1H), 1.35 (s, 3H), 1.28 (s, 3H), 1.22 (s, 3H), 1.15 (s, 3H), 1.12 (s, 3H), 0.82 (d, J=9.7 Hz, 1H). Anal. calcd for $C_{13}H_{20}F_3NO_3$: C 52.88; H 6.83; N 4.74. Found: C 51.13; H 6.73; N 4.75. HRMS: calcd for $C_{13}H_{20}F_3NO_3$: 295.1395, found 295.1392.

1.5.5. Introduction of *N*-Z-glycyl

1.5.5.1. (4*S*,1*R*,3*R*)-*trans*-*N*-(*N*′-Benzyloxycarbonyl-glycinyl)-3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-1,2,2-trimethyl-cyclo-propylamin (14d). Hydroxybenzotriazole (590 mg, 4.36 mmol, 2.0 equiv.) was added to a solution of *N*-Z-glycine (457 mg, 2.18 mmol, 1.0 equiv.) in dry THF (20 mL). After cooling to 0°C a solution of DCC (495 mg, 2.4 mmol, 1.1 equiv.) in dry THF (10 mL) was added under stirring. The mixture was stirred at 0°C for 1 h and at ambient temperature for 20 min while a turbidity appeared. After cooling to 0°C a solution of the aminocyclopropane **13a** (433 mg, 2.18 mmol, 1.0 equiv.) in dry THF (10 mL) was added dropwise under stirring over 5 min. Stirring at 0°C was continued for 15 min. Dicyclohexylurea was filtered off and the filtrate was concentrated with a rotatory evaporator. The remaining oil was mixed with AcOEt causing precipitation of hydroxybenzotriazole, which was filtered off and washed with AcOEt. The combined organic layers were washed with saturated aqueous $NaHCO_3$, 2 M aqueous citric acid and again with saturated aqueous $NaHCO_3$. Each of the aqueous phases was extracted with CH_2Cl_2. All combined organic layers (AcOEt and CH_2Cl_2) were dried ($MgSO_4$) and the solvents were evaporated. The remainder was purified by column chromatography (hexane/AcOEt, 1:1) affording **14d**. Colourless wax. r_f=0.15 (hexane/AcOEt, 1:1). ^{13}C NMR δ 170.0 (C), 157.0 (C), 136.9 (C), 128.9 (C), 128.7 (C), 128.6 (C), 128.4 (C), 128.1 (C), 108.9 (C), 74.5 (CH), 69.5 (CH_2), 67.5 (CH_2), 45.0 (CH_2), 38.5 (C), 36.6 (CH), 27.3 (CH_3), 26.3 (CH_3), 24.4 (C), 23.0 (CH_3), 16.6 (CH_3), 15.5 (CH_3). ^{1}H NMR δ 7.24 (m, 5H), 6.62 (s, 1H), 5.82 (s, 1H), 5.02 (s, 2H), 4.01 (m, 1H), 3.88 (m, 1H), 3.67 (m, 1H), 1.33 (s, 3H), 1.27 (s, 3H), 1.11 (s, 3H), 1.05 (s, 6H), 0.70 (d, J=9.7 Hz, 1H). CI-MS: m/z: 390 (M^+, 10), 375 (10), 333 (100), 315 (49), 289 (80), 232 (16), 170 (8), 142 (87), 124 (43).

1.5.6. Introduction of tosyl group

1.5.6.1. (4*S*,1*R*,3*R*)-*trans*-*N*-(4-Tolylsulfonyl)-3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-1,2,2-trimethyl-cyclopropylamine (14e). Ts-Cl (360 mg, 1.87 mmol, 1.1 equiv.) was added to a solution of aminocyclopropane **13a** (340 mg, 1.7 mmol, 1.0 equiv.), DMAP (22 mg, 0.18 mmol, 0.1 equiv.), and NEt_3 (0.46 mL, 3.74 mmol, 2.2 equiv.) in dry CH_2Cl_2 (30 mL) at room temperature. After stirring overnight saturated aqueous NH_4Cl (20 mL) was added and the mixture was extracted with CH_2Cl_2 (3 times 30 mL). The combined organic layers were dried (Na_2SO_4) and concentrated with a rotatory evaporator. Column chromatography (hexane/AcOEt, 7:3) of the remainder afforded the product **14e**. Colourless wax. r_f= 0.19 (hexane/AcOEt, 7:3). ^{13}C NMR δ 143.6 (C), 139.9 (C), 130.0 (CH). 127.3 (CH), 109.0 (C), 74.3 (CH), 69.2 (CH_2), 41.1 (C), 34.2 (CH), 27.2 (CH_3), 26.3 (CH_3), 24.6 (C), 23.0 (CH_3), 21.8 (CH_3), 18.0 (CH_3), 16.4 (CH_3). ^{1}H NMR δ 7.66 (d, J=8.2 Hz, 2H), 7.21 (d, J=8.2 Hz, 2H), 5.27 (s, 1H), 3.94 (dd, J=5.9, 8.2 Hz, 1H), 3.84 (dd→t, J=7.7 Hz, 1H),

3.56 (m, 1H), 2.34 (s, 3H), 1.26 (s, 3H), 1.24 (s, 3H), 1.11 (s, 3H), 1.00 (s, 3H), 0.97 (s, 3H), 0.82 (d, J=9.8 Hz, 1H).

1.5.6.2. (4*S*,1*R*,3*R*)-*trans*-*N*-Bis-(4-tolylsulfonyl)-3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-1,2,2-trimethyl-cyclopropylamine (15). A solution of monotosylate **14e** (200 mg, 0.56 mmol, 1.0 equiv.) in dry DMF (2 mL) was added to a solution of 95% NaH (20 mg, 0.6 mmol, 1.07 equiv.) in dry DMF (1 mL) dropwise under stirring in an argon atmosphere while the colour of the mixture turned from colourless to orange and the mixture became turbid. After stirring at room temperature for 30 min Ts-Cl (115 mg, 0.6 mmol, 1.07 equiv.) was added. The reaction mixture turned yellow and precipitation started. After stirring at room temperature for 14.5 h EtOH (3 mL) was added. The mixture was concentrated and the remainder was dissolved in CH_2Cl_2 (20 mL). After washing with water (15 mL)/1 M HCl (2 drops), water (15 mL), saturated aqueous NH_4Cl (15 mL), and brine (15 mL) the organic phase was dried (Na_2SO_4) and evaporated. The remainder was purified by column chromatography (silica, hexane/AcOEt, 9:1→7:3) affording the ditosylated product **15** (210 mg, 74%). Colourless crystals. Mp 110–112°C. r_f=0.32 (hexane/AcOEt, 7:3). ^{13}C NMR δ 145.1 (C), 144.8 (C), 139.7 (C), 138.5 (C), 130.0 (CH), 129.6 (CH), 129.5 (CH), 128.4 (CH), 108.9 (C), 74.4 (CH), 68.4 (CH_2), 50.1 (C), 32.6 (CH), 28.0 (C), 27.5 (CH_3), 26.2 (CH_3), 24.9 (CH_3), 22.0 (CH_3), 18.7 (CH_3), 16.3 (CH_3). ^{1}H NMR δ 7.93 (d, J=8.4 Hz, 2H), 7.88 (d, J=8.4 Hz, 2H), 7.25 (d, J=6.0 Hz, 2H), 7.22 (d, J=6.0 Hz), 4.16 (dd, J=5.8, 8.5 Hz, 1H), 3.96 (dd, J=5.7, 8.5 Hz, 1H), 3.71 (m, 1H), 2.36 (s, 3H), 2.34 (s, 3H), 1.47 (s, 3H), 1.24 (s, 6H), 1.06 (s, 3H), 0.96 (s, 3H), 0.88 (d, J=9.5 Hz, 1H). Anal. calcd for $C_{25}H_{33}NS_2O_6$ C, 59.14; H 6.55; N 2.76. S: 12.63. Found: C 59.03; H 7.01; N 2.74; S: 12.62.

1.5.6.3. Transformation of 15 into (1*R*,2*R*)-*trans*-2,3,3-trimethyl-2-(bis-4-tolylsulfonyl-amino)-cyclopropancarboxylic acid 16. For hydrolytic cleavage the acetonide **15** (170 mg, 0.34 mmol, 1.0 equiv.) was dissolved in MeOH (5 mL) and combined with water (0.5 mL) and *p*-TsOH (cat., 40 mg). After stirring at room temperature overnight the solvent was evaporated and the remainder was purified by column chromatography ($CHCl_3$/MeOH, 90:10) affording 136 mg (86%) of (1*R*,2*R*,1*S*)-*trans*-*N*-bis-4-tolylsulfonyl-1-(2-amino-2,3,3-trimethyl-cyclopropyl)-ethan-1,2-diol. Colourless foam. r_f=0.11 (hexane/AcOEt, 1:1). ^{13}C NMR δ 145.3 (C), 145.0 (C), 139.5 (C), 138.2 (C), 130.2 (CH), 129.7 (CH), 129.6 CH), 128.1 (CH), 70.7 (CH), 66.4 (CH_2), 50.8 (C), 33.2 (CH), 27.6 (C), 25.2 (CH_3), 22.0 (CH_3), 18.9 (CH_3), 16.4 (CH_3). ^{1}H NMR δ 7.93 (d, J=8.4 Hz, 2H), 7.85 (d, J=8.4 Hz, 2H), 7.23 (t, J=8.4 Hz, 4H), 3.77 (dd, J=3.6, 11.5 Hz, 1H), 3.58 (dd, J=6.7, 11.5 Hz, 1H), 3.39 (m, 1H), 2.35 (s, 3H), 2.32 (s, 3H), 1.50 (s, 3H), 1.05 (s, 3H), 0.95 (s, 3H), 0.79 (d, J=9.8 Hz, 1H). HRMS: calcd for (M^+−CHOH−CH_2OH) $C_{20}H_{24}O_4NS_2$: 406.1146, found 406.1148. The diol (125 mg, 0.267 mmol, 1.0 equiv.) was dissolved in a mixture of $CHCl_3$ (2 mL), MeCN (2 mL), and water (3 mL). $NaIO_4$ (228 mg, 1.07 mmol, 4.0 equiv.) and $RuCl_3$×H_2O (10 mg) were added under ice cooling. After stirring at room temperature for 2 h $NaIO_4$ (228 mg, 1.07 mmol, 4.0 equiv.) was added again. Stirring at room temperature was continued for 3 h while the dark solution turned temporarily light. After drying the reaction mixture with Na_2SO_4 it was filtered and the Na_2SO_4 was washed with CH_2Cl_2. The combined organic layers were evaporated and the remaining product was purified by twofold column chromatography ($CHCl_3$/MeOH, 90:10 and hexane/AcOEt, 7:3). The product was formed in 56% yield (65 mg) and was recrystallized from hexane/AcOEt, 7:3. (1*R*,2*R*)-*trans*-2,3,3-Trimethyl-2-(bis-4-tolylsulfonyl-amino)-cyclopropancarboxylic acid **16**. Colourless crystals. Mp 83–85°C. $[\alpha]_{546}^{20}$=−10.1 (*c* 1.0, CHCl). r_f=0.48 ($CHCl_3$/MeOH, 9:1). ^{13}C NMR δ 175.9 (C), 145.6 (C), 145.2 (C), 139.0 (C), 137.6 (C), 130.2 (CH), 129.9 (CH), 129.6 (CH), 128.7 (CH), 54.7 (C), 34.3 (C), 32.9 (CH), 25.3 (CH_3), 22.0 (CH_3), 16.8 (CH_3), 15.9 (CH_3). ^{1}H NMR δ 10.63 (b, 1H), 7.96 (d, J=8.3 Hz, 2H), 7.85 (d, 2H, J=8.3 Hz, 2H), 7.26 (m, 4H), 2.38 (s, 3H), 2.35 (s, 3H), 1.61 (s, 3H), 1.22 (s, 3H), 1.11 (s, 3H), 0.80 (s, 1H). EI-MS: *m/z*: 452 (M^++1, 7), 434 (100), 416 (15), 406 (28), 308 (15), 278 (18), 155 (96), 91 (100), 65 (27). HRMS: calcd for (M^+−OH) $C_{21}H_{24}NO_5S_2$: 434.1096, found 434.1099.

1.6. Conversion of dioxolane into the carboxylate moiety—synthesis of β-aminocyclopropane carboxylate derivatives 17–20

General procedure for hydrolytic removal of acetal protective group from **14** *to the corresponding diols*. Water (0.5 mL) and *p*-TsOH (cat., 25 mg) were added to a solution of **13** (100 mg) in MeOH (10 mL). After stirring overnight the progress of the reaction was checked (TLC) and eventually further water (0.5 mL) and *p*-TsOH (cat., 25 mg) were added. After the reaction had gone to completeness the mixture was concentrated and saturated aqueous $NaHCO_3$ (10 mL) was added. The solution was saturated with NaCl and extracted with CH_2Cl_2 (5–10 times 15 mL, TLC check). After drying the combined organic layers ($MgSO_4$) the solvent was evaporated. The remaining crude product was further used without prior purification. Column chromatography was possible (hexane/AcOEt, 1:1→3:7 or $CHCl_3$/MeOH, 90:10) but caused loss of product.

General procedure for the synthesis of **17** (Table 3). NEt_3 (0.412 mL, 2.96 mmol, 4.0 equiv.) and DMAP (10 mg, 0.074 mmol, 0.1 equiv.) were added to a solution of the diol (v.s. 0.74 mmol, 1.0 equiv.) in dry CH_2Cl_2 (20 mL). After cooling to −18°C TES-Cl (0.373 mL, 2.22 mmol, 3.0 equiv.) was added dropwise under stirring over a period of 10 min. The mixture was allowed to warm up to room temperature under stirring overnight. It was quenched with half-concentrated aqueous $NaHCO_3$. The organic layer was separated, dried (Na_2SO_4) and concentrated. Column chromatography (hexane/AcOEt, 9:1→7:3) afforded products **17**.

1.6.1. (1*S*,1*R*,3*R*)-*trans*-*N*-Trifluoroacetyl-3-(1,2-bis-triethylsilyloxy-ethyl)-1,2,2-trimethyl-cyclopropylamine (17c). Colourless oil. r_f=0.69 (hexane/AcOEt, 1:1).^{13}C NMR δ 157.6 (C, J_{CF}=36.3 Hz), 116.2 (C, J_{CF}=288.7 Hz), 72.1 (CH), 68.2 (CH_2), 39.5 (C), 37.7 (CH), 24.6 (C), 23.1 (CH_3), 16.9 (CH_3), 15.1 (CH_3), 7.2 (CH_3), 7.0 (CH_3), 5.7 (CH_2), 4.6 (CH_2). ^{1}H NMR δ 6.44 (s, 1H), 3.62 (dd, J=6.4, 10.3 Hz, 1H), 3.54 (dd, J=7.0, 10.3 Hz, 1H), 3.41 (m, 1H), 1.23 (s, 3H), 1.09 (s, 6H), 0.89 (t, J=7.9 Hz, 18H), 0.68 (d, J=9.8 Hz, 1H), 0.54 (q, J=7.9 Hz, 12H). Anal. calcd for

$C_{22}H_{44}F_5NSi_2O_3$: C 54.62; H 9.17; N 2.90. Found: C 54.26; H 8.90; N 2.92. EI-MS *m/z*: 484.4 (M^++1, 60), 454.3 (50), 352.4 (30), 338.3 (51), 322.3 (23), 261.3 (19), 220.3 (100), 206.2 (8), 145.3 (8), 115.5 (19), 107.3 (19), 87.2 (11).

1.6.2. (1*S*,1*R*,3*R*)-*trans*-*N*-(*N'*-Benzyloxycarbonyl-glycinyl)-3-(1,2-bis-triethylsilyloxy-ethyl)-1,2,2-trimethyl-cyclopropylamine (17d). Colourless foam. r_f=0.18 (hexane/AcOEt, 7:3); ^{13}C NMR δ 169.4 (C), 157.0 (C), 136.5 (C), 128.9 (CH), 128.6 (CH), 128.4 (CH), 72.8 (CH), 68.4 (CH_2), 67.4 (CH_2), 45.0 (CH_2), 39.1 (C), 37.5 (CH), 24.2 (C), 23.3 (CH_3), 17.0 (CH_3), 15.6 (CH_3), 7.3 (CH_3), 7.0 (CH_3), 5.8 (CH_3), 4.6 (CH_3). ^{1}H NMR δ 7.10 (b, 5H), 6.10 (s, 1H), 5.48 (s, 1H), 4.86 (s, 2H), 3.52 (m, 3H), 3.33 (m, 1H), 3.22 (m, 1H), 1.01 (s, 3H), 0.89 (s, 3H), 0.85 (s, 3H), 0.72 (t, 18H, *J*=7.9 Hz, 18H), 0.40 (m, 13H). EI-MS *m/z*: 578.5 (M^+, 38), 549 (100), 447 (4), 404 (5), 289 (57), 242 (18), 189 (18), 124 (52), 91 (100), 83 (32), 75 (23), 47 (7). Anal. calcd for $C_{30}H_{54}N_2Si_2O_5$: C 62.24; H 9.40; N 4.84. Found: C 61.57; H 9.28; N 4.82.

1.6.3. (1*S*,1*R*,3*R*)-*trans*-*N*-Benzoyl-3-(1,2-bis-triethylsilyloxy-ethyl)-1,2,2-trimethyl-cyclopropylamine (17g). Colourless wax. r_f=0.50 (hexane/AcOEt, 7:3). ^{13}C NMR δ 167.9 (C), 135.4 (C), 131.6 (CH), 128.8 (CH), 127.0 (CH), 72.6 (CH), 68.4 (CH_2), 39.8 (C), 37.8 (CH), 24.9 (C), 23.5 (CH_3), 17.2 (CH_3), 15.8 (CH_3), 7.3 (CH_3), 7.1 (CH_3), 6.1 (CH_2), 5.8 (CH_2). ^{1}H NMR δ 7.61 (d, *J*=6.8 Hz, 2H), 7.33 (m, 3H), 6.28 (s, 1H), 3.70 (m, 1H), 3.55 (m, 1H), 3.45 (m, 1H), 1.30 (s, 3H), 1.14 (s, 3H), 1.13 (s, 3H), 0.88 (t, *J*=7.8 Hz, 18H), 0.69 (d, *J*=9.8 Hz), 0.55 (q, *J*=7.9 Hz, 12 H). Anal. calcd for $C_{27}H_{49}NSi_2O_3$: C 65.93; H 10.04; N 2.85. Found: C 65.07; H 10.96; N 2.86.

Swern oxidation: *general procedure for the synthesis of aldehydes* **18** (Table 3). A solution of DMSO (0.243 mL, 3.41 mmol, 2.5 equiv.) in dry CH_2Cl_2 (4 mL) was added to a solution of oxalyl chloride (0.153 mL, 1.77 mmol, 1.3 equiv.) in dry CH_2Cl_2 (4 mL) dropwise under stirring at −78°C. After 5 min of stirring a solution of **17** (1.36 mmol, 1.0 equiv.) in dry CH_2Cl_2 was added. The mixture was allowed to warm up under stirring to −45°C during 1 h. NEt_3 (1.02 mL, 7.34 mmol) was added and the mixture was allowed to warm up to room temperature over 30 min. Water (20 mL) was added and the mixture was extracted with CH_2Cl_2 (3 times 15 mL). The combined organic layers were washed with brine, were dried ($MgSO_4$) and concentrated. Pure aldehydes **18** were obtained after column chromatography (hexane/AcOEt, 9:1→1:1).

1.6.4. (1*S*,1*R*,3*R*)-*trans*-*N*-(*N'*-Benzyloxycarbonyl-glycinyl)-3-(2-oxo-1-triethylsilyloxy-ethyl)-1,2,2-trimethyl-cyclopropylamine (18d). Light yellow oil. r_f=0.15 (hexane/AcOEt, 1:1); ^{13}C NMR δ 201.1 (CH), 169.6 (C), 157.0 (C), 136.5 (C), 128.9(CH), 128.5 (CH), 128.3 (CH), 76.0 (CH), 67.4 (CH_2), 45.0 (CH_2), 38.8 (C), 35.7 (CH), 24.7 (C), 23.0 (CH_3), 16.8 (CH_3), 16.1 (CH_3), 7.0 (CH_3), 5.3 (CH_2). ^{1}H NMR δ 9.57 (d, *J*=2.2 Hz, 1H), 7.25 (b, 5H), 6.55 (s, 1H), 5.68 (t, *J*=5.6 Hz, 1H), 5.01 (s, 2H), 3.65 (m, 3H), 1.20 (s, 3H), 1.17 (s, 3H), 1.06 (s, 3H), 0.87 (t, *J*=7.9 Hz, 9H), 0.78 (d, *J*=10.1 Hz, 1H), 0.53 (q, *J*=7.9 Hz, 6H). Anal. calcd for $C_{24}H_{38}NSi_2O_5$: C 62.31; H 8.28; N 6.05. Found: C 58.97; H 8.14; N 6.08.

1.6.5. (1*S*,1*R*,3*R*)-*trans*-*N*-Benzoyl-3-(2-oxo-1-triethylsilyloxy-ethyl)-1,2,2-trimethyl-cyclopropylamine (18g). Light yellow oil. r_f=0.25 (hexane/AcOEt, 7:3); ^{13}C NMR δ 200.0 (CH), 166.7 (C), 133.8 (C), 130.5 (CH), 127.6 (CH), 125.9 (CH), 74.9 (CH), 38.1 (C), 34.7 (CH), 23.9 (C), 22.0 (CH_3), 15.7 (CH_3), 15.0 (CH_3), 5.8 (CH_3), 4.1 (CH_2). ^{1}H NMR δ 9.66 (d, *J*=2.1 Hz, 1H), 7.61 (d, *J*=7.0 Hz, 2H), 7.31 (m, 3H), 6.60 (s, 1H), 3.71 (dd, *J*=2.1 Hz, 1H), 1.32 (s, 3H), 1.20 (s, 3H), 1.14 (s, 3H), 0.88 (m, *J*=7.9 Hz,10H), 0.53 (q, *J*=7.9 Hz, 6H).

Oxidation with $NaClO_2$—general procedure for the synthesis of carboxylic acids **19** (Table 3). A solution of the aldehyde **18** (0.293 mmol, 1.0 equiv.) in MeCN (3 mL) was combined with a solution of NaH_2PO_4 (cat., 10 mg) in water (0.5 mL). After cooling to 0°C 30% H_2O_2 (32 μL, 0.308 mmol, 1.05 equiv.) was added under stirring followed by the addition of a solution of $NaClO_2$ (47 mg, 0.410 mmol, 1.4 equiv.) in water (1 mL) over a period of 10 min while the mixture turned light yellow greenish. Stirring was continued at 0°C for 30 min and at room temperature for 30 min. After the reaction had gone to completion (TLC), Na_2SO_3 (5 mg) was added and the solvent was evaporated under vacuum. 1 M aqueous HCl (1 mL) and water (5 mL) were added to the remainder. After extraction with CH_2Cl_2 (3 times 10 mL) the combined organic layers were dried (Na_2SO_4) and concentrated. The remainder was purified by column chromatography ($CHCl_3$/MeOH, 9:1).

1.6.6. (1*R*,2*R*,2*S*)-*trans*-(2-*N*-Trifluoroacetyl-amino-2,3,3-trimethyl-cyclopropyl)-hydroxy-acetic acid (19c). Compound **17c** was oxidized according to the general procedure. The resulting aldehyde **18c** was oxidized without prior purification and analytical characterisation affording **19c**. Colourless foam. r_f=0.20 ($CHCl_3$/MeOH, 9:1). ^{13}C NMR (CD_3OD) δ 176.2 (C), 158.4 (C, J_{CF}=36.3 Hz), 116.4 (C, J_{CF}=287.8 Hz), 68.3 (CH), 40.5 (C), 36.0 (CH), 25.1 (C), 22.1 (CH_3), 15.6 (CH_3), 14.1 (CH_3). ^{1}H NMR δ 3.88 (d, *J*=10.5 Hz, 1H), 1.45 (s, 3H), 1.23 (s, 3H), 1.15 (s, 3H), 1.08 (d, *J*=10.5 Hz, 1H).

1.6.7. (1*R*,2*R*,2*S*)-*trans*-2-[*N*-(*N'*-Benzyloxycarbonyl-glycinyl)-amino]-2,3,3-trimethyl-cyclopropyl)-hydroxy-acetic acid (19d). Colourless foam. Mp 65–68°C. $[\alpha]_{546}^{20}$=−26.0 (*c* 1.0, $CHCl_3$). r_f=0.29 ($CHCl_3$/MeOH, 9:1); ^{13}C NMR δ 176.7 (C), 172.5 (C), 157.4 (C), 136.4 (C), 128.9 (CH), 128.7 (CH), 128.4 (CH), 69.3 (CH), 67.6 (CH_2), 44.7 (CH_2), 39.9 (C), 35.7 (CH), 24.7 (C), 23.0 (CH_3), 16.9 (CH_3), 15.5 (CH_3). ^{1}H NMR δ 7.43 (s, 1H), 7.21 (b, 5H), 6.12 (s, 1H), 4.98 (s, 2H), 3.71 (m, 3H), 1.22 (s, 3H), 1.05 (b, 6H), 0.86 (d, *J*=10.8 Hz, 1H). EI-MS: *m/z*: 365 (M^++1, 2), 289 (100), 188 (16), 98 (69), 91 (100), 65 (25). HR-MS: calcd M^++1, $\{C_{18}H_{25}N_2O_6\}$=365.1713. Found: 365.1717.

1.6.8. (1*R*,2*R*,2*S*)-*trans*-(2-*N*-Benzoyl-amino-2,3,3-trimethyl-cyclopropyl)-hydroxyacetic acid (19g). Colourless foam. Mp 110–112°C; $[\alpha]_{546}^{20}$=−15.0 (*c* 1.0, $CHCl_3$). r_f=0.17 ($CHCl_3$/MeOH, 9:1); ^{13}C NMR δ 176.6 (C), 170.1 (C), 133.0 (C), 132.8 (CH), 129.1(CH), 127.5 (CH), 69.5 (CH), 40.2 (C), 35.5 (CH), 24.8 (C), 23.3 (CH_3), 17.1 (CH_3), 15.6 (CH_3). ^{1}H NMR δ 11.62 (b, 1H), 7.70 (d, *J*=7.1 Hz, 2H), 7.40 (m, 4H), 3.83 (d, *J*=11.0 Hz, 1H), 1.40 (s, 3H),

1.25 (s, 3H), 1.17 (s, 3H), 1.02 (d, J=11.0 Hz, 1H). EI-MS: m/z: 278 (M^++1, 2), 202 (36), 112 (6), 105 (100), 85 (2), 77 (39), 55 (3), 42 (8), 31 (12).

1.6.9. (1*R*,2*R*,2*S*)-*trans*-2-Amino-2,3,3-trimethyl-cyclopropyl-2-hydroxyacetic acid (20). $Ba(OH)_2 \times 8H_2O$ (4 portions, 183 mg, 0.58 mmol each, 4.8 equiv.) were added to a solution of the trifluoroacetyl protected amino acid **19c** (130 mg, 0.483 mmol, 1.0 equiv.) in MeOH (10 mL) at room temperature over a period of 24 h. After refluxing for 2 h the solvent was removed under vacuum and the remainder was dissolved in 1 M H_3PO_4 (6 mL). This solution was transferred to a Dowex 50WX8 column (swelled in half concentrated HCl and washed chloride free with water). Eluation with 1 M H_3PO_4 (20 mL), water (200 mL) and 2% aqueous NH_3 (150 mL) afforded the amino acid **20** in the last 130 mL of eluent. Further purification by column chromatography was possible ($CHCl_3$/MeOH, 6:4). Colourless foam. r_f=0.14 ($CHCl_3$/MeOH, 6:4). ^{13}C NMR (CD_3OD) δ 180.5 (C), 71.0 (CH), 42.3 (C), 37.4 (CH), 23.6 (C_q), 22.4 (CH_3), 17.4 (CH_3), 15.5 (CH_3). ^{1}H NMR δ 3.49 (d, J=10.5 Hz, 1H), 1.40 (s, 3H), 1.18 (s, 3H), 1.08 (s, 3H), 1.98 (d, J=10.5 Hz, 1H).

1.6.10. (1*R*,2*R*)-*trans*-2,3,3-Trimethyl-2-nitro-cyclopropancarbaldehyde (21). Water (5 drops) and *p*-TsOH (cat., 25 mg) were added to a solution of the acetonide **10c** (100 mg, 0.44 mmol, 1.0 equiv.) in MeOH (5 mL). After stirring at room temperature for 12 h, solvents were removed and the deprotected diol was obtained in quantitative yield as colourless wax after column chromatography (hexane/AcOEt, 1:1. r_f=0.21). The diol (720 mg, 3.81 mmol, 1.0 equiv.) was dissolved in MeOH (30 mL) and was combined with a suspension of $NaIO_4$ (902 mg, 4.19 mmol, 1.1 equiv.) in buffer solution (pH=7,7 mL) under ice cooling. After 2 h stirring at room temperature the colourless precipitate was filtered off under suction and was washed with Et_2O. The combined filtrates were concentrated under vacuum and the remainder was dissolved in brine. The solution was extracted with Et_2O four times, the combined organic layers were dried (Na_2SO_4) and evaporated. After column chromatography hexane/AcOEt, 7:3) the product **21** (459 mg, 77%) was obtained. Light yellow oil. r_f=0.53 (hexane/AcOEt, 1:1). ^{13}C NMR δ 196.9 (CH), 78.5 (C), 41.3 (CH), 35.3 (C), 22.1 (CH_3), 16.2 (CH_3), 13.5 (CH_3). ^{1}H NMR δ 9.77 (d, J=3.3 Hz, 1H), 3.16 (d, J=3.3 Hz, 1H), 1.97, 1.37 (s, 3H), 1.28 (s, 3H). Anal. calcd for $C_7H_{11}NO_3$: C 53.49; H 7.05; N 8.91. Found: C 53.28; H 7.05; N 8.98.

1.6.11. (1*R*,2*R*)-*trans*-2,3,3-Trimethyl-2-nitro-cyclopropanecarboxylic acid (22a). *By oxidation with air.* A solution of the aldehyde **21** (242 mg, 1.54 mmol, 1.0 equiv.) in $CHCl_3$ (10 mL) was stirred at room temperature in an open flask. Eventually some $CHCl_3$ has to be added. After the reaction had gone to completion (TLC check, maximum 48 h), the solvent was evaporated and the remainder was purified by column chromatography (hexane/AcOEt, 1:1) affording product **22** (239 mg, 90%).

By oxidation with $RuCl_3$/$NaIO_4$. MeCN (6 mL) and water (9 mL) were added to a solution of the aldehyde **21** (850 mg, 5.41 mmol, 1.0 equiv.) in CCl_4 (6 mL). $NaIO_4$ (1.153 g, 5.41 mmol, 1.0 equiv.) and $RuCl_3 \times nH_2O$ (41% Ru, cat., 120 mg) were added and the resulting brownish-black solution was vigorously stirred at room temperature for 2.5 h. After the addition of brine (50 mL) and CH_2Cl_2 (100 mL) the organic layer was separated and the aqueous phase was extracted with CH_2Cl_2 (twice 50 mL). After drying of the combined organic layers ($MgSO_4$), removal of solvent and chromatography (hexane/AcOEt, 1:1) the product **22** (739 mg, 79%) was obtained. Colourless crystals. Mp 114°C. r_f=0.21 (hexane/AcOEt, 1:1). ^{13}C NMR (CD_3OD) δ 170.9 (C), 77.2 (C), 35.2 (CH), 32.3 (C), 21.9 (CH_3), 15.9 (CH_3) 13.3. ^{13}C NMR ($CDCl_3$) δ 174.4 (C), 33.9 (CH), 32.5 (C), 21.7 (CH), 15.7 (CH), 12.9 (CH). ^{1}H NMR ($CDCl_3$) δ 11.00 (b, 1H), 2.86 (s, 1H), 1.87 (s, 3H), 1.27 (s, 3H), 1.18 (s, 3H). Anal. calcd for $C_7H_{11}NO_4$: C, 48.55. H, 6.40; N 8.09. Found: C 48.88. H, 5.71; N 7.95.

1.6.12. Methyl (1*R*,2*R*)-*trans*-2,3,3-trimethyl-2-nitro-cyclopropanecarboxylate (22b). A cold 0.7 M solution of diazomethane in ether (3.8 mL, 2.68 mmol, 3.0 equiv.) was added to a solution of the acid **22a** (155 mg, 0.895 mmol, 1.0 equiv.) in Et_2O (5 mL) dropwise under stirring at 0°C. After stirring at 0°C for 1 h, the solvent was evaporated leaving back pure methyl ester **22b**. Light yellow oil. r_f=0.60 (hexane/AcOEt): ^{13}C NMR (δ 168.8 (C), 76.5 (C), 52.2 (CH_3), 34.4 (CH), 32.1 (C), 22.0 (CH_3), 16.0 (CH_3), 13.2 (CH_3). ^{1}H NMR δ 3.64 (s, 3H), 2.84 (s, 1H), 1.85 (s, 3H), 1.25 (s, 3H), 1.15 (s, 3H). Anal. calcd for $C_8H_{13}NO_4$ C, 51.33; H 7.00; N 7.48. Found: C 51.47; H 6.61; N 8.07.

1.6.13. (1*R*,2*S*)-*cis*-2,3,3-Trimethyl-2-nitro-cyclopropanecarboxylic acid (23). The *cis*-nitrocyclopropane **8b** (100 mg, 0.44 mmol, 1.0 equiv.) was hydrolysed (formation of the corresponding diol) and oxidized with $NaIO_4$ and $RuCl_3 \times nH_2O$ as reported for **22** affording the corresponding (1*R*,2*S*)-*cis*-2,3,3-trimethyl-2-nitro-cyclopropanecarbaldehyde (45 mg, 45%) after column chromatography (hexane/AcOEt, 8:2). Light yellow oil. r_f=0.48 (hexane/AcOEt, 1:1). ^{13}C NMR δ 196.1 (CH), 79.0 (C), 45.3 (CH), 32.8 (C), 22.9 (CH_3), 19.6 (CH_3), 16.6 (CH_3). ^{1}H NMR δ 9.48 (d, J=5.2 Hz, 1H), 1.77 (s, 3H), 1.69 (d, J=5.2 Hz, 1H), 1.40 (s, 3H), 1.25 (s, 3H). This aldehyde (342 mg, 2.18 mmol) was oxidized to the corresponding carboxylic acid **23** by the procedure applied for the synthesis of **22** (vide supra) using CCl_4 (3 mL), MeCN (3 mL), water (3.5 mL), $NaIO_4$ (930 mg, 4.35 mmol, 2.2 equiv.), $RuCl_3 \times nH_2O$ (41% Ru, cat., 92 mg) affording **24** (263 mg, 70%). Colourless wax. r_f=0.16 (hexane/AcOEt, 1:1). ^{13}C NMR (CD_3OD) δ 168.2 (C), 74.3 (C), 35.8 (CH), 28.9 (C), 20.5 (CH_3), 16.9 (CH_3), 14.3 (CH_3). ^{1}H NMR (CD_3OD) δ 1.82 (s, 1H), 1.70 (s, 3H), 1.26 (s, 3H), 1.16 (s, 3H). Anal. calcd for $C_7H_{11}NO_4$: C 48.55; H 6.40; N 8.09. Found: C 50.06; H 6.57; N 7.60.

1.6.14. (3*R*,4*S*)-1-(Hydroxy-2,2-dimethyl-tetrahydrofuran-3-yl)-ethanone 26. Compound **10c** (420 mg, 1.7 mmol, 1.0 equiv.) was dissolved in MeOH (15 mL). Aqueous concentrated HCl (5 drops) was added. The solution was stirred at room temperature for 8 h and then at 40°C for 30 min. The volatiles were evaporated under reduced pressure and the residue was diluted with CH_2Cl_2 (20 mL). The organic solution was washed with brine, dried with $MgSO_4$. After removal of the solvent the residue was purified by chromatography (hexane/AcOEt, 1:1) to afford

(109 mg, 41%) tetrahydrofurane **26**. Yellow liquid. r_f=0.11 (hexane/AcOEt, 1:1). ^{13}C NMR δ 206.7 (C), 81.6 (C), 73.9 (CH), 71.6 (CH_2), 69.8 (CH), 31.4 (CH_3), 29.6 (CH_3), 23.8 (CH_3). ^{1}H NMR δ 4.79 (dd, J=6.2, 12.2 Hz, 1H), 4.01 (dd, J=6.2, 9.3 Hz, 1H), 3.62 (dd, J=5.4, 9.3 Hz, 1H), 2.96 (d, J=6.2 Hz, 1H), 2.19 (s, 3H), 1.50 (s, 3H), 1.02 (s, 3H). Anal. calcd for $C_8H_{14}O_3$: C 60.73; H 8.92. Found: C 60.13; H 8.90.

References

1. (a) Barret, A. G. M.; Graboski, G. G. *Chem. Rev.* **1986**, *86*, 751. (b) Corey, E. J.; Estreicher, H. *J. Am. Chem. Soc.* **1978**, *100*, 6294. (c) *Nitroalkanes and Nitroalkenes in Synthesis, Tetrahedron Symposia*, Barret, A. G. M., Ed.;, 1990; Vol. 46, p 7313. (d) Li, C.-S.; Kozikowski, P. *J. Org. Chem.* **1985**, *50*, 778. (e) Seebach, D.; Knochel, P. *Synthesis* **1982**, 1017. (f) Cavallo, A.; Khiar, N. *J. Org. Chem.* **1990**, *55*, 4750. (g) Rosini, G.; Ballini, R.; Sorrenti, P. *Synthesis* **1983**, 1014. (h) Kozikowski, A. P.; Kitagawa, Y.; Springer, J. P. *J. Chem. Soc., Chem. Commun.* **1983**, 1460.
2. (a) Feuer, H.; Nielsen, A. T. *Nitro Compounds*; Chemie: New York, 1990. (b) Jackson, R. F. W.; Palmer, N. J.; Wythes, M. J.; Clegg, W.; Elsegood, M. R. J. *J. Org. Chem.* **1995**, *60*, 6431. (c) Ambroise, L.; Jackson, F. W. *Tetrahedron Lett.* **1996**, *37*, 2311. (d) Ayerbe, M.; Cossio, F. *Tetrahedron Lett.* **1995**, *36*, 4447. (e) Ayerbe, M.; Morao, I.; Arrieta, A.; Linden, A.; Cossio, F. *Tetrahedron Lett.* **1996**, *37*, 3055. (f) Rodríguez-García, C.; Ibarzo, J.; Álvarez-Larena, A.; Branchadell, V.; Oliva, A.; Ortuño, R. M. *Tetrahedron* **2001**, *57*, 1025.
3. Muray, E.; Alvarez-Larena, A.; Piniella, J. F.; Branchadell, V.; Ortuno, R. M. *J. Org. Chem.* **2000**, *65*, 388.
4. Galley, G.; Hübner, J.; Anklam, S.; Jones, P. G.; Pätzel, M. *Tetrahedron Lett.* **1996**, *37*, 6307.
5. (a) Gueritte-Voegelein, F.; Senilh, V.; David, B.; Guenard, D.; Potier, P. *Tetrahedron* **1986**, *42*, 4451. (b) Gueritte-Voegelein, F.; Mangatal, L.; Adeline, M. T.; Guenard, D. *Tetrahedron* **1989**, *45*, 4177.
6. (a) Battersby, A. F.; Staunton, J.; Tippett, J. *J. Chem. Soc., Perkin Trans. 1* **1982**, 455. (b) Silvermann, R. B.; Andruszkiewicz, R.; Yuen, P. -W.; Sobieray, D. M.; Franklin, L. C.; Schwindt, M. A. US Patent 5,710,304, January 20, 1998; *CAN 121*, 158191.
7. Compound **4a** was recently described by Cossio.[2d]
8. Barrow, R. A.; Hemscheidt, T.; Liang, J.; Paik, S.; Moore, R. E.; Tius, M. *J. Am. Chem Soc.* **1995**, *117*, 2479.
9. Caramella, P.; Rondan, N. G.; Paddon-Row, M. N.; Houk, K. N. *J. Am. Chem. Soc.* **1981**, *103*, 2438.
10. (a) Houk, K. N.; Paddon-Row, M. N.; Rondan, N. G.; Wu, Y. D.; Brown, F. K.; Spellmeyer, D. C.; Metz, J. T.; Li, Y.; Loncharich, R. J. *Science* **1986**, *231*, 1108. (b) Houk, K. N.; Wu, Y. D.; Duh, H.-Y.; Moses, S. R. *J. Am. Chem. Soc.* **1986**, *108*, 2754.
11. Apeloig, Y.; Karni, M.; Rappoport, Z. *J. Am. Chem. Soc.* **1983**, *105*, 2784.
12. Clagett, M.; Gooch, A.; Graham, P.; Holy, N.; Mains, B.; Strunk, J. *J. Org. Chem.* **1976**, *41*, 4033.
13. (a) Paulini, K.; Reißig, H.-U. *Liebigs Ann.Chem.* **1991**, 455. (b) Reißig, H.-U. *Top. Curr. Chem.* **1988**, *144*, 73. (c) Paulini, K.; Reißig, H.-U. *Liebigs Ann.Chem.* **1994**, 549.
14. For some recent examples see (a) Grieco, P. A.; Kaufman, M. D. *J. Org. Chem.* **1999**, *64*, 7586. (b) Csuk, R.; Scholz, v. Y. *Tetrahedron* **1994**, *50*, 10431. (c) Martin-Vila, M.; Muray, E.; Aguado, G.; Alvarez-Larena, A.; Branchadell, V.; Minguillon, C.; Giralt, E.; Ortuno, R. M. *Tetrahedron: Asymmetry* **2000**, *17*, 3569. (d) Beumer, R.; Reiser, O. *Tetrahedron* **2001**, *57*, 202. (e) Bubert, C.; Cabrele, C.; Reiser, O. *Synlett* **1997**, 827. (f) Maas, G.; Müller, A. *J. Prakt. Chem.* **1998**, *340*, 315.
15. Franck-Neumann, M.; Miesch, M.; Kempf, H. *Tetrahedron* **1988**, *44*, 2933.
16. Park, J. S.; Beak, P. *Tetrahedron* **1996**, *52*, 12333.
17. Wiedemann, S.; Marek, I.; de Meijere, A. *Synlett* **2002**, 879.
18. Fisera, L.; Goljer, I.; Jarovska, L. *Coll. Czech. Chem. Commun.* **1988**, *53*, 1753.
19. (a) Gaboury, J. A.; Sibi, M. P. *J. Org. Chem.* **1993**, *58*, 2173. (b) DeAmici, M.; DeMicheli, C.; Carrea, G. *Tetrahedron: Asymmetry* **1996**, *7*, 787.
20. Franzen, V.; Schmidt, H.-J.; Mertz, C. *Chem. Ber.* **1961**, *94*, 2942.