A New Strategy for the Stereoselective Synthesis of 1,2,3-Trisubstituted Cyclopropanes

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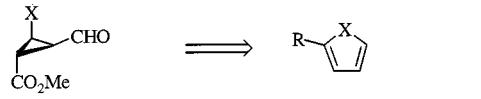
The stereoselective synthesis of highly functionalized 1,2,3-trisubstituted cyclopropanes **1** and **2**, starting from readily available furans **3** or *N*-protected pyrrole **4**, is described. Furthermore, exceptionally high diastereocontrol in agreement with the Felkin–Anh model was observed for the addition of nucleophiles to the title compounds.

Introduction

Cyclopropanes are an important class of compounds because of their occurrence in numerous natural products and drugs,[1] and because of their value as synthetic building blocks in organic synthesis.[2] Cyclopropanes vicinally substituted with donor and acceptor moieties[3] are particularly useful, since they easily undergo ring opening, giving rise to reactive intermediates, which can be intra- or intermolecularly trapped. A number of stoichiometric[4] and catalytic[5] methods are known for the stereoselective synthesis of mono- and 1,2-disubstituted cyclopropanes. However, fewer synthetic approaches towards 1,2,3-trisubstituted cyclopropanes are known.[6]

We report here an easy route from readily available heteroaromatic starting materials to amino- and hydroxy-substituted cyclopropanecarbaldehydes **1** and **2**, and their elaboration as synthetic building blocks (Scheme 1).



1a: X = OCHO
1b: X = $OCOCO_2Me$
2: X = NCHO(Boc)

3a: X = O, R = H
3b: X = O, R = CO_2Me
4: X = NBoc, R = H

Scheme 1

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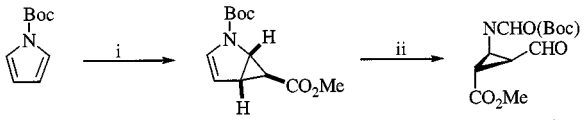
[+] X-ray crystallography of compounds **1b**, **9a**.
[++] X-ray crystallography of compounds **2**, **11d**, **11g**.

Results and Discussion

Based on the original report by Fowler et al.,[7] we have been able to develop an efficient diastereo- and enantioselective synthesis of the bicyclic adduct **5** (45% yield), (Scheme 2).[8] Ozonolysis of **5** smoothly yielded the β-amino aldehyde **2** (88% yield), which proved to undergo highly selective addition reactions with nucleophiles.[9] Only a few cases have been reported of nucleophilic additions to cyclopropanecarbaldehydes and cyclopropyl ketones proceeding with high diastereocontrol.[10] We would like to give here a full report describing the scope and limitations of **2** as a synthetic intermediate, as well as the extension of our synthetic strategy towards the β-hydroxy aldehyde **1**.

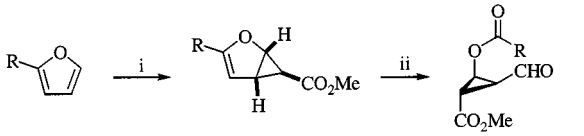


4 **5** **2**

i: $Cu(OTf)_2$, $PhNHNH_2$, N_2CHCO_2Me, ii: O_3, DMS

Scheme 2

In analogy with the synthesis of **5**, we were able to use furans **3** as starting materials for β-hydroxy-substituted cyclopropanecarbaldehydes **1** (Scheme 3).



3a: R = H
3b: R = CO_2Me

6a: R = H
6b: R = CO_2Me

1a: R = H
1b: R = CO_2Me

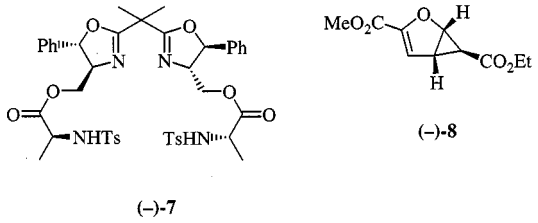
i: $Cu(OTf)_2$, $PhNHNH_2$, N_2CHCO_2Me; ii: O_3, DMS

Scheme 3

The cyclopropanation of furan (**3a**) with diazo esters has been reported to give rise to the bicyclic adduct **6a**, either

  1434−193X/00/0816−2955 $ 17.50+.50/0

photochemically[11] or by catalysis with $Rh_2(OAc)_4$ [12]. Using copper(II) triflate activated by phenylhydrazine as a catalyst, we were able to improve the yield of **6a** to 43% based on methyl diazoacetate. Ozonolysis of **6a**, followed by reductive work up with dimethyl sulfide (DMS) provided the cyclopropanecarbaldehyde **1a** in 81% yield. Unfortunately, **1a** turned out to be rather unstable because of the base-labile *O*-formyl group causing immediate ring opening upon its hydrolysis. Therefore, we turned our attention to the furan-2-carboxylic ester **3b**, which had previously been cyclopropanated with diazo esters, using $Rh_2(OAc)_4$ as a catalyst, by Wenkert et al., in 55% yield.[12] Following our protocol, we treated **3b** with methyl diazoacetate in the presence of $Cu(OTf)_2/PhNHNH_2$ as catalyst, and obtained exclusively the *exo* adduct **6b** in 64% yield on a 50-g scale. Moreover, using bis(oxazoline) (−)-**7**[13] as a chiral ligand, we were able to obtain **6b** in 39% yield and 88% *ee*. When this technique was used in combination with ethyl diazoacetate and $Cu(OTf)_2/PhNHNH_2$, the bicyclic adduct (−)-**8** could be isolated in 36% yield and 91% *ee* (Scheme 4). The enantiopurity of the latter was improved to 100% by a single recrystallization, and its absolute stereochemistry was determined by X-ray analysis.[14]



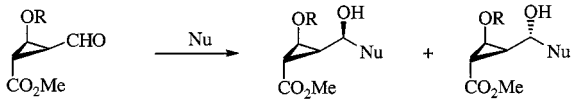
(–)-7 (–)-8

Scheme 4

Upon ozonolysis of **6b** the cyclopropanealdehyde **1b** was obtained (81% yield), which proved to be considerably more stable than **1a** due to the hydrolytically less labile oxalic ester functionality.

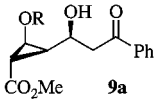
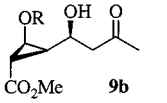
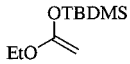
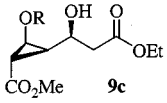
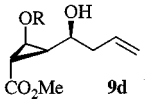
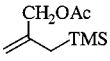
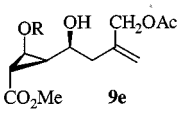
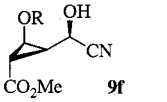
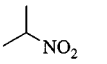
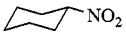
Although the aldehydes **1b** and **2** are quite sensitive towards basic conditions, reactions catalyzed by Lewis acids can readily be carried out. Both aldehydes underwent stereoselective additions with various nucleophiles (Table 1, Table 2). Especially good results were obtained for Mukaiyama aldol reactions catalyzed by boron trifluoride (Table 1, Entry 1−3; Table 2, Entry 1), which generally took place in high yield and with excellent 1,2 induction. However, attempts to achieve 1,2 and 1,3 stereocontrol using the prochiral silyl enol ether of cyclohexanone were not successful; **13** and **14** were obtained as a 1:1 mixture of diastereomers, which were tentatively assigned as depicted in Scheme 5. Sakurai allylations (Table 1, Entries 4, 5; Table 2, Entries 2, 3) also proceeded quite well; however, with these examples, it became apparent that **2** was superior to **1b** in terms of its 1,2 induction capability. These differences were even more pronounced in the addition of smaller nucleophiles like cyanide, in which the diastereoselectivity dropped to 2:1 in

Table 1. Addition of nucleophiles to **1b**



1b **9** **10**

R = $COCO_2Me$

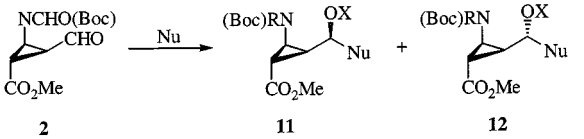
Entry	Nucleophile	Catalyst	Product	9:10	Yield [%]
1		$BF_3{\cdot}Et_2O$	 **9a**	99:01	87
2		$BF_3{\cdot}Et_2O$	 **9b**	99:01	86
3		$BF_3{\cdot}Et_2O$	 **9c**	99:01	86
4		$BF_3{\cdot}Et_2O$	 **9d**	90:10	82
5		$BF_3{\cdot}Et_2O$	 **9e**	80:20	85
6	TMSCN	$BF_3{\cdot}Et_2O$	 **9f**	65:35	91
7		NEt_3		–	–[a]
8		NEt_3		–	–[a]
9	H_3CNO_2	NEt_3		–	–[a]

[a] Decomposition

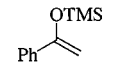
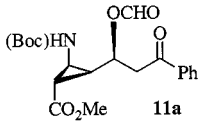
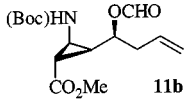
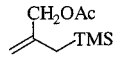
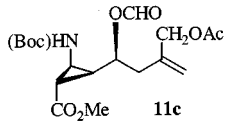
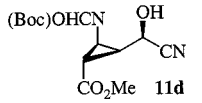
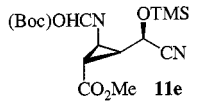
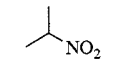
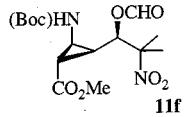
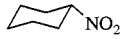
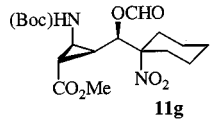
the case of **1b** (Table 1, Entry 6), while respectable selectivities of 9:1 were still obtained with **2** (Table 2, Entries 4, 5). We also noticed a difference in reactivity between **1b** and **2**; TMSCN addition in the absence of Lewis acids occurred only with **2**, and not with **1b**. Base-catalyzed nitro aldol reactions also only took place with **2** and, moreover, only secondary nitroalkanes could be used as reagents. In these reactions, a formyl shift occurs from the amino to the hydroxy group, thus making the latter a good leaving group. Therefore, with primary nitroalkanes like nitromethane, subsequent elimination of formic acid readily takes place, resulting in a mixture of products. Nevertheless, with nitroalkanes such as 2-nitropropane (Table 2, Entry 6) or nitrocyclohexane (Table 2, Entry 7) excellent selectivities were obtained even at ambient temperature.

The relative stereochemistries were determined by X-ray diffraction analysis[14] of **9a**, **11d** and **11g** (*N*−CO_2Me in-

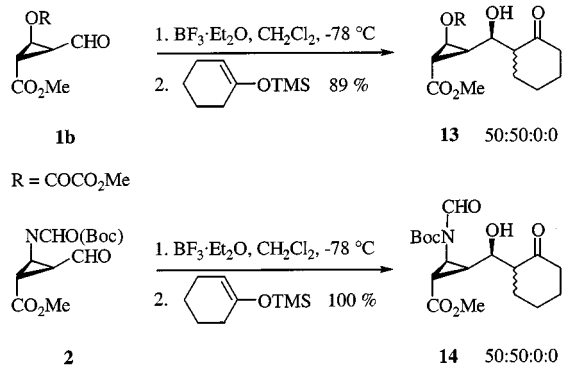
Table 2. Addition of nucleophiles to **2**



2 **11** **12**

Entry	Nucleophile	Catalyst	Product	11:12	Yield [%]
1		$BF_3{\cdot}Et_2O$	 **11a**	99:01	71
2		$BF_3{\cdot}Et_2O$	 **11b**	99:01	92
3		$BF_3{\cdot}Et_2O$	 **11c**	99:01	93
4	TMSCN	$BF_3{\cdot}Et_2O$	 **11d**	89:11	94
5	TMSCN	–	 **11e**	91:09	100
6		NEt_3	 **11f**	99:01	91
7		NEt_3	 **11g**	99:01	91
8	H_3CNO_2	NEt_3		–	–[a]

[a] Decomposition



Scheme 5

stead of *N*−Boc) (Figure 1, Figure 2 and Figure 3, Table 3) and by NOESY experiments on **16a−d**, derived from **11a−c**, **f** (Scheme 6).

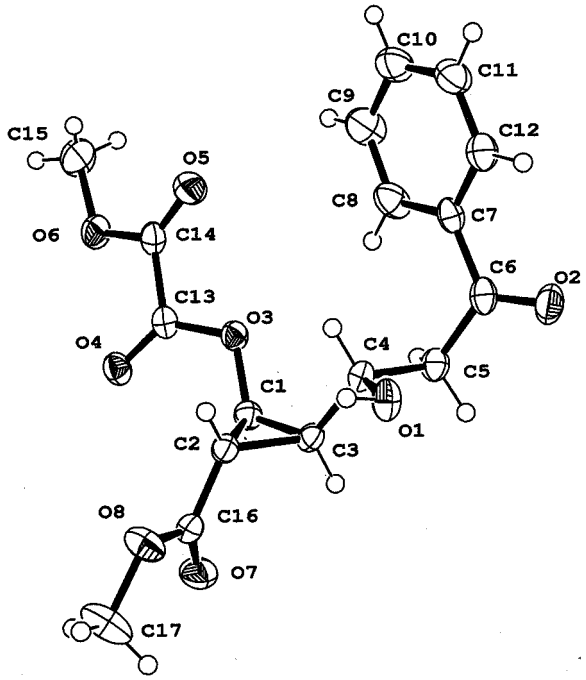


Figure 1. Structure of **9a** in the crystal

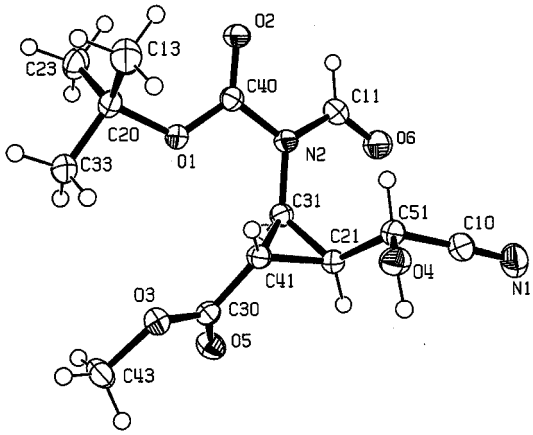


Figure 2. Structure of **11d** in the crystal

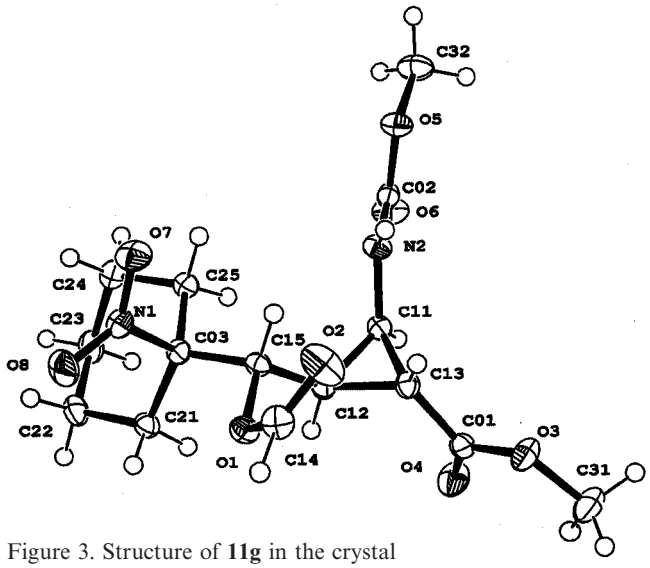
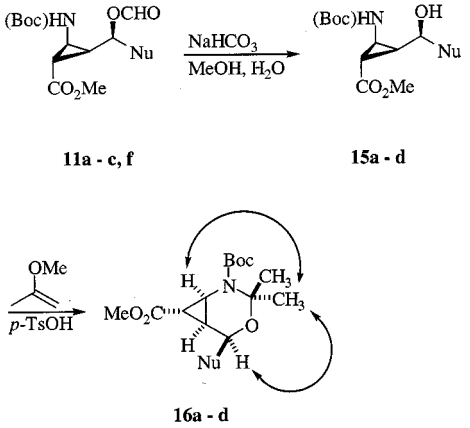


Figure 3. Structure of **11g** in the crystal

Table 3. Crystal data for compounds **1b**, **2**, **9a**, **11d**, **11g**

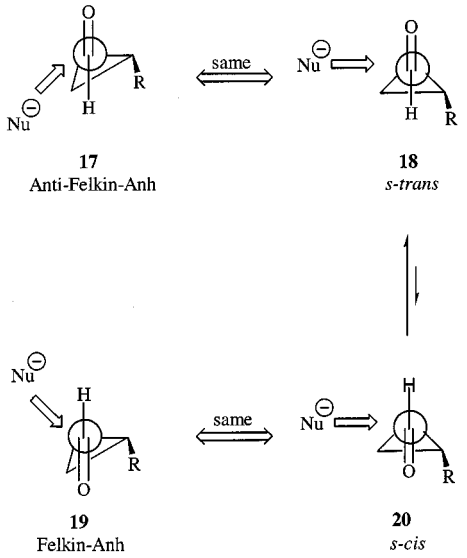
Compound	1b	2	9a	11d	11g
Empirical formula	$C_9H_{10}O_7$	$C_{12}H_{17}NO_6$	$C_{17}H_{18}O_8$	$C_{13}H_{18}N_2O_6$	$C_{15}H_{22}N_2O_8$
Formula weight	230.17	271.27	350.31	298.29	358.35
ρ [gcm^{-3}]	1.431	1.325	1.387	1.372	1.433
Z	4	8	4	4	2
Temperature [K]	297(2)	213(2)	173(2)	298(3)	133(2)
Crystal system	Monoclinic	Monoclinic	Monoclinic	Monoclinic	Triclinic
Space group	$P2_1/a$	C2/c	$P2_1/a$	$P2_1/n$	P_1
Radiation [Å]	*Mo-K*$_\alpha$(0.71073)	*Mo-K*$_\alpha$(0.71073)	*Mo-K*$_\alpha$(0.71073)	*Mo-K*$_\alpha$(0.71073)	*Mo-K*$_\alpha$(0.71073)
Crystal size [mm]	0.20 x 0.15 x 0.08	0.70 x 0.60 x 0.60	0.36 x 0.24 x 0.11	0.50 x 0.50 x 0.40	0.50 x 0.40 x 0.20
a [Å]	7.0935(4)	19.925(4)	11.2843(6)	9.5897(19)	9.4370(19)
b [Å]	11.9851(9)	8.704(2)	7.8257(4)	8.2777(17)	9.993(2)
c [Å]	12.7444(6)	15.879(3)	19.5704(10)	18.27.2(4)	9.995(2)
α [°]	90	90	90	90	65.04(3)
β [°]	99.4486(6)	98.98(3)	103.979(6)	95.19(3)	76.68(3)
γ [°]	90	90	90	90	81.89(3)
F(000)	480	1152	736	632	380
Volume [Å^3]	1068.67(11)	2720.2(9)	1677.0(2)	1444.5(5)	830.5(3)
Scan range [°]	3.24 < Θ < 25.92	3.53 < Θ < 27.57	2.82 < Θ < 25.78	2.24 < Θ < 25.35	2.22 < Θ < 26.37
Index ranges	*h*: -8/8	*h*: -25/25	*h*: -13/13	*h*: -11/11	*h*: -11/11
	k: -14/14	*k*: -11/11	*k*: -9/9	*k*: -10/10	*k*: -11/12
	l: -15/15	*l*: -6/20	*l*: -23/23	*l*: -22/20	*l*: -11/12
Collected reflections	14920	4238	21334	15694	11540
Independent reflections ($R_{int.}$)	1972 (0.0272)	2891 (0.0301)	3201 (0.0388)	2615 (0.0310)	3382 (0.0211)
Data/restraints/parameters	1972 / 0 / 185	2887 / 0 / 176	3291 / 0 / 298	2615 / 0 / 199	3382 / 1 / 241
Goodness-of-fit on F^2	1.033	1.120	1.010	1.144	1.040
Final R indices [$I > 2\sigma(I)$]; *R*1, *wR*2	0.0415, 0.1127	0.0474, 0.1170	0.0347, 0.0835	0.0514, 0.1293	0.0344, 0.0875
R indices (all data); *R*1, *wR*2	0.0509, 0.1159	0.0571, 0.1320	0.0506, 0.0883	0.0644, 0.1444	0.0399, 0.0911
Largest diff. Peak and hole [e Å^{-3}]	0.188, -0.149	0.223, -0.249	0.238, -0.148	0.275, -0.306	0.273, -0.299



Scheme 6

In all cases the Felkin−Anh[15] diastereomers **9** and **11** were obtained as the major product, both in noncatalyzed reactions and in those catalyzed by Lewis acids. This was unexpected in view of a previously proposed model,[10e] which assumed for steric and stereoelectronic reasons that the *s-trans* conformation **18** should be decisive in reactions with cyclopropanecarbaldehydes. Moreover, coordination of a Lewis acid to the aldehyde should disfavor the *s-cis* conformation **20** even more for steric reasons. By this analysis, the *anti*-Felkin−Anh products **10** and **12** would have been expected (Scheme 7).

To our surprise, the X-ray structure of **2**[14] was found to be in the *s-cis* conformation **20**, although the aldehyde functionality is pointing towards the cyclopropane moiety with the sterically demanding NCHO(Boc) group *cis* to it (Figure 4). A possible explanation for the preferred *s-cis* orientation might be the favorable antiparallel arrangement of the aldehyde and the *N*-formyl functionality for stereoelectronic reasons. In contrast, in the X-ray structure of **1b**, the *s-trans* conformation **18** was found (Figure 5), which should not, however, be the reactive conformation according to our experimental results and the Curtin−Hammett principle. Apparently, nucleophilic additions to **1b** and **2** adhere well to the Felkin−Anh paradigm designating **19** as the preferred arrangement between a nucleophile and the cyclopropanecarbaldehyde. The exceptionally high Felkin−Anh selectivities obtained with sterically demanding nucleo-



Scheme 7

philes suggest especially unfavorable interactions in the *anti*-Felkin−Anh transition state of cyclopropanealdehydes and nucleophiles.

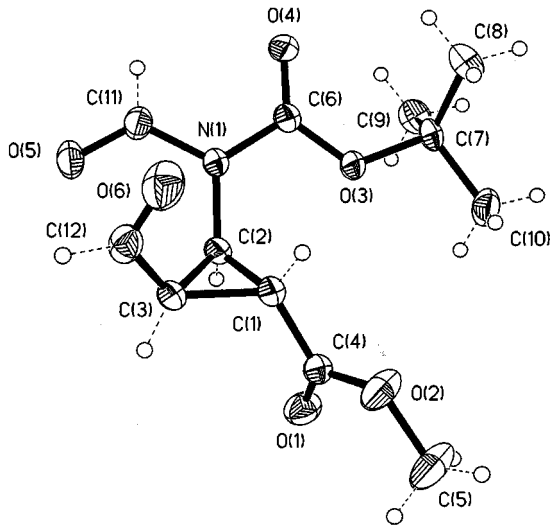


Figure 4. Structure of **2** in the crystal

Conclusion

1,2,3-Trisubstituted cyclopropanecarbaldehydes can be easily obtained, starting from readily available furans or pyrroles. These aldehydes can be further elaborated by the addition of various nucleophiles, leading with high stereocontrol to highly functionalized substituted cyclopropanes, which should prove to be useful building blocks thanks to their donor-acceptor properties. Such studies are currently under way in our laboratories.

Experimental Section

General Remarks: Reactions with moisture-sensitive chemicals were performed under nitrogen in a flame-dried reaction flask. Solvents were dried by standard methods. − Chromatography: Macherey−Nagel silica gel (0.03−0.06 mm). − Uncorrected melting points: Büchi SMP 20. − IR: Mattson Genesis Series FT-IR, Perkin−Elmer 298, Bruker IFS 66, $\tilde{\nu}$ in cm^{-1}. − ^1H and ^{13}C NMR: Bruker ARX 500, ARX 400, AC 250 F, AW 250, δ in ppm, *J* in Hz. $CDCl_3$ was freshly deactivated by basic alumina. − MS: Finnigan MAT 95, Varian MAT 311A. − Elemental analysis: Heraeus CHN-Rapid. − XRD: Stoe Imaging Plate System, Siemens Stoe AED2.

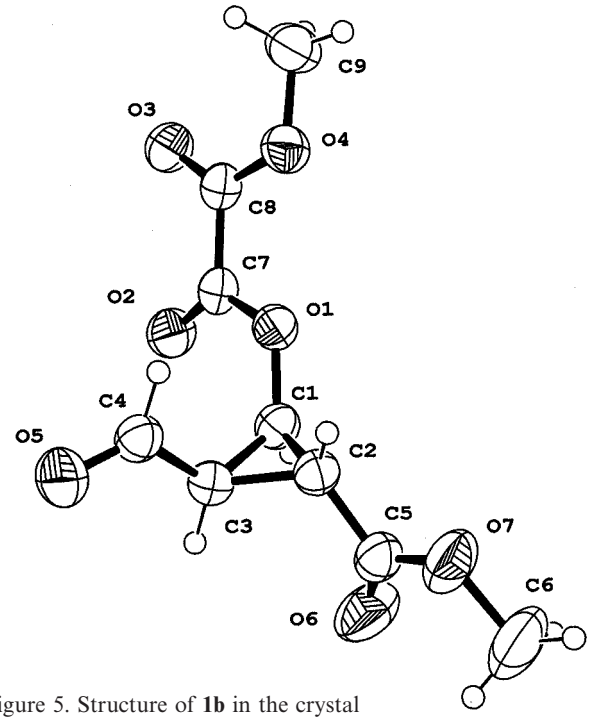


Figure 5. Structure of **1b** in the crystal

2-*tert*-Butyl 6-Methyl (1*S,5*S**,6*S**)-2-Azabicyclo[3.1.0]hex-3-ene-2,6-dicarboxylate (5):** To a solution of *tert*-butyl 1*H*-pyrrole-1-carboxylate (**4**) (22.0 g, 131.7 mmol) in dry CH_2Cl_2 (100 mL) was added $Cu(OTf)_2$ (101 mg, 0.28 mmol) and phenylhydrazine (1 mL), dissolved in CH_2Cl_2 (100 mL). A solution of methyl diazoacetate (16.5 g, 165.0 mmol) in dry CH_2Cl_2 (200 mL) was added slowly. Stirring was continued for 12 h. The reaction mixture was filtered through silica gel and the solvent was evaporated in vacuo. The residue was purified by chromatography (hexanes/ethyl acetate, 20:1 to 10:1, silica gel, R_f = 0.26) to provide **5** (14.21 g, 45%) as yellow oil containing 8% fumaric acid dimethyl ester. For analysis, the impurity was removed by sublimation (40 °C, 0.01 Torr). − ^1H NMR (250 MHz, $CDCl_3$): δ = 0.92 (br. s, 1 H, 5-H), 1.46 [s, 9 H, $C(CH_3)_3$], 2.77 (br. s, 1 H, 6-H), 3.62 (s, 3 H, OCH_3), 3.65 (s, 3 H, OCH_3), 4.26−4.40 (m, 1 H), 5.28−5.36 (m, 1 H), 6.40−6.55 (br. s, 1 H). − ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 22.6, 22.7 (+, C-5), 28.1 [+, $C(CH_3)_3$], 30.9, 32.1 (+, C-6), 44.0, 44.1 (+, C-1), 51.7 (+, OCH_3), 81.6 [C_{quat}, $OC(CH_3)_3$], 109.7 (+, olefin-C), 129.5, 129.7 (+, olefin-C), 150.8, 151.1 [C_{quat}, $NCO_2C(CH_3)_3$], 173.2, 173.5 (C_{quat}, CO). − IR (KBr): $\tilde{\nu}$ = 3180 cm^{-1}, 3126, 2999, 2981, 2958, 1716 (C=O), 1586, 1477, 1463, 1441, 1400, 1367, 1348, 1295, 1259, 1250, 1194, 1169, 1141, 1072, 1031, 1015, 1000, 951, 912, 893, 835, 815, 763, 746, 721, 563, 549, 428. − MS (DCI, NH_3): *m*/*z* (%) = 257 (100) [M + NH_4^+]. − $C_{12}H_{17}NO_4$ (239.3): calcd. C 60.24, H 7.16; found C 60.46, H 7.17.

Methyl (1*S,5*S**,6*S**)-2-Oxabicyclo[3.1.0]hex-3-ene-6-carboxylate (6a):** A mixture of furan (**3a**) (300 mL, 4.11 mol), $Cu(OTf)_2$ (217

mg, 0.60 mmol) and two drops of phenylhydrazine was stirred at 0 °C for 30 min to give a clear, light brown solution. A solution of methyl diazoacetate (20.0 g, 199.8 mmol) in dry CH_2Cl_2 (280 mL) was added dropwise over a period of 12 h. The reaction mixture was filtered through a short pad of alumina (basic, activity I) and the solvent was evaporated in vacuo. The brown residue was purified by chromatography (*n*-pentane/diethyl ether, 9:1, 1% NEt_3, silica gel) to yield **6a** as a colorless liquid (11.92 g, 43%). − R_f = 0.30. − ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.96 (d, *J* = 2.5 Hz, 1 H, 6-H), 2.79 (ddd, *J* = 5.5, 2.7, 2.5 Hz, 1 H, 5-H), 3.68 (s, 3 H, OCH_3), 4.86 (d, *J* = 5.5 Hz, 1 H, 1-H), 5.48 (dd, *J* = 2.7, 2.6 Hz, 1 H, 4-H), 6.38 (d, *J* = 2.6 Hz, 1 H, 3-H). − ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 21.9 (C-6), 31.7 (C-5), 51.8 (OCH_3), 67.1 (C-1), 106.3 (C-4), 147.3 (C-3), 173.3 (C_{quat}, CO). − IR (film): $\tilde{\nu}$ = 3080 cm^{-1}, 2920, 1710, 1580, 1430, 1370, 1280, 1180, 1150, 1130, 1070, 1040, 1030, 1000, 980, 950, 920, 900, 810, 700. − MS (EI, 70 eV): *m*/*z* (%) = 140.1 (62) [M$^+$], 125.1 (10), 109 (23), 81 (100), 53.0 (32), 28 (81), 17.9 (66). − $C_7H_8O_3$ (140.1): calcd. C 60.00, H 5.75; found C 59.89, H 5.77.

Dimethyl (1*S,5*S**,6*S**)-2-Oxabicyclo[3.1.0]hex-3-ene-3,6-dicarboxylate (6b):** A mixture of methyl 2-furancarboxylate (**3b**) (125 mL, 843 mmol), $Cu(OTf)_2$ (273 mg, 0.2 mol-%) and two drops of phenylhydrazine was stirred at room temp. for 30 min to give a clear, light brown solution. A solution of methyl diazoacetate (37.7 g, 377 mmol) in dry CH_2Cl_2 (320 mL) was added dropwise over a period of 48 h. The reaction mixture was filtered through a short pad of alumina (basic, activity I) and the solvent was evaporated in vacuo. Excess methyl 2-furancarboxylate was distilled off under reduced pressure and the residue was purified by chromatography (hexanes/ethyl acetate, 10:1, silica gel) to provide **6b** (47.82 g, 64%) as a white solid. − R_f = 0.04. − M.p. 64 °C. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.18 (dd, *J* = 2.7, 1.1 Hz, 1 H, 6-H), 2.88 (ddd, *J* = 5.3, 2.9, 2.7 Hz, 1 H, 5-H), 3.70 (s, 3 H, OCH_3), 3.81 (s, 3 H, OCH_3), 4.98 (dd, *J* = 5.3, 1.1 Hz, 1 H, 1-H), 6.39 (d, *J* = 2.9 Hz, 1 H, 4-H). − ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.3 (C-6), 32.0 (C-5), 52.1 (OCH_3), 52.2 (OCH_3), 67.5 (C-1), 116.0 (C-4), 149.3 (C-3), 159.5 (C_{quat}, CO), 172.1 (C_{quat}, CO). − IR (KBr): $\tilde{\nu}$ = 3130 cm^{-1}, 2960, 1720, 1440, 1305, 1170, 1115. − MS (EI, 70 eV): *m*/*z* (%) = 198.0 (14) [M$^+$], 138.9 (100), 110.9 (38), 79.0 (11), 59.0 (15). − $C_9H_{10}O_5$ (198.2): calcd. C 54.54, H 5.09; found C 54.54, H 5.14. − The analogous reaction was carried out in presence of chiral ligand **7** (for detailed procedure see synthesis of **8**) to yield **6b** in 39% yield and 88% ee. − $[\alpha]_D^{20}$ = −234 (*c* = 1.0, CH_2Cl_2).

6-Ethyl 3-Methyl (1*S*,5*S*,6*S*)-2-Oxabicyclo[3.1.0]hex-3-ene-3,6-dicarboxylate (8): To a mixture of **3b** (320 μL, 3.0 mmol), $Cu(OTf)_2$ (7 mg, 0.02 mmol) and **7** (18 mg, 0.022 mmol) under nitrogen were added two drops of a solution of one drop phenylhydrazine in abs. CH_2Cl_2 (1 mL). After 30 min, a solution of ethyl diazoacetate (100 mg, 0.88 mmol) in abs. CH_2Cl_2 (10 mL) was added via syringe over 12 h. The solvent was evaporated and the residue was purified by chromatography (hexanes/ethyl acetate, 10:1, silica gel) to provide **8** (76 mg, 36%, 91% ee). An enantiopure compound could be obtained by recrystallization from *n*-pentane. − M.p. 42 °C. − $[\alpha]_D^{20}$ = −272 (*c* = 1.0, CH_2Cl_2). − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.16 (dd, *J* = 2.7, 1.1 Hz, 1 H, 6-H), 1.23 (t, *J* = 7.1 Hz, 3 H, CH_3), 2.87 (ddd, *J* = 5.3, 2.9, 2.7 Hz, 1 H, 5-H), 3.78 (s, 3 H, OCH_3), 4.12 (q, *J* = 7.1 Hz, 2 H, CH_2), 4.97 (dd, *J* = 5.3, 1.1 Hz, 1 H, 1-H), 6.39 (d, *J* = 2.9 Hz, 1 H, 4-H). − ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 14.2 (+, CH_3), 21.5 (+, C-6), 31.9 (+, C-5), 52.1 (+, OCH_3), 61.0 (−, CH_2), 67.5 (+, C-1), 116.0 (+, C-4), 149.3 (C_{quat}, C-3), 159.5 (C_{quat}, CO), 171.7 (C_{quat}, CO). − IR (KBr): $\tilde{\nu}$ = 3118 cm^{-1}, 2956, 1720, 1617, 1428, 1380, 1297, 1166, 1124, 1041, 954, 831, 725. − MS (70 eV, EI): *m*/*z* (%) = 212.1 [M$^+$] (9.8), 153.0 [M$^+$ − CO_2Me] (11.5), 139.0 [M$^+$ − CO_2Et] (100), 124.9 (24.4), 98.9 (28.6), 96.9 (31.7), 78.9 (11.3), 59.0 (13.5), 52.1(11.5). − $C_{10}H_{12}O_5$ (212.2): calcd. C 56.60, H 5.70; found C 56.51, H 5.73.

General Ozonolysis Procedure (GP1): A solution of **5** or **6** in dry CH_2Cl_2 (5 mL/mmol) was cooled to −78 °C and treated with ozone until the mixture turned blue. Excess ozone was expelled by passing oxygen through the solution, followed by addition of dimethyl sulfide (0.4 mL/mmol). The mixture was allowed to warm to room temp. and stirring was continued for 24 h.

Methyl (1*S,2*S**,3*S**)-2-Formyl-3-(formyloxy)cyclopropanecarboxylate (1a):** Compound **6a** (3.00 g, 21.4 mmol) was ozonolyzed according to GP1. The solvent was evaporated and the residue distilled under reduced pressure (b.p. 70 °C/0.02 Torr) to yield **1a** as a colorless liquid (3.00 g, 81%). − ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.77 (ddd, *J* = 7.4, 5.9, 4.0 Hz, 1 H, 2-H), 2.85 (dd, *J* = 5.9, 3.6 Hz, 1 H, 1-H), 3.75 (s, 3 H, OCH_3), 4.79 (dd, *J* = 7.4, 3.6 Hz, 1 H, 3-H), 8.02 (s, 1 H, OHCO), 9.47 (d, *J* = 4.0 Hz, 1 H, OHC). − ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 26.2 (+, C-1), 34.9 (+, C-2), 52.7 (+, OCH_3), 57.0 (+, C-3), 159.8 (+, OCHO), 168.9 (C_{quat}, CO), 193.1 (+, CHO). − IR (film): $\tilde{\nu}$ = 3040 cm^{-1}, 2940, 1730, 1430, 1360, 1280, 1180, 1140, 1070, 980, 930, 850, 750. − MS (EI, 70 eV): *m*/*z* (%) = 172.0 (0.1) [M$^+$], 157.0 (0.3), 143.0 (9.3), 126.0 (14.6), 115.1 (26.4), 95.0 (10.4), 87.0 (21.8), 83.0 (52.1), 55.0 (35.0), 43.9 (10.0), 28.0 (100), 17.9 (5.7). − $C_7H_8O_5$ (172.1): calcd: C 48.84, H 4.68; found C 48.31, H 4.78.

(1*S,2*S**,3*S**)-2-Formyl-3-(methoxycarbonyl)cyclopropyl Methyl Oxalate (1b):** Compound **6b** (2.91 g, 14.7 mmol) was ozonolyzed according to GP1. The reaction mixture was washed with sat. $NaHCO_3$ (20 mL) and water (20 mL), dried ($MgSO_4$), and the solvent was evaporated. The residue was recrystallized from ethyl acetate to provide **1b** as a white solid (2.75 g, 81%). − M.p. 85 °C. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.81 (ddd, *J* = 7.3, 6.1, 3.9 Hz, 1 H, 2-H), 2.94 (dd, *J* = 6.1, 3.6 Hz, 1 H, 3-H), 3.77 (s, 3 H, OCH_3), 3.91 (s, 3 H, OCH_3), 4.84 (dd, *J* = 7.3, 3.6 Hz, 1 H, 1-H), 9.47 (d, *J* = 3.9 Hz, 1 H, CHO). − ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 26.1 (C-3), 34.8 (C-2), 52.8 (OCH_3), 53.9 (OCH_3), 58.7 (C-1), 156.5 (C_{quat}, CO), 156.8 (C_{quat}, CO), 168.6 (C_{quat}, CO), 192.5 (CHO). − IR (KBr): $\tilde{\nu}$ = 3066 cm^{-1}, 3015, 2963, 2892, 1785, 1751, 1735, 1706, 1445, 1345, 1313, 1210, 1167, 1086, 1011, 963, 867, 790, 715, 613, 495. − MS (DCI, NH_3): *m*/*z* (%) = 478.2 (2) [2 M + NH_4^+], 248.1 (100) [M + NH_4^+]. − $C_9H_{10}O_7$ (230.2): calcd. C 46.96, H 4.38; found C 46.77, H 4.43.

Methyl (1*S,2*S**,3*S**)-2-[(*tert*-Butyloxycarbonyl)(formyl)amino]-3-formylcyclopropanecarboxylate (2):** A solution of **5** (5.98 g, 24.9 mmol) was ozonolyzed according to GP1. The solvent was evaporated and the residue was purified by chromatography (hexanes/ethyl acetate, 5:1, silica gel) to provide **2** (5.96 g, 88%) as a colorless oil, which was recrystallized from diethyl ether/cyclohexane. − R_f = 0.19. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.52 [s, 9 H, $C(CH_3)_3$], 2.75 (dd, *J* = 6.0, 4.8 Hz, 1 H, 1-H), 2.96 (ddd, *J* = 8.2, 6.0, 2.3 Hz, 1 H, 3-H), 3.20 (dd, *J* = 8.2, 4.8 Hz, 1 H, 2-H), 3.75 (3 H, OCH_3), 9.07 (s, 1 H, NCHO), 9.54 (d, *J* = 2.3 Hz, 1 H, CHO). − ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 27.6 (+), 27.7 [+, $C(CH_3)_3$], 34.8 (+), 36.5 (+), 52.5 (+, OCH_3), 85.2 [C_{quat}, $C(CH_3)_3$], 151.8 [C_{quat}, $NCO_2C(CH_3)_3$], 163.3 (+, NCHO), 169.9 (C_{quat}, CO), 193.0 (+, CHO). − IR (KBr): $\tilde{\nu}$ = 3070 cm^{-1}, 3041, 3007, 2979, 2958, 2859, 2752, 1727 (C=O), 1698 (C=O), 1552, 1456, 1433, 1395, 1385, 1372, 1349, 1325, 1285, 1203, 1177, 1145, 1101, 1060, 1028, 975, 913, 897, 885, 843, 819, 806, 777, 752, 737, 721, 666, 575. − MS (EI, 70 eV): *m*/*z* (%) = 171.1 (7) [M − Boc],

142.1 (10) [M − Boc-CHO], 126.1 (34), 57.1 (100), 41.0 (25). − $C_{12}H_{17}NO_6$ (271.3): calcd. C 53.13 H 6.32 N 5.16; found C 53.02 H 6.29 N 5.02.

General Procedure (GP2) for BF_3-Catalyzed Additions of Nucleophiles to 1b or 2: A solution of the aldehyde **1b** or **2** (1.0 mmol) in CH_2Cl_2 (10 mL) was treated with $BF_3{\cdot}Et_2O$ (126 μL, 1.0 mmol) at −78 °C. After 10 min, the nucleophile was added and stirring was continued for 12 h. The reaction was quenched with saturated $NaHCO_3$ (0.2 mL) and the mixture was allowed to warm to 0 °C. After separation of the organic layer and drying with $MgSO_4$, the solvent was evaporated under vacuum to yield the products (purity > 95%). All products derived from **1b** turned out to be hydrolytically too labile to be further purified by chromatography and were taken as such or recrystallized if possible. The products derived from **2** were further purified by chromatography on a silica gel column and/or by recrystallization.

(1*S,1′*S**,2*R**,3*S**)-2-(1′-Hydroxy-3′-oxo-3′-phenylpropyl)-3-(methoxycarbonyl)cyclopropyl Methyl Oxalate (9a):** Treatment of aldehyde **1b** (230 mg, 1.0 mmol), $BF_3{\cdot}Et_2O$ (126 μL, 1.0 mmol) and trimethyl(1-phenylvinyloxy)silane (192 mg, 1.0 mmol) according to GP2 yielded **9a**, after recrystallization from $CHCl_3$/*n*-pentane, as colorless crystals (305 mg, 87%) which were subjected to X-ray crystallography.[13] − M.p. 112−113 °C. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.04 (ddd, *J* = 8.7, 7.3, 6.1 Hz, 1 H, 2-H), 2.27 (dd, *J* = 6.1, 2.8 Hz, 1 H, 3-H), 3.26 (dd, *J* = 17.6, 7.0 Hz, 1 H, 2′-H), 3.34 (dd, *J* = 17.6, 4.4 Hz, 1 H, 2′-H), 3.55 (br. s, 1 H, OH), 3.72 (s, 3 H, OCH_3), 3.85 (s, 3 H, OCH_3), 4.15 (ddd, *J* = 8.7, 7.0, 4.4 Hz, 1 H, 1′-H), 4.71 (dd, *J* = 7.3, 2.8 Hz, 1 H, 1-H), 7.45−7.51 (m, 2 H, Ar-H), 7.57 − 7.64 (m, 1 H, Ar−H), 7.95 (m, 2 H, Ar−H). − ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 25.2 (C-3), 30.9 (C-2), 44.7 (C-2′), 52.3 (CO_2CH_3), 53.7 (CO_2CH_3), 58.7 (C-1), 65.4 (C-1′), 128.2 (Ar−C), 128.8 (Ar−C), 133.8 (Ar−C), 136.5 (Ar−C), 157.1 (C_{quat}, CO), 157.4 (C_{quat}, CO), 170.8 (C_{quat}, CO), 199.7 (C-3′). − IR (KBr): $\tilde{\nu}$ = 3503 cm^{-1}, 3064, 3025, 2956, 1776, 1752, 1731, 1683, 1597, 1449, 1315, 1268, 1202, 1161, 984. − MS (DCI, NH_3): *m*/*z* (%) = 368.2 (30) [M + NH_4^+], 264.2 (64), 248.1 (100). − MS (HR-DCI): 368.13435 ($C_{17}H_{22}NO_8$: calcd. 368.13452 [M + NH_4^+]). − $C_{17}H_{18}O_8$ (230.2): calcd. C 58.29, H 5.18; found C 57.78, H 5.19.

(1*S,1′*S**,2*R**,3*S**)-2-(1′-Hydroxy-3′-oxobutyl)-3-(methoxycarbonyl)cyclopropyl Methyl Oxalate (9b):** Treatment of aldehyde **1b** (115 mg, 0.5 mmol), $BF_3{\cdot}Et_2O$ (63 μL, 0.5 mmol) and (isopropenyloxy)trimethylsilane (65 mg, 0.5 mmol) according to GP2 yielded **9b** as a colorless oil (123.9 mg, 86%). − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.04 (ddd, *J* = 8.5, 7.2, 6.3 Hz, 1 H, 2-H), 2.20 (m, 4 H, 3-H, CH_3), 2.77 (m, 2 H, 2′-H, CH_2), 3.71 (s, 3 H, OCH_3), 3.80 (br. s, 1 H, OH), 3.90 (s, 3 H, OCH_3), 3.96 (m, 1 H, 1′-H), 4.66 (dd, *J* = 7.3, 2.7 Hz, 1 H, 1-H). − ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 24.9 (C-3), 30.7 (C-2), 31.3 (C-4′), 49.3 (C-2′), 52.6 (OCH_3), 53.8 (OCH_3), 58.6 (C-1), 64.9 (C-1′), 157.1 (C_{quat}, CO), 157.4 (C_{quat}, CO), 170.8 (C_{quat}, CO), 208.7 (C-3′). − IR (film): $\tilde{\nu}$ = 3506 cm^{-1}, 3062, 3005, 2958, 1756, 1632, 1442, 1316, 1202, 1160, 1083, 1006, 916, 733. − MS (DCI, NH_3): *m*/*z* (%) = 306.2 (10) [M + NH_4^+], 288.2 (100), 202.1 (30), 186.1 (40). − MS (HR-DCI): 306.11833 ($C_{12}H_{20}NO_8$: calcd. 306.11889 [M + NH_4^+]).

(1*S,1′*S**,2*R**,3*S**)-2-(2′-Ethoxycarbonyl-1′-hydroxyethyl)-3-(methoxycarbonyl)cyclopropyl Methyl Oxalate (9c):** Treatment of aldehyde **1b** (115 mg, 0.5 mmol), $BF_3{\cdot}Et_2O$ (63 μL, 0.5 mmol) and *tert*-butyl(1-ethoxyvinyloxy)dimethylsilane (101 mg, 0.5 mmol) according to GP2 yielded **9c** as a colorless oil (137 mg, 86%). − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.28 (t, *J* = 7.1 Hz, 3 H, CH_3), 1.90−2.06 (m, 1 H, 2-H), 2.23 (dd, *J* = 6.4, 2.8 Hz, 1 H, 3-H), 2.63−2.71 (m, 2 H, 2′-H, CH_2), 3.71 (s, 3 H, OCH_3), 3.90 (s, 3 H, OCH_3), 3.94−4.00 (m, 1 H, 1′-H), 4.18 (q, *J* = 7.1 Hz, 2 H, CH_2), 4.68 (dd, *J* = 7.6, 2.8 Hz, 1 H, 1-H). − ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 14.1 (+, CH_3), 24.9 (+, C-3), 30.7 (+, C-2), 41.0 (−, CH_2), 52.3 (OCH_3), 53.8 (OCH_3), 58.6 (C-1), 60.9 (−, CH_2), 65.2 (C-1′), 157.0 (C_{quat}, CO), 157.3 (C_{quat}, CO), 170.8 (C_{quat}, CO), 171.9 (C_{quat}, CO). − IR (film): $\tilde{\nu}$ = 3500 cm^{-1}, 3063, 2957, 2857, 1780, 1731, 1624, 1443, 1316, 1258, 1200, 1160, 978. − MS (DCI, NH_3): *m*/*z* (%) = 336.2 (30) [M + NH_4^+], 264.2 (64), 248.1 (100). − MS (HR-FAB): 319.10329 ($C_{13}H_{19}O_9$: calcd. 319.10291 [M + H^+]).

(1*S,1′*R**/*S**,2*R**,3*S**)-2-(1′-Hydroxy-but-3′-enyl)-3-(methoxycarbonyl)cyclopropyl Methyl Oxalate (9d/10d):** Treatment of aldehyde **1b** (230 mg, 1.0 mmol), $BF_3{\cdot}Et_2O$ (126 μL, 1.0 mmol) and allyltrimethylsilane (171 mg, 1.5 mmol) according to GP 2 yielded **9d/10d** (90:10) as a colorless liquid (223 mg, 82%). − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.89 (m, 1 H, 2-H), 1.97 (br. s, 1 H, OH), 2.19 (dd, *J* = 6.1, 2.7 Hz, 1 H, 3-H), 2.30−2.49 (m, 2 H, 2′-H), 3.71 (s, 3 H, OCH_3), 3.73 (m, 1 H, 1′-H), 3.91 (s, 3 H, OCH_3), 4.75 (dd, *J* = 7.3, 2.7 Hz, 1 H, 1-H), 5.14−5.22 (m, 2 H, 4′-H), 5.76−5.93 (m, 1 H, 3′-H); characteristic signals of the diastereomer **10d**: δ = 4.70 (dd, *J* = 6.8, 2.8 Hz, 1 H, 1-H). − ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 24.4 (C-3), 31.3 (C-2), 41.7 (C-2′), 52.2 (OCH_3), 53.7 (OCH_3), 58.8 (C-1), 67.7 (C-1′), 118.8 (C-4′), 133.3 (C-3′), 157.1 (C_{quat}, CO), 157.2 (C_{quat}, CO), 170.9 (C_{quat}, CO); characteristic signals of the diastereomer **10d**: δ = 24.8 (C-3), 41.3 (C-2′), 58.6 (C-1), 68.6 (C-1′), 118.5 (C-4′), 133.4 (C-3′). − IR (film): $\tilde{\nu}$ = 3503 cm^{-1}, 3076, 2957, 2852, 1778, 1752, 1730, 1641, 1450, 1316, 1202, 1162, 1076, 996, 921, 867, 784. − MS (DCI, NH_3): *m*/*z* (%) = 562.2 (1) [2 M + NH_4^+], 290.2 (100) [M + NH_4^+]. − MS (HR-DCI): 290.12326 ($C_{12}H_{20}NO_7$: calcd. 290.12396 [M + NH_4^+]).

(1*S,1′*R**/*S**,2*R**,3*S**)-2-(3′-Acetoxymethyl-1′-hydroxybut-3′-enyl)-3-(methoxycarbonyl)cyclopropyl Methyl Oxalate (9e/10e):** Treatment of **1b** (230 mg, 1.0 mmol), $BF_3{\cdot}Et_2O$ (126 μL, 1.0 mmol) and 2-(trimethylsilylmethyl)allyl acetate (279 mg, 1.5 mmol) according to GP2 yielded **9e/10e** (80:20) as a colorless liquid (293 mg, 85%). − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.81 −1.91 (m, 1 H, 2-H), 2.04 (s, 3 H, Acyl-H), 2.14 (dd, *J* = 6.1, 2.7 Hz, 1 H, 3-H), 2.32−2.44 (m, 2 H, 2′-H), 2.89 (br. s, 1 H, OH), 3.66 (s, 3 H, OCH_3), 3.72 (m, 1 H, 1′-H), 3.86 (s, 3 H, OCH_3), 4.51 (m, 2 H, CH_2) 4.67 (dd, *J* = 7.4, 2.7 Hz, 1 H, 1-H), 5.05 (m, 1 H, 4′-H), 5.13 (m, 1 H, 4′-H); characteristic signals of the diastereomer **10e**: δ = 1.86−1.96 (m, 1 H, 2-H), 2.05 (s, 3 H, CH_3), 2.17 (dd, *J* = 6.1, 2.7 Hz, 1 H, 3-H), 3.67 (s, 3 H, OCH_3), 3.87 (s, 3 H, OCH_3), 4.65 (dd, *J* = 7.4, 2.7 Hz, 1 H, 1-H). − ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.7 (CH_3), 24.8 (C-3), 31.6 (C-2), 41.5 (C-2′), 52.2 (OCH_3), 53.7 (OCH_3), 58.7 (C-1), 66.5 (−, CH_2), 67.4 (C-1′), 116.1 (C-4′), 140.1 (C-3′), 157.0 (C_{quat}, CO), 157.1 (C_{quat}, CO), 170.5 (C_{quat}, CO), 170.8 (C_{quat}, CO); characteristic signals of the diastereomer **10e**: δ = 20.9 (CH_3), 25.2 (C-3), 31.5 (C-2), 41.0 (C-2′), 52.2 (OCH_3), 53.8 (OCH_3), 58.4 (C-1), 66.9 (−, CH_2), 67.8 (C-1′), 116.2 (C-4′), 157.5 (C_{quat}, CO), 170.6 (C_{quat}, CO), 170.7 (C_{quat}, CO). − IR (film): $\tilde{\nu}$ = 3506 cm^{-1}, 2957, 1779, 1736, 1442, 1374, 1315, 1234, 1201, 1160, 1028, 980, 915, 860. − MS (DCI, NH_3): *m*/*z* (%) = 362.2 (100) [M + NH_4^+], 258.1 (69), 200.1 (18). − MS (HR-DCI): 362.14384 ($C_{15}H_{24}NO_9$: calcd. 362.14511 [M + NH_4^+]).

(1*S,1′*R**/*S**,2*R**,3*S**)-2-(Cyanohydroxymethyl)-3-(methoxycarbonyl)cyclopropyl Methyl Oxalate (9f/10f):** Treatment of aldehyde **1b** (230 mg, 1.0 mmol), $BF_3{\cdot}Et_2O$ (126 μL, 1.0 mmol) and TMSCN (149 mg, 1.5 mmol) according to the general procedure

yielded **9f/10f** (65:35) as a colorless liquid (234 mg, 91%). – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.26–2.39 (m, 2 H, 2-H, 3-H), 3.75 (s, 3 H, OCH_3), 3.93 (s, 3 H, OCH_3), 4.18 (br. s, 1 H, OH), 4.60 (d, *J* = 7.9 Hz, 1 H, 1′-H), 4.76–4.83 (m, 1 H, 1-H); characteristic signals of the diastereomer **10f**: δ = 2.24 (dd, *J* = 6.1, 2.8 Hz, 1 H, 3-H), 3.76 (s, 3 H, OCH_3), 4.48 (d, *J* = 9.1 Hz, 1 H, 1′-H). – ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 25.5 (C-3), 28.5 (C-2), 52.7 (OCH_3), 54.0 (OCH_3), 57.2 (C-1′), 58.1 (C-1), 117.9 (C_{quat}, CN), 156.8 (C_{quat}, CO), 156.9 (C_{quat}, CO), 169.7 (C_{quat}, CO); characteristic signals of the diastereomer **10f**: δ = 24.3 (C-3), 28.6 (C-2), 52.8 (OCH_3), 54.1 (OCH_3), 57.6 (C-1′), 58.3 (C-1), 118.2 (C_{quat}, CN), 156.7 (C_{quat}, CO), 157.0 (C_{quat}, CO), 169.4 (C_{quat}, CO). – IR (film): $\tilde{\nu}$ = 3459 cm^{-1}, 3065, 2960, 1781, 1754, 1735, 1456, 1318, 1203, 1163, 1080, 1063, 980, 858. – MS (DCI, NH_3): *m/z* (%) = 275.0 (100) [M + NH_4^+], 248.0 (69) [M – HCN + NH_4^+]. – MS (HR-DCI): 275.08866 ($C_{10}H_{15}N_2O_7$: calcd. 275.08792 [M + NH_4^+]).

Methyl (1*S,1′*S**,2*S**,3*S**)-2-(*tert*-Butoxycarbonylamino)-3-(1′-formyloxy-3′-oxo-3′-phenylpropyl)cyclopropanecarboxylate (11a):** Treatment of aldehyde **2** (271 mg, 1.0 mmol), $BF_3{\cdot}Et_2O$ (126 μL, 1.0 mmol) and trimethyl(1-phenylvinyloxy)silane (192 mg, 1.0 mmol) according to GP2 yielded **11a** as colorless crystals (139 mg, 71%) after chromatography (hexanes/ethyl acetate, 3:1) and recrystallization from CH_2Cl_2/hexanes. – R_f = 0.36. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.35 [s, 9 H, $C(CH_3)_3$], 1.83–2.01 (m, 1 H, cyclopropyl–H), 2.03 (br. s, 1 H, cyclopropyl–H), 3.19 (br. s, 1 H, cyclopropyl–H), 3.56–3.63 (m, 2 H, 2′-H), 3.65 (s, 3 H, OCH_3), 5.35–5.44 (m, 1 H, 1′-H), 5.77 (br. s, 1 H, NH), 7.41–7.59 (m, 3 H, phenyl–H), 7.90–7.94 (m, 2 H, phenyl–H), 8.03 (s, 1 H, OCHO). – ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 26.2 (+, C-3), 28.0 [+, $C(CH_3)_3$], 30.9 (+, C-1), 36.0 (+, C-2), 43.5 (–, C-2′), 52.0 (+, OCH_3), 68.0 (+, C-1′), 80.0 [C_{quat}, $OC(CH_3)_3$], 128.0 (+, phenyl–C), 128.6 (+, phenyl–C), 133.6 (+, phenyl–C), 136.0 (C_{quat}, phenyl–C), 156.2 [C_{quat}, $NCO_2C(CH_3)_3$], 160.3 (+, OCHO), 171.6 (C_{quat}, CO), 196.5 (C_{quat}, C-3′). – IR (KBr): $\tilde{\nu}$ = 3346 cm^{-1} (NH), 2982, 1710 (C=O), 1700 (C=O), 1679 (C=O), 1512, 1452, 1416, 1392, 1367, 1335, 1265, 1238, 1172, 1068, 994, 982, 855, 759, 692, 458. – MS (DCI, NH_3): *m/z* (%) = 409 (100) [M + NH_4^+]. – $C_{20}H_{25}NO_7$ (391.4): calcd. C 61.37 H 6.44; found C 61.47 H 6.27.

Methyl (1*S,1′*S**,2*S**,3*S**)-2-(*tert*-Butoxycarbonylamino)-3-(1′-formyloxybut-3′-enyl)cyclopropanecarboxylate (11b):** Treatment of aldehyde **2** (271 mg, 1.0 mmol), $BF_3{\cdot}Et_2O$ (126 μL, 1.0 mmol) and allyltrimethylsilane (171 mg, 1.5 mmol) according to GP2 yielded **11b** as a colorless oil (288 mg, 92%) after chromatography (hexanes/ethyl acetate, 5:1). – R_f = 0.30. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.41 [s, 9 H, $C(CH_3)_3$], 1.76–1.91 (m, 2 H, 1-H + 3-H), 2.40–2.59 (m, 2 H, 2′-H), 3.23 (br. s, 1 H, 2-H), 3.65 (s, 3 H, OCH_3), 4.81–4.89 (m, 1 H, 1′-H), 4.98 (br. s, 1 H, NH), 5.09–5.17 (m, 2 H, olefin-H), 5.67–5.84 (m, 1 H, olefin-H), 8.04 (s, 1 H, OCHO). – ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 25.5 (+), 27.7 (+), 28.1 [+, $C(CH_3)_3$], 30.3 (+), 35.84 (+), 38.7 (–, C-2′), 52.0 (+, OCH_3), 71.1 (+), 80.2 [C_{quat}, $OC(CH_3)_3$], 118.9 (–, C-4′), 132.3 (+, C-3′), 155.3 [C_{quat}, $NCO_2C(CH_3)_3$], 160.5 (+, OCHO), 171.6 (C_{quat}, CO). – IR (film): $\tilde{\nu}$ = 3361 cm^{-1} (NH), 3079, 2979, 2933, 1736 (C=O), 1643, 1513, 1455, 1392, 1368, 1335, 1240, 1173, 1068, 1026, 986, 921, 851, 783, 737, 703, 621, 461. – MS (DCI, NH_3): *m/z* (%) = 644.6 (8) [2 M + NH_4^+], 331.3 (100) [M + NH_4^+]. – MS (HR-DCI): 331.18688 ($C_{15}H_{27}N_2O_6$: calcd. 331.1869 [M + NH_4^+]).

Methyl (1*S,1′*S**,2*S**,3*S**)-2-(3′-Acetoxymethyl-1′-formyloxybut-3′-enyl)-3-(*tert*-butoxycarbonylamino)cyclopropanecarboxylate (11c):** Treatment of aldehyde 2 (271 mg, 1.0 mmol), $BF_3{\cdot}Et_2O$ (126 μL, 1.0 mmol) and acetic acid 2-trimethylsilanylmethyl-allyl ester (279 mg, 1.5 mmol) according to GP2 yielded 11c as a colorless oil (358 mg, 93%) after chromatography (hexanes/ethyl acetate, 5:1). R_f = 0.23. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.40 [s, 9 H, $C(CH_3)_3$], 1.79 (ddd, *J* = 9.8, 7.7, 5.5 Hz, 1 H, 2-H), 1.89 (dd, *J* = 5.4, 3.7 Hz, 1 H, 1-H), 2.05 [s, 3 H, $C(O)CH_3$], 2.41–2.60 (m, 2 H, 2′-H), 3.20 (br. s, 1 H, 3-H), 3.63 (s, 3 H, OCH_3), 4.45–4.60 (m, 2 H, CH_2), 4.94–5.21 (m, 3 H, 1′-H + olefin–H), 5.22 (br. s, 1 H, NH), 8.00 (s, 1 H, NCHO). – ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.7 (+), 25.5 (+), 28.1 [+, $C(CH_3)_3$], 30.7 (+), 35.9 (+), 38.7 (–), 52.0 (+, OCH_3), 66.7 (–), 70.0 (+), C-1′), 80.2 [C_{quat}, $OC(CH_3)_3$], 117.0 (–, C-4′), 138.6 (C_{quat}, C-3′), 155.9 [C_{quat}, $NCO_2C(CH_3)_3$], 160.4 (+, OCHO), 170.6 (C_{quat}, CO), 171.5 (C_{quat}, CO). – IR (film): $\tilde{\nu}$ = 3360 cm^{-1} (NH), 2979, 1721 (C=O), 1511, 1455, 1368, 1335, 1236, 1165, 1029, 989, 918, 849, 784, 732, 606, 431. – MS (DCI, NH_3): *m/z* (%) = 788.7 (5) [2 M + NH_4^+], 403.4 (100) [M + NH_4^+].

Methyl (1*S,1′*R**/*S**,2*S**,3*S**)-2-[(*tert*-Butoxycarbonyl)(formyl)-amino]-3-(cyanohydroxymethyl)cyclopropanecarboxylate (11d/12d):** Treatment of aldehyde **2** (271 mg, 1.0 mmol), $BF_3{\cdot}Et_2O$ (126 μL, 1.0 mmol) and TMSCN (149 mg, 1.5 mmol) according to GP2 yielded **11d/12d** (89:11) as a colorless oil (280 mg, 94%) after chromatography (hexanes/ethyl acetate, 3:1). The major diastereomer **11d** was obtained pure by recrystallization (215 mg, 72%) from cyclohexane/$CHCl_3$ and analyzed by X-ray crystallography.[13] – R_f = 0.18. – M.p. 83 °C. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.55 [s, 9 H, $C(CH_3)_3$], 2.20–2.30 (m, 2 H, 1-H + 3-H), 3.04 (dd, *J* = 7.3, 4.6 Hz, 1 H, 2-H), 3.76 (s, 3 H, OCH_3), 4.63 (d, *J* = 10.7 Hz, 1 H, OH), 4.93 (dd, *J* = 10.7, 3.7 Hz, 1 H, 1′-H), 9.18 (s, 1 H, NCHO). – ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 24.3 (+, C-3), 27.7 (+, C-1), 29.1 [+, $C(CH_3)_3$], 34.1 (+, C-2), 52.5 (+, CO_2CH_3), 58.4 (+, C-1′), 86.2 [C_{quat}, $OC(CH_3)_3$], 117.2 (CN), 152.2 [C_{quat}, $NCO_2C(CH_3)_3$], 165.0 (+, NCHO), 170.6 (C_{quat}, CO). – IR (KBr): $\tilde{\nu}$ = 3417 cm^{-1} (OH), 3035, 3007, 2987, 1727 (C=O), 1704 (C=O), 1456, 1413, 1399, 1368, 1321, 1274, 1210, 1181, 1147, 1119, 1063, 1041, 994, 929, 917, 894, 840, 805, 774, 748, 727, 593, 529, 498, 473, 407. – MS (DCI, NH_3): *m/z* (%) = 289 (100) [M – HCN + NH_4^+]. – $C_{13}H_{18}N_2O_6$ (298.3): calcd. C 52.35 H 6.08; found C 52.12 H 5.94.

Methyl (1*S,1′*R**/*S**,2*S**,3*S**)-2-[(*tert*-Butoxycarbonyl)(formyl)-amino]-3-[cyano(trimethylsilyloxy)methyl]cyclopropanecarboxylate (11e/12e):** To a solution of **2** (56 mg, 0.21 mmol) in CH_2Cl_2 (2 mL) was added TMSCN (99 mg, 1.0 mmol). The mixture was stirred for 24 h and then concentrated in vacuo to yield a mixture of **11e/12e** (91:9) as a colorless oil (74 mg, 97%). – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.13 [s, 9 H, $Si(CH_3)_3$], 1.51 [s, 9 H, $C(CH_3)_3$], 2.17 (ddd, *J* = 7.9, 6.3, 2.5 Hz, 1 H, 3-H), 2.36–2.41 (m, 1 H, 1-H), 3.04 (dd, *J* = 7.9, 4.5 Hz, 1 H, 2-H), 3.73 (s, 3 H, OCH_3), 4.76 (d, *J* = 2.5 Hz, 1 H, 1′-H), 9.03 (s, 1 H, NCHO). – ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = –0.6 [+, $Si(CH_3)_3$], 21.6 (+, C-3), 27.7 [+, $C(CH_3)_3$], 30.3 (+, C-1), 34.7 (+, C-2), 52.3 (+, OCH_3), 57.3 (+, C-1′), 84.9 [C_{quat}, $OC(CH_3)_3$], 118.4 (C_{quat}, CN), 151.9 [C_{quat}, $NCO_2C(CH_3)_3$], 163.5 (+, NCHO), 171.2 (C_{quat}, CO). – IR (film): $\tilde{\nu}$ = 2957 cm^{-1}, 1736 (C=O), 1457, 1371, 1291, 1207, 1148, 1064, 990, 952, 899, 850, 775, 753. – MS (DCI, NH_3): *m/z* (%) = 388 (100) [M + NH_4^+]. – MS (HR-DCI): 388.18861 ($C_{16}H_{30}N_3O_6Si$: calcd. 388.19039 [M + NH_4^+]).

Methyl (1*S,1′*R**/*S**,2*S**,3*S**)-2-(*tert*-Butoxycarbonylamino)-3-(1′-formyloxy-2′-methyl-2′-nitropropyl)cyclopropanecarboxylate (11f):** A solution of **2** (271 mg, 1.0 mmol) in 2-nitropropane (3 mL) was treated with triethylamine (100 μL) at 0 °C and stirred for 6 h. The

solvent was evaporated in vacuo and the residue was purified by chromatography (hexanes/ethyl acetate, 2:1) to yield **11f** as a colorless oil. Recrystallization from CH_2Cl_2/cyclohexane gave white needles (329 mg, 91%). − R_f = 0.53. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.43 [s, 9 H, $C(CH_3)_3$], 1.64 (s, 3 H, CH_3), 1.73 (s, 3 H, CH_3), 1.76−1.80 (m, 1 H, 3-H), 1.28−2.02 (m, 1 H, 1-H), 3.47 (br. s, 1 H, 2-H), 3.68 (s, 3 H, OCH_3), 5.05 (br. s, 1 H, NH), 5.55 (d, J = 10.0 Hz, 1 H, 1′-H), 8.02 (s, 1 H, OCHO). − ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.5 (+), 23.4 (+), 24.6 (+), 27.1 (+), 28.1 [+, $C(CH_3)_3$], 37.4 (+), 52.3 (+, OCH_3), 72.4 (+, C-1′), 80.7 [C_{quat}, $OC(CH_3)_3$], 89.8 (C_{quat}, C-2′), 155.4 [C_{quat}, $NCO_2C(CH_3)_3$], 159.7 (+, OCHO), 171.1 (C_{quat}, CO). − IR (KBr): $\tilde{\nu}$ = 3350 cm^{-1} (NH), 2984, 1702 (C=O), 1544, 1455, 1402, 1368, 1346, 1288, 1249, 1164, 1075, 1042, 992, 974, 928, 847, 788, 754, 732, 540, 446. − MS (DCI, NH_3): m/z (%) = 378 (100) [M + NH_4^+], 322 (53). − $C_{15}H_{24}N_2O_8$ (360.4): calcd. C 49.99 H 6.71; found C 50.18 H 6.67.

Methyl (1*S,1′*R**/*S**,2*S**,3*S**)-2-(*tert*-Butoxycarbonylamino)-3-[formyloxy(1′-nitrocyclohexyl)methyl]cyclopropanecarboxylate (11g)**: A solution of **2** (271 mg, 1.0 mmol) in nitrocyclohexane (2 mL) was treated with triethylamine (500 μL) at 0 °C and stirred for 12 h at room temp. The mixture was concentrated in vacuo and the residue was purified by chromatography (hexanes/ethyl acetate, 3:1) to yield **11g** as a white solid, which was recrystallized from CH_2Cl_2/cyclohexane to yield white needles (337 mg, 84%). − R_f = 0.36. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.20−1.42 (m, 2 H), 1.49 [s, 9 H, $C(CH_3)_3$], 1.57−171 (m, 6 H), 1.83−1.95 (m, 2 H), 2.45−2.50 (m, 1 H), 2.63−2.69 (m, 1 H), 3.42 (br. s, 1 H, 2-H), 3.68 (s, 3 H, OCH_3), 4.77 (br. s, 1 H, N H), 5.21 (d, J = 9.2 Hz, 1 H, 1′-H), 8.07 (s, 1 H, OCHO). − ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.6 (−), 24.3 (−), 24.8 (+), 26.7 (+), 28.1 [+, $C(CH_3)_3$], 29.1 (−), 30.5 (−), 37.3 (+), 52.3 (+, OCH_3), 73.0 (+, C-1′), 80.8 [C_{quat}, $OC(CH_3)_3$], 93.1 (C_{quat}), 153.4 [C_{quat}, $NCO_2C(CH_3)_3$], 159.7 (+, OCHO), 171.0 (C_{quat}, CO). − IR (KBr): $\tilde{\nu}$ = 3375 cm^{-1} (NH), 2941, 2869, 1735 (C=O), 1699 (C=O), 1541, 1452, 1392, 1367, 1335, 1298, 1272, 1252, 1162, 1074, 1031, 983, 951, 895, 846, 787, 728, 549, 460, 425. − MS (DCI, NH_3): m/z (%) = 418 (100) [M + NH_4^+], 362 (88). − $C_{18}H_{28}N_2O_8$ (400.4): calcd: C 53.99 H 7.05; found C 54.12 H 7.15.

(1*S,1′*R**,1′′*R**/*S**,2*R**,3*S**)-2-[Hydroxy(2′-oxocyclohexyl)-methyl]3-(methoxycarbonyl)cyclopropyl Methyl Oxalate (13):** Treatment of aldehyde **1b** (230 mg, 1.0 mmol), BF_3·Et_2O (126 μL, 1.0 mmol) and (cyclohex-1-enyloxy)trimethylsilane (170 mg, 1.0 mmol) according to GP2 yielded **13** (1:1 mixture of two diastereomers) as a colorless liquid (292 mg, 89%). − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.55−1.79 (m, 2 H), 1.80−2.02 (m, 3 H), 2.03−2.25 (m, 3 H), 2.26−2.62 (m, 3 H), 3.36 (br. s, 1 H, OH), 3.61 (dd, J = 9.2, 7.3 Hz, 1 H, 1′-H, diastereomer 1), 3.94 (dd, J = 7.7, 2.9 Hz, 1 H, 1′-H, diastereomer 2), 3.66 (s, 3 H, OCH_3), 3.86 (s, 3 H, OCH_3), 4.62 (dd, J = 7.3, 2.8 Hz, 1 H, 1-H, diastereomer 1), 4.67 (dd, J = 7.3, 2.8 Hz, 1 H, 1-H, diastereomer 2). − ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 24.7, 24.9 (−, CH_2), 24.8, 25.1 (+, C-2), 27.0, 27.1, 27.4, 27.6 (−, CH_2), 28.5, 30.1 (+, C-3), 42.4, 42.7 (−, CH_2), 52.3, 53.8, 54.8, 56.4 (+, OCH_3), 58.9, 59.3 (+, C-1), 66.8, 68.6 (+, C-1′), 157.2, 157.3, 175.4, 157.5 (C_{quat}, CO), 170.9, 171.0 (C_{quat}, CO), 213.7, 214.5 (C_{quat}, C-2′′). − IR (film): $\tilde{\nu}$ = 3506 cm^{-1}, 2952, 2866, 1780, 1753, 1708, 1450, 1313, 1201, 1160, 979, 866, 735. − MS (DCI, NH_3): m/z (%) = 346.1 (100) [M + NH_4^+], 328.1 (12) [M^+], 242.1 (54). − MS (HR-DCI): 346.14956 ($C_{15}H_{24}NO_8$: calcd. 346.15021 [M + NH_4^+]).

Methyl (1*S,1′*R**,1′′*R**/*S**,2*S**,3*S**)-2-[(*tert*-Butoxycarbonyl)-(formyl)amino]-3-[hydroxy(2′′-oxocyclohexyl)methyl]cyclopropane-carboxylate (14):** Treatment of aldehyde **2** (134 mg, 0.49 mmol), BF_3·Et_2O (65 μL, 0.49 mmol) and (cyclohex-1-enyloxy)trimethylsilane (84 mg, 0.49 mmol) according to GP2 yielded **14** as a colorless oil (183 mg, quant.) after concentration in vacuo. − ^{1}H NMR (400 MHz, [D_6]DMSO): δ = 1.39−1.48 (m, 2 H), 1.51 [s, 9 H, $C(CH_3)_3$], 1.53 [s, 9 H, $C(CH_3)_3$]}, 1.56−2.06 (m, 14 H), 2.20−2.31 (m, 2 H), 2.33−2.45 (m, 2 H), 2.49−2.60 (m, 2 H), 2.84−2.89 (m, 2 H), 3.36 (s, 2 H), 3.67 (s, 3 H, OCH_3), 3.68 (s, 3 H, OCH_3), 4.01 (m, 1 H, OH), 4.18 (m, 1 H, OH), 4.59 (m, 2 H), 9.00 (s, 1 H, NCHO), 9.01 (s, 1 H, NCHO). − ^{13}C NMR (100.6 MHz, [D_6]DMSO): δ = 21.8, 22.7 (+), 23.9, 24.0 (−), 26.1, 26.4 (−), 26.8 (−), 27.5 (+), 27.7 (−), 29.3 31.1 (+), 33.9, 35.0 (+), 51.8, 51.9 (+, OCH_3), 55.4, 56.5 (+), 62.5, 63.6 (+), 83.2, 83.5 [C_{quat}, $C(CH_3)_3$], 152.4, 152.2 [C_{quat}, $NCO_2C(CH_3)_3$], 163.5, 163.7 (+, NCHO), 172.4, 172.5 (C_{quat}, CO), 210.6 (C_{quat}, C-2′′), 211.2 (C_{quat}, C-2′′). − MS (HR-FAB): 370.18590 ($C_{18}H_{28}NO_7$: calcd. 370.18658 [M + H^+]).

General Procedure for the Saponification of the *N*-Formyl Group (GP3): A solution of **11** in methanol (10 mL) was treated with $NaHCO_3$ and H_2O (10 mL). Stirring was continued for 1 h and brine (10 mL) was added. The aqueous layer was extracted with ethyl acetate (3 × 30 mL) and the combined organic layers were washed twice with water and dried ($MgSO_4$). The solvent was evaporated under vacuum and the residue was purified by chromatography (hexanes/ethyl acetate, 2:1).

Methyl (1*S,1′*S**,2*S**,3*S**)-2-(*tert*-Butoxycarbonylamino)-3-(1′-hydroxy-3′-phenyl-3′-oxopropyl)cyclopropanecarboxylate (15a):** Treatment of **11a** (100 mg, 0.26 mmol) with $NaHCO_3$ (100 mg, 1.19 mmol) according to GP3 yielded **15a** as a colorless oil (57 mg, 53%) after chromatography (hexanes/ethyl acetate, 2:1). The crude product could be recrystallized from hexanes/CH_2Cl_2. − R_f = 0.18. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.38 [s, 9 H, $C(CH_3)_3$], 1.71−1.80 (m, 1 H, 3-H), 1.96 (dd, J = 5.5, 3.6 Hz, 1 H, 1-H), 3.26−3.43 (m, 3 H, 2′-H + OH), 3.66 (s, 3 H, OCH_3), 3.68−3.71 (m, 1 H, 2-H), 4.25−4.31 (m, 1 H, 1′-H), 5.67 (br. s, 1 H, NH), 7.41−7.60 (m, 3 H, phenyl-H), 7.92−7.95 (m, 2 H, phenyl−H). − ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 23.6 (+, C-3), 28.1 [+, $C(CH_3)_3$], 30.9 (+, C-1), 36.4 (+, C-2), 45.2 (−, C-2′), 51.9 (+, OCH_3), 64.9 (+, C-1′), 79.9 [C_{quat}, $OC(CH_3)_3$], 128.1 (+, phenyl−C), 128.6 (+, phenyl−C), 133.7 (+, phenyl−C), 136.2 (C_{quat}, phenyl−C), 156.1 [C_{quat}, $NCO_2C(CH_3)_3$], 172.4 (C_{quat}, CO), 200.5 (C_{quat}, C-3′). − IR (KBr): $\tilde{\nu}$ = 3436 cm^{-1}, 3341, 3002, 2981, 1723 (C=O), 1679, 1598, 1581, 1521, 1450, 1392, 1369, 1351, 1266, 1217, 1166, 1116, 1071, 1002, 974, 919, 881, 845, 785, 752, 730, 692, 665, 593, 534. − MS (DCI, NH_3): m/z (%) = 381 (100) [M + NH_4^+].

Methyl (1*S,1′*S**,2*S**,3*S**)-2-(*tert*-Butoxycarbonylamino)-3-(1′-hydroxybut-3′-enyl)cyclopropanecarboxylate (15b):** Treatment of **11b** (254 mg, 0.81 mmol) with $NaHCO_3$ (135 mg, 1.6 mmol) according to GP3 yielded **15b** as a colorless oil (188 mg, 81%) after chromatography (hexanes/ethyl acetate, 2:1). − R_f = 0.21. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.43 [s, 9 H, $C(CH_3)_3$], 1.68−1.74 (m, 1 H, 3-H), 1.88 (dd, J = 5.7, 3.6 Hz, 1 H, 1-H), 2.05 (br. s, 1 H, OH), 2.27−2.49 (m, 2 H, 2′-H), 3.37 (br. s, 1 H, 2-H), 3.67 (s, 3 H, OCH_3), 3.75−3.81 (m, 1 H, 1′-H), 5.14−5.17 (m, 1 H, olefin-H), 5.21 (s, 1 H, olefin−H), 5.27 (br. s, 1 H, NH), 5.74−5.91 (m, 1 H, olefin−H). − ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 23.3 (+, C-3), 28.2 [+, $C(CH_3)_3$], 30.7 (+, C-1), 36.4 (+, C-2), 42.2 (−, C-2′), 51.9 (+, OCH_3), 67.2 (+, C-1), 80.0 (C_{quat}, $OC(CH_3)_3$), 119.4 (−, C-4′), 133.4 (+, C-3′), 156.0 [C_{quat}, $NCO_2C(CH_3)_3$], 172.5 (C_{quat}, CO). − IR (film): $\tilde{\nu}$ = 3463 cm^{-1}, 3318, 2979, 1734 (C=O), 1706 (C=O), 1675 (C=O), 1641, 1523, 1454, 1392, 1368, 1139, 1285, 1257, 1237, 1174, 1067, 989, 909, 841, 758, 733, 609. − MS (DCI,

NH_3): *m/z* (%) = 303 (34) [M + NH_4^+], 163 (100). − $C_{14}H_{23}NO_5$ (285.3): calcd. C 58.93 H 8.12; found C 59.17 H 8.19.

Methyl (1*S,1′*S**,2*S**,3*S**)-2-(3′-Acetoxymethyl-1′-hydroxybut-3′-enyl)-3-(*tert*-butoxycarbonylamino)cyclopropanecarboxylate (15c):** Treatment of 11c (155 mg, 0.40 mmol) with $NaHCO_3$ (84 mg, 1.0 mmol) according to GP3 yielded 15c as a colorless oil (105 mg, 73%) after chromatography (hexanes/ethyl acetate, 2:1). R_f = 0.19. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.40 [s, 9 H, $C(CH_3)_3$], 1.63−1.71 (m, 1 H, 2-H), 1.86−1.90 (m, 1 H, 1-H), 2.07 (s, 3 H, CH_3), 2.28 (dd, *J* = 14.0, 8.9 Hz, 2′-H), 2.40−2.47 (m, 1 H, 2′-H), 2.75 (br. s, 1 H, OH), 3.36 (br. s, 1 H, 3-H), 3.64 (s, 3 H, OCH_3), 3.85−3.88 (m, 1 H, 1′-H), 4.49 (d, *J* = 13.5 Hz, 1 H, CH_2), 4.55 (d, *J* = 13.5 Hz, 1 H, CH_2), 5.05 (s, 1 H, olefin-H), 5.14 (s, 1 H, olefin−H), 5.46 (br. s, 1 H, NH). − ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.8 (+), 23.1 (+), 28.2 [+, $C(CH_3)_3$], 31.1 (+), 36.6 (+), 41.9 (−, C-2′), 51.9 (+, OCH_3), 66.6 (−, CH_2), 66.7 (+, C-1′), 79.9 [C_{quat}, $OC(CH_3)_3$], 116.0 (−, C-4′), 139.9 (C_{quat}, C-3′), 156.0 [C_{quat}, $NCO_2C(CH_3)_3$], 170.9 (C_{quat}, CO), 172.5 (C_{quat}, CO). − IR (film): $\tilde{\nu}$ = 3500 cm^{-1}, 3356, 2977, 1732 (C=O), 1719 (C=O), 1682 (C=O), 1649, 1518, 1453, 1392, 1369, 1343, 1278, 1254, 1226, 1166, 1070, 985, 896, 849, 784, 735, 607. − MS (DCI, NH_3): *m/z* (%) = 375.4 (4) [M + NH_4^+], 296.2 (20), 279.2 (49), 233.2 (100), 216.2 (20), 177.1 (57), 160.1 (96), 116.1 (19). − MS (HR-DCI): 375.21189 ($C_{17}H_{31}N_2O_7$: calcd. 375.21313 [M + NH_4^+]).

Methyl (1*S,1′*R**,2*S**,3*S**)-2-(*tert*-Butoxycarbonylamino)-3-(1′-hydroxy-2′-methyl-2′-nitropropyl)cyclopropanecarboxylate (15d):** Treatment of **11f** (720 mg, 2.0 mmol) with $NaHCO_3$ (168 mg, 2.0 mmol) according to GP3 yielded **15d** as a colorless oil (472 mg, 71%) after chromatography (hexanes/ethyl acetate, 3:1). − R_f = 0.13. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.44 [s, 9 H, $C(CH_3)_3$], 1.55−1.74 (m, 7 H), 2.00−2.04 (m, 1-H), 3.10−3.55 (m, 2 H, 2-H, OH), 3.69 (s, 3 H, OCH_3), 4.31 (br. s, 1 H, 1′-H), 5.30 (br. s, 1 H, NH). − ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.2 (+), 23.1 (+), 26.6 (+), 27.8 (+), 28.2 [+, $C(CH_3)_3$], 36.2 (+), 52.2 (+, CO_2CH_3), 70.8 (+, C-1′), 80.6 [C_{quat}, $OC(CH_3)_3$], 92.0 (C_{quat}), 156.2 [C_{quat}, $NCO_2C(CH_3)_3$], 172.2 (C_{quat}, CO). − IR (film): $\tilde{\nu}$ = 3428 cm^{-1}, 3350, 2980, 1716, 1676, 1548, 1401, 1278, 1201, 1105, 905, 732. − MS (DCI, NH_3): *m/z* (%) = 350 (100) [M + NH_4^+]. − $C_{14}H_{24}N_2O_7$ (332.4): calcd. C 50.60 H 7.28; found C 50.73 H 7.17.

General Procedure for the Cyclization of 15 with 2-Methoxypropene (GP4): A solution of **15** and *p*-toluenesulfonic acid (5 mg) in DMF (5 mL) was treated with 2-methoxypropene and stirred for 1 h at room temp. Diethyl ether (50 mL) was added, the organic layer was washed with H_2O (20 mL), saturated $NaHCO_3$ (20 mL) and brine (20 mL), dried ($MgSO_4$) and the solvent was evaporated. The residue was purified by chromatography (hexanes/ethyl acetate, 10:1).

Methyl (1*S,5*S**,6*S**,7*S**)-2-(*tert*-Butoxycarbonyl)-3,3-dimethyl-5-(2′-oxo-2′-phenylethyl)-4-oxa-2-azabicyclo[4.1.0]heptane-7-carboxylate (16a):** Treatment of **15a** (72 mg, 0.20 mmol) and 2-methoxypropene (125 μL) according to GP4 yielded **16a** as a colorless solid (75 mg, 94%) after chromatography (hexanes/ethyl acetate, 10:1) and recrystallization from CH_2Cl_2/hexanes. − R_f = 0.09. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.44 [s, 9 H, $C(CH_3)_3$], 1.55 (s, 3 H, CH_3), 1.59 (s, 3 H, CH_3), 1.82 (dd, *J* = 5.4, 2.9 Hz, 1 H, cyclopropyl−H), 2.13 (ddd, *J* = 8.4, 5.4, 2.9 Hz, 1 H, cyclopropyl−H), 3.09 (dd, *J* = 16.9, 6.4 Hz, 1 H, 1′-H), 3.33 (dd, *J* = 16.9, 6.1 Hz, 1 H, 1′-H), 3.63 (s, 4 H, OCH_3 + cyclopropyl−H), 4.79 (ddd, *J* = 6.4, 6.1, 2.9 Hz, 1 H, 5-H), 7.42−7.60 (m, 3 H, phenyl−H), 7.93−7.96 (m, 2 H, phenyl−H). − ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 22.5 (+), 22.9 (+), 24.7 (+), 28.2 [+, $C(CH_3)_3$], 29.0 (+), 38.9 (+), 43.6 (−), 51.6 (+, OCH_3), 61.5 (+), 80.3 [C_{quat}, $OC(CH_3)_3$], 86.3 (C_{quat}), 128.0 (+, phenyl−C), 128.5 (+, phenyl−C), 133.2 (+, phenyl−C), 136.7 (C_{quat}, phenyl−C), 153.6 [C_{quat}, $NCO_2C(CH_3)_3$], 172.2 (C_{quat}, CO), 197.2 (C_{quat}). − IR (KBr): $\tilde{\nu}$ = 3026 cm^{-1}, 2981, 2970, 1708 (C=O), 1679 (C=O), 1597, 1581, 1444, 1383, 1365, 1349, 1323, 1314, 1286, 1241, 1212, 1197, 1176, 1089, 1032, 981, 924, 888, 860, 840, 788, 760, 716, 690, 657, 593, 570. − MS (70 eV, EI): *m/z* (%) = 403 (1) [M^+], 189 (17), 155 (18), 105 (87), 57 (100). − $C_{22}H_{29}NO_6$ (403.5): calcd. C 65.49 H 7.24; found C 65.99 H 7.09.

Methyl (1*S,5*S**,6*S**,7*S**)-5-Allyl-2-(*tert*-butoxycarbonyl)-3,3-dimethyl-4-oxa-2-azabicyclo[4.1.0]heptane-7-carboxylate (16b):** Treatment of **15b** (143 mg, 0.50 mmol) and 2-methoxypropene (200 μL) according to GP4 yielded **16b** as a colorless oil (149 mg, 91%) after chromatography (hexanes/ethyl acetate, 10:1). − R_f = 0.28. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.40 [s, 9 H, $C(CH_3)_3$], 1.46 (s, 3 H, CH_3), 1.59 (s, 3 H, CH_3), 1.73 (dd, *J* = 5.4, 3.0 Hz, 1 H, 7-H), 1.86 (ddd, *J* = 8.5, 5.4, 2.9 Hz, 1 H, 6-H), 2.12−2.35 (m, 2 H, 1′-H), 3.51−3.55 (m, 1 H, 1-H), 3.64 (s, 3 H, OCH_3), 4.07 (dt, *J* = 6.7, 2.9 Hz, 1 H, 5-H), 5.00−5.10 (m, 2 H, olefin-H), 5.67−5.84 (m, 1 H, olefin−H). − ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 22.2 (+), 22.9 (+), 24.6 (+), 28.2 [+, $C(CH_3)_3$], 29.0 (+, C-7), 38.8 (+, C-1), 39.2 (−, C-1′), 51.6 (+, OCH_3), 64.2 (+, C-5), 80.2 [C_{quat}, $OC(CH_3)_3$], 86.0 (C_{quat}, C-3), 117.6 (−, C-3′), 133.2 (+, C-2′), 153.6 [C_{quat}, $NCO_2C(CH_3)_3$], 172.5 (C_{quat}, CO). − IR (film): $\tilde{\nu}$ = 2979 cm^{-1}, 1711 (C=O), 1444, 1350, 1305, 1170, 1083, 1013, 925, 850, 770, 719. − MS (DCI, NH_3): *m/z* (%) = 343 (100) [M + NH_4^+].

Methyl (1*S,5*S**,6*S**,7*S**)-5-[2′-(Acetoxymethyl)allyl]-2-(*tert*-butoxycarbonyl)-3,3-dimethyl-4-oxa-2-azabicyclo[4.1.0]heptane-7-carboxylate (16c):** Treatment of **15c** (107 mg, 0.30 mmol) and 2-methoxypropene (75 μL) according to GP4 yielded **16c** as a colorless oil (109 mg, 92%) after chromatography (hexanes/ethyl acetate, 5:1). − R_f = 0.23. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.41 [s, 9 H, $C(CH_3)_3$], 1.47 (s, 3 H, CH_3), 1.59 (s, 3 H, CH_3), 1.75 (dd, *J* = 5.4, 3.0 Hz, 1 H, 7-H), 1.86 (ddd, *J* = 8.7, 5.4, 2.9 Hz, 1 H, 6-H), 2.06 [s, 3 H, $C(O)CH_3$], 2.27 (d, *J* = 6.6 Hz, 2 H, 1′-H), 3.53−3.57 (m, 1 H, 1-H), 3.64 (s, 3 H, OCH_3), 4.21 (dt, *J* = 6.6, 2.9 Hz, 1 H, 5-H), 4.43−4.55 (m, 2 H, CH_2), 4.99 (s, 1 H, olefin−H), 5.07 (s, 1 H, olefin−H). − ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.8 (+), 22.3 (+), 22.9 (+), 24.7 (+), 28.2 [+, $C(CH_3)_3$], 29.0 (+), 38.6 (−, C-1′), 38.7 (+, C-1), 51.7 (+, OCH_3), 63.6 (+, C-5), 66.6 (−), 80.3 [C_{quat}, $OC(CH_3)_3$], 86.1 (C_{quat}, C-3), 115.1 (−, C-3′), 139.8 (C_{quat}, C-2′), 153.6 [C_{quat}, $NCO_2C(CH_3)_3$], 170.5 (C_{quat}, CO), 172.4 (C_{quat}, CO). − IR (film): $\tilde{\nu}$ = 2981 cm^{-1}, 1710 (C=O), 1445, 1350, 1303, 1230, 1174, 1084, 1030, 919, 802, 770, 734, 648. − MS (DCI, NH_3): *m/z* (%) = 415 (98) [M + NH_4^+], 357 (100).

Methyl (1*S,5*R**,6*S**,7*S**)-2-(*tert*-Butoxycarbonyl)-3,3-dimethyl-5-(1′-methyl-1′-nitroethyl)-4-oxa-2-azabicyclo[4.1.0]heptane-7-carboxylate (16d):** Treatment of **15d** (166 mg, 0.50 mmol) and 2-methoxypropene (120 μL) according to GP4 yielded **16d** as a yellow oil (113 mg, 61%) after chromatography (hexanes/ethyl acetate, 10:1). − R_f = 0.08. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.40 [s, 9 H, $C(CH_3)_3$], 1.45 (s, 3 H, CH_3), 1.52 (s, 3 H, CH_3), 1.55 (s, 6 H, CH_3), 1.81 (ddd, *J* = 7.7, 5.3, 2.3 Hz, 1 H, 6-H), 1.92 (dd, *J* = 5.4, 2.7 Hz, 1 H, 7-H), 3.65 (s, 4 H, 1-H, OCH_3), 4.69 (d, *J* = 2.1 Hz, 1 H, 5-H). − ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 19.8 (+), 19.9 (+), 22.8 (+), 23.0 (+), 23.7 (+), 28.2 [+, $C(CH_3)_3$], 36.3 (+, C-1), 51.9 (+, OCH_3), 68.5 (+, C-5), 80.8 [C_{quat}, $OC(CH_3)_3$], 87.8 (C_{quat}, C-3), 90.5 (C_{quat}), 153.4 [C_{quat}, $NCO_2C(CH_3)_3$], 171.5 (C_{quat}, CO). − IR (film): $\tilde{\nu}$ = 2982 cm^{-1}, 1707, 1546, 1445, 1367, 1344, 1302, 1167, 1083, 1041, 984, 924, 852, 769, 703.

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