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Synthesis of Highly Functionalized Enantiopure Halocyclopropanes Derived from Carbohydrates

Humberto Rodríguez-Solla,*[a] Carmen Concellón,[a] Vicente del Amo,[a] Ainhoa Díaz-Pardo,[a] Elena G. Blanco,[a] Santiago García-Granda,[a] M. Rosario Díaz,[a] Ricardo Llavona,[a] and Raquel G. Soengas[b]

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A chromium-mediated synthesis of enantiopure sugar-based halocyclopropanecarboxamides is reported. This reaction can be stereospecifically carried out on (*E*)- or (*Z*)-α,β-unsaturated amides and takes place with the formation of a new C-Hal stereogenic center, which is generated with total stereoselectivity. Synthetic applications of the obtained halocyclopropanecarboxamides are also reported. The structure of the halocyclopropanes and derivatives were established by X-ray analysis. A mechanism to explain these transformations is proposed.

Introduction

A great deal of attention has been focused on the preparation of cyclopropanes because of their fascinating structure. The highly strained nature of the cyclopropane rings makes them very reactive and useful synthetic building blocks in organic chemistry.[1] Additionally, cyclopropane moieties are present in a wide range of natural products. While non-activated cyclopropanes have limited use in chemical synthesis, activated derivatives, such as cyclopropanes substituted with electron-withdrawing or electron-donating groups, have been used extensively as precursors in several chemical syntheses.[2] In particular, it is known that the presence of a carbonyl or imine group further activates cyclopropanes towards ring-enlargement and cycloaddition reactions.[3] Cyclopropanes have been extensively used to introduce a conformational restriction in drugs to enhance their activity and avoid undesired effects. In this regard, chiral cyclopropanes substituted at all three ring carbon atoms are of great interest.[4] Moreover, much effort has been devoted to substitution of the cyclopropane moiety by means of either the formation of organometallic cyclopropanes or palladium cross-coupling reactions. For this purpose, halocyclopropanes have proven to be useful starting materials.[5]

An important advance in cyclopropane chemistry has been the integration of cyclopropanes and carbohydrates.[6] The incorporation of cyclopropanes into a carbohydrate scaffold provides a combination of strained and reactive cyclopropanes with the well-defined stereochemistry inherent of carbohydrates. However, although there are several reports on the synthesis of cyclopropane units on the furanosyl and pyranosyl rings of carbohydrates,[7] construction of cyclopropanes on acyclic sugars[8] or in acyclic chains of pyranoses and furanoses,[9] has been much less studied.

Chromium dichloride ($CrCl_2$) has become an important reagent in synthetic organic chemistry because of its versatility in electron transfer reactions, and this reagent has been applied to a multitude of organic transformations, which generally proceeded with high selectivity.[10] In particular, previous contributions by us (the stereospecific cyclopropanation of α,β-unsaturated amides,[11] the highly stereoselective *tert*-butyl- and silyl-cyclopropanation,[12] and the chloro- and bromocyclopropanation of α,β-unsaturated amides with total or high stereoselectivity[13]) and other[14] laboratories, have demonstrated the utility of $CrCl_2$ for the cyclopropanation of unsaturated compounds.

In this communication we report a stereoselective preparation of sugar-based chloro and bromocyclopropanes in moderate to good yields by means of the reaction of α,β-unsaturated amides derived from sugar aldehydes and chromium carbenoids.

Results and Discussion

The (*E*)- and (*Z*)-α,β-unsaturated amides used as starting materials were easily prepared from sugar aldehydes **1**, and *N*,*N*-diethyl-(dimethylphosphono)acetamide (**2**) through the Horner–Wadsworth–Emmons protocol.[15] By using the method described in the Experimental Section, it was possible to isolate α,β-unsaturated amides **3** and **4** as a stereo-

[a] Departamento de Química Orgánica e Inorgánica and Química Física y Analítica, Facultad de Química, Universidad de Oviedo,
Julián Clavería 7, 33006 Oviedo, Spain
E-mail: hrsolla@uniovi.es
[b] Departamento de Química & QOPNA, Universidade de Aveiro, 3810-193 Aveiro, Portugal

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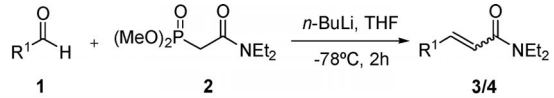
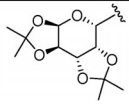
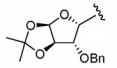
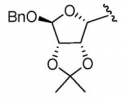
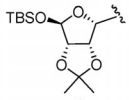
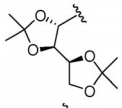
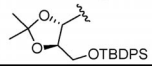
isomeric mixture, which was easily separated by simple column chromatography (Table 1).

Table 1. Synthesis of (*E*/*Z*)-α,β-unsaturated amides **3**/**4**.



1 2 3/4

Entry	1	(*E*)-3/(*Z*)-4	R1	*E*/*Z*[a]	Yield (%)[b]
1	1a	3a/4a		2:1	89 (61/28)
2	1b	3b/4b		1.6:1	66 (26/40)
3	1c	3c/4c		1.6:1	71 (28/43)
4	1d	3d/4d		1:1	68 (31/37)
5	1e	3e/4e		1.8:1	63 (15/48)
6	1f	3f/4f		2:1	72 (26/46)

[a] *E*/*Z* ratio determined by ^{1}H NMR spectroscopic analysis of crude reaction mixtures. [b] Isolated yield of analytically pure *E*/*Z* mixtures and, in parentheses, percentage yield of the isolated *E*- and *Z*-stereoisomer (**3** and **4**, respectively), after column purification.

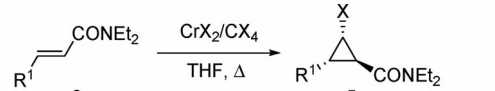
On the basis of the results of the halocyclopropanation of (*E*)-α,β-unsaturated amides previously reported by our group,[13] we initially tested the same reaction conditions to perform the chlorocyclopropanation of the (*E*)-α,β-unsaturated amide derived from galactose **3a**. Thus, when a mixture of $CrCl_2$ (3 equiv.) and CCl_4 (1 equiv.) in tetrahydrofuran (THF) was heated to reflux for 16 h in the presence of (*E*)-α,β-unsaturated amide **3a**, chlorocyclopropanamide **5a** was obtained, after hydrolysis, in high yield and with total stereoselectivity (Table 2, entry 1). These reaction conditions were used to generalize the process, with the reaction being performed on various (*E*)-α,β-unsaturated amides **3** (Table 2).

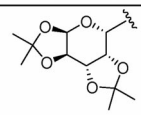
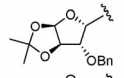
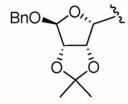
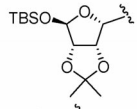
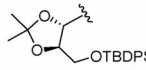
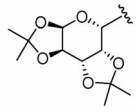
In the case of the synthesis of bromocyclopropane **5f**, a similar process was carried out. In this case, a mixture of $CrBr_2$[13]/CBr_4 was employed instead $CrCl_2$/CCl_4. Carbenoid sources, CCl_4 and CBr_4, are both commercially available.

When this reaction was performed on (*Z*)-α,β-unsaturated amides **4**, no significant differences were observed when compared with the same process carried out on (*E*)-α,β-unsaturated amides **3**. Table 3 summarizes the results obtained on the chloro- and bromocyclopropanation of sugar-based (*Z*)-α,β-unsaturated amides **4**.

Analysis of the results compiled in Tables 2 and 3 indicates that: (a) all halocyclopropanation reactions took place

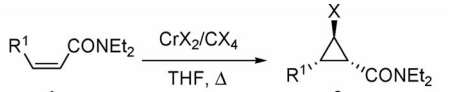
Table 2. Synthesis of halocyclopropanecarboxamides **5** derived from (*E*)-α,β-unsaturated amides **3**.

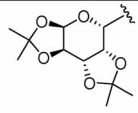
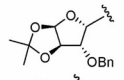
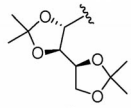
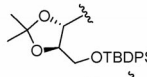
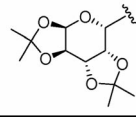


Entry	3	5[a]	R1	X	Yield (%)[b]
1	3a	5a		Cl	86
2	3b	5b		Cl	53
3	3c	5c		Cl	69
4	3d	5d		Cl	81
5	3f	5e		Cl	73
6	3a	5f		Br	63

[a] Only one stereoisomer was observed by ^{1}H NMR spectroscopic analysis of the crude reaction mixture. [b] Isolated yield of analytically pure **5** based on **3**.

Table 3. Synthesis of halocyclopropanecarboxamides **6** derived from (*Z*)-α,β-unsaturated amides **4**.



Entry	4	6[a]	R1	X	Yield (%)[b]
1	4a	6a		Cl	55
2	4b	6b		Cl	64
3	4e	6c		Cl	73
4	4f	6d		Cl	76
5	4a	6e		Br	60

[a] Only one stereoisomer was observed by ^{1}H NMR spectroscopic analysis of the crude reaction mixture. [b] Isolated yield of analytically pure **6** based on **4**.

in moderate to good yields, with total stereoselectivity and in the absence of epimerization of any chiral center; (b) this process tolerated a broad range of sugar-derived (*E*)- or (*Z*)-α,β-unsaturated amides bearing different protection on the hydroxyl groups; (c) the determination of the structure for compounds **5** and **6** has proven that the halocyclopropanation reaction took place with complete stereospecificity because the geometry of the C–C double bond of both (*E*)- and (*Z*)-α,β-unsaturated amides was conserved during the cyclopropanation process (see Tables 2 and 3), and (d) no significant differences were observed in terms of yield or stereoselectivities when the reaction was carried out using $CrCl_2/CCl_4$ or $CrBr_2/CBr_4$.

The total stereoselectivity of this process was established by ^1H NMR spectroscopic experiments with the crude reaction mixtures. Analysis of the spectra showed that all halocyclopropanes were isolated as single stereoisomers. The structures of halocyclopropanes **5** and **6** were assigned based on ^1H, ^{13}C, COSY, and HSQC NMR experiments. Because the stereochemistry of the sugar backbone is fixed in the starting material, and no epimerization of any chiral center took place, the absolute configuration of **5** and **6** was established by means of NOESY and NOE difference experiments. Furthermore, the assigned absolute configuration of **5c**, **6a**, and **6e** was unambiguously confirmed by single-crystal X-ray diffraction analysis (Figure 1).[16] The structure and the absolute configuration of other halocyclopropanes were assigned by analogy.

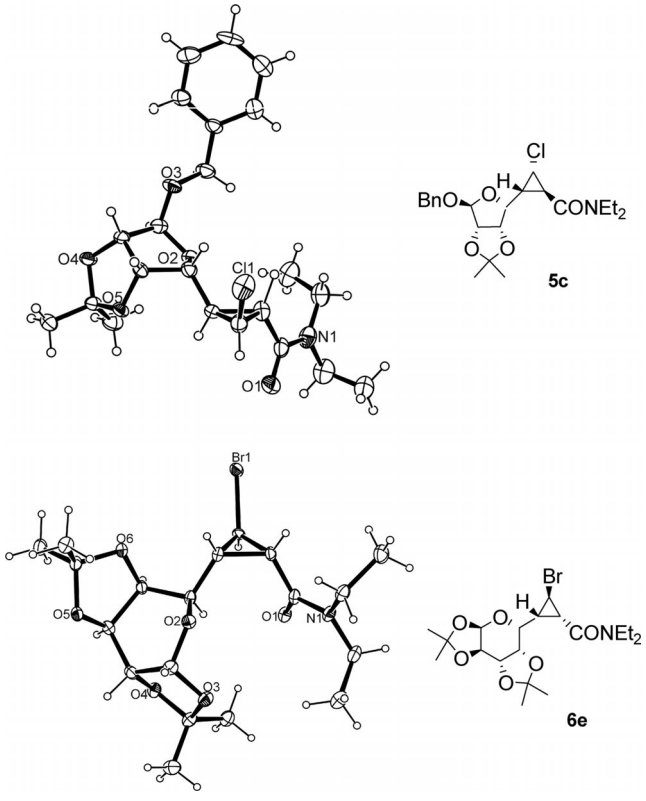


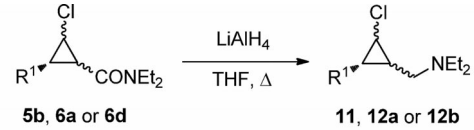
Figure 1. Ortep diagram for **5c** and **6e**.

Mechanism

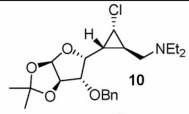
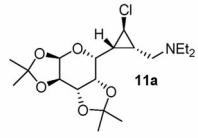
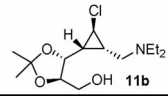
This halocyclopropanation process could be explained by assuming the formation of a chromium(III) geminal dicarbenoid intermediate **8**, after the reaction of CrX_2 (4.0 equiv.) with CX_4 (X = Cl, or Br; 1.0 equiv.). This chromium(III) geminal dicarbenoid has been previously proposed by Takai et al. for the halocyclopropanation of acrylic esters using the $CrCl_2/CCl_4$ system.[17] In this sense, dicarbenoid **8** could react with α,β-unsaturated amides **3b** or **4b** through a similar mechanism to that proposed by Houk for the addition of carbenoids to olefins.[18] Tentatively, we propose the transition states **A** and **B** depicted in Scheme 1, in which the formation of the new stereogenic centers, with total stereoselectivity, could be explained on the basis of steric hindrance between the halogen atom X and the carboxamide group. The attack of carbenoid **8** to olefins **3b** and **4b** would take place from the less hindered *si* face. In the transition state, the halogen atom would occupy a *trans* relative position with respect to the carboxamide group as depicted in Scheme 1. Moreover, internal coordination of the chromium(III) center with the amide oxygen would play a crucial role because it would afford an additional stabilization of intermediates **9** and **10**.[17,19] Hydrolysis of these intermediates during workup would finally yield halocyclopropanes **5b** or **6b**, respectively. It is noteworthy that when this process was carried out on sugar-based (*E*)- or (*Z*)-α,β-unsaturated esters, no reaction took place. In this sense, the presence of the amide group was necessary to obtain sugar-based halocyclopropanes **5** and **6**.

To demonstrate synthetic applications of the obtained chlorocyclopropanecarboxamides **5** and **6**, selected examples were readily transformed into enantiopure chlorocy-

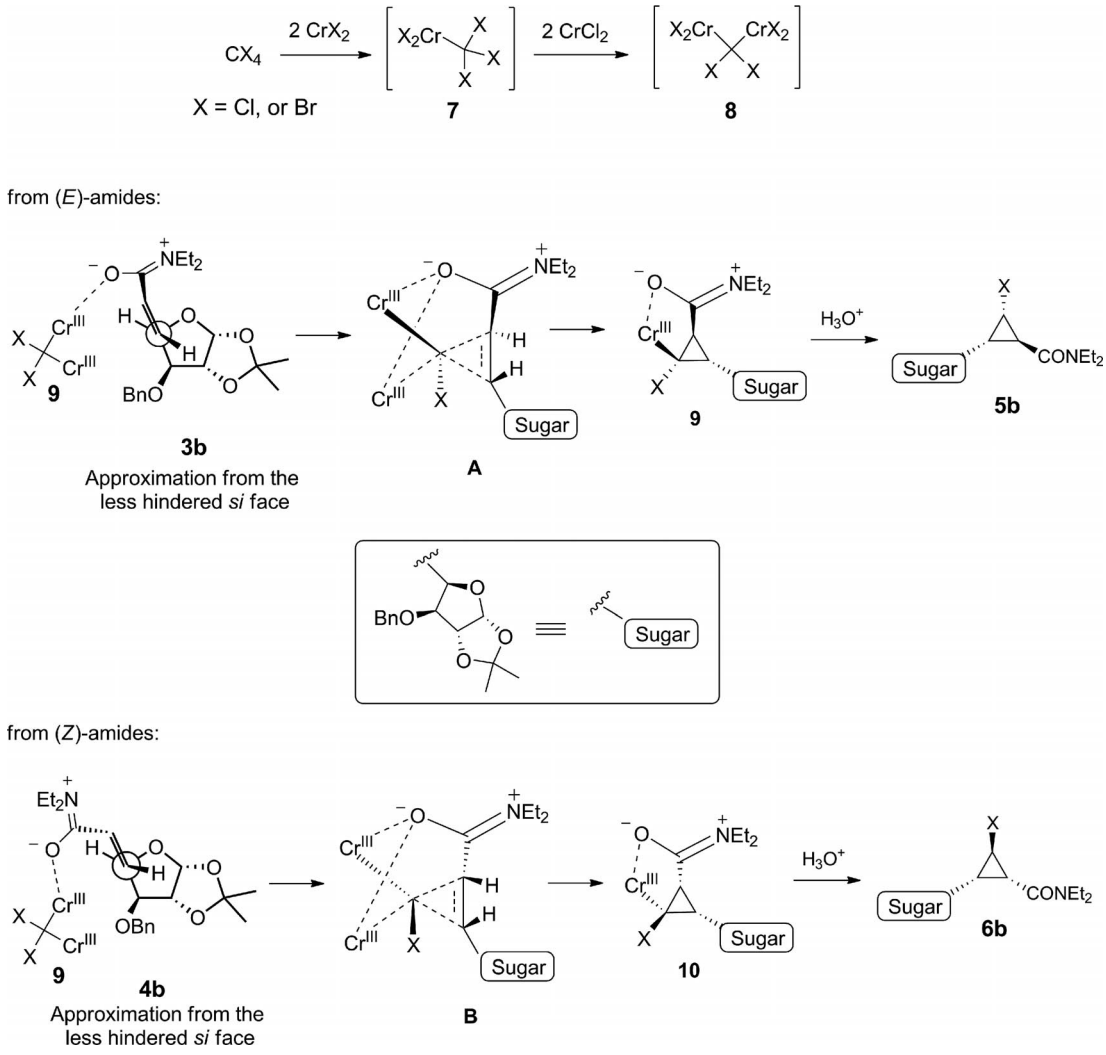
Table 4. Synthesis of enantiopure chlorocyclopropylamines **11** and **12**.



5b, **6a** or **6d** → **11**, **12a** or **12b**

Entry	5/6	11/12[a]	Yield (%)[b]
1	**5b**	 **10**	74
2	**6a**	 **11a**	71
3	**6d**	 **11b**	52

[a] Only one stereoisomer was observed by ^1H NMR spectroscopic analysis of the crude reaction mixture. [b] Isolated yield of analytically pure compound based on **5** or **6**.



Scheme 1. Mechanistic proposal.

clopropylamines (Table 4). Thus, **5b**, **6a**, or **6d** in THF was treated with lithium aluminum hydride at reflux for 12 h, affording the corresponding chlorocyclopropylamines **11**, **12a**, or **12b**, in good yields, without loss of stereoisomeric purity (^{1}H NMR spectroscopic analsysis of the crude reaction products), following a previously described procedure.[12b] No significant differences in terms of yield or stereoisomeric purity were observed when this transformation was performed using different chlorocyclopropanecarboxamides. In the case of the reaction of **6d** with $LiAlH_4$, *O*-deprotection took place under the reaction conditions and the *O*-desilylated chlorocyclopropylamine **12b** was obtained.

Conclusions

We have described a general method for the synthesis of highly functionalized sugar-based halocyclopropanecarboxamides in a stereospecific manner and in good yields. This process is carried out through a stereospecific chromium(III)-promoted halocyclopropanation of (*E*)- or (*Z*)-α,β-unsaturated amides derived from carbohydrates. Studies aimed towards fully delineating the factors involved in this transformation and other synthetic applications of the products obtained are under investigation in our laboratory.

Experimental Section

General: Reactions requiring an inert atmosphere were conducted under dry nitrogen, and the glassware was oven dried (120 °C). THF was distilled from sodium/benzophenone immediately prior to use. All reagents were purchased in the highest quality available and were used without further purification. Flash column chromatography was carried out on silica gel 230–400 mesh; compounds were visualized on analytical thin-layer chromatograms (TLC) by UV light (254 nm). ^{1}H NMR spectra were recorded at 300 MHz; ^{13}C NMR spectra and DEPT experiments were determined at 75 MHz. Chemical shifts are given in ppm relative to tetramethylsilane (TMS), which was used as an internal standard, and coupling constants (*J*) are reported in Hz. The diastereoisomeric ratios were obtained by ^{1}H NMR analyses (300 MHz) of crude products. GC–MS and HRMS were measured by using EI (70 eV) or FAB conditions. When HRMS could not be measured

on the molecular ion, the HRMS of a significant fragment is given. Only the most important IR bands (cm^{-1}) and the molecular ions and/or base peaks in MS are given.

Synthesis of 3/4. General Procedure: To a solution of *N,N*-diethylbromoacetamide (1.1 equiv.) in ethyl acetate was added trimethylphosphite (1.1 mmol, 1.1 equiv.) at room temperature and the solution was heated to reflux for 72 h to give *N,N*-diethyl-(dimethylphophono)acetamide (**2**). The solution of *N,N*-diethyl-(dimethylphosphono)acetamide (1.1 mmol, 1.1 equiv.) in anhydrous THF (3 mL) was treated under a nitrogen atmosphere with *n*-butyllithium (1.6 M in hexanes, 1.05 mmol, 1.05 equiv.) at –78 °C. After stirring for 10 min, the corresponding aldehyde (1.0 mmol, 1.0 equiv.) in THF (2 mL) was added and the mixture was stirred for 2 h at –78 °C. The reaction was quenched by the addition of saturated NH_4Cl solution, and extracted with ethyl acetate (3 × 5 mL). Usual work-up and separation by column chromatography on silica gel (hexane/EtOAc, 5:1) afforded pure compounds **3** and **4**. Compounds **3a**, **3b**, and **3d** have previously been fully characterized.[20]

(*E*)-*N,N*-Diethyl-1-*O*-benzyl-5,6-dideoxy-2,3-*O*-isopropylidene-α-D-*lyxo*-hept-5-enofuranosiduronamide (3c): Starting from **1c** (1.0 mmol, 278.3 mg), yield 105.1 mg (28%); yellow oil; $[\alpha]_D^{20} = -5.0$ (c = 1.00, $CHCl_3$); R_f = 0.38 (hexane/EtOAc, 1:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.38–7.29 (m, 5 H), 6.90 (dd, J = 15.2, 5.2 Hz, 1 H), 6.55 (d, J = 15.0 Hz, 1 H), 5.15 (s, 1 H), 4.72–4.69 (m, 1 H), 4.63 (d, J = 4.5 Hz, 1 H), 4.60–4.57 (m, 2 H), 4.44 (d, J = 11.8 Hz, 1 H), 3.44–3.38 (m, 4 H), 1.42 (s, 3 H), 1.29 (s, 3 H), 1.26–1.18 (m, 6 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.7 (C), 137.8 (CH), 137.6 (C), 128.8 (2×CH), 128.3 (2×CH), 128.2 (CH), 123.2 (CH), 113.2 (CH), 105.6 (C), 85.6 (CH), 81.3 (CH), 79.8 (CH), 69.4 (CH_2), 42.6 (CH_2), 42.4 (CH_2), 26.4 (CH_3), 25.3 (CH_3), 15.2 (CH_3), 13.5 (CH_3) ppm. MS (ESI^+-TOF): m/z (%) = 376 (100) $[M + H]^+$, 398 (78) $[M + Na]^+$, 414 (31) $[M + K]^+$. HRMS: m/z calcd. for $C_{21}H_{30}NO_5$ $[M + H]^+$ 376.2124; found 376.2123. IR (neat): $\tilde{\nu}$ = 3056, 1720, 1657, 1620, 1086 cm^{-1}.

(*E*)-*N,N*-Diethyl-2,3-dideoxy-4,5:6,7-di-*O*-isopropylidene-L-*xylo*-hept-2-enamide (3e): Starting from **1e** (1.0 mmol, 230.1 mg), yield 49.1 mg (15%); yellow oil; $[\alpha]_D^{20} = +3.8$ (c = 1.00, $CHCl_3$); R_f = 0.38 (hexane/EtOAc, 1:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 6.92 (dd, J = 15.0, 5.9 Hz, 1 H), 5.58 (dd, J = 15.0, 1.2 Hz, 1 H), 4.58–4.54 (m, 1 H), 4.18–4.09 (m, 2 H), 3.97–3.86 (m, 1 H), 3.73 (t, J = 7.1 Hz, 1 H), 3.47–3.31 (m, 4 H), 1.43 (s, 3 H), 1.40 (s, 3 H), 1.39 (s, 3 H), 1.33 (s, 3 H), 1.25–1.11 (m, 6 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.5 (C), 142.4 (CH), 121.2 (CH), 110.3 (C), 110.1 (C), 81.4 (CH), 79.7 (CH), 76.9 (CH), 67.7 (CH_2), 42.5 (CH_2), 41.2 (CH_2), 27.3 (CH_3), 27.0 (2×CH_3), 25.5 (CH_3), 15.2 (CH_3), 13.5 (CH_3) ppm. MS (ESI^+-TOF): m/z (%) = 328 (100) $[M + H]^+$. HRMS: m/z calcd. for $C_{17}H_{30}NO_5$ $[M + H]^+$ 328.2124; found 328.2127. IR (neat): $\tilde{\nu}$ = 2986, 2935, 1628, 1064 cm^{-1}.

(*E*)-*N,N*-Diethyl-6-*O*-*tert*-butyldiphenylsilyl-2,3-dideoxy-4,5-*O*-isopropylidene-D-*threo*-hex-2-enamide (3f): Starting from **1f** (1.0 mmol, 398.2 mg), yield 128.9 mg (26%); yellow oil; $[\alpha]_D^{20} = -6.8$ (c = 1.00, $CHCl_3$); R_f = 0.20 (hexane/EtOAc, 1:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.71–7.65 (m, 4 H), 7.45–7.34 (m, 6 H), 6.89 (dd, J = 15.0, 5.3 Hz, 1 H), 6.51 (d, J = 14.9 Hz, 1 H), 4.68 (app. dd, J = 7.5, 5.4 Hz, 1 H), 3.92–3.76 (m, 3 H), 3.47–3.32 (m, 4 H), 1.47 (s, 3 H), 1.43 (s, 3 H), 1.25–1.12 (m, 6 H), 1.06 (s, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.3 (C), 141.9 (CH), 136.0 (4×CH), 133.5 (C), 133.4 (C), 130.1 (CH), 130.0 (CH), 128.1 (4×CH), 121.8 (CH), 110.1 (C), 81.4 (CH), 77.7 (CH), 63.3 (CH_2), 42.6 (CH_2), 41.2 (CH_2), 27.4 (CH_3), 27.3 (3×CH_3), 27.1 (CH_3), 19.6 (C), 15.3 (CH_3), 13.5 (CH_3) ppm. MS (ESI^+-TOF): m/z (%) = 518 (100) $[M + Na]^+$, 519 (41), 487 (19), 496 (13) $[M + H]^+$, 520 (13). HRMS: m/z calcd. for $C_{29}H_{41}NNaO_4Si$ $[M + Na]^+$ 518.2703; found 518.2710. IR (neat): $\tilde{\nu}$ = 3049, 1650, 1127, 824 cm^{-1}.

(*Z*)-*N,N*-Diethyl-6,7-dideoxy-1,2:3,4-di-*O*-isopropylidene-β-D-*galacto*-oct-6-enopyranosiduronamide (4a): Starting from **1a** (1.0 mmol, 258.3 mg), yield 99.5 mg (28%); white solid; m.p. 79–81 °C (Et_2O/Hex); $[\alpha]_D^{20} = -136.9$ (c = 1.00, $CHCl_3$); R_f = 0.45 (hexane/EtOAc, 3:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 6.15 (d, J = 11.6 Hz, 1 H), 5.97 (dd, J = 11.7, 7.6 Hz, 1 H), 5.47 (d, J = 5.1 Hz, 1 H), 5.08 (d, J = 7.6 Hz, 1 H), 4.57–4.51 (m, 2 H), 4.24 (d, J = 5.3 Hz, 1 H), 3.41–3.18 (m, 4 H), 1.46 (s, 3 H), 1.41 (s, 3 H), 1.27 (s, 6 H), 1.11 (t, J = 7.1 Hz, 3 H), 1.04 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.4 (C), 139.7 (CH), 122.7 (CH), 109.2 (C), 109.0 (C), 96.7 (CH), 73.9 (CH), 71.2 (CH), 70.6 (CH), 66.3 (CH), 42.9 (CH_2), 40.4 (CH_2), 26.3 (2×CH_3), 25.4 (CH_3), 24.5 (CH_3), 14.7 (CH_3), 13.3 (CH_3) ppm. MS (ESI^+-TOF): m/z (%) = 378 (100) $[M + Na]^+$, 356 (31) $[M + H]^+$, 379 (25). HRMS: m/z calcd. for $C_{18}H_{29}NNaO_6$ $[M + Na]^+$ 378.1893; found 378.1892. IR (neat): $\tilde{\nu}$ = 3400, 1654, 1040, 756 cm^{-1}.

(*Z*)-*N,N*-Diethyl-3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hept-5-enofuranosiduronamide (4b): Starting from **1b** (1.0 mmol, 278.3 mg), yield 150.2 mg (40%); yellow oil; $[\alpha]_D^{20} = -9.2$ (c = 1.00, $CHCl_3$); R_f = 0.54 (hexane/EtOAc, 1:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.24–7.16 (m, 5 H), 6.18 (d, J = 11.4 Hz, 1 H), 6.08 (dd, J = 12.0, 7.2 Hz, 1 H), 5.90 (d, J = 3.15 Hz, 1 H), 5.26 (dd, J = 3.66, 3.0 Hz, 1 H), 4.55–4.50 (m, 3 H), 4.27 (d, J = 2.7 Hz, 1 H), 3.44–3.17 (m, 4 H), 1.41 (s, 3 H), 1.23 (s, 3 H), 1.20–1.04 (m, 6 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.9 (C), 138.2 (C), 138.0 (CH), 128.6 (2×CH), 127.9 (CH), 127.8 (2×CH), 124.1 (CH), 111.9 (C), 105.4 (CH), 85.1 (CH), 83.8 (CH), 78.9 (CH), 72.8 (CH_2), 43.0 (CH_2), 40.3 (CH_2), 27.2 (CH_3), 26.7 (CH_3), 14.7 (CH_3), 13.4 (CH_3) ppm. MS (ESI^+-TOF): m/z (%) = 376 (31) $[M + H]^+$, 398 (100) $[M + Na]^+$. HRMS: m/z calcd. for $C_{21}H_{29}NNaO_5$ $[M + Na]^+$ 398.1943; found 398.1945. IR (neat): $\tilde{\nu}$ = 3440, 1745, 1240, 1101 cm^{-1}.

(*Z*)-*N,N*-Diethyl-1-*O*-benzyl-5,6-dideoxy-2,3-*O*-isopropylidene-α-D-*lyxo*-hept-5-enofuranosiduronamide (4c): Starting from **1c** (1.0 mmol, 278.3 mg), yield 161.4 mg (43%); yellow oil; $[\alpha]_D^{20} = -38.4$ (c = 1.00, $CHCl_3$); R_f = 0.62 (hexane/EtOAc, 1:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.25–7.19 (m, 5 H), 6.23 (d, J = 11.7 Hz, 1 H), 6.08 (dd, J = 11.7, 7.0 Hz, 1 H), 5.21–5.18 (m, 1 H), 5.04 (s, 1 H), 5.03–5.01 (m, 1 H), 4.63–4.58 (m, 2 H), 4.39 (d, J = 11.9 Hz, 1 H), 3.36–3.25 (m, 4 H), 1.39 (s, 3 H), 1.22 (s, 3 H), 1.15–1.05 (m, 6 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.4 (C), 138.9 (CH), 137.7 (C), 128.7 (2×CH), 128.2 (2×CH), 128.0 (CH), 123.2 (CH), 112.5 (C), 105.7 (CH), 85.5 (CH), 82.7 (CH), 78.3 (CH), 68.9 (CH_2), 42.9 (CH_2), 40.5 (CH_2), 26.4 (CH_3), 24.9 (CH_3), 14.8 (CH_3), 13.4 (CH_3) ppm. MS (ESI^+-TOF): m/z (%) = 376 (100) $[M + H]^+$, 398 (34) $[M + Na]^+$, 377 (28), 400 (22). HRMS: m/z calcd. for $C_{21}H_{30}NO_5$ $[M + H]^+$ 376.2124; found 376.2119. IR (neat): $\tilde{\nu}$ = 3056, 1720, 1657, 1620, 1086 cm^{-1}.

(*Z*)-*N,N*-Diethyl-*O*-*tert*-buthyldimehyilsilyl-5,6-dideoxy-2,3-*O*-isopropylidene-α-D-*lyxo*-hept-5-enofuranosiduronamide (4d): Starting from **1d** (1.0 mmol, 302.4 mg), yield 147.9 mg (37%); colorless oil; $[\alpha]_D^{20} = -75.4$ (c = 1.00, $CHCl_3$); R_f = 0.78 (hexane/EtOAc, 1:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 6.26 (dd, J = 11.7, 1.3 Hz, 1 H), 6.06 (dd, J = 11.7, 7.3 Hz, 1 H), 5.32 (s, 1 H), 5.20 (dd, J = 7.3, 3.7 Hz, 1 H), 5.06 (dd, J = 5.8, 3.7 Hz, 1 H), 4.52 (d, J = 5.8 Hz, 1 H), 3.47–3.28 (m, 4 H), 1.45 (s, 3 H), 1.28 (s, 3 H), 1.16 (t, J = 7.1 Hz, 3 H), 1.14 (t, J = 7.1 Hz, 3 H), 0.85 (s, 9 H), 0.09 (s, 3 H), 0.06 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.9 (C), 138.7 (CH), 123.5 (CH), 112.4 (C), 102.0 (CH), 87.4 (CH), 82.9 (CH), 78.2 (CH), 43.0 (CH_2), 40.4 (CH_2), 26.4 (CH_3), 26.0

(3 × CH_3), 25.0 (CH_3), 18.2 (C), 14.7 (CH_3), 13.4 (CH_3), –4.2 (CH_3), –5.1 (CH_3) ppm. MS (ESI$^+$-TOF): *m*/*z* (%) = 400 (100) [M + H]$^+$, 473 (75), 422 (34) [M + Na]$^+$. HRMS: *m*/*z* calcd. for $C_{20}H_{38}NO_5Si$ [M + H]$^+$ 400.2519; found 400.2513. IR (neat): $\tilde{\nu}$ = 2976, 1721, 1114 cm^{-1}.

(*Z*)-*N*,*N*-Diethyl-2,3-dideoxy-4,5:6,7-di-*O*-isopropylidene-L-*xylo*-hept-2-enamide (4e): Starting from **1e** (1.0 mmol, 230.1 mg), yield 157.2 mg (48%); yellow oil; $[\alpha]_D^{20}$ = –26.5 (*c* = 1.00, $CHCl_3$); R_f = 0.47 (hexane/EtOAc, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.21 (d, *J* = 12.3 Hz, 1 H), 5.85 (t, *J* = 9.0 Hz, 1 H), 4.89 (t, *J* = 8.6 Hz, 1 H), 4.25 (q, *J* = 6.0 Hz, 1 H), 4.13 (t, *J* = 8.1 Hz, 1 H), 3.95 (t, *J* = 8.1 Hz, 1 H), 3.89–3.84 (m, 1 H), 3.40–3.26 (m, 4 H), 1.39–1.37 (m, 9 H), 1.30 (s, 3 H), 1.11 (q, *J* = 8.4 Hz, 6 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.3 (C), 136.9 (CH), 125.9 (CH), 109.7 (C), 109.1 (C), 80.4 (CH), 75.3 (CH), 75.1 (CH), 65.2 (CH_2), 42.4 (CH_2), 39.6 (CH_2), 27.0 (CH_3), 26.7 (CH_3), 26.3 (CH_3), 25.3 (CH_3), 14.1 (CH_3), 12.9 (CH_3) ppm. MS (ESI$^+$-TOF): *m*/*z* (%) = 328 (100) [M + H]$^+$. HRMS: *m*/*z* calcd. for $C_{17}H_{30}NO_5$ [M + H]$^+$ 328.2124; found 328.2126. IR (neat): $\tilde{\nu}$ = 2998, 1614, 1031, 701 cm^{-1}.

(*Z*)-*N*,*N*-Diethyl-6-*O*-*tert*-butyldiphenylsilyl-2,3-dideoxy-4,5-*O*-isopropylidene-D-*threo*-hex-2-enamide (4f): Starting from **1f** (1.0 mmol, 398.2 mg), yield 228.0 mg (46%); colorless oil; $[\alpha]_D^{20}$ = +8.7 (*c* = 1.00, $CHCl_3$); R_f = 0.33 (hexane/EtOAc, 3:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.76–7.72 (m, 4 H), 7.40–7.33 (m, 6 H), 6.16 (dd, *J* = 11.7, 1.0 Hz, 1 H), 5.85 (dd, *J* = 11.7, 8.4 Hz, 1 H), 5.05 (t, *J* = 7.6 Hz, 1 H), 3.97–3.86 (m, 3 H), 3.35 (q, *J* = 7.2 Hz, 2 H), 3.27 (c, *J* = 7.2 Hz, 2 H), 1.43 (d, *J* = 7.8 Hz, 6 H), 1.12 (t, *J* = 6.8 Hz, 3 H), 1.08–1.06 (m, 12 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.6 (C), 138.1 (CH), 136.1 (2 × CH), 136.0 (2 × CH), 134.0 (C), 133.8 (C), 130.0 (2 × CH), 127.8 (4 × CH), 125.8 (CH), 109.9 (C), 82.6 (CH), 74.3 (CH), 64.2 (CH_2), 42.8 (CH_2), 39.9 (CH_2), 27.5 (CH_3), 27.4 (CH_3), 27.1 (3 × CH_3), 19.5 (C), 14.5 (CH_3), 13.2 (CH_3) ppm. MS (ESI$^+$-TOF): *m*/*z* (%) = 518 (100) [M + Na]$^+$, 519 (41), 520 (13), 496 (6) [M + H]$^+$. HRMS: *m*/*z* calcd. for $C_{29}H_{41}NNaO_4Si$ [M + Na]$^+$ 518.2703; found 518.2700. IR (neat): $\tilde{\nu}$ = 3041, 1624, 1100, 1067 cm^{-1}.

Synthesis of Chlorocyclopropanecarboxamides 5a–e and 6a–d: To a suspension of anhydrous $CrCl_2$ (1.5 mmol, 3.0 equiv.) in THF (5 mL) was added **3** or **4** (0.5 mmol, 1.0 equiv.) in THF (2 mL) and CCl_4 (0.5 mmol, 1.0 equiv.) at room temperature, under an inert atmosphere. After stirring for 16 h at reflux, the reaction mixture was quenched by the addition of 1.0 M aqueous HCl (5 mL), extracted with Et_2O (3 × 10 mL) and washed with saturated NH_4Cl solution and water. Usual work-up and further purification by column chromatography on silica gel (hexane/EtOAc, 10:1) afforded pure **5** and **6**.

(1*S*,2*S*,3*S*)-2-Chloro-*N*,*N*-diethyl-3-[(5*R*)-1,2:3,4-di-*O*-isopropylidene-β-L-arabinopyran-5-*C*-yl]cyclopropanecarboxamide (5a): Starting from **3a** (0.5 mmol, 177.7 mg), yield 173.7 mg (86%); yellow oil; $[\alpha]_D^{20}$ = –37.5 (*c* = 1.00, $CHCl_3$); R_f = 0.61 (hexane/EtOAc, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.52 (d, *J* = 5.0 Hz, 1 H), 4.62 (dd, *J* = 7.9, 2.5 Hz, 1 H), 4.43–4.16 (m, 2 H), 3.75 (dd, *J* = 8.2, 2.8 Hz, 2 H), 3.60–3.25 (m, 4 H), 2.16–2.00 (m, 1 H), 1.98 (dd, *J* = 5.8, 3.6 Hz, 1 H), 1.48 (s, 3 H), 1.46 (s, 3 H), 1.36 (s, 3 H), 1.32 (s, 3 H), 1.26 (t, *J* = 7.2 Hz, 3 H), 1.10 (t, *J* = 7.1 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.3 (C), 109.3 (C), 108.5 (C), 96.5 (CH), 71.9 (CH), 70.7 (CH), 70.4 (CH), 67.9 (CH), 42.2 (CH_2), 40.8 (CH_2), 37.6 (CH), 28.4 (CH), 26.1 (CH), 25.9 (2 × CH_3), 24.9 (CH_3), 24.3 (CH_3), 14.5 (CH_3), 13.1 (CH_3) ppm. MS (ESI$^+$-TOF): *m*/*z* (%) = 404 (100) [M + H]$^+$, 406 (11), 356 (4). HRMS: *m*/*z* calcd. for $C_{19}H_{31}ClNO_6$ [M + H]$^+$ 404.1840; found 404.1834. IR (neat): $\tilde{\nu}$ = 3420, 1637, 1041, 752 cm^{-1}.

(1*S*,2*S*,3*S*)-2-Chloro-*N*,*N*-diethyl-3-[(4*R*)-3-*O*-benzyl-1,2-*O*-isopropylidene-β-L-threofuran-4-*C*-yl]cyclopropanecarboxamide (5b): Starting from **3b** (0.5 mmol, 187.7 mg), yield 112.4 mg (53%); yellow oil; $[\alpha]_D^{20}$ = –18.5 (*c* = 1.00, $CHCl_3$); R_f = 0.62 (hexane/EtOAc, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.29–7.19 (m, 5 H), 5.87 (d, *J* = 3.9 Hz, 1 H), 4.66 (d, *J* = 12.0 Hz, 1 H), 4.58 (d, *J* = 3.9 Hz, 1 H), 4.54 (d, *J* = 12.0 Hz, 1 H), 4.04 (dd, *J* = 8.6, 3.2 Hz, 1 H), 3.92 (d, *J* = 3.2 Hz, 1 H), 3.56 (dd, *J* = 7.5, 3.8 Hz, 1 H), 3.48 (q, *J* = 7.4 Hz, 1 H), 3.29 (hept, *J* = 6.8 Hz, 3 H), 2.11–2.03 (m, 2 H), 1.41 (s, 3 H), 1.26 (s, 3 H), 1.19 (t, *J* = 7.1 Hz, 3 H), 1.03 (t, *J* = 7.1 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.5 (C), 137.6 (C), 128.8 (2 × CH), 128.3 (CH), 128.1 (2 × CH), 111.1 (CH), 104.9 (C), 83.3 (CH), 81.9 (CH), 80.6 (CH), 72.6 (CH_2), 42.6 (CH_2), 41.3 (CH_2), 37.3 (CH), 28.5 (CH), 27.1 (CH), 26.5 (CH_3), 24.8 (CH_3), 15.2 (CH_3), 13.5 (CH_3) ppm. MS (ESI$^+$-TOF): *m*/*z* (%) = 446 (100) [M + Na]$^+$, 448 (50) [M + 2 + Na]$^+$, 424 (16) [M + H]$^+$. HRMS: *m*/*z* calcd. for $C_{22}H_{30}ClNNaO_5$ [M + Na]$^+$ 446.1710; found 446.1705. IR (neat): $\tilde{\nu}$ = 2982, 1713, 997 cm^{-1}.

(1*S*,2*S*,3*S*)-2-Chloro-*N*,*N*-diethyl-3-[(4*R*)-1-*O*-benzyl-2,3-*O*-isopropylidene-β-L-erythrofuran-4-*C*-yl]cyclopropanecarboxamide (5c): Starting from **3c** (0.5 mmol, 187.7 mg), yield 146.3 mg (69%); colorless solid; m.p. 146–147 °C (Et_2O/Hex); $[\alpha]_D^{20}$ = +13.2 (*c* = 1.00, $CHCl_3$); R_f = 0.32 (hexane/EtOAc, 3:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.34–7.19 (m, 5 H), 5.77 (d, *J* = 3.8 Hz, 1 H), 4.52 (d, *J* = 3.8 Hz, 1 H), 3.84–3.78 (m, 1 H), 3.62–3.51 (m, 4 H), 3.19 (sext, *J* = 7.2 Hz, 2 H), 2.99 (sext, *J* = 7.2 Hz, 2 H), 2.25 (dd, *J* = 10.2, 3.6 Hz, 1 H), 2.13 (dt, *J* = 10.0, 4.6 Hz, 1 H), 1.30 (s, 3 H), 1.20 (s, 3 H), 1.17 (t, *J* = 7.1 Hz, 3 H), 1.02 (t, *J* = 7.1 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.6 (C), 137.7 (C), 128.9 (2 × CH), 128.3 (CH), 128.2 (2 × CH), 112.2 (CH), 105.1 (C), 83.1 (CH), 82.3 (CH), 77.6 (CH), 72.6 (CH_2), 42.4 (CH_2), 40.9 (CH_2), 34.5 (CH), 28.8 (CH), 28.7 (CH), 27.2 (CH_3), 26.9 (CH_3), 14.7 (CH_3), 13.0 (CH_3) ppm. MS (ESI$^+$-TOF): *m*/*z* (%) = 424 (100) [M + H]$^+$, 426 (44) [M + 2 + H]$^+$, 496 (28), 446 (25). HRMS: *m*/*z* calcd. for $C_{22}H_{31}ClNO_5$ [M + H]$^+$ 424.1891; found 424.1871. IR (neat): $\tilde{\nu}$ = 2932, 1634, 1464, 1259, 1075 cm^{-1}.

(1*S*,2*S*,3*S*)-2-Chloro-*N*,*N*-diethyl-3-[(4*R*)-1-*O*-*tert*-butyldimethylsilyl-2,3-*O*-isopropylidene-β-L-erythrofuran-4-*C*-yl]cyclopropanecarboxamide (5d): Starting from **3d** (0.5 mmol, 199.8 mg), yield 181.5 mg (81%); yellow oil; $[\alpha]_D^{20}$ = +39.9 (*c* = 1.00, $CHCl_3$); R_f = 0.45 (hexane/EtOAc, 3:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.29 (s, 1 H), 4.80–4.77 (m, 1 H), 4.55 (d, *J* = 5.8 Hz, 1 H), 4.00–3.96 (m, 1 H), 3.78–3.74 (m, 1 H), 3.58–3.26 (m, 4 H), 2.09–2.02 (m, 2 H), 1.44 (s, 3 H), 1.31 (s, 3 H), 1.23 (t, *J* = 7.1 Hz, 3 H), 1.10 (t, *J* = 7.1 Hz, 3 H), 0.87 (s, 9 H), 0.08 (d, *J* = 4.5 Hz, 6 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.2 (C), 112.4 (C), 100.8 (CH), 87.2 (CH), 79.8 (CH), 79.5 (CH), 42.0 (CH_2), 40.9 (CH_2), 36.9 (CH), 28.5 (CH), 26.0 (CH), 25.5 (3 × CH_3), 25.0 (CH_3), 24.7 (CH_3), 17.8 (C), 14.8 (CH_3), 13.0 (CH_3), –4.5 (CH_3), –5.4 (CH_3) ppm. MS (ESI-TOF): *m*/*z* (%) = 448 (100) [M + H]$^+$, 496 (94), 450 (38) [M + 2 + H]$^+$, 438 (22), 470 (16). HRMS: *m*/*z* calcd. for $C_{21}H_{39}ClNO_5Si$ [M + H]$^+$ 448.2286; found 448.2265. IR (neat): $\tilde{\nu}$ = 2976, 1721, 1114 cm^{-1}.

(1*S*,2*S*,3*S*)-2-Chloro-*N*,*N*-diethyl-3-(3-*O*-*tert*-butyldiphenylsilyl-1,2-isopropilidene-D-threitol-1-*C*-yl)cyclopropanecarboxamide (5e): Starting from **3f** (0.5 mmol, 247.9 mg), yield 198.7 mg (73%); colorless oil; $[\alpha]_D^{20}$ = –35.0 (*c* = 1.00, $CHCl_3$); R_f = 0.33 (hexane/EtOAc, 3:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.75–7.66 (m, 4 H), 7.45–7.35 (m, 6 H), 4.14–4.08 (m, 1 H), 4.04–3.99 (m, 1 H), 3.92 (dd, *J* = 11.4, 3.6 Hz, 1 H), 3.80 (dd, *J* = 11.4, 4.0 Hz, 1 H), 3.55

(dd, J = 7.5, 3.5 Hz, 1 H), 3.52–3.40 (m, 2 H), 3.39–3.30 (m, 2 H), 2.20 (dd, J = 5.9, 3.6 Hz, 1 H), 1.79 (td, J = 7.8, 5.8 Hz, 1 H), 1.42 (d, J = 2.7 Hz, 6 H), 1.28 (t, J = 7.2 Hz, 3 H), 1.12 (t, J = 7.1 Hz, 3 H), 1.06 (s, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.8 (C), 136.1 (4 × CH), 133.6 (2 × C), 130.0 (2 × CH), 128.0 (4 × CH), 109.5 (C), 82.7 (CH), 76.0 (CH), 63.1 (CH_2), 42.6 (CH_2), 41.3 (CH_2), 37.9 (CH), 29.3 (CH), 27.6 (CH), 27.5 (CH_3), 27.3 (CH_3), 27.2 (3 × CH_3), 19.6 (C), 15.2 (CH_3), 13.5 (CH_3) ppm. MS (ESI-TOF): m/z (%) = 566 (100) [M + Na]$^+$, 568 (58) [M + 2 + Na]$^+$, 569 (19), 582 (16). HRMS: m/z calcd. for $C_{30}H_{42}ClNNaO_4Si$ [M + Na]$^+$ 566.2469; found 566.2473. IR (neat): $\tilde{\nu}$ = 2932, 1639, 1463, 1428, 1381 cm^{-1}.

(1*R*,2*S*,3*S*)-2-Chloro-*N*,*N*-diethyl-3-[(5*R*)-1,2:3,4-di-*O*-isopropylidene-β-L-arabinopyran-5-*C*-yl]cyclopropanecarboxamide (6a): Starting from **4a** (0.5 mmol, 177.7 mg), yield 111.1 mg (55%); colorless solid; m.p. 145–146 °C (Et_2O/Hex); $[\alpha]_D^{20}$ = –175.4 (c = 1.00, $CHCl_3$); R_f = 0.38 (hexane/EtOAc, 3:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.38 (d, J = 5.1 Hz, 1 H), 4.58 (dd, J = 9.6, 1.8 Hz, 1 H), 4.25–4.20 (m, 2 H), 3.66 (t, J = 4.08 Hz, 1 H), 3.63–3.56 (m, 1 H), 3.54–3.45 (m, 2 H), 3.36–3.21 (m, 2 H), 2.22 (dd, J = 10.3, 3.6 Hz, 1 H), 2.14 (td, J = 9.9, 4.5 Hz, 1 H), 1.48 (s, 3 H), 1.46 (s, 3 H), 1.37 (s, 3 H), 1.27–1.23 (m, 6 H), 1.13 (t, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.5 (C), 109.5 (C), 109.0 (C), 96.5 (CH), 72.8 (CH), 71.2 (CH), 70.6 (CH), 65.0 (CH), 42.6 (CH_2), 40.7 (CH_2), 34.4 (CH), 31.4 (CH), 28.6 (CH), 26.3 (CH_3), 26.2 (CH_3), 25.3 (CH_3), 24.7 (CH_3), 14.8 (CH_3), 13.6 (CH_3) ppm. MS (ESI-TOF): m/z (%) = 426 (100) [M + Na]$^+$, 428 (56) [M + 2 + Na]$^+$, 404 (16) [M + H]$^+$, 429 (13). HRMS: m/z calcd. for $C_{19}H_{30}ClNNaO_6$ [M + Na]$^+$ 426.1659; found 426.1652. IR (neat): $\tilde{\nu}$ = 3420, 1637, 1041, 752 cm^{-1}.

(1*R*,2*S*,3*S*)-2-Chloro-*N*,*N*-diethyl-3-[(4*R*)-3-*O*-benzyl-1,2-*O*-isopropylidene-β-L-threofuran-4-*C*-yl]cyclopropanecarboxamide (6b): Starting from **4b** (0.5 mmol, 187.7 mg), yield 135.7 mg (64%); yellow oil; $[\alpha]_D^{20}$ = –47.5 (c = 1.00, $CHCl_3$); R_f = 0.52 (hexane/EtOAc, 3:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.31–7.27 (m, 5 H), 5.77 (d, J = 4.7 Hz, 1 H), 4.62 (q, J = 12.0 Hz, 2 H), 4.53 (d, J = 4.9 Hz, 1 H), 3.82 (d, J = 5.7 Hz, 1 H), 371–3.43 (m, 2 H), 3.19 (dq, J = 14.6, 7.1 Hz, 2 H), 3.00 (dq, J = 13.9, 7.0 Hz, 2 H), 2.24 (dd, J = 9.8, 4.7 Hz, 1 H), 2.13 (td, J = 9.9, 4.4 Hz, 1 H), 1.30 (s, 3 H), 1.20 (s, 3 H), 1.18 (t, J = 7.1 Hz, 3 H), 1.02 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.2 (C), 137.2 (C), 128.4 (2 × CH), 127.9 (CH), 127.7 (2 × CH), 111.8 (CH), 104.6 (C), 82.7 (CH), 81.9 (CH), 77.4 (CH), 72.2 (CH_2), 42.0 (CH_2), 40.5 (CH_2), 34.1 (CH), 28.4 (CH), 28.3 (CH), 26.8 (CH_3), 26.5 (CH_3), 14.2 (CH_3), 12.6 (CH_3) ppm. MS (ESI-TOF): m/z (%) = 446 (100) [M + Na]$^+$, 448 (44) [M + 2 + Na]$^+$, 449 (13). HRMS: m/z calcd. for $C_{22}H_{30}ClNNaO_5$ [M + Na]$^+$ 446.1710; found 446.1705. IR (neat): $\tilde{\nu}$ = 2982, 1713, 997 cm^{-1}.

(1*R*,2*S*,3*S*)-2-Chloro-*N*,*N*-diethyl-3-(1,2:3,4-di-*O*-isopropylidene-L-xylitol-1-*C*-yl)cyclopropanecarboxamide (6c): Starting from **4e** (0.5 mmol, 163.7 mg), yield 137.2 mg (73%); yellow oil; $[\alpha]_D^{20}$ = –41.5 (c = 1.00, $CHCl_3$); R_f = 0.78 (hexane/EtOAc, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.13 (dd, J = 8.1, 5.9 Hz, 1 H), 4.01 (dt, J = 7.5, 5.4 Hz, 1 H), 3.94 (dd, J = 8.1, 4.9 Hz, 1 H), 3.81–3.77 (m, 2 H), 3.77–3.54 (m, 3 H), 3.29 (sext, J = 7.1 Hz, 1 H), 3.13 (sext, J = 7.1 Hz, 1 H), 2.24 (dd, J = 10.0, 3.9 Hz, 1 H), 1.76 (dt, J = 9.7, 4.3 Hz, 1 H), 1.47 (s, 3 H), 1.36 (s, 3 H), 1.34 (s, 3 H), 1.24 (t, J = 7.1 Hz, 3 H), 1.23 (s, 3 H), 1.07 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.4 (C), 109.6 (C), 108.8 (C), 81.4 (CH), 76.8 (CH), 76.3 (CH), 67.5 (CH_2), 42.1 (CH_2), 40.4 (CH_2), 35.2 (CH), 32.8 (CH), 28.4 (CH), 27.1 (CH_3), 26.6 (CH_3), 26.5 (CH_3), 25.0 (CH_3), 14.2 (CH_3), 12.4 (CH_3) ppm. MS (ESI-TOF): m/z (%) = 376 (100) [M + H]$^+$. HRMS: m/z calcd. for $C_{18}H_{31}ClNO_5$ [M + H]$^+$ 376.1891; found 376.1888. IR (neat): $\tilde{\nu}$ = 2986, 1634, 1069, 737 cm^{-1}.

(1*R*,2*S*,3*S*)-2-Chloro-*N*,*N*-diethyl-3-(3-*O*-*tert*-butyldiphenylsilyl-1,2-isopropilidene-D-threitol-1-*C*-yl)cyclopropanecarboxamide (6d): Starting from **4f** (0.5 mmol, 247.9 mg), yield 206.8 mg (76%); colorless oil; $[\alpha]_D^{20}$ = +9.5 (c = 1.00, $CHCl_3$); R_f = 0.68 (hexane/EtOAc, 3:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.75–7.71 (m, 4 H), 7.43–7.37 (m, 6 H), 4.07–4.02 (m, 1 H), 3.85–3.70 (m, 3 H), 3.68–3.59 (m, 3 H), 3.29 (dq, J = 14.6, 7.2 Hz, 1 H), 3.12 (dq, J = 13.9, 7.0 Hz, 1 H), 2.24 (dd, J = 10.1, 3.6 Hz, 1 H), 1.80 (dt, J = 10.0, 4.0 Hz, 1 H), 1.40 (s, 3 H), 1.27 (s, 3 H), 1.25 (t, J = 7.2 Hz, 3 H), 1.11–1.06 (m, 12 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.4 (C), 136.0 (4 × CH), 133.4 (C), 133.3 (C), 130.0 (2 × CH), 128.0 (4 × CH), 109.1 (C), 82.0 (CH), 75.0 (CH), 64.2 (CH_2), 42.2 (CH_2), 40.7 (CH_2), 34.5 (CH), 33.0 (CH), 28.5 (CH), 27.7 (CH_3), 27.1 (3 × CH_3), 26.9 (CH_3), 19.5 (C), 14.6 (CH_3), 12.8 (CH_3) ppm. MS (ESI-TOF): m/z (%) = 566 (100) [M + Na]$^+$, 568 (56) [M + 2 + Na]$^+$, 569 (19), 582 (13), 553 (9). HRMS: m/z calcd. for $C_{30}H_{42}ClNNaO_4Si$ [M + Na]$^+$ 566.2469; found 566.2473. IR (neat): $\tilde{\nu}$ = 2932, 1639, 1463, 1428, 1381 cm^{-1}.

Synthesis of Bromocyclopropanes 5f and 6e: Bromocyclopropanes **5f** and **6e** were synthesized following the same procedure used for the synthesis of chlorocyclopropanecarboxamides **5a**–**e**, and **6a**–**d** using anhydrous $CrBr_2$[13] instead of $CrCl_2$ and commercial CBr_4 as the carbenoid source.

(1*S*,2*S*,3*S*)-2-Bromo-*N*,*N*-diethyl-3-[(5*R*)-1,2:3,4-di-*O*-isopropylidene-β-L-arabinopyran-5-*C*-yl]cyclopropanecarboxamide (5f): Starting from **3a** (0.5 mmol, 177.7 mg), yield 141.2 mg (63%); colorless oil; $[\alpha]_D^{20}$ = –23.6 (c = 0.50, $CHCl_3$); R_f = 0.10 (hexane/EtOAc, 3:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.52 (d, J = 5.1 Hz, 1 H), 4.63 (dd, J = 7.9, 2.4 Hz, 1 H), 4.33 (m, 2 H), 3.69 (dd, J = 9.0, 1.9 Hz, 1 H), 3.63 (dd, J = 7.5, 4.2 Hz, 1 H), 3.58–3.26 (m, 4 H), 2.04–1.94 (m, 2 H), 1.51 (s, 3 H), 1.46 (s, 3 H), 1.37 (s, 3 H), 1.33 (s, 3 H), 1.27 (t, J = 7.1 Hz, 3 H), 1.11 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.9 (C), 109.8 (C), 109.0 (C), 97.0 (CH), 72.0 (CH), 71.1 (CH), 70.9 (CH), 70.4 (CH), 42.7 (CH_2), 41.3 (CH_2), 29.0 (CH), 26.4 (CH_3), 26.3 (CH_3), 25.9 (CH_3), 25.8 (CH_3), 25.4 (CH), 24.8 (CH), 15.0 (CH_3), 13.6 (CH_3) ppm. MS (ESI$^+$-TOF): m/z (%) = 470 (100) [M + Na]$^+$, 472 (100) [M + 2 + Na]$^+$, 473 (28); 448 (16), 450 (16). HRMS: m/z calcd. for $C_{19}H_{30}BrNNaO_6$ [M + Na]$^+$ 470.1154; found 470.1162. IR (neat): $\tilde{\nu}$ = 3434, 2984, 1634, 1069, 737 cm^{-1}.

(1*R*,2*S*,3*S*)-2-Bromo-*N*,*N*-diethyl-3-[(5*R*)-1,2:3,4-di-*O*-isopropylidene-β-L-arabinopyran-5-*C*-yl]cyclopropanecarboxamide (6e): Starting from **4a** (0.5 mmol, 177.7 mg), yield 134.5 mg (60%); colorless solid; m.p. 135–137 °C (Et_2O/Hex); $[\alpha]_D^{20}$ = –78.5 (c = 0.50, $CHCl_3$); R_f = 0.35 (hexane/EtOAc, 3:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.31 (d, J = 5.0 Hz, 1 H), 4.52 (dd, J = 7.9, 2.4 Hz, 1 H), 4.16 (dt, J = 6.6, 2.0 Hz, 1 H), 4.15 (s, 1 H), 3.60–3.39 (m, 4 H), 3.32–3.14 (m, 2 H), 2.20 (dd, J = 10.1, 3.9 Hz, 1 H), 2.11 (td, J = 9.8, 4.8 Hz, 1 H), 1.41 (d, J = 6.4 Hz, 6 H), 1.31 (s, 3 H), 1.18 (s, 3 H), 1.18 (t, J = 7.2 Hz, 3 H), 1.07 (t, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.9 (C), 109.5 (C), 109.0 (C), 96.5 (CH), 72.8 (CH), 71.2 (CH), 70.6 (CH), 65.4 (CH), 42.6 (CH_2), 40.8 (CH_2), 31.6 (CH), 28.4 (CH), 26.4 (CH_3), 26.3 (CH_3), 25.3 (CH_3), 24.7 (CH_3), 20.3 (CH), 14.9 (CH_3), 13.6 (CH_3) ppm. MS (ESI-TOF): m/z (%) = 470 (100) [M + Na]$^+$, 472 (100) [M + 2 + Na]$^+$, 473 (22), 448 (9), 450 (9). HRMS: m/z calcd. for $C_{19}H_{30}BrNNaO_6$ [M + Na]$^+$ 470.1154; found 470.1161. IR (neat): $\tilde{\nu}$ = 3434, 2984, 1634, 1069, 737 cm^{-1}.

Chlorocyclopropanamines 11 and 12[12b]

(4*R*)-3-*O*-Benzyl-[(1*S*,2*R*,3*S*)-2-chloro-3-diethylaminomethylcyclopropanyl]-1,2-isopropylidene-β-L-threofuranose (11): Starting from **5b** (0.4 mmol, 169.6 mg), yield 121.3 mg (74%); colorless oil; $[\alpha]_D^{20}$ = –143.3 (*c* = 0.50, $CHCl_3$); R_f = 0.15 (hexane/EtOAc, 1:10). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.32–7.21 (m, 5 H), 5.87 (d, *J* = 3.9 Hz, 1 H), 4.68 (d, *J* = 12.0 Hz, 1 H), 4.56 (s, 1 H), 4.54 (d, *J* = 8.4 Hz, 1 H), 3.97–3.91 (m, 2 H), 2.90 (dd, *J* = 7.7, 4.0 Hz, 1 H), 2.66 (dd, *J* = 13.7, 5.4 Hz, 1 H), 2.58 (q, *J* = 7.2 Hz, 4 H), 2.30 (dd, *J* = 13.6, 7.4 Hz, 1 H), 1.41 (s, 3 H), 1.38–1.29 (m, 2 H), 1.26 (s, 3 H), 0.98 (t, *J* = 7.1 Hz, 6 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.6 (C), 128.8 (2×CH), 128.3 (CH), 128.1 (2×CH), 111.7 (CH), 104.7 (C), 83.3 (CH), 82.1 (CH), 82.0 (CH), 72.6 (CH_2), 54.3 (CH_2), 46.8 (2×CH_2), 36.4 (CH), 27.1 (CH), 26.5 (2×CH_3), 21.0 (CH), 11.8 (2×CH_3) ppm. MS (ESI-TOF): *m*/*z* (%) = 410 (100) $[M + H]^+$, 412 (38) [M + 2 + H], 413 (9). HRMS: *m*/*z* calcd. for $C_{22}H_{33}ClNO_4$ $[M + H]^+$ 410.2098; found 410.2096. IR (neat): ṽ = 3419, 2973, 2936, 1634, 1005 cm^{-1}.

(5*R*)-[(1*S*,2*R*,3*R*)-2-Chloro-3-diethylaminomethylcyclopropanyl]-1,2:3,4-di-*O*-isopropylidene-β-L-arabinopyranose (12a): Starting from **6a** (0.4 mmol, 161.6 mg), yield 110.7 mg (71%); yellow oil; $[\alpha]_D^{20}$ = –52.5 (*c* = 0.60, $CHCl_3$); R_f = 0.13 (hexane/EtOAc, 1:10). ^1H NMR (300 MHz, $CDCl_3$): δ = 5.54 (d, *J* = 5.2 Hz, 1 H), 4.59 (dd, *J* = 7.9, 2.3 Hz, 1 H), 4.27 (dd, *J* = 5.2, 2.3 Hz, 1 H), 4.23 (dd, *J* = 7.9, 1.9 Hz, 1 H), 3.23 (dd, *J* = 7.9, 1.9 Hz, 1 H), 3.07 (dd, *J* = 13.3, 3.3 Hz, 1 H), 2.64 (q, *J* = 6.0 Hz, 4 H), 2.11 (dd, *J* = 13.3, 9.6 Hz, 1 H), 1.48 (s, 3 H), 1.49 (s, 3 H), 1.36 (s, 3 H), 1.31 (s, 3 H), 1.16–1.07 (m, 1 H), 1.04 (t, *J* = 7.1 Hz, 6 H), 0.96–0.89 (m, 1 H), 0.18 (q, *J* = 5.4 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 109.4 (C), 108.4 (C), 97.1 (CH), 73.3 (CH), 71.4 (CH), 70.6 (CH), 69.2 (CH), 52.7 (CH_2), 47.0 (2×CH_2), 26.4 (2×CH_3), 25.1 (CH_3), 24.7 (CH_3), 14.7 (CH), 13.9 (CH), 11.6 (2×CH_3), 10.3 (CH_2) ppm. MS (ESI-TOF): *m*/*z* (%) = 392 (100) $[M – Cl + H + K]^+$, 304 (90), 365 (53) $[M – Cl + H + NH_4]^+$. HRMS: *m*/*z* calcd. for $C_{19}H_{32}KNO_5$ $[M – Cl + H + K]^+$ 393.1918; found 393.1127. IR (neat): ṽ = 3435, 2981, 2935, 1645, 1003 cm^{-1}.

(1*S*,2*R*,3*R*)-2-Chloro-3-diethylaminomethyl-1-(1,2-*O*-isopropylidene-D-threitol-1-*C*-yl)cyclopropane (12b): Starting from **6d** (0.4 mmol, 217.7 mg); Yield: 58.36 mg (52%); colorless oil; $[\alpha]_D^{20}$ = –4.5 (*c* = 1.00, $CHCl_3$); R_f = 0.09 (hexane/EtOAc, 1:10). ^1H NMR (300 MHz, $CDCl_3$): δ = 3.99 (dt, *J* = 8.2, 3.3 Hz, 1 H), 3.91 (dd, *J* = 12.2, 3.3 Hz, 1 H), 3.68 (dd, *J* = 12.3, 3.4 Hz, 1 H), 3.60 (t, *J* = 8.4 Hz, 1 H), 3.00 (dd, *J* = 13.7, 4.8 Hz, 1 H), 2.96–2.93 (m, 1 H), 2.69 (dq, *J* = 7.1, 2.4 Hz, 4 H), 2.42 (dd, *J* = 13.6, 8.3 Hz, 1 H), 1.99 (br. s, 1 H), 1.58–1.42 (m, 2 H), 1.44 (s, 3 H), 1.38 (s, 3 H), 1.10 (t, *J* = 7.2 Hz, 6 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 109.4 (C), 82.0 (CH), 75.0 (CH), 61.4 (CH_2), 50.4 (CH_2), 46.8 (2×CH_2), 35.7 (CH), 28.4 (CH), 27.5 (CH_3), 27.2 (CH_3), 24.4 (CH), 11.6 (2×CH_3) ppm. MS (ESI-TOF): *m*/*z* (%) = 292 (100) $[M + H]^+$, 294 (38) [M + 2 + H]. HRMS: *m*/*z* calcd. for $C_{14}H_{27}ClNO_3$ $[M + H]^+$ 292.1679; found 292.1683. IR (neat): ṽ = 3435, 2983, 2935, 1641, 1381 cm^{-1}.

Supporting Information (see footnote on the first page of this article): Copies of ^1H and ^{13}C NMR spectra for compounds **3**–**6**, and **11**–**12**.

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