Titanium-Mediated Diastereoselective Formation of (*E*)- or (*Z*)-2-Substituted 1-Vinylcyclopropanols: Scope and Limitation, Applications[‡]

Sandrine Racouchot,[a] Isabelle Sylvestre,[a] Jean Ollivier,[a] Yuri Yu. Kozyrkov,[a,b] Alexei Pukin,[a,b] Oleg G. Kulinkovich,*[b] and Jacques Salaün*[a]

Keywords: Azidation / Cyclopropanation / 2,3-Methanoamino acids / Palladium / Titanium

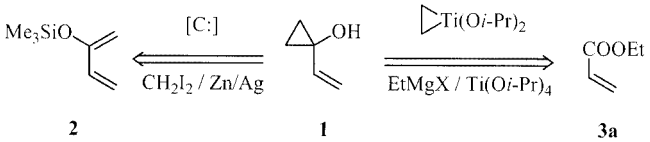
Titanium-mediated cyclopropanation of α,β-unsaturated esters failed to provide 1-vinylcyclopropanol derivatives in useful yields, but (*E*)-2-substituted-1-vinylcyclopropanols were formed diastereoselectively from *O*-protected β-oxo- and β-halo esters, with the allylic double bond being created subsequently (Knoevenagel condensation or dehydrohalogenation). Titanium-mediated cyclopropanation of homoallyl alk-2-enoates, on the other hand, directly provided the corresponding *Z* diastereomers. Palladium(0)-catalysed azidation of their sulfonic esters (tosylate, mesylate), azide reduction, and subsequent double bond cleavage afforded (*E*)- or (*Z*)-2-alkyl-2,3-methanoamino acids, although improvements are required to perform the total asymmetric syntheses of molecules with three membered-rings by these methods.

Introduction

Among the functionalized cyclopropanes, building blocks of matchless synthetic potential,[1] the derivatives of the 1-vinylcyclopropanol (**1**) − available through, for example, the simple cyclopropanation of the 2-trimethylsiloxybutadiene (**2**)[2] − constitute an outstanding class of synthons. These unique conjugated homoenols or their silyl ethers can undergo regio- and diastereoselective acid-, base-, or thermally induced $C_3 \rightarrow C_{4-8}$ ring expansions,[1b] and fluoride ion-induced $C_3 \rightarrow C_{10-20}$ ring enlargements.[3] These useful rearrangements have been demonstrated by the total syntheses of various natural products (i.e., jasmone and dihydrojasmone,[1b] dicranenone A,[1b] methylenomycin B,[1b] prostaglandins,[1b] aphidicolin,[4] spirovetivane,[1b] butanolides such as (3*S*,4*S*)-Quercus lactones,[5] macrocycles and azamacrocycles[3]). Moreover, it has been pointed out that the sulfonic esters (tosylates, mesylates) of the allylic alcohol **1** form significant π- or σ-1,1-ethyleneallyl metal complexes, which may then undergo chemo-, regio-, and diastereoselective nucleophilic[6] or electrophilic substitutions.[7]

Applications of these intermediaries to, for example, the asymmetric syntheses of alkylidenecyclopropanes, cyclobutanones and γ-butyrolactones,[8] cyclopentenones,[9] 2,3-methanoamino acids,[10] isoxazolidines and pyrrolo[3,4-*b*]pyridinones,[11] and β-lactams[12] have recently been reported. Natural and non-natural cyclopropane-containing compounds are also endowed with a large spectrum of biological properties,[13] and so these derivatives are of great general interest to both synthetic organic and bioorganic chemists.

Although the parent 1-ethenylcyclopropanol (**1**) and its derivatives were already available, from 1,3-dichloroacetone,[14] cyclopropanone hemiacetals[15] or 1-hydroxycyclopropanecarboxylic acids,[16] it appeared worthwhile to examine the titanium-mediated cyclopropanation of ethyl acrylate **3a** and its derivatives as a new and direct route to these functional three-membered rings (Scheme 1). In this article we report the scope and limitations of this new procedure, including new applications to the diastereoselective syntheses of (*E*)- and (*Z*)-2,3-methanoamino acids.



Scheme 1. Syntheses of 1-ethenylcyclopropanol

[‡] In contrast to IUPAC nomenclature rules, the (*E*)/(*Z*) descriptors used in this article refer to the relative stereochemistry of the cyclopropane substituents.

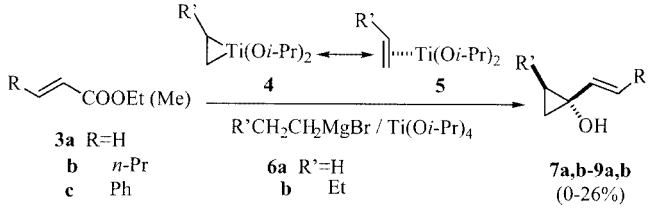
[a] Laboratoire des Carbocycles, UMR 8615, Institut de Chimie Moléculaire d'Orsay, Université de Paris-Sud, 91405 Orsay, France
Fax: (internat.) +33−1/6915-6278
E-mail: jasalaun@icmo.u-psud.fr
[b] Department of Chemistry, Belarussian State University, Fr. Skariny av. 4, Minsk 220050, Belarus
Fax: (internat.) + 375−17/226-4998
E-mail: kulinkovich@bsu.by

Results and Discussion

Cyclopropanation of α,β-Unsaturated Esters

Effectively, the diisopropyloxytitana(IV)cyclopropanes **4**, also shown in their resonance forms, the (η^2-olefin) diisopropyloxytitanium(II) complexes **5**, arising from the reaction of two equivalents of alkylmagnesium bromides with titanium tetraisopropoxide [Ti(O*i*Pr)$_4$], have been considered to act as 1,2-dicarbanionic equivalents performing an overall twofold alkylation of alkoxy-carbonyl groups, most often providing (*E*)-cyclopropanols in good or excellent yields (74−98%).[17,18]

Despite many attempts under various experimental conditions, however, treatment of the conjugated esters **3a−c** (R = H, *n*Pr, Ph) with the Grignard reagents **6a** and **6b** (R′ = H, Et) in the presence of Ti(O*i*Pr)$_4$ gave the expected 1-(alk-1-enyl) cyclopropanols **7a−9a/9b** only in unusably low yields (Scheme 2 and Table 1). Thus, for instance, treatment of ethyl hex-2-enoate **3b** (R = *n*Pr) with 2.1−3.3 equivalents of *n*-butylmagnesium bromide (**6b**, R′ = Et) in the presence of 0.2−1 equivalent of Ti(O*i*Pr)$_4$ in a 1:1 solution of tetrahydrofuran and diethyl ether at room temperature for 60 min provided the expected (*E*)-2-ethyl-1-(pent-1-enyl)cyclopropanol (**8b**) in only 11−15% yields (Table 1, entry 4). Use of longer reaction times or heating of the reaction mixture (45−90 °C) did not improve the yield appreciably, and neither did the use of different titanium catalysts [ClTi(O*i*Pr)$_3$, MeTi(O*i*Pr)$_3$]. For comparison, treatment of **3b** with 2.5 equivalents of EtMgBr (**6a**, R′ = H) in the presence of Ti(O*i*Pr)$_4$ resulted in the 1-(pent-1-enyl)cyclopropanol (**8a**) in 26% yield, thus revealing a steric effect (Table 1, entry 3).

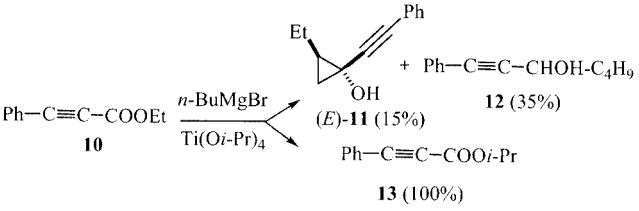


Scheme 2. Titanium-mediated cyclopropanation of α,β-unsaturated esters

Table 1. Syntheses of 1-(1-alkenyl)cyclopropanols by titanium-mediated cyclopropanation of α,β−unsaturated esters

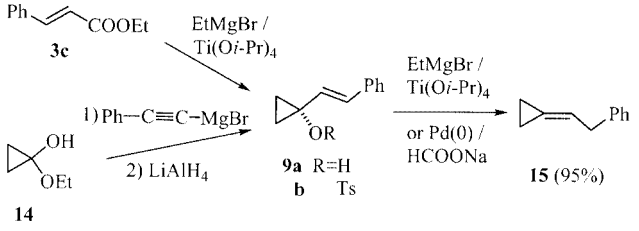
Entry	Ester	R	Grignard reagent	R′	Product	Yield (%)
1	**3a**	H	**6a**	H	**7a**	11[19]
2	**3a**	H	**6b**	Et	**7b**	0
3	**3b**	*n*Pr	**6a**	H	**8a**	26
4	**3b**	*n*Pr	**6b**	Et	**8b**	15
5	**3c**	Ph	**6a**	H	**9a**	25
6	**3c**	Ph	**6b**	Et	**9b**	0

Similarly, ethyl phenylpropiolate (**10**) underwent cyclopropanation on treatment with 2.5 equivalents of *n*BuMgBr (**6b**) in the presence of 0.2 equivalent of Ti(O*i*Pr)$_4$ to provide (*E*)-2-ethyl-1-(phenylethynyl)cyclopropanol (**11**) in only 15% yield, together with propargylic alcohol (**12**) as the main product. Compound **12** probably resulted from reduction of 1-phenylhept-1-yn-3-one formed as by-product, as previously observed on treatment of conjugated esters with alkylmagnesium halides.[20] Alternatively, above −78 °C in the presence of one equivalent of Ti(O*i*Pr)$_4$, **10** quantitatively underwent the well known transesterification into isopropyl phenylpropiolate (**13**), even in the absence of any Grignard reagent (Scheme 3). This result was deeply disappointing, because it is known that simple lithium aluminum hydride reduction of propargylic alcohols such as **11** can produce 1-ethenyl cyclopropanols in high yield.[21]



Scheme 3. Titanium-mediated cyclopropanation of phenylpropiolate

The 1-styrylcyclopropanol **9a** (X = OH) resulting from the titanium-mediated cyclopropanation of ethyl cinnamate **3c** (26%) was univocally obtained in 90% overall yield from treatment of cyclopropanone hemiacetal **14** with two equivalents of phenylethynylmagnesium bromide, followed by LiAlH$_4$ reduction.[21] Upon treatment with the EtMgBr/Ti(O*i*Pr)$_4$ reagent, under the conditions of the cyclopropanation reaction,[17] the allylic alcohol **9a** then underwent reductive elimination of the hydroxy group to provide the (2-phenylethylidene)cyclopropane **15** in 95% yield. It was noteworthy that **15** was also obtained from the palladium(0) [PdP(*o*-anisyl)$_3$]$_4$-catalysed reduction (HCOONa) of the tosylate **9b** (R = Ts) (prepared from **9a**) (Scheme 4).[6b,23]



Scheme 4. Titanium-mediated cyclopropanation of allylic alcohols

Most probably, this subsequent reaction of allylic alcohols such as **7a/7b−9a/9b** with Grignard reagents in the presence of Ti(O*i*Pr)$_4$ was responsible for the low yields obtained in the cyclopropanation of conjugated esters **3a−c**.[24] It therefore appeared that, to provide acceptable yields of 1-(1-alkenyl)cyclopropanols, the allylic double bond would have to be created after the cyclopropanation reaction.

(*E*)-Cyclopropanation of α- and β-Oxyesters

While ethyl 2-hydroxypropionate (**16**) was reported to undergo cyclopropanation [2 EtMgBr/0.2 TiCl(O*i*Pr)$_3$] to give

1-hydroxycyclopropylcarbinol (**17**) in 62% yield (Table 2, entry 1),[26] treatment of ethyl 2,2-dimethoxypropionate (**18**) with 2.5 EtMgBr/0.2 Ti(O*i*Pr)$_4$, on the other hand, gave the corresponding tertiary alcohol 2,2-dimethoxy-3-ethylpentan-3-ol in 72% yield rather than the expected 1-hydroxycyclopropanecarboxaldehyde dimethylacetal (**19**, entry 2), a potential precursor of 1-(1-alkenyl)cyclopropanols **7a**−**9a** after simple deacetalisation and Wittig reaction ($Ph_3P{=}CH{-}R$).[27]

By comparison, treatment of ethyl 3-(1,3-dioxolan-2-yl)-butanoate (**20**) with EtMgBr in the presence of 0.2 equivalent of Ti(O*i*Pr)$_4$ gave the cyclopropanol **21a**[25] in 86% yield (Table 2, entry 3). However, treatment of **20** with *n*BuMgBr suffered from steric hindrance, since the 2-ethylcyclopropanol **21b** was not formed under these conditions (entry 4). Cyclopropanation of ethyl 3-(tetrahydropyranyloxy)butanoate (**22**) by 2.5 *n*BuMgBr/0.2 Ti(O*i*Pr)$_4$, though, afforded (*E*)-2-ethyl-1-(2-tetrahydropyranyloxypropyl)cyclopropanol (**23**) in 65% yield. In fact, formation of a separable 1:1 diastereomeric mixture of **23** was observed, due to the presence of a chiral carbon substituted by the *O*-protecting group. Comparison of the ^{1}H and ^{13}C NMR spectra of (*E*)-**23** with literature data,[28] led us to conclude an exclusive *cis* relationship between the two alkyl substituents on the cyclopropanol ring (entry 5).[29] Cyclopropanation of β-siloxy esters **24** and **26** under the same conditions gave the 1,2-disubstituted cyclopropanols (*E*)-**25** and (*E*)-**27**[30] in 54 and 60% yields, respectively (entries 6, 7), while the ethyl 3,3-diethoxypropionate **28** furnished (*E*)-1-(2,2-diethoxyethyl)-2-ethylcyclopropanol (**29**) in 92% yield and as a single diastereomer, as confirmed by ^{1}H and ^{13}C NMR spectroscopic analysis and from its further transformation into (*E*)-2,3-methanoamino acid (vide infra).[31]

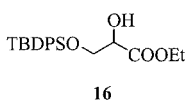
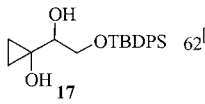
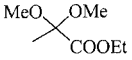
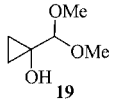
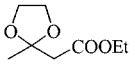
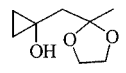
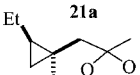
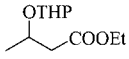
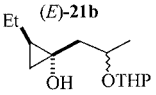
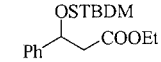
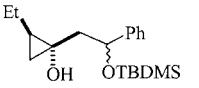
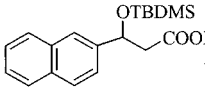
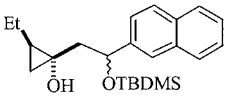
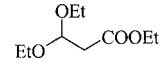
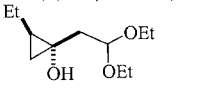
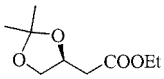
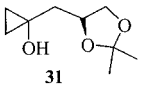
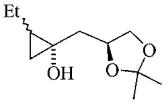
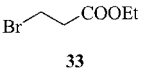
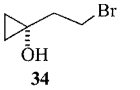
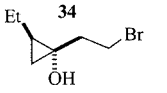
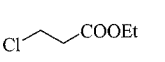
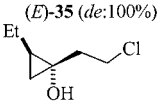
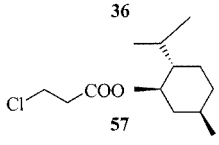
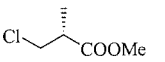
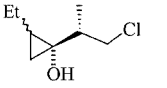
Cyclopropanation of the chiral ester (3*S*)-**30**, available from dimethyl (*S*)-malate, with 2.5 EtMgBr/0.2 Ti(O*i*Pr)$_4$ provided the cyclopropanol derivative **31** in 78% yield (Table 2, entry 9).[32a] In sharp contrast with the previous examples (entries 5−8), however, treatment of ester (3*S*)-**30** with 2.5 *n*BuMgBr/O.2 Ti(O*i*Pr)$_4$ afforded an 80% yield of an 80:20 diastereomeric mixture of (*E*)- and (*Z*)-1,2-disubstituted cyclopropanols **32** [in fact a 4:4:2 mixture of (*SSS*), (*SRR*), and (*SRS*) diastereomers], difficulty in their separation precluding their further investigation (entry 10).[32b]

(*E*)-Cyclopropanation of β-Halo Esters

Upon treatment with two equivalents of EtMgBr in the presence of 0.2 equivalents of Ti(O*i*Pr)$_4$, ethyl 2-bromopropionate (**33**) provided 1-(2-bromoethyl)cyclopropanol (**34**) in 86% yield (Table 2, entry 11).[33] Under the same conditions, treatment with *n*BuMgBr and Ti(O*i*Pr)$_4$ transformed **33** into (*E*)-1-(2-bromoethyl)-2-ethyl cyclopropanol (**35**) in 48% yield (entry 12). A better yield was obtained from the 2-chloropropionate **36**, which provided the chlorocyclopropanol (*E*)-**37** (65%), probably due to reduced steric hindrance (entry 13).[34]

Examination of Table 2 shows that the presence of one oxy substituent β to a carboxylate group provided beneficial effects for the cyclopropanation reaction and allowed the

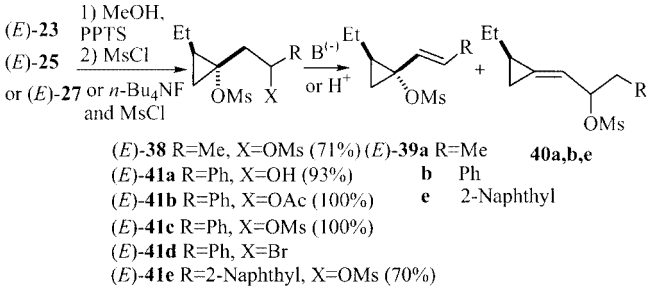
Table 2. Titanium-mediated cyclopropanation of α- and β-oxy- and halo-esters

Entry	Starting ester	Grignard reagent	Product	Yield %[ref.]
1	 **16**	EtMgBr	 **17**	62[26]
2	 **18**	EtMgBr	 **19**	0
3	 **20**	EtMgBr	 **21a**	86[25]
4	**20**	*n*BuMgBr	 (*E*)-**21b**	0
5	 **22**	*n*BuMgBr	 (*E*)-**23** (*de*: 100%)	65
6	 **24**	*n*BuMgBr	 (*E*)-**25** (*de*: 100%)	54
7	 **26**	*n*BuMgBr	 (*E*)-**27** (*de*: 100%)	60
8	 **28**	*n*BuMgBr	 (*E*)-**29** (*de*: 100%)	92
9	 (3*S*)-**30**	EtMgBr	 **31**	78[32a]
10	(3*S*)-**30**	*n*BuMgBr	 (*E*)-**32** (*de*: 60%)	80
11	 **33**	EtMgBr	 **34**	86[33]
12	**33**	*n*BuMgBr	 (*E*)-**35** (*de*:100%)	48
13	 **36**	*n*BuMgBr	 (*E*)-**37** (*de*:100%)	65
14	 **57**	*n*BuMgBr	(*E*)-**37**	0
15	 (2*S*)-**58**	*n*BuMgBr	 (*E*, *Z*)-**59** (*de*: 0%)	24

diastereoselective formation of 2-alkyl-1-ethenylcyclopropanols in good yields (entries 5−8), with a comparable beneficial effect being produced by a β-halo substituent (entries 11−13)

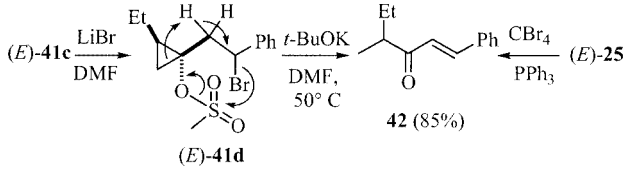
Dehydrosulfonatation and Dehydrohalogenation of 1-(2-Hydroxyalkyl)- and 1-(2-Haloalkyl)cyclopropyl Esters to Give (*E*)-2-Alkyl-1-vinylcyclopropanols

O-Deprotection of, for example, cyclopropanol (*E*)-**23** (PPTs, EtOH) gave the corresponding diol, which underwent diesterification (MsCl, NEt_3) to afford the dimesylate (*E*)-**38** (R = Me, X = OMs) in 71% yield. Subsequent attempted base-induced (DBU/THF, *t*BuOK/DMSO, or NaH/THF at 50 °C for 20 h),[36] or acid-induced (*p*TsOH/DMF, H_2SO_4/CH_2Cl_2)[36] elimination of methanesulfonic acid (MsOH), however, surprisingly failed to produce from (*E*)-**38** the regioisomeric 1,1- or 3,3-ethyleneallyl mesylates (*E*)-**39a** (R = Me) or **40a** (R = Me), potential precursors of π-1,1-ethyleneallyl metal complexes (Scheme 5).[6,7] Alternatively, esterification of cyclopropanol (*E*)-**25** (MsCl, NEt_3), followed by desilylation (nBu_4NF/THF), produced the cyclopropyl mesylate (*E*)-**41a** (R = Ph, X = OH) in 93% yield. Esterification of (*E*)-**41a** then quantitatively afforded either the acetate (*E*)-**41b** (R = Ph, X = OAC; Ac_2O/DMAP) or the dimesylate (*E*)-**41c** (R = Ph, X = OMs; MsCl/NEt_3). Despite several attempts under various basic or acidic conditions, the esters (*E*)-**41a−c** again did not undergo any AcOH or MsOH elimination, although the formation of (*E*)-2-ethyl-1-styrylcyclopropyl mesylate [(*E*)-**39b**, R = Ph] should be favoured by phenyl ring conjugation of the expected nascent double bond (Scheme 5).



Scheme 5. Base- and acid-induced dehydrosulfonatation

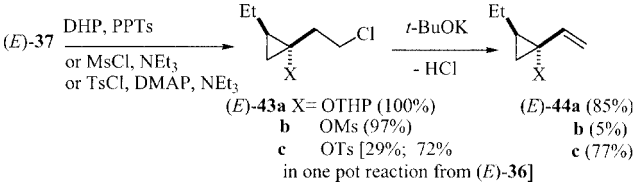
Treatment of the cyclopropanol (*E*)-**25** with carbon tetrabromide and triphenylphosphane gave 4-methyl-1-phenylhex-1-en-3-one (**42**) in 40% yield. Treatment of the dimesylate (*E*)-**41c** with lithium bromide in DMF at 40 °C for 3 h,[37] however, gave the monobromide (*E*)-**41d**, which upon treatment with *t*BuOK in DMF at 50 °C for 20 h also



Scheme 6. Ring-opening of bromomesylate

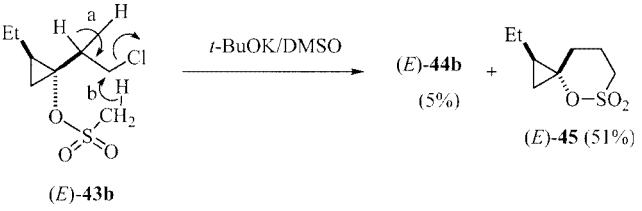
underwent ring-opening into **42** in preference to the expected elimination of BrH or MsOH to provide the regioisomeric allylic mesylates (*E*)-**39b** or **40b** (R = Ph; Schemes 5 and 6).[30]

Similarly, desilylation of (*E*)-**27** (nBu_4NF/THF) followed by double esterification (2 MsCl, NEt_3) gave the dimesylate (*E*)-**41e** (R = 2-naphthyl, X = OMs) in 70% overall yield. Subsequent attempted palladium(0)-induced {$Pd(dba)_2$, dppe} and base-induced (DBU/DMF at 60 °C) elimination of MsOH by a reported procedure[38] also failed to provide (*E*)-**39e** and **40e** (R = 2-naphthyl) (Scheme 5). *O*-Protection of (*E*)-**37** (DHP, PPTs) quantitatively furnished the tetrahydropyranyl ether (*E*)-**43a** (X = OTHP), which was then able to undergo dehydrochlorination (*t*BuOK/THF at reflux for 12 h) to afford the (*E*)-2-ethyl-2-ethenylcyclopropanol derivative **44a** (X = OTHP) in 85% yield (Scheme 7).[34]



Scheme 7. Base-induced dehydrochlorination

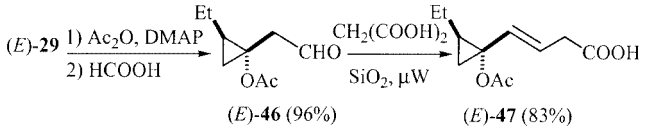
On the other hand, esterification of (*E*)-**37** (MsCl, NEt_3) gave the mesylate (*E*)-**43b** (X = OMs) in 97% yield. Upon treatment with *t*BuOK in DMSO at room temperature for 16 h, (*E*)-**43b** underwent competitive hydrochloric acid elimination to give a mixture of the allylic mesylate (*E*)-**44b** (5%) (pathway a) and of (*E*)-1-ethyl-4-oxa-5-thiaspiro[2.5]octane 5,5-dioxide (**45**, 51%) (pathway b) (Scheme 8).



Scheme 8. Base-induced cyclisation

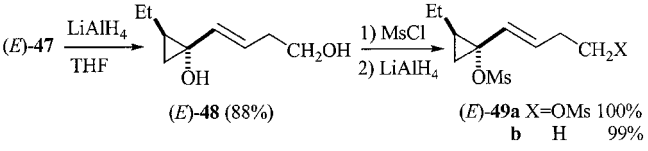
Alternatively, one-pot cyclopropanation of the β-chloro ester **36** [2.5 equiv. of *n*BuMgBr, 0.2 equiv. of $Ti(OiPr)_4$] and in situ addition of 2.5 equiv. of tosyl chloride instead of the usual aqueous acidic workup[17] directly provided (*E*)-1-(2-chloroethyl)-2-ethyl-1-tosyloxycyclopropane (**43c**), in 72% overall yield from **36**. It must be underlined that tosylation of cyclopropanol (*E*)-**37** under classical conditions (TsCl, DMAP, NEt_3 in CH_2Cl_2 at room temperature for 13 h) gave a lower yield of (*E*)-**43c** (29%). Base-induced dehydrochlorination of (*E*)-**43c** (*t*BuOK/THF at reflux for 12 h) then occurred selectively to afford, in 77% yield, *exclusively* (*E*)-1-ethenyl-2-ethylcyclopropyl tosylate [(*E*)-**44c**] (Scheme 7). Hence, the titanium-mediated cyclopropanation of commercially available and cheap ethyl 2-chloropropionate (**36**), followed by in situ tosylation and base-induced selective dehydrochlorination, allowed the problem

encountered with α,β-unsaturated esters to be overcome in two steps.[34] Alternatively, *O*-protection of (*E*)-1-(2,2-diethoxyethyl)-2-ethylcyclopropanol (**29**) (Ac_2O, DMAP, Et_2O) and cleavage of the acetal (HCOOH/pentane) provided (*E*)-2-(1-acetoxy-2-ethylcyclopropyl)acetaldehyde (**46**) in 96% overall yield. In order to provide a vinylcyclopropane moiety, the aldehyde (*E*)-**46** was then treated with a three-molar excess of malonic acid in the presence of 0.001 mol of piperidine in refluxing xylene for 2 h, by a reported procedure,[39] to produce (*E*)-4-(1-acetoxy-2-ethylcyclopropyl)but-3-enoic acid (**47**) in 40% yield. However, this modified Knoevenagel condensation was simplified, and the yield improved to 83%, when equimolar quantities of aldehyde (*E*)-**46** and malonic acid adsorbed on silica gel were subjected to microwave irradiation (300 W) at 130 °C for 15 min (Scheme 9).[40]



Scheme 9. Modified Knoevenagel condensation

Lithium aluminum hydride reduction of (*E*)-**47** in THF then provided (*E*)-1-(4-hydroxybut-1-enyl)-2-ethylcyclopropanol (**48**) in 88% yield. Double mesylation of (*E*)-**48** (2.5 MsCl, Et_3N) gave the corresponding mesylate (*E*)-**49a** (X = OMs), which upon treatment with $LiAlH_4$ (2 equivalents at 0 °C for 2 h) provided the monomesylate (*E*)-**49b** (X = H) in 99% yield (Scheme 10).[31]

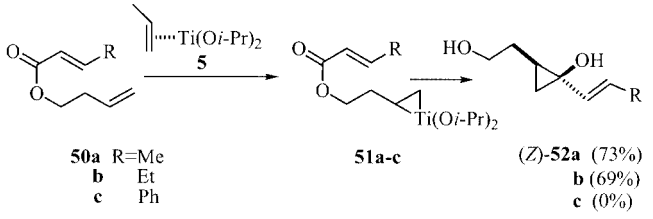


Scheme 10. Formation of (*E*)-1-vinylcyclopropyl esters

In conclusion, (*E*)-2-substituted 1-vinylcyclopropanol derivatives and their corresponding sulfonic esters, useful precursors of π-1,1-ethyleneallyl metal complexes,[6,7] were now readily available in diastereomerically pure form, from the titanium(IV)-mediated cyclopropanation of either β−halo or β,β-dialkoxyesters.

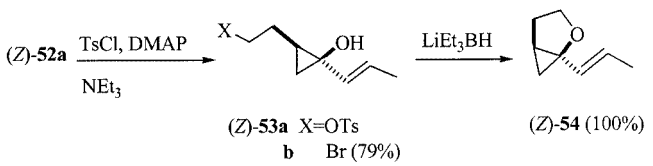
(*Z*)-Cyclopropanation of Homoallyl Alk-2-enoates

It has been shown that the coordinated propene in the (η^2-propene)Ti(O*i*Pr)$_2$ complex **5** (R′ = Me), readily formed by treatment of Ti(O*i*Pr)$_4$ with two equivalents of isopropylmagnesium halide,[17c] can be replaced by other olefinic or acetylenic moieties, either inter- or intramolecularly, sometimes more easily than in other titanium-olefin complexes.[18] Thus, homoallyl or bis-homoallyl esters, on treatment with **5** (R′ = Me), provide cyclopropanols in good yields.[41] Slow addition of an ethereal solution of *i*PrMgBr to solutions of homoallyl α,β-unsaturated esters **50a−c** (R = Me, Et, Ph) in Et_2O containing two equivalents of Ti(O*i*Pr)$_4$ at −40 °C and slow warming of the reaction mixture to room temperature gave diastereomerically pure (*Z*)-1-(prop-1-enyl)- and (*Z*)-1-(but-1-enyl)-2-(2-hydroxyethyl)cyclopropanols **52a** and **52b** in 73 and 69% yields, respectively, but under the same conditions **50c** did not afford the expected 1-styrylcyclopropanol **52c**.[43] The reactions of **50a** and **50b** probably involved the formation of the intermediate titanium complexes **51a** and **51b** (Scheme 11).[44] The notable difference in reactivity between the intermolecular reactions of esters **3a−c** (see Table 1 and Scheme 2) and the intramolecular reactions of the homoallylic esters **50a** and **50b** with the complexes **4** or **5** (Scheme 11) may be the result of protection of the conjugated double bond by the primary hydroxy groups on **52a** and **52b**, which might form complexes with the titanium catalyst more easily than the tertiary hydroxy group on the cyclopropane ring, thus removing the titanium away from the double bond. The failure of the formation of **52c** by this reaction may then be explained by the higher reactivity of the styryl double bond in the formation of titanium complexes. It has previously been reported that homoallyl alcohols were hydroxycyclopropanated with esters by **4** or **5** much more readily than usual alkenes.[17f]



Scheme 11. Intramolecular titanium-mediated cyclopropanation of homoallyl α,β-unsaturated esters

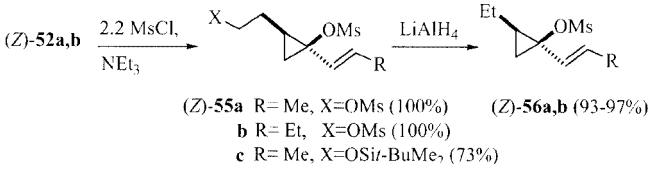
Treatment of the diol (*Z*)-**52a** with tosyl chloride (DMAP, NEt_3, CH_2Cl_2) regioselectively provided the monotosylate (*Z*)-**53a** (X = OTs), which upon treatment with lithium bromide afforded the bromoalcohol (*Z*)-**53b** (X = Br), in 79% overall yield. Lithium triethylborohydride ($LiEt_3BH$) reduction both of the tosylate (*Z*)-**53a** and of the bromide (*Z*)-**53b** quantitatively gave the 2-oxa-1-(1-propenyl)bicyclo[3.1]hexane (**54**), therefore confirming the *Z* stereochemistry of the diol **52a** (i.e., the *cis* relationship between the 1-hydroxy and 2-hydroxyethyl substituents) (Scheme 12).



Scheme 12. Confirmation of the *Z* configuration of 2-(2-hydroxyethyl)-1-(1-propenyl)cyclopropanol

On the other hand, treatment of diols (*Z*)-**52a** and (*Z*)-**52b** with 2.2 equivalents of mesyl chloride quantitatively gave the dimesylates (*Z*)-**55a** and (*Z*)-**55b** (X = OMs), which then underwent selective lithium aluminum hydride

reduction to yield the (*Z*)-1-(prop-1-enyl)- and the (*Z*)-1-(but-1-enyl)-2-ethylcyclopropyl mesylates **56a** and **56b** (93−97%). Alternatively, regioselective *O*-silylation of the diol (*Z*)-**52a** (TBDMSCl, imidazole, DMF) and subsequent mesylation (MsCl, NEt_3) furnished the mesylate (*Z*)-**55c** (R = Me, X = OSi-*t*BuMe$_2$) in 73% overall yield (Scheme 13).



Scheme 13. Formation of (*Z*)-1-vinylcyclopropyl esters

Therefore, while the catalytic titanium-mediated cyclopropanation of β-halo-esters followed by base-induced dehydrohalogenation (vide supra) opens a new route to (*E*)-2-substituted-1-vinylcyclopropanols, the complementary synthesis of their *Z* diastereomers can be achieved by the stoichiometric titanium-mediated cyclopropanation of conjugated homoallyl esters. In view of the fact that the corresponding sulfonic esters of these 1-vinylcyclopropanols allow the ready preparation of π-1,1-ethyleneallyl metal complexes of significant synthetic potential, the usefulness of these two strategies is obvious.

Attempted Asymmetric Syntheses of (*E*)- and (*Z*)-2-Substituted 1-Vinylcyclopropanols

The use of titanium chiral ligands such as (4*R*,5*R*)-2,2-(diethyl)-α,α,α′,α′-tetrakis[3.5-bis(trifluoromethyl)phenyl]-1,3-dioxolane-4,5-dimethanol has been reported to afford [from ethyl acetate and (2-phenylethyl)magnesium bromide] (1*S*)-methyl-(2*R*)-phenylcyclopropanol in 65−72% yield with 70−78% enantioselectivity.[28] However, an attempted cyclopropanation of ethyl 2-chloropropionate **36** by *n*BuMgBr in the presence of Ti(TADDOL)$_2$, [generated by mixing Ti(O*i*Pr)$_4$ and 2 equivalents of (*R*)-2,2-α,α,α′,α′-tetraphenyl-2,2-dimethyl-1,3-dioxolane-4,5-dimethanol[45]] indeed gave the expected cyclopropanol (*E*)-**37** (Table 2, entry 13) in 52% enantiomeric excess, as determined by ^{1}H and ^{19}F NMR analysis of the corresponding Mosher (MTPA) ester, but in low yield (6%). Use of various reaction conditions (higher or lower temperatures), addition of molecular sieves,[46] or use of other chiral ligands such as BINOL,[47] BINOL/TADDOL,[48] or (*S*)-1,3-butanediol[49] did not significantly improve the cyclopropanation yield and enantioselectivity. Thus, for instance, the use of (*S*)-1,3-butanediol as the titanium ligand[49] provided (*E*)-**37** in 44% yield but in only 6% *ee*.

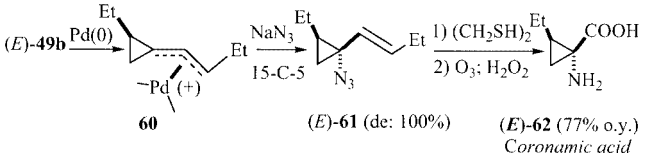
On the other hand, asymmetric β−chloroesters such as the (1*R*,2*S*,5*R*)-menthyl-3-chloropropionate (**57**) [from (−)-menthol and 3-chloropropanoic acid esterification] failed to undergo cyclopropanation to give the chiral cyclopropanol (*E*)-**37** (Table 2, entry 14), although the methyl (2*S*)-3-chloro-2-methylpropionate (**58**) [from chlorination of commercially available methyl (2*S*)-3-hydroxy-2-methylpropionate], upon treatment with 2.5 *n*BuMgBr/0.2 Ti(O*i*Pr)$_4$, provided a 24% yield of an inseparable 1:1 diastereomeric mixture of (*E*)- and (*Z*)-1-[(1*R*)-2-chloro-1-methylethyl]-2-ethylcyclopropanol **59** (entry 15). These reactions most probably suffered from steric repulsion between the hindered ester moieties of **57** and of (2*S*-)-**58** and the R′ substituent of the Grignard reagent **6b**, as pointed out recently.[49]

Otherwise, treatment of the homoallyl ester **50b** with 4 equivalents of *i*PrMgBr and 2 equivalents of Ti(TADDOL)$_2$[45] provided the cyclopropanol (*Z*)-**52b** in only 20% yield (see Scheme 11 for comparison) and in 22% enantiomeric excess, also determined by ^{1}H and ^{19}F NMR analysis of its Mosher ester. Attempted asymmetric hydroxycyclopropanations with other titanium chiral ligands such as BINOL[47] were also ineffective.

Applications: Diastereoselective Syntheses of (*E*)- or (*Z*)-2-Alkyl-2,3-methanoamino Acids

Considerable effort has been, and currently still is, devoted towards the synthesis of 1-aminocyclopropanecarboxylic acids (“2,3-methanoamino acids”), due to their physiological importance.[13,50] They not only provide enzyme inhibitors and biological probes for mechanistic studies and allow the design of new drugs, but their incorporation into peptide chains affords conformationally constrained peptidomimetics with enhanced biological activities and stabilities (reduced proteolytic degradation).[13] Among the different methodologies recently reported for the total synthesis of these α-amino acids,[13,50] the selective reaction of organometallic species, generated from 1-vinylcyclopropanol sulfonic esters,[6] has shown high efficiency. Thus, palladium(0)-catalysed [Pd(dba)$_2$, 2 PPh$_3$] azidation (N_3Na, 10% [15]-crown-5 ether)[51] of the allylic mesylate (*E*)-**49b** took place through the π-1,1-ethyleneallyl palladium complex **60**,[6] with complete retention of configuration,[10] to give the single 1-(but-1-enyl)-2-ethylcyclopropyl azide [(*E*)-**61**, *de*: 100%], in 86% yield, as determined by ^{1}H, ^{13}C, and 2D-NOESY NMR analysis.

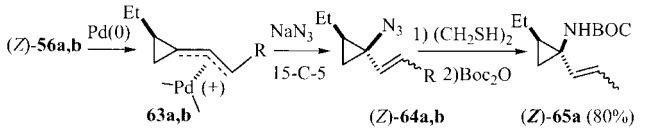
Simple azide reduction (1,3-propanedithiol, NEt_3/MeOH) followed by double bond oxidative cleavage (O_3/H_2O_2, HCOOH, aq. H_2O_2)[52] then afforded the diastereomerically pure coronamic acid [(*E*)-**62**][53] in 77% overall yield, (Scheme 14)



Scheme 14. Synthesis of (*E*)-2,3-methanoamino acids

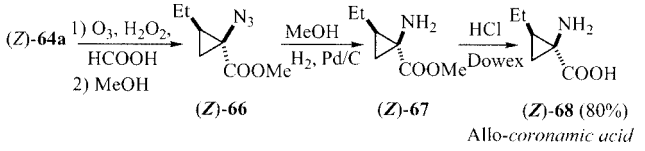
Although the cyclopropanation of the chiral ester **30**, derived from (*S*)-malate, was unfortunately not sufficiently diastereoselective (Table 2, entry 10) to achieve a convenient asymmetric synthesis of coronamic acid [(*E*)-**62**], it must, however, be underlined that resolution of such 2,3-me-

thanoamino acids should be achievable by simple enzymic or chemical methods.[54] [For a recent asymmetric synthesis of natural (*E*)-2,3-methanoamino acids involving π-allyl palladium complexes, cf. ref.[53]]. On the other hand, similar Pd^0-catalysed azidation (NaN_3, [15]-crown-5 ether) of the allylic mesylates (*Z*)-**56a** and (*Z*)-**56b**, which probably took place by way of the π-allyl palladium complexes **63a** and **63b**, afforded the 2-ethyl-1-(prop-1-enyl)- and 1-(but-1-enyl)-2-ethylcyclopropyl azides (*Z*)-**64a** and (*Z*)-**64b**, respectively, which, being extremely volatile, were used crude for the following steps (Scheme 15). In fact, ^1H NMR analysis of both isolated azides (*Z*)-**64a** and (*Z*)-**64b** revealed the formation of 75:25 mixtures of *trans*- and *cis*-1-(1-alkenyl)-2-ethylcyclopropylazides (e.g. dd at δ = 5.32 ppm, *J* = 15.3, 1.1 Hz and dd at δ = 5.51 ppm, *J* = 10.5, 1.1 Hz for (*Z*)-**64a**; ddd at δ = 5.28 ppm, *J* = 15.3, 1.4 Hz and d at δ = 5.48 ppm, *J* = 10.7 Hz for (*Z*)-**64b**). Reduction [$HS(CH_2)_3SH$, NEt_3/MeOH] of (*Z*)-**64a**, for instance, gave the corresponding cyclopropylamine, which, also being highly volatile, was directly transformed into the carbamate derivative (*Z*)-**65a** (Boc_2O, KOH/*t*BuOH, H_2O) in 80% overall yield. However, oxidative cleavage ($RuCl_3$/$NaIO_4$) of the prop-1-enylic double bond of (*Z*)-**65a** did not furnish the corresponding cyclopropanecarboxylic acid as reported from (1*R*,2*S*)-2-methyl-1-styrylcyclopropylamine,[10] but gave (*Z*)-*N*-*tert*-butyloxycarbonyl-2-ethylcyclopropanecarboxaldehyde in 97% yield, as recently observed for oxidation of such propenyl derivatives (Scheme 15).[55]



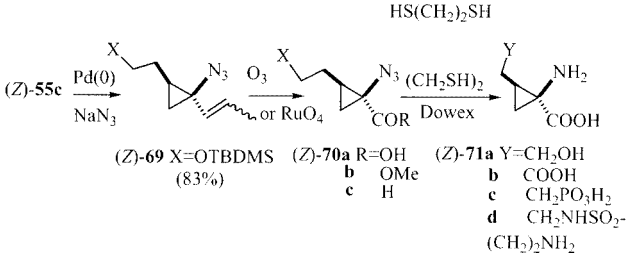
Scheme 15. Synthesis of (*Z*)-1-vinylcyclopropylamines

In order to avoid the formation of volatile cyclopropylamines, the cyclopropylazide (*Z*)-**64a** could first be subjected to selective ozonolysis (O_3, AcOH, HCO_2H; aq. H_2O_2)[52] and esterification (MeOH) to make purification easier, to give the corresponding azido ester (*Z*)-**66**. Azide reduction (H_2, Pd/C)[56] quantitatively afforded the amino ester (*Z*)-**67**. Finally, acidic hydrolysis (6 N HCl) and ion-exchange chromatography (Dowex 50WX 18) afforded an 80% yield of the diastereomerically pure *allo-coronamic acid* [(*Z*)-**68**], which is converted into 1-butene by plant tissues, allowing plant growth and fruit ripening control (Scheme 16).[13]



Scheme 16. Synthesis of (*Z*)-2,3-*allo*-coronamic acid

Alternatively, Pd^0-catalysed azidation of (*Z*)-**55c** (NaN_3, [15]-crown-5 ether) gave an 83% yield of a 75:25 mixture of *trans*- (dd at δ = 5.30 ppm, *J* = 15.1, 1.5 Hz) and *cis*-2-(2-*tert*-butyldimethylsiloxyethyl)-1-(prop-1-enyl)cyclopropylazide [(*Z*)-**69**; dd at δ = 5.95 ppm, *J* = 10.3, 1.5 Hz]. Subsequent acidic ozonolysis (O_3, HCO_2H, AcOH; aq. H_2O_2, O °C)[52] of (*Z*)-**69** produced a 78% yield of the single (*Z*)-azido acid **70a** (R=OH), while basic ozonolysis (O_3, NaOH, MeOH/CH_2Cl_2, 78 °C),[57] on the other hand, gave an 80% yield of a 84:16 mixture of azido esters (*Z*)- and (*E*)-**70b** (R = OMe). However, RuO_4-mediated ($RuCl_3$, $NaIO_4$) double bond cleavage of (*Z*)-**69** produced the corresponding cyclopropanecarboxaldehyde (*Z*)-**70c** (R = H),[55] which upon further oxidation ($NaClO_2$, NaH_2PO_4, *t*BuOH, 2-methylbut-2-ene)[58] also furnished the azido acid (*Z*)-**70a** in 85% yield. Finally, reduction of cyclopropylazide (*Z*)-**70a** [$HS(CH_2)_3SH$, NEt_3/MeOH][59] and ion-exchange chromatography provided the (*Z*)-*methanobishomo serine* **71a** (Y = CH_2OH).[24a,60] Other known 2,3-methanoamino acids of biological interest[13] are now available by this diastereoselective procedure: for instance, the (*Z*)-*2,3-methanoglutamic acid* **71b** (Y = COOH), a potential agonist of metabotropic glutamate receptors (mGLuRs),[61] the cyclopropyl analogue of 2-amino-5-phosphono pentanoic acid (*Z*)-**71c** (Y = $CH_2PO_3H_2$), assessed as a competitive antagonist for the *N*-methyl-D-aspartate (NMDA) receptor[62] and (*Z*)-**71d** (Y = $CH_2NHSO_2CH_2CH_2NH_2$), used to prepare thermally stable peptide table salt substitutes[63] (Scheme 17).



Scheme 17. Synthesis of (*Z*)-methanoamino acids

In conclusion, the use of titanium-mediated cyclopropanation for the diastereoselective preparation of (*E*)- and (*Z*)-2-substituted-1-vinyl cyclopropanols described here appeared to be competitive with the previously reported approaches. To perform the total asymmetric syntheses of these attractive synthons with useful yields and enantiomeric excesses, however, still requires improvements.

Experimental Section

General Remarks: Melting points (uncorrected) were determined with a Mettler FP51 apparatus. FT-IR: Perkin−Elmer spectrophotometer. ^1H NMR: Bruker AM 250 (250 MHz), AC 250 (250 MHz), and AC 200 (200 MHz): δ = 7.27 for $CHCCl_3$. ^{13}C NMR: Bruker AM 250 and AC 250 (63 MHz), AC 200 (50 MHz): δ = 77 for $CDCl_3$, the NMR spectroscopic data are reported as δ values (ppm) relative to TMS. The DEPT-135 pulse was used for the determination of signal types. MS: Nermag R-10 coupled with a OKI DP 125 gas chromatograph. Relative percentages are shown in brackets; high-resolution mass spectra were recorded with a Fin-

nigan MAT 95S. Elemental analyses were performed with a Perkin−Elmer 240 C analyzer by the Service de Microanalyse, Institut de Chimie des Substances Naturelles, Gif-sur-Yvette (France). Preparative column chromatography was performed on SDS normal silica gel (70−230 mesh), on SDS flash silica gel (35−70 mesh) or on Fluka neutral alumina 507c (100−200 mesh). Microwave experiments were performed on a monomode Prolabo Synthewave 402 oven. Solvents were dried by standard procedures. All reactions requiring anhydrous conditions were performed under argon. All Grignard reagents were generated from the corresponding alkyl halides by standard laboratory procedures.

General Procedure for the Cyclopropanation of α,β-Unsaturated Esters: A solution of the alkylmagnesium bromide (2.5 equiv. 25 mmol in diethyl ether) was added dropwise over one hour at room temperature to a solution of the conjugated esters **3a−c** (10 mmol) and titanium tetraisopropoxide (0.2 equiv.) in 25 mL of anhydrous THF; the solution turned brown immediately. After stirring for one hour, the reaction mixture was cooled to 0 °C, and 75 mL of diethyl ether and 10 mL of water were added, to give a white precipitate, which was filtered off through a plug of Celite. The aqueous phase was extracted three times with 50 mL of diethyl ether. The combined organic extracts were dried with anhydrous Na_2SO_4. After evaporation of the solvents the residue was purified by flash chromatography on silica gel (eluent dichloromethane) to give the 1-(alk-1-enyl)cyclopropanols **7a−9b** in 11−26% yields.

1-Ethenylcyclopropanol (7a): Colourless oil, 92.4 mg (11% yield). Spectroscopic data (IR, NMR, Mass) were in total agreement with those reported.[59]

1-(Pent-1-enyl)cyclopropanol (8a): Colourless oil, 328 mg (26% yield). IR (neat): ν(CO) = 3326 cm^{-1}, 3087, 3006, 2958, 2929, 2872, 1463, 1378, 1291, 1014, 965. ^1H NMR (250 MHz, $CDCl_3$): δ = 5.68 (dt, *J* = 15.1, 6.8 Hz, 1 H), 5.27 (d, *J* = 15.1 Hz, 1 H), 2.09−1.98 (m, 2 H), 1.60−1.03 (m, 3 H), 1.00 (dd, *J* = 7.3, 4.9 Hz, 2 H), 0.91 (t, *J* = 7.3 Hz, 3 H), 0.68 (dd, *J* = 7.3, 4.9 Hz, 2 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 133.7, 126.7, 54.1, 34.1, 22.4, 15.2, 13.4 ppm. MS (EI): *m*/*z* = 126 (0.6) [M^+], 97 (15), 83 (100), 69 (15), 57 (16), 55 (74), 43 (40), 41 (55), 39 (35) ppm. MS (DCI, NH_3): *m*/*z* = 144 (100) [M^+ + 18], 127 (85) [M^+ + 1]. HRMS: found 126.1053, $C_8H_{14}O$ requires 126.1045.

(*E*)-2-Ethyl-1-(pent-1-enyl)cyclopropanol (8b): Yellow oil, 160 mg (15% yield). R_f = 0.25 (eluent pentane/diethyl ether, 3:1). ^1H NMR (200 MHz, $CDCl_3$): δ = 5.73 (dt, *J* = 15.5, 6.8 Hz, 1 H), 5.44 (d, *J* = 15.4 Hz, 1 H), 2.07 (dq, *J* = 7, 1 Hz, 2 H), 1.99 (s, 1 H), 1.51−1.36 (m, 2 H), 1.33−1.12 (m, 3 H), 1.07−1.02 (m, 1 H), 0.93 (t, *J* = 7.2 Hz, 6 H), 0.46 (dd, *J* = 6, 5 Hz, 1 H) ppm. MS (EI): *m*/*z* = 154 (0.6) [M^+], 111 (34) [M^+ − Pr], 97 (12), 83 (36), 69 (15), 55 (100), 54 (34), 43 (39), 41 (46), 39 (25). MS (DCI, NH_3): *m*/*z* = 172 (23) [M^+ + 18], 171 (17) [M^+ + 17], 155 (100) [M^+ + 1]. HRMS: found 154.1361, $C_{10}H_{18}O$ requires 154.1357.

1-Styrylcyclopropanol (9a): Colourless oil, 400 mg (25% yield). Spectroscopic data (IR, NMR, Mass) were in total agreement with those reported.[21]

(*E*)-2-Ethyl-1-(2-phenylethynyl)cyclopropanol (11): Colourless oil, 66 mg (15% yield). R_f = 0.4 (eluent pentane/diethyl ether, 3:1). ^1H NMR (250 MHz, $CDCl_3$): δ = 7.43−7.18 (m, 5 H), 2.21 (s, 1 H), 1.77−1.50 (m, 2 H), 1.35−1.19 (m, 2 H), 1.08 (t, *J* = 7.4 Hz, 3 H), 0.78−0.74 (m, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 131.5, 128.2, 128, 123, 92, 81.8, 48.8, 30, 22.5, 20.6, 13.8 ppm. MS (EI): *m*/*z* = 187 (4) [M^+ + 1], 186 (27) [M^+], 158 (15), 157 (100), 156 (37), 129 (56), 128 (30), 115 (20), 102 (14), 75 (15), 55 (37). HRMS: found 186.1047, $C_{13}H_{14}O$ requires 186.1044.

1-Styryl-1-(tosyloxy)cyclopropane (9b): Colourless oil prepared from cyclopropanone hemiacetal **14**, by a reported procedure, giving 184 mg (90% yield).[6a] Spectroscopic data (IR, NMR, Mass) were in total agreement with those reported.[6a]

2-(Phenylethylidene)cyclopropane (15): Colourless oil prepared from 1-styryl-1-(tosyloxy)cyclopropane (**9b**), by a reported procedure, giving 137 mg (95% yield).[6a] Spectroscopic data (IR, NMR, Mass) were in agreement with those reported.[6a]

(*E*)-2-Ethyl-1-[2-(tetrahydropyran-2-yloxy)propyl]cyclopropanol (23): Yellow oil, 372 mg (65% yield). Purification by chromatography on silica gel (eluent pentane/diethyl ether, 9:1).

First Diastereomer: R_f = 0.43 (eluent pentane/diethyl ether, 1:1). ^1H NMR (250 MHz, $CDCl_3$): δ = 4.72−4.65 (m, 1 H), 4.37 (s, 1 H), 4.27−4.13 (m, 1 H), 3.58−3.45 (m, 2 H), 2.00 (dd, *J* = 12, 7 Hz, 1 H), 1.84−1.68 (m, 4 H), 1.63−1.50 (m, 6 H), 1.47−1.30 (m, 1 H), 1.18 (d, *J* = 7.0 Hz, 3 H), 0.99 (d, *J* = 6.6 Hz, 3 H), 0.92−0.80 (m, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 97.2, 96.7, 71.5, 70.9, 63.6, 63.4, 57.6, 56.5, 40.5, 39.8, 31, 30.9, 26.8, 25.7, 25, 22.9, 22.8, 20.4, 20.3, 19.8, 19.7, 18.2, 13.7, 13.5 ppm. MS (EI): *m*/*z* = 229 (0.1) [M^+ + 1], 85 (100), 84 (23), 67 (18), 57 (22), 55 (28), 43 (28), 42 (23), 41 (34). MS (DCI): *m*/*z* = 246 (6) [M^+ + 18], 229 (10), 162 (100), 161 (46), 145 (47), 144 (26).

Second Diastereomer: R_f = 0.33 (eluent pentane/diethyl ether, 1:1). ^1H NMR (250 MHz, $CDCl_3$): δ = 4.86−4.78 (m, 1 H), 4.23−4.11 (m, 1 H), 3.93 (s, 1 H), 3.59−3.49 (m, 2 H), 1.92 (dd, *J* = 16, 4 Hz, 1 H), 1.84−1.64 (m, 4 H), 1.64−1.50 (m, 6 H), 1.50−1.40 (m, 1 H), 1.33 (d, *J* = 6.6 Hz, 3 H), 1.00 (d, *J* = 5.5 Hz, 3 H), 0.92−0.85 (m, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 99.4, 98.9, 75.8, 74, 62.5, 57.9, 57, 39.6, 39.4, 31.2, 30.9, 26.3, 25.7, 25.2, 22.9, 22, 19.6, 19.2, 18.3, 13.7, 13.6 ppm. MS (EI): *m*/*z* = 228 (0.1) [M^+], 86 (100), 85 (12), 68 (19), 58 (23), 57 (18), 44 (27), 42 (26).

(*E*)-1-[2-(*tert*-Butyldimethylsiloxy)-2-phenylethyl]-2-ethylcyclopropanol (25): Colourless oil, 489 mg (54% yield). Purification by chromatography on silica gel (eluent pentane/diethyl ether, 95:5) furnished two diastereomers (ratio 1:1).

First Diastereomer: R_f = 0.57 (eluent pentane/diethyl ether, 3:1). ^1H NMR (250 MHz, $CDCl_3$): δ = 7.36−7.26 (m, 5 H), 4.97 (d, *J* = 4.1 Hz, 1 H), 4.17 (s, 1 H), 2.38 (dd, *J* = 12, 1.5 Hz, 1 H), 1.49 (d, *J* = 4.0 Hz, 1 H), 1.16−0.98 (m, 2 H), 0.95−0.85 (m, 5 H), 0.85 (s, 9 H), 0.12 (dd, *J* = 7, 6 Hz, 1 H), 0.07 (s, 3 H), −0.23 (s, 3 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 144.6, 128.2, 127.4, 126, 125.9, 77, 58.9, 42.9, 26.2, 25.6, 22.8, 18.1, 17.8, 13.6, −4.6, −5.2 ppm. MS (EI): *m*/*z* = 305 [M^+ − 15], 263 (14), 221 (42), 181 (14), 171 (10), 129 (11), 104 (53), 91 (20), 75 (100), 74 (14), 73 (77), 55 (12). MS (DCI, NH_3): *m*/*z* = 338 (1.5) [M^+ + 18], 321 (35) [M^+ + 1], 262 (100), 263 (30), 222 (27), 221 (73), 207 (28), 206 (89), 190 (27), 189 (100), 188 (25), 172 (16), 171 (64), 132 (13). $C_{19}H_{32}O_2Si$ (320.22): calcd. C 71.19, H 10.06; found C 71.25, H 10.06.

Second Diastereomer: R_f = 0.48 (eluent pentane/diethyl ether, 3:1). IR (neat): ν(CO) = 3445 cm^{-1}, 2957, 2929, 2858, 1472, 1463, 1453, 1257, 1205, 1086, 1086, 836, 778, 699. ^1H NMR (250 MHz, $CDCl_3$): δ = 7.33−7.27 (m, 5 H), 5.10 (d, *J* = 4.0 Hz, 1 H), 4.01 (s, 1 H), 2.07 (d, *J* = 7.6 Hz, 1 H), 1.99 (d, *J* = 4.0 Hz, 1 H), 1.01−0.90 (m, 7 H), 0.92 (s, 9 H), 0.74 (dd, *J* = 7, 5.5 Hz, 1 H), 0.10 (s, 3 H), −0.16 (s, 3 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 144.5, 128, 127.2, 125.7, 125.5, 75.7, 57.8, 43.3, 25.8, 25.7, 23,

18.9, 17.8, 13.8, −4.7, −5.3. $C_{19}H_{32}O_2Si$ (320.22): calcd. C 71.19, H 10.06; found C 71.33, H 10.14.

(*E*)-1-[2-(*tert*-Butyldimethylsiloxy)-2-naphthylethyl]-2-ethylcyclopropanol (27): Pale yellow oil, 158 mg (60% yield). R_f = 0.50 (eluent pentane/diethyl ether, 3:1). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.87−7.47 (m, 14 H), 5.27 (dd, *J* = 7.3, 3 Hz, 1 H), 5.15 (dd, *J* = 10, 3.4 Hz, 1 H), 4.17 (s, 1 H), 4.05 (s, 1 H), 2.47 (dd, *J* = 16, 6.5 Hz, 1 H), 2.10 (m, 2 H), 0.94 (s, 3 H), 0.93 (s, 9 H), 1.00−0.87 (m, 14 H), 0.12 (s, 3 H), 0.10 (s, 3 H), 0.18−0.08 (m, 2 H), 0.16 (s, 3 H), −0.28 (s, 3 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 142.2, 133.1, 132.9, 128.2, 127.8, 127.7, 126.1, 125.8, 124.5, 124.9, 77.2, 59.1, 43.1, 26.3, 25.8, 22.9, 18.4, 17.9, 13.7, −4.3, −5 ppm. MS (EI): *m*/*z* = 313 (89) [M^+ − 57], 157 (100), 76 (41), 75 (96), 73 (28). MS (DCI, NH_3): *m*/*z* = 371 (5) [M^+ + 1], 313 (28), 256 (72), 240 (33), 239 (100).

(*E*)-1-(2,2-Diethoxyethyl)-2-ethylcyclopropanol (29): Colourless oil, 1.86 g (92% yield), purified by chromatography on silica gel (eluent pentane/diethyl ether, 3:1) or by distillation; b.p. 58−62 °C/mm. R_f = 0.45 (eluent pentane/diethyl ether, 3:1). IR (neat): ν(CO) = 3445 cm^{-1}, 2974, 2930, 2973, 1455, 1374, 1270, 1197, 1163, 1128, 1060, 935. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 4.79 (dd, *J* = 6.7, 5.2 Hz, 1 H), 3.90−3.45 (m, 4 H), 2.11 (dd, *J* = 14.6, 5.2 Hz, 1 H), 1.76 (dd, *J* = 14.6, 5.2 Hz, 1 H), 1.30−1.50 (m, 3 H), 1.24 (t, *J* = 7.0 Hz, 6 H), 1.30−1.0 (m, 1 H), 0.98 (t, *J* = 6.7 Hz, 3 H), 0.92−0.78 (m, 1 H), 0.08 (dd, *J* = 5.8 Hz, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 103.1, 61.8, 61.4, 56.4, 36.6, 25.9, 22.9, 18.2, 15.2, 13.7 ppm. MS (EI): *m*/*z* = 128 (11) [M^+ − 74], 127 (23), 113 (11), 111 (37), 110 (13), 103 (16), 85 (22), 83 (18), 82 (14), 75 (53), 73 (16), 72 (100), 71 (30), 57 (20), 56 (96), 55 (62), 53 (10), 47 (68), 45 (16), 44 (53), 43 (67), 42 (11), 41 (36), 39 (14). MS (DCI, NH_3): *m*/*z* = 220 (1) [M^+ + 18], 174 (14), 157 (11), 128 (100), 127 (38). HRMS: found 202.1571, $C_{11}H_{22}O_3$ requires 202.1569.

(*E*)-1-(2-Bromoethyl)-2-ethylcyclopropanol (35): Yellow oil, 827 mg (48% yield). R_f = 0.41 (eluent pentane/diethyl ether, 8:2). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.65 (dd, *J* = 6.0 Hz, 2 H), 2.32 (dt, *J* = 14, 6.9 Hz, 1 H), 2.00 (dt, *J* = 14, 7.3 Hz, 1 H), 1.45 (m, 2 H), 1.34−0.81 (m, 5 H), 0.21 (dd, *J* = 6.0 Hz, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 57.8, 37.4, 30.0, 27.6, 19.5, 13.8 ppm.

(*E*)-1-(2-Chloroethyl)-2-ethylcyclopropanol (37): Yellow oil, 1.76 g (65% yield). R_f = 0.40 (eluent pentane/diethyl ether, 3:1). IR (neat): ν(CO) = 3339.5 cm^{-1}, 3072.6, 2995, 2962, 2932, 2872. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.83 (dd, *J* = 6.0 Hz, 2 H), 2.20 (dt, *J* = 14.3, 6.8 Hz, 1 H), 1.95 (dt, *J* = 14.3, 7.3 Hz, 1 H), 1.45 (m, 2 H), 1.38−0.82 (m, 5 H), 0.21 (dd, *J* = 6.0 Hz, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 57.4, 42.1, 37.1, 27.3, 22.8, 19.2, 13.7 ppm. MS (EI): *m*/*z* = 149 (12), 147 (44), 119 (11), 93 (35), 91 (100), 75 [(12), 63 (65), 57 (48), 43 (75 (41), 414 (29). HRMS (M + Na): found 171.05525, $C_7H_{13}NaOCl$ requires 171.05527.

(*E*)-2-Ethyl-1-mesyloxy-1-(2-mesyloxypropyl)cyclopropane (38): A solution of cyclopropanol (*E*)-**23** (150 mg, 0.66 mmol) in methanol (6 mL) containing PPTS (0.1 equivalent) was heated at 40−45 °C for 3 h. After cooling to room temperature and evaporation of the solvent in vacuo, the residue was dissolved in diethyl ether (20 mL) and then washed with half-saturated brine and dried with anhydrous Na_2SO_4. The solvent was removed in vacuo to give crude 2-ethyl-1-(2-hydroxypropyl)cyclopropanol, which was purified by chromatography on silica gel (eluent dichloromethane/diethyl ether, 7:3). Colourless oil, 237 mg (85% yield). R_f = 0.21 (eluent dichloromethane/diethyl ether, 3:1). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 4.33−4.13 (m, 2 H), 3.02 (s, 2 H), 2.53 (s, 2 H), 2.09−1.68 (m, 4 H), 1.63−1.48 (m, 4 H), 1.25 (d, *J* = 6.3 Hz, 6 H), 1.06−0.83 (m, 10 H), 0.19−0.06 (m, 2 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 68.9, 68.1, 59.4, 58.3, 41.6, 40.9, 27.2, 26.6, 24, 23.7, 22.9, 22.9, 19.5, 18.4, 13.8, 13.8 ppm. MS (EI): *m*/*z* = 144 (1.1) [M^+], 87 (32), 57 (53), 45 (55), 43 (100), 42 (23), 41 (25). MS (DCI, NH_3): *m*/*z* = 162 (61) [M^+ + 18], 145 (56) [M^+], 127 (97), 126 (33), 118 (22).

Methanesulfonyl chloride (0.4 mL, 4.95 mmol, 2.2 equiv.) was added dropwise at 0 °C to a solution of this diol (325 mg, 2.25 mmol) in diethyl ether (30 mL), containing triethylamine (1 mL, 3 equiv.). The reaction was over within 2 h, as determined by thin layer chromatography; the mixture was then allowed to warm to room temperature, and diethyl ether (10 mL) and water (2 mL) were added. The aqueous phase was extracted twice with 5 mL of diethyl ether; the combined organic phases were successively washed with 0.5 N hydrochloric acid (2 × 2 mL), saturated $NaHCO_3$ solution (2 mL), and brine (2 mL), and dried with anhydrous $MgSO_4$. The solvent was removed in vacuo, and chromatography of the residue (eluent dichloromethane/diethyl ether, 85:15) gave the dimesylate **38** as an orange-yellow oil (480 mg, 71% yield). R_f = 0.60 (eluent dichloromethane/diethyl ether, 3:1). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 5.20−5.12 (m, 2 H), 3.04 (s, 6 H), 3.02 (s, 6 H), 2.66−2.57 (m, 2 H), 1.89 (dd, *J* = 15, 6.6 Hz, 1 H), 1.79 (dd, *J* = 15.2, 8.7 Hz, 1 H), 1.55 (dd, *J* = 6.3, 3 Hz, 6 H), 1.44−1.30 (m, 4 H), 1.28−1.24 (m, 4 H), 1.06 (t, *J* = 7.1 Hz, 6 H), 0.53 (t, *J* = 6.8 Hz, 1 H), 0.40 (t, *J* = 6.8 Hz, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 66.6, 66.4, 53.4, 39.8, 38.6, 36.4, 29.5, 25.6, 24.3, 22, 21.4, 17.6, 17.2, 13.2, 13.1 ppm. MS (EI): *m*/*z* = 221 (0.6) [M^+ − 79], 175 (19), 109 (12), 93 (23), 83 (42), 79 (40), 69 (100), 67 (21), 55 (53), 43 (27), 42 (20), 41 (38). MS (DCI, NH_3): *m*/*z* = 319 (19) [M^+ + 19], 318 (100) [M^+ + 18], 317 (14), 222 (7).

(*E*)-2-Ethyl-1-[2-hydroxy-2-phenylethyl]-1-mesyloxycyclopropane (41a): By the mesylation procedure used to obtain (*E*)-**38**, methanesulfonyl chloride (115 μL, 1.48 mmol, 1.5 equiv.) was added to a solution of cyclopropanol (*E*)-**25** (315 mg, 0.984 mmol) in diethyl ether (25 mL) containing triethylamine (0.4 mL, 2.95 mmol, 3 equiv.). When the reaction was complete as determined by thin layer chromatography, the usual workup gave 390 mg (100% yield) of (*E*)-1-[2-(*tert*-butyldimethylsiloxy)-2-phenylethyl]-2-ethyl-1-mesyloxycyclopropane as an orange oil. R_f = 0.36 (eluent pentane/diethyl ether, 3:1). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.39−7.31 (m, 10 H), 4.15−4.10 (d, *J* = 3.0 Hz, 2 H), 2.94 (s, 6 H), 1.65 (dd, *J* = 12, 7 Hz, 2 H), 1.42 (d, *J* = 9.0 Hz, 2 H), 1.26−1.17 (m, 8 H), 0.98 (t, *J* = 9.0 Hz, 6 H), 0.89 (s, 18 H), 0.61 (dd, *J* = 9, 0.70 Hz, 2 H), 0.70 (s, 6 H), −0.17 (s, 6 H) ppm. MS (DCI, NH_3): *m*/*z* = 416 (1) [M^+ + 18], 399 (2) [M^+ + 1], 284 (42), 283 (20), 221 (22), 188 (17), 171 (100), 170 (31).

A solution of tetra-*n*-butylammonium fluoride in THF (1 M, 2.2 mL, 2.205 mmol, 2.5 equiv.) was added dropwise under argon to a solution of the obtained cyclopropyl mesylate (390 mg, 0.98 mmol) in tetrahydrofuran (10 mL). The mixture was stirred overnight at room temperature, the solvent was removed in vacuo, and 35 mL of diethyl ether were added to the residue. The organic phase was washed with 6 mL of brine, dried with anhydrous Na_2SO_4, and concentrated in vacuo. Chromatography on silica gel (eluent pentane/diethyl ether, 50:50) gave 259 mg (93% yield) of (*E*)-**41a** as a pale yellow oil. R_f = 0.18 (eluent pentane/diethyl ether, 1:1). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.45−7.28 (m, 10 H), 5.15−5.03 (m, 2 H), 2.99 (s, 6 H), 2.64−2.54 (dd, *J* = 7.7, 2.9 Hz, 2 H), 2.35 (s, 1 H), 2.00 (dd, *J* = 15.3, 5.3 Hz, 2 H), 1.58−1.50 (m, 4 H), 1.21 (dt, *J* = 7, 4 Hz, 6 H), 1.05−1.00 (m, 4 H), 0.1 (dt, *J* = 7, 3.8 Hz, 2 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 144.3, 144.1, 128.4, 127.6, 127.4, 126, 125.6, 71.9, 71.3, 68.4, 69.1, 41.5, 41.2, 39.8, 39.7, 25.8, 24.4, 22.7, 22.3, 17.6, 17, 13.3, 13.1 ppm.

(*E*)-1-[2-Acetoxy-2-phenylethyl]-2-ethyl-1-mesyloxycyclopropane (41b): Acetic anhydride (110 μL, 1.15 mmol, 1.5 equiv.) was added dropwise at 0 °C to a solution of (*E*)-**41a** (217 mg, 0.764 mmol) in anhydrous diethyl ether (7 mL), containing dimethylaminopyridine (103 mg, 0.84 mmol, 1.1 equiv.). The resulting mixture was stirred overnight at room temperature, then filtered through Celite and concentrated in vacuo. Chromatography of the residue on deactivated silica gel (NEt_3) (eluent pentane/diethyl ether, 1:1) gave 294 mg (100%) of acetate **41b**, as a colourless oil. R_f = 0.48 (eluent pentane/diethyl ether, 1:1). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.41−7.29 (m, 10 H), 6.10 (t, *J* = 7.0 Hz, 2 H), 3.00 (s, 6 H), 2.73 (dd, *J* = 15.2, 7 Hz, 2 H), 2.14−2.05 (m, 2 H), 2.10 (s, 6 H), 1.60−1.43 (m, 4 H), 1.19−1.09 (m, 4 H), 1.02 (t, *J* = 6.5 Hz, 6 H), 0.07 (t, *J* = 7.0 Hz, 2 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 169.9, 140.5, 128.2, 128.1, 126.8, 73.3, 67, 58.7, 37.9, 25.3, 22.6, 21.2, 17.1, 13.1 ppm. MS (DCI, NH_3): *m*/*z* = 344 (100) [M^+ + 18], 267 (6) [M^+ − 77], 188 (12), 171 (40).

(*E*)-2-Ethyl-1-mesyloxy-1-(2-mesyloxy-2-phenylethyl)cyclopropane (41c): By the mesylation procedure used to obtain (*E*)-**38**, methanesulfonyl chloride (110 μL, 1.42 mmol, 1.5 equiv.) was added dropwise to a solution of (*E*)-**41a** (296 mg, 0.947 mmol) in anhydrous diethyl ether (7 mL), containing triethylamine (0.4 mL, 2.84 mmol, 3 equiv.). When the reaction was over, as determined by thin layer chromatography, the usual workup gave 343 mg (100% yield) of dimesylate **41c**, as an orange oil. R_f = 0.57 (eluent dichloromethane/diethyl ether, 9:1). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.43−7.35 (m, 10 H), 5.99 (dd, *J* = 9.5, 3.5 Hz, 1 H), 5.90 (t, *J* = 7.0 Hz, 1 H), 3.02 (s, 3 H), 2.95 (s, 3 H), 2.90−2.80 (m, 2 H), 2.72 (s, 3 H), 2.70 (s, 3 H), 2.19 (dd, *J* = 9.5, 6.5 Hz, 2 H), 1.44−1.18 (m, 8 H), 1.02 (t, *J* = 7.3 Hz, 6 H), 0.62 (t, *J* = 7.3 Hz, 1 H), 0.02 (t, *J* = 7.5 Hz, 1 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 138.4, 138, 128.9, 126.7, 126.2, 81.9, 81.8, 66.2, 66.1, 39.6, 39.4, 39.2, 39.1, 38.9, 38.8, 25.3, 24.3, 22.4, 22.3, 17.4, 16.7, 13.1, 12.9 ppm.

4-Methyl-1-phenylhex-1-en-3-one (42):[64] Carbon tetrabromide (150 mg, 0.45 mmol, 1.5 equiv.) was added to a solution of (*E*)-**41a** (95 mg, 0.30 mmol) in acetonitrile (2 mL). The solution was cooled to 0 °C, and a solution of triphenylphosphane (117 mg, 0.45 mmol, 1.5 equiv.) in acetonitrile (1.5 mL) was added dropwise. The reaction mixture was allowed to warm to room temperature and stirred for one hour, acetone (50 μL, 0.45 mmol, 1.5 equiv.) was added, and the solution was stirred overnight. The solvent was removed in vacuo, and purification of the residue by chromatography on silica gel (eluent pentane/diethyl ether, 9:1) gave 34 mg (0.18 mmol, 64% yield) of ketone **42** as a yellow oil. R_f = 0.74 (eluent pentane/diethyl ether, 3:1). IR (neat): ν(CO) = 2963 cm^{-1}, 2931, 2873, 2360, 2341, 1687, 1660, 1609, 1576, 1449, 1197, 1063, 979, 759. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.62 (d, *J* = 1 6.0 Hz, 1 H), 7.60−7.39 (m, 5 H), 6.83 (d, *J* = 1 6.0 Hz, 1 H), 2.85−2.72 (m, 1 H), 1.86−1.63 (m, 1 H), 1.56−1.33 (m, 1 H), 1.17 (d, *J* = 7.0 Hz, 3 H), 0.93 (t, *J* = 7.5 Hz, 3 H) ppm. MS (EI): *m*/*z* = 188 (8) [M^+], 131 (100), 130 (15), 103 (51), 102 (19), 77 (44), 51 (15). MS (DCI, NH_3): *m*/*z* = 206 (2) [M^+ + 18], 190 (14), 189 (100) [M^+ + 1], 188 (7.5) [M^+], 131 (11).

(*E*)-2-Ethyl-1-mesyloxy-1-[2-mesyloxy-2-(2-naphthyl)ethyl]-cyclopropane (41e): A solution of tetrabutylammonium fluoride in THF (1 M, 2.2 mL, 2.22 mmol, 2.5 equiv.) was added dropwise to a solution of cyclopropanol (*E*)-**27** (329 mg, 0.89 mmol) in tetrahydrofuran (10 mL). The mixture was stirred overnight at room temperature, the solvent was removed in vacuo, and diethyl ether (30 mL) was added. The organic phase was washed with 6 mL of brine, dried with anhydrous Na_2SO_4, and concentrated in vacuo. Chromatography on silica gel (eluent pentane/diethyl ether, 7:3) gave 158 mg (70% yield) of (*E*)-2-ethyl-1-[2-hydroxy-2-(2-naphthyl)-ethyl]cyclopropanol as a colourless solid. R_f = 0.55 (eluent dichloromethane/diethyl ether, 9:1). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.87−7.46 (m, 14 H), 5.26−5.21 (d, *J* = 2.0 Hz, 2 H), 3.63 (s, 2 H), 3.25 (s, 2 H), 2.46 (dd, *J* = 15, 10.3 Hz, 2 H), 1.57 (dd, *J* = 15, 2.7 Hz, 2 H), 1.32−1.02 (m, 8 H), 0.96 (t, *J* = 7.0 Hz, 6 H), 0.20 (t, *J* = 4.5 Hz, 2 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 141.7, 133.2, 132.8, 128.2, 127.8, 127.6, 126.1, 125.7, 124.2, 123.9, 75.2, 59.5, 41.6, 27.2, 22.8, 18.5, 13.7 ppm. MS (EI): *m*/*z* = 238 (31) [M^+ + 2], 181 (100), 152 (36). MS (DCI, NH_3): *m*/*z* = 258 (31) [M^+ + 2], 257 (8) [M^+ + 1], 241 (20), 240 (28), 239 (100), 238 (27).

By the dimesylation procedure used for (*E*)-**38**, the obtained diol (158 mg, 0.6 mmol) was treated with methanesulfonyl chloride (206 mg, 1.8 mmol, 3 equiv.) in diethyl ether (30 mL), containing triethylamine (364 mg, 3.6 mmol, 6 equiv.). The usual workup and chromatography on silica gel (eluent dichloromethane/ether, 9:1) gave 247 mg (100% yield) of dimesylate (*E*)-**41e** as an orange oil. R_f = 0.50 (eluent dichloromethane/diethyl ether, 9:1). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.94−7.52 (m, 14 H), 6.19−6.14 (d, *J* = 3.5 Hz, 1 H), 6.08 (t, *J* = 7.0 Hz, 1 H), 3.23−3.12 (m, 2 H), 3.05 (s, 6 H), 2.95 (s, 6 H), 3.32 (dd, *J* = 15.3, 6.5 Hz, 2 H), 1.69−1.50 (m, 4 H), 1.39 (t, *J* = 7.3 Hz, 6 H), 1.26−1.14 (m, 2 H), 1.11−1.00 (m, 2 H), 0.66 (t, *J* = 7.2 Hz, 1 H), 0.005 (t, *J* = 7.1 Hz, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 135.6, 135.1, 133.2, 132.6, 128.8, 127.9, 127.5, 127.4, 126.7, 126.6, 126.4, 125.9, 125.7, 123.4, 123.2, 66.3, 66.1, 52.3, 46.1, 39.6, 39.4, 39.1, 38.7, 25.3, 24.2, 22.4, 22.2, 17.4, 16.7, 13, 12.9 ppm.

(*E*)-1-(2-Chloroethyl)-2-ethyl-1-(tetrahydropyranyloxy)cyclopropane (43a): A solution of PPTS (33.5 mg, 0.14 mmol) in dichloromethane (1 mL) was added dropwise, whilst stirring at room temperature, to a solution of cyclopropanol (*E*)-**37** (100 mg, 0.67 mmol) in dichloromethane (20 mL), containing dihydropyran (114 mg, 1.34 mmol). The reaction mixture was stirred at room temperature overnight. The solvent was then removed in vacuo, and 10 mL of diethyl ether were added. The organic phase was washed with 2 mL of brine, dried with anhydrous Na_2SO_4, and concentrated in vacuo. Chromatography of the residue over silica gel (eluents pentane/diethyl ether, 95:5) gave 155 mg (100%) of (tetrahydropyranyloxy)cyclopropane **43a** as a pale yellow oil. IR (neat): ν(CO) = 2958 cm^{-1}, 2941, 2872, 1453, 1442, 1219, 1201, 1124, 1077, 1034, 989. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 4.69 (m, 2 H), 3.93−3.84 (m, 4 H), 3.82−3.70 (m, 8 H), 3.55−3.45 (m, 4 H), 2.57−0.80 (m, 22 H), 0.20 (dd, *J* = 5.8 Hz, 1 H), 0.213 (dd, *J* = 6.3 Hz, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 99.4, 98.5, 63.7, 63.5, 63.4, 63.3, 41.9, 41.5, 35.7, 35.6, 31.7, 31.7, 25.8, 25.1, 24.9, 22.6, 22.5, 20.2, 20.1, 18.4, 16.7, 13.7, 13.5 ppm. MS (EI): *m*/*z* = 177 (2) [M^+ − 55], 133 (5), 101 (17), 97 (10), 85 (100), 67 (5), 57 (7), 56 (20), 55 (14).

(*E*)-1-(2-Chloroethyl)-2-ethyl-1-mesyloxycyclopropane (43b): Colourless oil, 275 mg (97% yield). R_f = 0.63 (eluent pentane/diethyl ether, 1:3). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.80 (t, *J* = 7.8 Hz, 2 H), 3.03 (s, 3 H), 2.61 (m, 2 H), 2.07 (dt, *J* = 15, 7.5 Hz, 2 H), 1.60−1.10 (m, 5 H), 1.03 (t, *J* = 7.5 Hz, 3 H) 0.51 (dd, *J* = 6.8 Hz, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 65.8, 40.7, 39.9, 35.2, 25.1, 22.5, 17.4, 13.2 ppm. MS (EI): *m*/*z* = 149 (5), 147 (15), 93 (33), 91 (100), 665 (26), 63 (77). HRMS [of the parent 1-(2-chloroethyl)-2-ethylcyclopropanol]: found 148.0654, $C_7H_{13}ClO$ requires 148.0655.

(*E*)-1-(2-Chloroethyl)-2-ethyl-1-tosyloxycyclopropane (43c): A solution of butylmagnesium bromide (4.45 g, 27.6 mmol, 2.5 equiv.) in diethyl ether (30 mL) was added dropwise, whilst stirring at room

temperature, to a solution of ethyl 3-chloropropionate (1.50 g, 11 mmol) in tetrahydrofuran (40 mL), containing $Ti(OiPr)_4$ (625 mg 2.21 mmol, 0.2 equiv.). When the addition was over, the reaction mixture was cooled to 0 °C and a solution of tosyl chloride (5.26 g, 27.6 mmol, 2.5 equiv.) in diethyl ether (20 mL) was added. The mixture was stirred overnight at room temperature. After addition of diethyl ether (20 mL) containing saturated aqueous ammonium chloride solution (1 mL) and filtration through Celite, the organic phase was dried with anhydrous Na_2SO_4, and concentrated in vacuo. Chromatography of the residue over silica gel (eluents pentane/diethyl ether, 8:2 and then dichloromethane) gave 2.40 g (72%) of tosylate (*E*)-**43c**, as a yellow oil. R_f = 0.47 (eluent dichloromethane). IR (neat): ν(CO) = 3067 cm^{-1}, 2964, 2933, 2874, 1598, 1363, 1174, 1095, 927. ^1H NMR (250 MHz, $CDCl_3$): δ = 7.77 (d, *J* = 8.0 Hz, 2 H), 7.35 (d, *J* = 5.8 Hz, 2 H), 3.71 (dd, *J* = 7.3 Hz, 2 H), 2.58 (dt, *J* = 14.7, 7.3 Hz, 2 H), 2.46 (s, 3 H), 1.99 (dt, *J* = 14.7, 7.3 Hz, 2 H), 1.05−1.60 Hz (m, 2 H), 0.99 (t, *J* = 7.3 Hz, 3 H), 0.39 (dd, *J* = 6.8 Hz, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 144.5, 135.1, 129.6, 127.5, 70.2, 40.6, 35.1, 24.7, 22.3, 21.6, 18.4, 13.2 ppm. MS (EI): *m*/*z* = 239 (0.1) [M^+ − 85], 149 (3), 147 (9), 93 (20), 92 (10), 91 (100), 65 (22), 63 24), 55 (5), 41 (8). MS (DCI, NH_3): *m*/*z* = 325 (0.4) [M^+ + 1], 324 (0.6) [M^+], 323 (2.30), 322 (21), 321 (25), 320 (100), 3147 (37). HRMS: found 324.0272, $C_{14}H_{19}O_3SCl$ requires 324.0273.

(*E*)-2-Ethyl-1-ethenyl-1-tetrahydropyranyloxycyclopropane (44a): A solution of **43a** (106 mg, 0.47 mmol) in tetrahydrofuran (3 mL) containing potassium *tert*-butoxide (106 mg, 0.95 mmol) was stirred at 80−90 °C for 14 h. The solvent was removed in vacuo, and the residue was purified by chromatography on silica gel (eluent pentane/diethyl ether, 8:2) to give 79 mg (85% yield) of (*E*)-**44a** as a pale yellow oil. R_f = 0.76 (eluent pentane/ether, 3:1). IR (neat): ν(CO) = 3084 cm^{-1}, 2941, 2872, 1636, 1454, 1201, 11321, 1110, 1077, 1027, 991, 971, 904, 869. ^1H NMR (250 MHz, $CDCl_3$): δ = 5.83 (dd, *J* = 17, 11 Hz, 1 H), 5.82 (dd, *J* = 17, 11 Hz, 1 H), 5.24−5.08 (m, 4 H), 4.83 (m, 1 H), 4.878 (m, 1 H), 3.87 (m, 2 H), 3.47 (m, 2 H), 2.0−0.90 (m, 26 H), 0.52 (dd, *J* = 6.3 Hz, 2 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 136.9, 114.3, 112.5, 99, 98.4, 66.7, 62.8, 62.7, 31.4, 28.1, 27.8, 25.3, 22.3, 19.9, 19.8, 18.4, 17.8, 13.5, 13.4 ppm. MS (EI): *m*/*z* = 196 (0.2) [M^+], 126 (4), 95 (8), 86 (13), 85 (100), 84 (12), 83 (13), 67 (42), 57 (31), 55 (16). HRMS: found 196.1464, $C_{12}H_{20}O_2$ requires 196.1463.

(*E*)-2-Ethyl-1-ethenyl-1-tosyloxycyclopropane (44c): By the procedure used to prepare **44a**, a solution of tosylate **43c** (99.8 mg, 0.33 mmol) in tetrahydrofuran (5 mL), containing potassium *tert*-butoxide (37 mg, 0.33 mmol), was stirred at 80−90 °C for 14 h. The solvent was removed in vacuo, and the residue was purified by chromatography on silica gel (eluent pentane/diethyl ether, 8:2) to give 88 mg (77% yield) of (*E*)-**44c** as a pale yellow oil. R_f = 0.76 (eluent pentane/ether, 3:1). IR (neat): ν(CO) = 3092 cm^{-1}, 3068, 2963, 2932, 2874, 1643, 1599, 1365. ^1H NMR (250 MHz, $CDCl_3$): δ = 7.79 (d, *J* = 8.3 Hz, 2 H), 7.32 (d, *J* = 8.7 Hz, 2 H), 5.88 (dd, *J* = 17.10 Hz, 1 H), 5.69 (dd, *J* = 17.10, 10 Hz, 2 H), 2.46 (s, 3 H), 1.50−1.10 (m, 4 H), 0.91 (t, *J* = 7.3 Hz, 3 H) 0.72 (dt, *J* = 6.8 Hz, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 144.4, 133.1, 129.6, 127.8, 125.4, 116.5, 69.6, 34.1, 27.6, 21.7, 17, 13.1 ppm. MS (EI): *m*/*z* = 226 (0.6) [M^+ − 40], 208 (0.50), 111 (16), 92 (8), 91 (59), 65 (20), 56 (5), 55 (100). MS (DCI, NH_3): *m*/*z* = 284 (12) [M^+ + 18], 243 (7), 191 (10), 190 (100), 155 (17), 140 (4).

(*E*)-1-Ethyl-4-oxa-5-thiaspiro[2.5]octane 5,5-Dioxide (45): Potassium *tert*-butoxide (370 mg, 3.31 mmol, 2 equiv.) in DMSO (4 mL) was added at 0 °C to a solution of cyclopropyl mesylate **43b** (357 mg, 1.65 mmol) in benzene (4 mL). The mixture was stirred at room temperature for 8 h, the solvents were removed in vacuo, and 10 mL of diethyl ether and 5 mL of water were added. The organic phase was washed twice with 3 mL of water, dried with Na_2SO_4, and concentrated in vacuo. Chromatography of the residue on silica gel (eluent pentane/diethyl ether, 8:2 then 5:5) gave, in addition to 15.7 mg (5% yield) of (*E*)-**44b**, 160 mg (51% yield) of the dioxide **45** as a colourless oil. R_f = 0.41 (eluent pentane/diethyl ether, 1:3). ^1H NMR (250 MHz, $CDCl_3$): δ = 3.18 (dd, *J* = 6.8 Hz, 2 H), 2.33 (m, 2 H), 1.91 (m, 2 H), 1.60−1.20 (m, 4 H), 1.05 (t, *J* = 7.5 Hz, 3 H), 0.38 (dd, *J* = 6.3 Hz, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 71.4, 47.9, 25.8, 24.9, 21.8 (two carbons), 16.7, 13.3 ppm. MS (EI): *m*/*z* = 190 (0.2) [M^+], 161 (19), 98 (10), 97 (11), 55 (49), 54 (11), 43 (14), 42 (100), 41 (50). HRMS: found 190.0667, $C_8H_{14}O_3S$ requires 190.0664.

(*E*)-2-(1-Acetoxy-2-ethylcyclopropyl)acetaldehyde (46): Acetic anhydride (0.47 mL, 15 mmol) was added dropwise at 0 °C to a solution of cyclopropanol (*E*)-**29** (2.02 g, 10 mmol) in diethyl ether (30 mL), containing DMAP (1.44 g, 11 mmol). When the reaction was complete, as determined by thin layer chromatography, the solvent was removed in vacuo and 20 mL of pentane were added. After filtration through Celite, the solvent was removed to give 2.32 g (95%) of 1-acetoxy-1-(2,2-diethoxyethyl)-2-ethylcyclopropane as a colourless oil. IR (neat): ν(CO) = 2974 cm^{-1}, 2932, 1749, 1651, 1557, 1444, 1370, 1228, 1189, 1123, 1069, 771. ^1H NMR (200 MHz, $CDCl_3$): δ = 4.73 (dd, *J* = 6.4, 4 Hz, 1 H), 3.79−3.40 (m, 4 H), 2.36 (dd, *J* = 14.8 Hz, 1 H), 1.97(s, 3 H), 1.76 (dd, *J* = 14.8, 6 Hz, 1 H), 1.60−1.40 (m, 1 H), 1.30−1.15 (m, 1 H), 1.22 (t, *J* = 7.0 Hz, 3 H), 1.21 (t, *J* = 7.0 Hz, 3 H), 1.10−0.90 (m, 1 H), 1.02 (t, *J* = 7.3 Hz, 3 H), 0.38 (s, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 170.5, 101.5, 61.6, 61.6, 60.4, 34.6, 25.7, 22.7, 21.2, 16.7, 15.2, 15.1, 13.2 ppm. MS (EI): *m*/*z* = 111 (14) [M^+ − 133], 103 (40), 99 (11), 83 (13), 82 (13), 75 (44), 72 (43), 56 (22), 55 (16), 47 (67), 44 (36), 43 (100), 41 (22). MS (DCI, NH_3): *m*/*z* = 262 (0.2) [M^+ + 18], 200 (17), 199 (100), 139 (29), 103 (14).

Formic acid (4.5 mL) was added to a solution of this 1-acetoxycyclopropane (2.32 g, 9.5 mmol) in pentane (20 mL). The mixture was stirred at room temperature until disappearance of the starting material, determined by thin layer chromatography. Water (10 mL) was then added, and the aqueous phase was extracted with pentane (3 × 10 mL). The combined organic extracts were washed with 5 mL of saturated $NaHCO_3$ solution and dried with Na_2SO_4. Removal of solvent in vacuo, and chromatography of the residue (eluent pentane/diethyl ether) gave 1.49 g (87% yield) of pure aldehyde (*E*)-**46**, as a colourless oil. R_f = 0.50 (eluent pentane/diethyl ether, 3:1). IR (neat): ν(CO) = 2965 cm^{-1}, 2935, 2876, 1744, 1457, 1370, 1247, 1218, 1179, 1156, 1008, 1063, 1023, 975, 609. ^1H NMR (250 MHz, $CDCl_3$): δ = 9.90 (t, *J* = 2.2 Hz, 1 H), 2.90 (dd, *J* = 17.2, 2.2 Hz, 1 H), 2.64 (dd, *J* = 17.2, 2.2 Hz, 1 H), 1.98 (s, 3 H), 1.60−1.43 (m, 1 H), 1.30−1.10 (m, 3 H), 1.05 (t, *J* = 6.8 Hz, 3 H), 0.51 (s, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 200.5, 170.8, 58.5, 45, 24.9, 22.9, 21, 17.1, 13.1 ppm. MS (EI): *m*/*z* = 171 (0.2) [M^+ + 1], 99 (5), 83 (2), 82 (3), 56 (6), 55 (6), 43 (100), 42 (5), 41 (9), 39 (6). MS (DCI, NH_3): *m*/*z* = 188 (32) [M^+ + 18], 172 (10), 171 (100), 170 (13).

(*E*)-4-(1-Acetoxy-2-ethylcyclopropyl)but-3-enoic Acid (47): A mixture of aldehyde (*E*)-**47** (1 g, 6 mmol), malonic acid (630 mg, 6 mmol) and silica gel (2.1 g) was subjected to microwave irradiation (300 W) at 130 °C for 15 min. Filtration through silica gel and extraction from silica gel by ethyl acetate then gave, after removal of the solvent in vacuo, 1.04 g (83% yield) of practically pure butenoic acid (*E*)-**47**, as a brown oil. ^1H NMR (200 MHz, $CDCl_3$): δ = 5.7−5.6 (m, 2 H), 3.16 (d, *J* = 5.5 Hz, 2 H), 2.04 (s, 3 H),

1.50−1.10 (m, 4 H), 0.99 (t, J = 7.15 Hz, 3 H), 0.76 (dd, J = 6, 5.2 Hz, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 177.1, 170, 130, 122, 62, 37, 28, 22.4, 21.2, 18.7, 13.2 ppm. MS (EI): m/z = 212 (1.6) [M^+], 141 (21), 123 (15), 111 (29), 110 (21), 95 (20), 85 (10), 71 (12), 55 (11), 43 (100), 41 (16), 39 (21). MS (DCI, NH_3): m/z = 230 (100) [M^+ + 18], 126 (84), 125 (79), 124 (63), 112 (63), 111 (68), 109 (68).

(*E*)-2-Ethyl-1-(4-hydroxybut-1-enyl)cyclopropanol (48): A solution of lithium aluminum hydride in tetrahydrofuran (1.14 M, 4.14 mL, 1.94 mmol) was added at −10 °C to a solution of butenoic acid (*E*)-**47** (500 mg, 2.4 mmol) in tetrahydrofuran (20 mL). The mixture was stirred at room temperature for 3 h and then diluted with 30 mL of diethyl ether. Addition of wet Na_2SO_4, filtration, and removal of solvents in vacuo gave 329.5 mg (88% yield) of sufficiently pure (*E*)-**48**, which was used in the next step without further purification. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 5.74 (dt, J = 15.5, 6.2 Hz, 1 H), 5.55 (d, J = 15.5 Hz, 1 H), 2.38 (q, J = 6.3 Hz, 2 H), 1.40−1.20 (m, 2 H), 1.15−1.05 (m, 1 H), 1.05−0.85 (m, 4 H), 0.49 (dd, J = 6.1, 5.2 Hz, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 134.2, 124.5, 62.1, 58.3, 35.8, 30, 23, 21.8, 13.7 ppm. MS (EI): m/z = 127 (12) [M^+ − 29], 111 (29), 99 (12), 83 (17), 81 (28), 79 (17), 77 (11), 71 (15), 70 (11), 69 (65), 68 (24), 65 (34), 66 (27), 65 (15), 57 (19), 56 (12), 55 (100), 54 (12), 43 (48), 42 (11), 41 (54), 40 (11), 39 (38). MS (DCI, NH_3): m/z = 174 (100) [M^+ + 18], 158 (19), 157.

(*E*)-2-Ethyl-1-mesyloxy-1-(4-mesyloxybut-1-enyl)cyclopropane (49a): By the procedure used for the preparation of the dimesylate (*E*)-**38**, methanesulfonoyl chloride (0.2 mL, 2.5 mmol) was added dropwise at 0 °C to a solution of the diol (*E*)-**48** (130 mg, 0.83 mmol) in diethyl ether (10 mL). When the reaction was complete, within one hour as determined by thin layer chromatography, the usual workup gave 230 mg (88% yield) of the dimesylate (*E*)-**49a**. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 6.0−5.7 (m, 2 H), 4.28 (dt, J = 6.35 Hz, 2 H), 3.02 (s, 3 H), 3.00 (s, 3 H), 2.58 (q, J = 6.35, 5.86 Hz, 2 H), 1.60−1.50 (m, 1 H), 1.40−1.20 (m, 2 H), 1.10−0.80 (m, 5 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 133.1, 124.5, 68.7, 67.9, 39.7, 37.4, 31.7, 27.3, 21.6, 18.5, 13.5 ppm. MS (EI): m/z = 123 (14) [M^+ − 189], 97 (6), 85 (11), 79 (30), 59 (13), 58 (23), 57 (100), 56 (29), 45 (41), 44 (13), 43 (16), 41 (32). MS (DCI, NH_3): m/z = 217 (18) [M^+ − 95], 212 (13), 121 (100), 120 (16).

(*E*)-1-(But-1-enyl)-2-ethyl-1-mesyloxycyclopropane [(*E*)-49b]: A solution of lithium aluminum hydride (0.86 M, 2 mL, 1.7 mmol) in tetrahydrofuran was added dropwise at 0 °C to a solution of the dimesylate (*E*)-**49a** (260 mg, 0.83 mmol) in tetrahydrofuran (10 mL). The mixture was stirred for 2 h, and workup as for (*E*)-**48** gave 180 mg (99% yield) of sufficiently pure monomesylate (*E*)-**49b**. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 5.86 (dt, J = 15.4, 5.9 Hz, 1 H), 5.72 (d, J = 15.4 Hz, 1 H), 2.90 (s, 3 H), 2.09 (q, J = 6.7 Hz, 2 H), 1.50−1.40 (m, 1 H), 1.30−1.10 (m, 2 H), 1.10−0.70 (m, 8 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 138.1, 122.9, 39.9, 26.6, 25.1, 21.7, 16.5, 13.2, 13 ppm. MS (EI): m/z = 189 (13) [M^+ − 15], 111 (19), 93 (35), 91 (10), 83 (100), 81 (16), 80 (20), 77 (10), 55 (87), 53 (20), 43 (10), 41 (29), 39 (31). MS (DCI, NH_3): m/z = 222 (22) [M^+ + 18], 124 (11), 123 (100), 122 (20), 114 (14), 107 (12).

(*Z*)-2-[2-Hydroxyethyl]-1-(prop-1-enyl)cyclopropanol (52a): A solution of isopropylmagnesium bromide in diethyl ether (1.4 M, 204 mL, 285.7 mmol, 4 equiv.) was added dropwise over 3 h at −40 °C to a solution of but-3-enyl but-2-enoate (10 g, 71.43 mmol) in anhydrous diethyl ether (850 mL), containing Ti(O*i*Pr)$_4$ (42.5 mL, 142.9 mmol, 2 equiv.). When the addition was over, the mixture was stirred for 1 h at −40 °C, and then for 2 h at 0 °C, and was allowed to come to room temperature slowly whilst stirring overnight. Addition of 200 mL of diethyl ether and 100 mL of water gave, after stirring for 1 h, a clear solution and a blue-grey precipitate. After filtration through Celite, the aqueous phase was extracted three times with diethyl ether (3 × 100 mL); the combined extracts were then dried with Na_2SO_4 and concentrated in vacuo. Chromatography of the residue on silica gel (eluent pentane/ethyl acetate, 3:1) gave 7.36 g (51.83 mmol, 73% yield) of (*Z*)-**52a** as a colourless oil. R_f = 0.45 (eluent pentane/ethyl acetate, 1:1). IR (neat): ν(CO) = 3386 cm^{-1}, 2941, 2882, 1709, 1657, 1445, 1379, 1292, 1198, 1103, 1048, 968. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 5.72 (dq, J = 15.3, 6.5 Hz, 1 H), 5.25 (dd, J = 15.2, 1.45 Hz, 1 H), 3.87−3.80 (m, 1 H), 3.69 (dt, J = 10.8, 3 Hz, 1 H), 2.10−1.98 (m, 2 H), 1.72 (dd, J = 6.9, 1.5 Hz, 3 H), 1.69−1.57 (m, 2 H), 0.89−0.80 (m, 2 H), 0.71−0.67 (m, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 135.9, 121.1, 62.2, 56.9, 30.8, 24.4, 20.9, 17.4 ppm. MS (EI): m/z = 141 (1.3) [M^+ − 1], 127 (16) [M^+ − 15], 109 (16), 97 (35), 81 (13), 70 (33), 69 (100), 68 (15), 55 (28), 41 (54), 39 (35). MS (DCI, NH_3): m/z = 160 (23) [M^+ + 18], 144 (17), 143 (100), 142 (16), 125 (47). HRMS: found 142.0991, $C_8H_{14}O_2$ requires 142.0993. $C_8H_{14}O_2$ (142.10): calcd. C 67.57, H 9.92; found C 65.04, H 9.74.

(*Z*)-1-(But-1-enyl)-2-(2-hydroxyethyl)cyclopropanol (52b): By the procedure to prepare (*Z*)-**52a**, but-3-enyl pent-2-enoate (1 g, 6.49 mmol) was transformed into 701 mg (4.49 mmol, 69% yield) of diol **52b**, obtained as a colourless oil. R_f = 0.36 (eluent pentane/ethyl acetate, 1:1). IR (neat): ν(CO) = 3339 cm^{-1}, 2961, 2933, 2874, 1666, 1438, 1290, 1033, 964. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 5.76 (dt, J = 15.1, 6.6 Hz, 1 H), 5.21 (dd, J = 15.1, 2 Hz, 1 H), 3.88−3.71 (m, 1 H), 3.68 (dt, J = 10, 1 Hz, 1 H), 2.04 (dq, J = 6.6, 2 Hz, 2 H), 1.74 (s, 2 H), 1.72−1.58 (m, 1 H), 1.24 (dd, J = 6.6, 4 Hz, 1 H), 1.01 (t, J = 7.3 Hz, 3 H), 0.93−0.82 (m, 2 H), 0.72−0.68 (m, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 133.7, 128.1, 60.4, 56.9, 30.9, 25, 24.6, 21.1, 13.7 ppm. MS (EI): m/z = 156 (0.2) [M^+], 83 (21), 55 (45), 43 (100), 39 (22). HRMS (M + Na): found 179.104799, $C_9H_{16}O_2Na$ requires 179.104803.

(*Z*)-1-(Prop-1-enyl)-2-(2-tosyloxyethyl)cyclopropanol (53a): A solution of *p*-toluenesulfonyl chloride (2.82 g, 14.79 mmol, 1 equiv.) in dichloromethane (10 mL) was added dropwise at 0 °C to a solution of the diol (*Z*)-**52a** (2.1 g, 14.79 mmol) in dichloromethane (35 mL), containing triethylamine (2.3 mL, 16.27 mmol) and DMAP (181 mg, 1.48 mmol, 0.1 equiv.), and the reaction mixture was stirred at room temperature for 17 h. A saturated solution of ammonium chloride (10 mL) was then added, and the aqueous phase was extracted three times with dichloromethane (3 × 10 mL). The combined extracts were washed with brine (10 mL) and dried with Na_2SO_4, and the solvent was removed in vacuo. Chromatography of the residue on silica gel (eluent dichloromethane/diethyl ether, 97:3) gave 2.215 g (7.5 mmol, 51% yield) of the tosylate **53a** as an orange oil. R_f = 0.34 (eluent pentane/ethyl acetate, 3:1). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.80 (d, J = 8.3 Hz, 2 H), 7.35 (d, J = 8.1 Hz, 2 H), 5.64 (dq, J = 15.3, 6.5 Hz, 1 H), 5.22 (dd, J = 15.3, 1.5 Hz, 1 H), 4.20−4.03 (m, 2 H), 3.14 (s, 1 H), 2.46 (s, 3 H), 1.96−1.86 (m, 2 H), 1.72 (dd, J = 6.6, 1.5 Hz, 3 H), 0.89−0.78 (m, 2 H), 0.64−0.58 (m, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 143.7, 132.7, 129.8, 129.2, 127.7, 126.3, 68.5, 53.4, 31.5, 21.5, 21.3, 18.2, 16.9 ppm. MS (EI): m/z = 296 (0.9) [M^+], 155 (14), 91 (45), 83 (24), 82 (100), 68 (23.4), 67 (38.1), 53 (25.9). MS (DCI, NH_3): m/z = 315 (22) [M^+ + 18 + 1], 314 (100) [M^+ + 18], 313 (35), 125 (18).

(*Z*)-2-(2-Bromoethyl)-1-(prop-1-enyl)cyclopropanol (53b): A solution of lithium bromide (190 mg, 2.18 mmol, 1.5 equiv.) in NMP (2 mL) was added to a solution of the tosylate **53a** (430 mg, 1.45 mmol) in 1-methyl-2-pyrrolidinone (NMP, 1.5 mL). When the

reaction was complete (after stirring at room temperature for 3 h as determined by thin layer chromatography), 5 mL of diethyl ether and 5 mL of water were added. The aqueous phase was extracted three times with diethyl ether (3 × 5 mL) and the combined organic extracts were washed three times with water (3 × 5 mL), dried with Na_2SO_4, and concentrated in vacuo. Chromatography of the residue on silica gel (eluent pentane/ethyl acetate, 95:5) gave 235 mg (1.15 mmol, 79% yield) of bromide **53b** as a pale yellow oil. R_f = 0.6 (eluent pentane/ethyl acetate, 3:1). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 5.69 (dq, *J* = 15.3, 6.5 Hz, 1 H), 5.30 (dd, *J* = 15.3, 1.4 Hz, 1 H), 3.58−3.42 (m, 2 H), 2.28 (s, 1 H), 2.23−2.02 (m, 2 H), 1.73 (dd, *J* = 6.5, 1.3 Hz, 3 H), 1.01−0.86 (m, 1 H), 0.95 (dd, *J* = 5, 1.5 Hz, 1 H), 0.66 (dd, *J* = 5.5, 4.5 Hz, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 135, 122.6, 57.6, 33.9, 30.8, 24.8, 19.7, 17.3 ppm.

1-(Prop-1-enyl)-2-oxabicyclo[3.1]hexane (54): A solution of lithium triethylborohydride in tetrahydrofuran (1 M, 1.45 mL, 1.45 mmol) was added to a solution of the tosylate (*Z*)-**53a** (141 mg, 0.476 mmol) in tetrahydrofuran (2 mL). After this had stirred for 3 h, a saturated potassium carbonate solution (1 mL) was added. The mixture was then extracted three times with diethyl ether (3 × 5 mL), and the combined organic extracts were dried with Na_2SO_4 and concentrated in vacuo. Chromatography of the residue on silica gel (eluent pentane/diethyl ether, 9:1) gave 59 mg (0.476 mmol, 100% yield) of the bicyclofuran **54** as a colourless oil. R_f = 0.50 (eluent pentane/diethyl ether, 9:1). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 5.82 (dq, *J* = 16, 8 Hz, 1 H), 5.54 (dd, *J* = 16, 1.5 Hz, 1 H), 4.12 (dt, *J* = 9.5, 4 Hz, 1 H), 3.66−3.55 (m, 1 H), 2.28−2.05 (m, 1 H), 1.98−1.83 (m, 1 H), 1.78 (dd, *J* = 7, 1.5 Hz, 3 H), 1.52−1.46 (m, 1 H), 1.08 (dd, *J* = 4.5 Hz, 1 H), 0.74 (dd, *J* = 9, 6.7 Hz, 1 H) ppm. MS (EI): *m*/*z* = 124 (21) [M^+], 123 (20), 109 (96), 95 (23), 81 (23), 69 (100), 68 (40), 55 (23), 41 (74), 40 (33), 39 (66). MS (DCI, NH_3): *m*/*z* = 142 (4) [M^+ + 18], 125 (100) [M^+ + 1], 124 (9) [M^+].

(*Z*)-1-Mesyloxy-2-(2-mesyloxyethyl)-1-(prop-1-enyl)cyclopropane (55a): By the procedure to obtain the dimesylate (*E*)-**38**, diol **52a** (2.413 g, 17 mmol) was treated with methanesulfonyl chloride (29 mL, 37.38 mmol, 2.2 equiv.) in diethyl ether (200 mL), containing triethylamine (7.15 mL, 51 mmol, 3 equiv.). The usual workup gave 5.064 g (17 mmol, 100% yield) of (*Z*)-**55a** as an orange oil. R_f = 0.51 (eluent pentane/ethyl acetate, 1:1). IR (neat): ν(CO) = 3471 cm^{-1}, 3031, 2941, 1353, 1173, 971, 909, 843, 812, 529. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 5.80 (m, 2 H), 4.34 (t, *J* = 6.3 Hz, 2 H), 3.04 (s, 6 H), 2.06−1.97 (m, 2 H), 1.75 (dd, *J* = 4.7, 1.9 Hz, 3 H), 1.34 (dd, *J* = 8.5, 2.1 Hz, 2 H), 1.18−1.10 (m, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 128.8, 128.3, 69.2, 67.7, 39.8, 37.2, 28, 20.7, 17.5, 17.3 ppm. MS (EI): *m*/*z* = 219 (5) [M^+ − 79], 123 (28), 107 (15), 106 (13), 95 (23), 91 (20), 79 (27), 69 (100), 68 (17), 41 (41), 39 (18). MS (DCI, NH_3): *m*/*z* = 316 (100) [M^+ + 18], 222 (21), 220 (25), 205 (14), 203 (16), 141 (16), 126 (19), 125 (28), 124 (83), 123 (42), 122 (18).

(*Z*)-1-(But-1-enyl)-1-mesyloxy-2-(2-mesyloxyethyl)cyclopropane (55b): By the procedure used to obtain (*E*)-**38**, diol (*Z*)-**52b** (520.5 mg, 3.34 mmol) was treated with methanesulfonyl chloride (570 μL, 7.34 mmol, 2.2 equiv.) in diethyl ether (40 mL), containing triethylamine (1.4 mL, 10 mmol, 3 equiv.). The usual workup gave 1.041 g (3.33 mmol, 100% yield) of dimesylate **55b** as an orange oil. R_f = 0.42 (eluent pentane/diethyl ether, 1:1). IR (neat): ν(CO) = 2964 cm^{-1}, 2398, 1618, 1352, 1172, 971. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 5.91−5.77 (m, 2 H), 4.36 (t, *J* = 5.3 Hz, 2 H), 3.08 (s, 6 H), 2.16−1.89 (m, 4 H), 1.38 (dd, *J* = 7.9, 3.9 Hz, 2 H), 1.26−1.08 (m, 1 H), 1.03 (t, *J* = 6.8 Hz, 3 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 135.5, 126.2, 69.2, 67.8, 37.9, 28.1, 24.9, 20.8, 17.6, 13 ppm. MS (EI): *m*/*z* = 233 (3.8) [M^+ − 79], 217 (0.2) [M^+ − 95], 137 (18), 109 (30), 105 (29), 93 (17), 91 (27), 83 (100), 79 (29), 55 (43), 43 (17), 39 (20). MS (DCI, NH_3): *m*/*z* = 330 (11) [M^+ + 18], 234 (15), 138 (36), 137 (36), 123 (55), 122 (30), 121 (100), 120 (21).

(*Z*)-2-(2-*tert*-Butyldimethylsiloxyethyl)-1-mesyloxy-1-(prop-1-enyl)-cyclopropane (55c): A solution of *tert*-butyldimethylsilyl chloride (2.65 g, 17.6 mmol, 1.1 equiv.) in dimethylformamide (5 mL) was added dropwise at room temperature to a solution of diol (*Z*)-**52a** (2.27 g, 16 mmol) in dimethylformamide (5 mL), containing imidazole (2.72 g, 40 mmol, 2.5 equiv.). The mixture was stirred for 36 h and, after addition of 50 mL of diethyl ether, was cooled to 0 °C and 5 mL of water were added. The organic phase was washed three times with water (3 × 5 mL), dried with $MgSO_4$, and concentrated in vacuo. Chromatography of the residue on silica gel (eluent pentane/diethyl ether, 9:1) gave 2.99 g (11.68 mmol, 73% yield) of (*Z*)-2-(2-*tert*-butyldimethylsiloxyethyl)-1-(prop-1-enyl)cyclopropanol as a colourless oil. R_f = 0.79 (eluent pentane/diethyl ether, 9:1). IR (neat): ν(CO) = 3434 cm^{-1}, 2956, 2930, 2858, 1682, 1472, 1288, 1256, 1084, 1032, 963, 836, 779. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 5.70 (dq, *J* = 15.1, 6.9 Hz, 1 H), 5.19 (dd, *J* = 15.1, 0.3 Hz, 1 H), 3.94 (s, 1 H), 3.79 (dt, *J* = 7.9, 4 Hz, 3 H), 3.61 (dt, *J* = 11, 1.5 Hz, 1 H), 2.05 (m, 1 H), 1.70 (dd, *J* = 6.9 Hz, 1 H), 1.60−1.52 (m, 1 H), 0.92 (s, 9 H), 0.84−0.80 (m, 2 H), 0.69−0.65 (m, 1 H), 0.09 (s, 6 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 136.2, 121, 63.6, 56.8, 31.5, 25.9, 24.9, 21.4, 18.3, 17.4, −5.4, −5.7 ppm. MS (EI): *m*/*z* = 256 (0.5) [M^+], 199 (15), 109 (25), 107 (25), 105 (29), 91 (12), 81 (35), 75 (100), 73 (38), 69 (80), 55 (21), 41 (14). MS (DCI, NH_3): *m*/*z* = 274 (7) [M^+ + 18], 258 (21), 257 (100) [M^+ + 1], 256 (31) [M^+], 199 (8), 125 (52), 124 (30). HRMS: found 256.1855, $C_{14}H_{28}O_2Si$ requires 256.1855.

By the procedure used to obtain (*E*)-**38**, this cyclopropanol (2.125 g, 8.3 mmol) was treated with methanesulfonyl chloride (0.77 mL, 9.96 mmol, 1.2 equiv.) in diethyl ether (20 mL), containing triethylamine (3.5 mL, 24.9 mmol, 3 equiv.). The usual workup gave 2.77 g (8.3 mmol, 100% yield) of mesylate (*Z*)-**55c**, as a colourless oil. R_f = 0.25 (eluent pentane/diethyl ether, 8:2). IR (neat): ν(CO) = 2957 cm^{-1}, 2930, 2857, 1472, 1361, 1258, 1166, 1102, 963, 914, 836, 811, 776. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 5.77−5.75 (m, 2 H), 3.71 (t, *J* = 6.3 Hz), 3.02 (s, 3 H), 1.86 (d, *J* = 7.0 Hz, 1 H), 1.74 (dd, *J* = 4.8, 1.6 Hz, 3 H), 1.68 (d, *J* = 7.0 Hz, 1 H), 1.28 (dd, *J* = 8.5, 6.5 Hz, 2 H), 1.17−1.02 (m, 1 H), 0.90 (s, 9 H), 0.06 (s, 6 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 129.4, 127.5, 68.2, 62.4, 39.8, 31.5, 25.9, 21.9, 18.2, 17.7, 17.4, −5.4 ppm. MS (EI): *m*/*z* = 255 (6) [M^+ − 79], 153 (90), 152 (20), 123 (21), 107 (62), 89 (32), 81 (26), 79 (72), 75 (65), 73 (100), 69 (78), 59 (37), 57 (26), 42 (34), 41 (43). MS (DCI, NH_3): *m*/*z* = 352 (25) [M^+ + 18], 335 (58) [M^+ + 1], 334 (20) [M^+], 240 (77), 239 (100), 238 (34), 124 (17).

(*Z*)-2-Ethyl-1-mesyloxy-1-(prop-1-enyl)cyclopropane (56a): A solution of lithium aluminum hydride in tetrahydrofuran (0.93 M, 14.5 mL, 13.43 mmol, 1.85 equiv.) was added dropwise to a solution of dimesylate (*Z*)-**55a** (2 g, 6.71 mmol) in tetrahydrofuran (80 mL). The reaction mixture was stirred at room temperature for 2 h, 100 mL of diethyl ether were then added, and the solution was cooled at 0 °C. Addition of wet Na_2SO_4 gave a clear solution and a grey precipitate. Filtration through Celite and concentration in vacuo gave 1.28 g (6.25 mmol, 93% yield) of sufficiently pure (*Z*)-**56a**, as a pale yellow oil. R_f = 0.70 (eluent pentane/diethyl ether, 1:1). IR (neat): ν(CO) = 3440 cm^{-1}, 2963, 1651, 1455, 1357, 1174, 1047, 967. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 5.74−5.70 (m, 2 H), 2.99 (s, 3 H), 1.70 (d, *J* = 4.6 Hz), 1.64−1.34 (m, 2 H), 1.23 (dd,

J = 8.3, 1.5 Hz, 2 H), 0.99 (t, J = 7.5 Hz, 3 H), 0.89−0.81 (m, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 129.5, 127.2, 67.4, 63.7, 26.7, 21.6, 17.8, 17.4, 13.5 ppm. MS (EI): m/z = 189 (11) [M^+ − 15], 109 (16) [M^+ − 95], 108 (10), 97 (20), 95 (17), 94 (42), 91 (15), 72 (25), 77 (16), 69 (100), 67 (22), 55 (24), 41 (59), 39 (47). MS (DCI, NH_3): m/z = 222 (5) [M^+ + 18], 126 (10), 125 (11), 114 (14), 111 (14), 110 (13), 109 (100), 198 (15). HRMS: found 204.0818, $C_9H_{16}O_3S$ requires 204.0820.

(*Z*)-2-(But-1-enyl)-2-ethyl-1-mesyloxycyclopropane (56b): A solution of dimesylate (*Z*)-**55b** (853 mg, 2.734 mmol) in tetrahydrofuran was treated with lithium aluminum hydride (229 mg, 6.02 mmol, 2.2 equiv.), by the procedure to obtain (*Z*)-**56a**. The usual workup gave 580 mg (2.658 mmol, 97% yield) of sufficiently pure (*Z*)-**56b**, as an turbid oil. R_f = 0.80 (eluent pentane/ethyl acetate, 1:1). IR (neat): ν(CO) = 2964 cm^{-1}, 2936, 2876, 1666, 1458, 1359, 1165, 1938, 971. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 5.77−5.71 (m, 2 H), 3.03 (s, 3 H), 2.08 (dq, J = 7.3, 3.6 Hz, 2 H), 1.66−1.39 (m, 2 H), 1.23 (dd, J = 5, 3.4 Hz, 2 H), 1.01 (q, J = 7.3 Hz, 6 H), 0.92−0.86 (m, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 133.9, 127.5, 68.9, 39.8, 26.9, 24.9, 21.7, 18, 13.6, 13.2 ppm. MS (EI): m/z = 218 (0.2) [M^+], 189 (29), 139 (3), 111 (74), 93 (44), 83 (100), 79 (30), 55 (78), 53 (17), 41 (36), 39 (31). MS (DCI, NH_3): m/z = 236 (100) [M^+ + 18], 139 (13), 123 (45), 122 (14), 114 (21).

(*E*)-1-Azido-1-(but-1-enyl)-2-ethylcyclopropanol (61): A solution of mesylate (*E*)-**49b** (180 mg, 0.83 mmol) in DMF (2 mL) was added to a solution of $Pd(dba)_2$ (24 mg, 0.04 mmol) in dimethyl formamide (DMF, 2 mL), containing PPh_3 (26 mg, 0.1 mmol); the mixture was stirred under an argon stream in order to obtain a clear solution. This solution was then added to a solution of sodium azide (110 mg, 1.67 mmol) in DMF (2 mL) containing [15]-crown-5 ether (20.4 mg, 17 mmol). The reaction mixture was stirred for 12 h at room temperature, and 20 mL of diethyl ether and 3 mL of water were added. The organic layer was washed with saturated ammonium chloride, dried with Na_2SO_4, filtered through Celite and concentrated in vacuo. Chromatography on silica gel (eluent pentane) gave 98 mg (0.71 mmol, 86% yield) of azidocyclopropane (*E*)-**61** as a colourless oil. R_f = 0.49 (eluent pentane). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 5.83 (dt, J = 15.1, 6.5 Hz, 1 H), 5.40 (d, J = 15.1 Hz, 1 H), 2.13 (q, J = 7.3 Hz, 2 H), 1.40−1.20 (m, 3 H), 1.20−1.10 (m, 1 H), 1.03 (t, J = 7.3 Hz, 3 H), 0.96 (t, J = 7.3 Hz, 3 H), 0.63 (dd, J = 5.4, 4.9 Hz, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 135.1, 124.4, 65.8, 28, 25.5, 22.4, 18.4, 13.8, 13.5 ppm. MS (EI): m/z = 137 (17) [M^+], 122 (12), 108 (24), 94 (15), 82 (46), 81 (35), 80 (18), 79 (30), 77 (12), 68 (17), 67 (39), 66 (12), 65 (11), 56 (36), 55 (36), 54 (53), 53 (42), 52 (15), 51 (16), 50 (10), 42 (13), 41 (100), 40 (15), 39 (63). MS (DCI, NH_3): m/z = 139 (10) [M^+ + 2], 138 (100) [M^+ + 1], 137 (9) [M^+]. HRMS: found 137.1197, $C_9H_{15}N_3$ requires 137.1204.

(*E*)-1-Amino-2-ethylcyclopropanecarboxylic Acid (*Coronamic Acid*) (62):[53,65] 1,3-Propanedithiol (440 mg, 4.4 mmol, 4 equiv.) and triethylamine (610 mg, 4.4 mmol) were added to a solution of the azidocyclopropane (*E*)-**61** (180 mg, 1.1 mmol) in methanol (3 mL). The reaction mixture was stirred for 20 h at room temperature, hydrolysed with 0.5 N hydrochloric acid until neutrality, and diluted by addition of 50 mL of diethyl ether. The organic phase was extracted twice with water (2 × 50 mL). The combined aqueous phases were washed twice with diethyl ether, and a saturated $NaHCO_3$ solution was added in order to reach pH 9. After extraction three times by diethyl ether (3 × 50 mL), the combined organic phase was dried with Na_2SO_4, and concentrated in vacuo, to give 153 mg (100% yield) of sufficiently pure (*Z*)-1-(1-but-1-enyl)-2-ethylcyclopropylamine. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 5.6 (dt, J = 15.13, 6.35 Hz, 1 H), 5.39 (d, J = 15.13 Hz, 1 H), 2.08 (q, J = 7.27 Hz, 2 H), 1.70 (s, 2 H), 1.28 (q, J = 7.27 Hz, 2 H), 1.1−0.8 (m, 8 H), 0.38 (dd, J = 5.84, 4.35 Hz, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 132.8, 129.6, 38.5, 30.5, 25.5, 22.9, 22.2, 14.2, 13.9 ppm. MS (EI): m/z = 139 (0.6) [M^+], 111 (25), 110 (100), 82 (21), 81 (10), 54 (10), 42 (17), 41 (21), 29 (12). MS (DCI, NH_3): m/z = 157 (1.4) [M^+ + 18], 141 (11), 140 (100) [M^+ + 1], 139 (18) [M^+], 123 (26), 110 (36).

A solution of the above cyclopropylamine (139 mg, 1 mmol) in acetic acid (5 mL) containing formic acid (3 mL) was ozonolysed for 6 h at 0 °C. A hydrogen peroxide solution (30%, 1 mL) was then added, and the mixture was allowed to reach room temperature overnight. After addition of 6 mL of water, the aqueous phase was extracted three times with dichloromethane (3 × 50 mL). The combined organic phases were dried with $MgSO_4$ and concentrated in vacuo to give 99 mg (77% overall yield from (*E*)-**61**) of the amino acid (*E*)-**62** (coronamic acid), with spectral and analytical data in total agreement with reported data.[65]

(*E*)-1-Azido-2-ethyl-1-(prop-1-enyl)cyclopropane (64a): By the procedure used to obtain the azidocyclopropane (*E*)-**61**, cyclopropyl mesylate (*Z*)-**56a** (650 mg, 3.19 mmol) was treated with $Pd(dba)_2$ (92 mg, 0.16 mmol, 0.05 equiv.), PPh_3 (100 mg, 0.38 mmol, 0.06 equiv.) and sodium azide (415 mg, 6.37 mmol, 2 equiv.) in DMF (5 mL). After the usual workup, careful concentration of a part of the resulting solution in vacuo gave the volatile azidocyclopropane (*Z*)-**64a** as a colourless oil containing a 75:25 mixture of two diastereomers. R_f = 0.45 and 0.38 (eluent pentane). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 5.92 (dd, J = 10.6, 7 Hz, 1 H, *cis*-prop-1-enyl), 5.70 (dq, J = 15.2, 6.5 Hz, 1 H, *trans*-prop-1-enyl), 5.51 (dd, J = 10.5, 1.1 Hz, 1 H, *cis*-prop-1-enyl), 5.32 (dd, J = 15.3, 1.1 Hz, 1 H, *trans*-prop-1-enyl), 1.86 (dd, J = 7, 1.3 Hz, 3 H, *cis*-prop-1-enyl), 1.73 (dd, J = 6.7, 1.1 Hz, 3 H, *trans*-prop-1-enyl), 1.53−1.44 (m, 4 H), 1.00 (t, J = 7.3 Hz, 6 H), 0.98−0.90 (m, 4 H), 0.66−0.63 (m, 1 H, *trans*-prop-1-enyl), 0.53−0.47 (m, 1 H, *cis*-prop-1-enyl) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 131.2, 124.6, 48.1, 28.3, 22.1, 18.5, 17.5, 13.9 ppm.

(*Z*)-1-Azido-1-(but-1-enyl)-2-ethylcyclopropane (64b): By the procedure used to obtain the azidocyclopropane (*E*)-**61**, cyclopropyl mesylate (*Z*)-**56b** (457 mg, 2.10 mmol) was treated with $Pd(dba)_2$ (60.5 mg, 0.105 mmol, 0.05 equiv.), PPh_3 (66 mg, 0.252 mmol, 0.06 equiv.), and sodium azide (273 mg, 4.2 mmol, 2 equiv.) in DMF (5 mL). After the usual workup, chromatography of the residue (eluent pentane) gave 173 mg (50% yield) of the azidocyclopropane (*Z*)-**64b** as a colourless oil containing a 75:25 mixture of diastereomers. R_f = 0.42 (eluent pentane). IR (neat): ν(CO) = 2965 cm^{-1}, 2934, 2876, 2103, 1664, 1462, 1292, 1261, 964. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 5.73 (dt, J = 15.3, 6.4 Hz, 2 H), 5.48 (d, J = 10.75 Hz, 1 H, *cis*-but-1-enyl), 5.28 (ddd, J = 15.3, 1.4 Hz, 1 H, *trans*-but-1-enyl), 2.32 (dq, J = 7.6, 2.3 Hz, 2 H, *cis*-but-1-enyl), 2.09 (dq, J = 7.6, 2.2 Hz, 2 H, *trans*-but-1-enyl), 1.50 (dq, J = 7, 1.7 Hz, 4 H), 1.01 (t, J = 7.5 Hz, 12 H), 0.97−0.91 (m, 4 H), 0.66 (dd, J = 5.5, 4.4 Hz, 1 H, *trans*-but-1-enyl), 0.49 (t, J = 5.5 Hz, 1 H, *cis*-but-1-enyl) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): (*trans*-but-1-enyl): δ = 131.6, 129.1, 48, 28.4, 25.1, 22.1, 18.6, 13.8, 13.6; (*cis*-but-1-enyl): δ = 141.2, 122.5, 47.9, 28.4, 25.9, 22.8, 19.7, 14, 13.4 ppm. HRMS: found 137.1199, $C_9H_{15}N$ requires 137.1204.

(*Z*)-*N*-*tert*-Butyloxycarbonyl-2-ethyl-1-(prop-1-enyl)cyclopropylamine (65a): By the procedure used to obtain the amino acid (*E*)-**62**, a solution of the cyclopropyl azide (*Z*)-**64a** (481 mg, 3.19 mmol) was treated with 1,3-propanedithiol (2.05 mL) and methanol (7 mL) containing triethylamine (2.9 mL, 20.7 mmol, 6.3

equiv.). Acidification with 0.5 N hydrochloric acid solution gave 700 mg of (*Z*)-2-ethyl-1-(prop-1-enyl)cyclopropylamine hydrochloride, containing some triethylamine hydrochloride [which was not totally separable by chromatography on silica gel (eluent dichloromethane/pentane, 9:1)], as a colourless oil. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 5.96 (dd, *J* = 10.5, 7 Hz, 1 H), 5.78 [dq, *J* = 15.2, 6 Hz, 1 H), 5.65 (dd, *J* = 10.5, 1.5 Hz, 1 H), 5.22 (dd, *J* = 15.6, 1.5 Hz, 1 H), 1.75 (dd, *J* = 7.1, 1.5 Hz, 3 H), 1.54 (dd, *J* = 6.5, 1.3 Hz, 3 H), 1.06−0.80 (m, 8 H), 0.92 (t, *J* = 7.3 Hz, 6 H), 0.43−0.37 (m, 2 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): (*trans*-prop-1-enyl): δ = 128.8, 125.8, 38.4, 25.9, 20.6, 17.6, 17.4, 16.4; (*cis*-prop-1-enyl): δ = 136.1, 122.24, 33.9, 23.3, 21.8, 17.61, 17.1, 12.9 ppm.

Di-*tert*-butyl carbonate (402 mg, 51.84 mmol, 1.1 equiv.) and potassium hydroxide (103 mg, 1.84 mmol, 1.1 equiv.) were added successively to a solution of the above cyclopropylamine hydrochloride (270 mg, 1.67 mmol) in water (4 mL) and *tert*-butyl alcohol (3 mL). The reaction mixture was stirred at room temperature overnight, acidified to pH 2 with $NaHSO_4{\cdot}2H_2O$, and extracted three times with diethyl ether (3 × 20 mL). The combined organic phases were dried with $MgSO_4$ and concentrated in vacuo. Chromatography of the residue on silica gel (eluent pentane/diethyl ether, 1:1) gave 456 mg (80% yield) of (*Z*)-**65a** as a yellow oil. IR (neat): ν(CO) = 3384 cm^{-1}, 2963, 1703, 1652, 1455, 1366, 1260, 1173, 1075, 798. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 5.61−5.37 (m, 2 H), 5.10 (dd, *J* = 15.1, 1.5 Hz, 2 H), 1.78 (d, *J* = 5.4 Hz, 3 H), 1.67 (dd, *J* = 6.5, 1.5 Hz, 3 H), 1.45 (s, 18 H), 1.33−1.15 (m, 8 H), 1.00 (t, *J* = 7.3 Hz, 6 H), 0.89 (t, *J* = 7.3 Hz, 2 H), 0.71−0.67 (m, 1 H), 0.55−0.50 (m, 1 H) ppm.

(*Z*)-Methyl 1-Azido-2-ethylcyclopropanecarboxylate (66): Ozone was bubbled for 16 h through a solution of cyclopropylazide (*Z*)-**64a** (370 mg, 2.45 mmol) in acetic acid (15 mL) and formic acid (9 mL). A solution of hydroperoxide (30%, 6 mL) was then added at 0 °C and the reaction mixture was allowed to warm slowly to room temperature overnight. After addition of 30 mL of water and extraction three times by dichloromethane (3 × 100 mL), the combined organic phases were dried with $MgSO_4$ and concentrated in vacuo. Addition of 5 mL of methanol gave, after removal of the solvent in vacuo, 207 mg [1.22 mmol, 50% yield from mesylate (*Z*)-**56a**] of (*Z*)-**66** as a colourless oil. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.80 (s, 3 H), 1.72−1.49 (m, 2 H), 1.08−0.98 (m, 5 H), 0.97−0.81 (m, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 173.6, 52.6, 50, 21.6, 21.3, 19.9, 13.4 ppm.

(*Z*)-Methyl 1-Amino-2-ethylcyclopropanecarboxylate (67): A solution of azido ester (*Z*)-**66** (205 mg, 1.21 mmol) in ethanol (15 mL), containing palladium on carbon (20 mg), was stirred under hydrogen atmosphere at room temperature overnight. After filtration through Celite and removal of solvent in vacuo, chromatography of the residue on silica gel (eluent pentane/diethyl ether, 1:1) gave 173 mg (100% yield) of (*Z*)-**67** as a colourless oil. R_f = 0.28 (eluent dichloromethane/diethyl ether, 7:3). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.69 (s, 3 H), 2.43 (s, 2 H), 1.60−1.39 (m, 4 H), 1.00 (t, *J* = 7.0 Hz, 3 H), 0.67−0.66 (m, 1 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 170.4, 52.2, 39.1, 30.4, 23.3, 21.1, 13.9 ppm. MS (EI): *m*/*z* = 143 (6) [M$^+$], 128 (19), 114 (100), 84 (24). HRMS: found 143.0939, $C_7H_{13}NO_2$ requires 143.0946.

(*Z*)-1-Amino-2-ethylcyclopropanecarboxylic Acid (*allo*-*Coronamic Acid*, 68): A solution of amino ester (*Z*)-**67** (50 mg, 0.35 mmol) in hydrochloric acid (6 N, 5 mL) was heated under reflux for 1 h. The reaction mixture was then cooled to room temperature and most of the hydrochloride acid was removed in vacuo. The residue was dissolved in distilled water and purified by chromatography through an ion-exchange resin (Dowex 50 WX-18) to give 36 mg (0.28 mmol, 80% yield) of the amino acid (*Z*)-**68** as a white solid (m.p. 183 °C. ^{1}H NMR (250 MHz, D_2O): δ = 1.55−0.94 (m, 4 H), 0.84 (t, *J* = 7.0 Hz, 3 H), 0.78−0.62 (m, 1 H) ppm. ^{13}C NMR (50 MHz, D_2O): δ = 176, 39.9, 25.8, 20.7, 17.9, 13 ppm.

(*Z*)-1-Azido-2-[2-(*tert*-butyldimethylsiloxyethyl]-1-(prop-1-enyl)-cyclopropane (69): By the procedure used to obtain the azidocyclopropane (*E*)-**61**, a solution of the cyclopropyl mesylate (*Z*)-**55c** (2.44 g, 7.3 mmol) in DMF (10 mL) was treated with sodium azide (955 mg, 14.6 mmol, 2 equiv.) in the presence of $Pd(dba)_2$ (211 mg, 0.36 mmol, 0.05 equiv.) and PPh_3 (231 mg, 0.87 mmol, 0.12 equiv.). After the usual workup, chromatography of the residue on silica gel (eluent pentane/diethyl ether, 95:5) gave 1.69 g (6.04 mmol, 83% yield) of a 75:25 mixture of *trans*- and *cis*-1-(prop-1-enyl)azidocyclopropane (*Z*)-**69**, as a colourless oil. R_f = 0.9 (eluent pentane/diethyl ether, 8:2). IR (neat): ν(CO) = 2957 cm^{-1}, 2928, 2857, 2099, 1472, 1256, 1105, 961, 836, 776. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 5.95 (dd, *J* = 10.5, 6.8 Hz, 1 H, *cis*-prop-1-enyl), 5.72 (dq, *J* = 15.1, 6.5 Hz, 1 H, *trans*-prop-1-enyl), 5.56 (dd, *J* = 10.3, 1.5 Hz, 1 H, *cis*-prop-1-enyl), 5.33 (dd, *J* = 15.1, 1.5 Hz, 1 H), 3.68 (dt, *J* = 6.9, 1.5 Hz, 4 H), 1.86 (dd, *J* = 6.9, 2.0 Hz, 3 H, *cis*-prop-1-enyl), 1.75 (dd, *J* = 6.5, 1.5 Hz, 3 H, *trans*-prop-1-enyl), 1.69−1.59 (m, 2 H), 1.31−0.93 (m, 6 H), 0.90 (s, 18 H), 0.70 (dd, *J* = 6.5, 5.4 Hz, 1 H, *trans*-prop-1-enyl), 0.59−0.56 (m, 1 H, *cis*-prop-1-enyl), 0.065 (s, 12 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): *trans*-prop-1-enyl: δ = 131.1, 125, 62.7, 47.6, 32.1, 25.9, 23.3, 18.3, 17.5, −5.4; *cis*-prop-1-enyl: δ = 134.05, 124.34, 62.50, 43.02, 32.80, 25.92, 21.18, 19.47, 18.32, 15.25, −5.35 ppm. MS (EI): *m*/*z* = 239 (9), 238 (11), 198 (17), 197 (71), 196 (100), 166 (20), 122 (52), 101 (34), 100 (32), 99 (34), 75 (36), 73 (49), 59 (21), 42 (18). MS (DCI): *m*/*z* = 257 (4) [M$^+$ − 28], 256 (16), 255 (31), 254 (100), 196 (15), 122 (11). $C_{14}H_{27}NO_3Si$ (285.17): calcd. C 59.74, H 9.67, N 14.93; found C 59.74, H 9.69, N 14.41.

(*Z*)-1-Azido-2-[2-(*tert*-butyldimethylsiloxy)ethyl]cyclopropanecarboxylic Acid (70a)

a) From Azidocyclopropane (Z)-69: Ozone was bubbled for 6 h at 0 °C through a solution of (*Z*)-**69** (195 mg, 0.69 mmol) in acetic acid (8 mL) and formic acid (4 mL). A hydrogen peroxide solution (30%, 2 mL) was added, and the reacting solution was allowed to warm to room temperature. Workup as for (*E*)-**62** gave 155 mg (0.54 mmol, 78% yield) of the azido acid (*Z*)-**70a**.

b) From Azidocyclopropane Carbaldehyde (Z)-70c: Sodium periodate (335 mg, 1.57 mmol, 4 equiv.) and ruthenium chloride (2 mg, 8 mmol, 0.02 equiv.) were added to a solution of (*Z*)-**69** (110 mg, 0.39 mmol) in a mixture of acetonitrile (2.6 mL), carbon tetrachloride (2.6 mL), and water (3.9 mL). The reaction mixture was stirred at room temperature overnight, the solvents were then removed in vacuo and the residue was dissolved in 10 mL of ethyl acetate. After filtration through Celite and concentration in vacuo, chromatography of the residue on silica gel (eluent pentane/diethyl ether, 95:5) gave 67 mg (0.25 mmol, 64% yield) of (*Z*)-1-azido-2-[2-(*tert*-butyldimethylsiloxyethyl]cyclopropanecarbaldehyde **70c** as a yellow oil. R_f = 0.3 (eluent pentane/diethyl ether, 9:1). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 9.01 (s, 1 H), 3.78−3.86 (m, 2 H), 1.83−1.73 (m, 3 H), 1.68−1.59 (m, 1 H), 0.89 (s, 10 H), 0.05 (s, 6 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 196.6, 62, 53.6, 31, 25.9, 25.1, 19.8, 18.3, −5.4 ppm. MS (EI): *m*/*z* = 132 (67), 131 (100), 102 (67), 101 (94), 76 (38), 74 (20), 60 (31), 59 (23). MS (DCI): *m*/*z* = 206 (21), 190 (23), 189 (100), 188 (55), 132 (23), 131 (39) ppm.

An aqueous solution of sodium chlorite and sodium dihydrophosphate monohydrate (10%, 5.5 mL) was added to a solution of the

aldehyde (*Z*)-**70c** (67 mg, 0.25 mmol) in a mixture of *tert*-butyl alcohol and 2-methylbut-2-ene (8:3, 11.6 mL). The reaction mixture was then stirred for 30 min, until complete discolouration. After addition of 17 mL of water and five extractions of the aqueous phase with ethyl acetate (5 × 20 mL), the combined organic phase were washed with brine, dried with Na_2SO_4, and concentrated in vacuo. Chromatography of the residue on silica gel (eluent dichloromethane/diethyl ether, 9:1) gave 60 mg (0.21 mmol, 85% yield) of the azido acid (*Z*)-**70a**, as a colourless oil. R_f = 0.74 (eluent dichloromethane/methanol, 9:1). IR (neat): ν(CO) = 3425 cm^{-1}, 2955, 2930, 2858, 2111, 1700, 1257, 1104, 836, 777. ^1H NMR (200 MHz, $CDCl_3$): δ = 4.27 (*t*, *J* = 6.0 Hz, 2 H), 1.96−1.78 (m, 2 H), 1.39−1.13 (m, 2 H), 1.05−0.99 (m, 1 H), 0.88 (s, 9 H), 0.06 (s, 6 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 74.4, 62.8, 45.5, 27, 25.94, 25.5, 21.9, 20.7, −3.9 ppm.

(*E*)- and (*Z*)-Methyl 1-Azido-[2-(*tert*-butyldimethylsiloxy)ethyl]cyclopropanecarboxylate (70b): Ozone was bubbled for 1 h at −78 °C through a solution of the cyclopropylazide (*Z*)-**69** (212 mg, 0.75 mmol) in dichloromethane (6 mL), containing a sodium hydroxide solution in methanol (2.5 M, 1.5 mL), until a persistent blue solution and a yellow precipitate were obtained. After elimination of excess ozone by oxygen bubbling, 10 mL of diethyl ether and 5 mL of water were added, and the mixture was allowed to reach room temperature. The aqueous phase was extracted three times with diethyl ether (3 × 5 mL). The combined organic phases were dried with $MgSO_4$ and concentrated in vacuo. Chromatography of the residue on silica gel (eluent pentane/diethyl ether: 93:7) gave 181 mg (0.60 mmol, 80% yield) of a 16:84 mixture of (*E*)- and (*Z*)-**70b**. R_f = 0.35 and 0.40 (eluent pentane/diethyl ether, 9:1). IR (neat): ν(CO) = 2956 cm^{-1}, 2930, 2858, 2111, 1736, 1258, 1104, 836, 777.

(*Z*)-**70b**: ^1H NMR (250 MHz, $CDCl_3$): δ = 3.82 (s, 3 H), 3.63 (t, *J* = 6.0 Hz, 2 H), 1.79−1.64 (m, 2 H), 1.44−1.24 (m, 3 H), 0.90 (s, 9 H), 0.05 (s, 6 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 170.5, 62.2, 52.6, 46.7, 29.9, 27.9, 25.9, 21.4, 18.23, −5.5 ppm.

(*E*)-**70b**: ^1H NMR (250 MHz, $CDCl_3$): δ = 3.79 (s, 3 H), 3.75−3.59 (m, 2 H), 1.89−1.72 (m, 2 H), 1.63−1.56 (m, 2 H), 0.90 (s, 10 H), 0.05 (s, 6 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 171.9, 62.2, 52.6, 46.1, 31.5, 26.1, 25.8, 21.6, 18.2, −5.5 ppm.

(*Z*)-1-Amino-2-[2-hydroxyethyl)cyclopropanecarboxylic Acid (Methano-Bishomoserine, 71a): By the procedure used to obtain the 2,3-methanoamino acid (*E*)-**62**, 1,3-propanedithiol (60 μL, 0.6 mmol, 6.3 equiv.) and triethylamine (80 μL, 0.62 mmol, 6.5 equiv.) were added to a solution of azido acid (*Z*)-**70a** (27 mg, 95 μmol) in methanol (0.5 mL). After the mixture had been stirred at room temperature for 20 h, the usual workup and chromatography of the residue through ion-exchange resin (Dowex 50WX-18) afforded 9 mg (65% yield) of (*Z*)-**71a** as a colourless oil. ^1H NMR (250 MHz, D_2O): δ = 3.39 (dd, *J* = 6.0 Hz, 2 H), 1.58 (t, *J* = 6.5 Hz, 2 H), 1.51−1.42 (m, 1 H), 1.30−1.28 (m, 1 H), 0.77 (t, *J* = 6.0 Hz, 1 H) ppm. ^{13}C NMR (63 MHz, D_2O): δ = 177.9, 63.1, 41.5, 32, 23.8, 20 ppm. HRMS (M + Na): found 168.06371, $C_6H_{11}NNaO_3$ requires 168.06366.

(*Z*)-2-[2-(But-1-enyl)-2-hydroxycyclopropyl]ethyl-3,3,3-trifluoro-2-methoxy-2-phenyl Propanoate [*Mosher Ester* of *Z*-(52b)]: A solution of asymmetric cyclopropanol (*Z*)-**52b** (produced by treatment of the ester **50b** with *i*PrMgBr in the presence of $Ti(TADDOL)_2$, 28.5 mg, 0.183 mmol) in dichloromethane (1 mL) containing DMAP (3 mg, 22 μmol, 0.12 equiv.) was added dropwise at 0 °C to a solution of (*R*)-2-methoxy-α-(trifluoromethyl)phenylacetic acid (51.5 mg, 0.22 mmol, 1.2 equiv.) in dichloromethane (0.5 mL). Then, under an argon stream, *N*,*N*-dicyclohexylcarbodiimide (DCC, 46 mg, 0.22 mmol, 1.2 equiv.) was added. When the reaction was complete as determined by thin layer chromatography, the mixture was allowed to warm to room temperature and was filtered through Celite. The organic phase was washed three times with hydrochloric acid (0.5 N, 3 × 0.5 mL) until acidity and then with a saturated solution of sodium bicarbonate and saturated brine. The organic phase was dried with Na_2SO_4, and chromatography on silica gel (eluent pentane/ethyl acetate; 3:1) gave 55 mg (0.15 mmol, 82% yield) of the corresponding Mosher ester as a diastereomeric mixture. R_f = 0.49 (eluent pentane/ethyl acetate, 1:1). IR (neat): ν(CO) = 3401 cm^{-1}, 2962, 1749, 1650, 1452, 1273, 1169, 1024. ^1H NMR (250 MHz, D_2O): δ = 7.54−7.40 (m, 1OH), 5.72−5.52 (m, 2 H), 5.21−5.07 (m, 2 H), 4.51−4.41 (m, 2 H), 4.34−4.23 (m, 2 H), 3.55 (s, 6 H), 2.12−1.95 (m, 8 H), 0.98 (dt, *J* = 7.3, 2 Hz, 6 H), 0.83(d, *J* = 2.0 Hz, 4 H), 0.64 (dd, *J* = 4, 1.5 Hz, 4 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 166.6, 133.1, 132.2, 129.6, 128.5, 127.3, 121, 95.1, 66.2, 57.8, 55.4, 26.8, 25.1, 23.4, 20.1, 13.7 ppm. ^{19}F NMR (250 MHz, $CDCl_3$, external reference C_6F_6): δ = −72.15 (s, 3F), −72.55 (s, 3F) ppm. HRMS (M + Na): found 395.144613, $C_{19}H_{23}F_3NaO_4$ requires 395.144610.

Acknowledgments

This work was financially supported by the CNRS and the Université de Paris-Sud (XI), by the INCO-COPERNICUS programme of cooperation of the European Community, for a project called "A new protocol for sustainable environmental management (PROSEM)" and by the International Association for the Promotion of Cooperation with Scientists from the Independent states of the former Soviet Union (INTAS) for a project called "Novel metal mediated transformation for efficient organic synthesis". The authors are grateful to Dr. André Loupy for the use of his Prolabo Synthewave 402 microwave oven.

[1] [1a] J. Salaün, in: *The Chemistry of the Cyclopropyl Group* (Ed.: Z. Rappoport), Rearrangements Involving the Cyclopropyl Group; Wiley, New York, **1987**, pp. 809−878. [1b] J. Salaün, *Top. Curr. Chem.* **1988**, *144*, 1−71 and references cited therein. [1c] *Carbocyclic Three- and Four-membered Ring systems in Methods of Organic Chemistry*; Houben-Weyl; (Ed.: A. de Meijere), **1997**, Vol. E 17a−f and references cited therein.

[2] [2a] J. P. Barnier, B. Garnier, C. Girard, J. M. Denis, J. Salaün, J. M. Conia, *Tetrahedron Lett.* **1973**, 1747−1750. [2b] C. Girard, P. Amice, J. P. Barnier, J. M. Conia, *Tetrahedron Lett.* **1974**, 3329−3332.

[3] [3a] J. Schnaubelt, A. Ullmann, H.-U. Reissig, *Synlett* **1995**, 1223−1225. [3b] A. Ulmann, H.-U. Reissig, O. Rademacher, *Eur. J. Org. Chem.* **1998**, 2541−2549. [3c] P. K. Patra, H.-U. Reissig, *Synlett* **2001**, 33−36. [3d] P. K. Patra, H.-U. Reissig, *Eur. J. Org. Chem.* **2001**, 4195−4206.

[4] B. M. Trost, Y. Nishimura, K. Yamamoto, S. S. McElvain, *J. Am. Chem. Soc.* **1979**, *101*, 1328−1330.

[5] [5a] J. Salaün, B. Karkour, *Tetrahedron Lett.* **1987**, *28*, 4669−4672. [5b] J. Salaün, B. Karkour, J. Ollivier, *Tetrahedron* **1989**, *45*, 3151−3162.

[6] [6a] A. Stolle, J. Ollivier, P. P. Piras, J. Salaün, A. de Meijere, *J. Am. Chem. Soc.* **1992**, *114*, 4051−4067. [6b] J. Ollivier, P. Dorizon, P. P. Piras, A. de Meijere, J. Salaün, *Inorg. Chim. Acta* **1994**, *222*, 37−49. [6c] J. Salaün, *Russian, J. Org. Chem.* **1997**, *33*, 742−780.

[7] [7a] J. Ollivier, N. Girard, J. Salaün, *Synlett* **1999**, 1539−1542. [7b] V. Paschetta, F. M. Cordero, R. Paugam, J. Ollivier, A. Brandi, J. Salaün, *Synlett* **2001**, 1233−1236.

[8] T. Chevtchouk, J. Ollivier, J. Salaün, *Tetrahedron: Asymmetry* **1997**, *8*, 1005−1009. T. Chevtchouk, J. Ollivier, J.; Salaün, *Tetrahedron: Asymmetry* **1997**, *8*, 1011−1014.

[9] A. Stolle, H. Becker, J. Salaün, A. de Meijere, *Tetrahedron Lett.* **1994**, *35*, 3517−3520; A. Stolle, H. Becker, J. Salaün, A. de Meijere, *Tetrahedron Lett.* **1994**, *35*, 3521−3524.
[10] V. Atlan, S. Racouchot, M. Rubin, C. Bremer, J. Ollivier, A. de Meijere, J. Salaün, *Tetrahedron: Asymmetry* **1998**, *9*, 1131−1135.
[11] [11a] K. Estieu, R. Paugam, J. Ollivier, J. Salaün, F. M. Cordero, A. Goti, A. Brandi, *J. Org. Chem.* **1997**, *62*, 8276−8277. [11b] M. Ferrara, F. M.; Cordero, A. Goti, A.; Brandi, K. Estieu, R. Paugam, J. Ollivier, J. Salaün, *Eur. J. Org. Chem.* **1999**, 2725−2739. [11c] F. Pisaneschi, F. M. Cordero, A. Goti, R. Paugam, J. Ollivier, A. Brandi, J. Salaün, *Tetrahedron: Asymmetry* **2000**, *11*, 897−909.
[12] F. M. Cordero, F. Pisaneschi, A. Goti, J. Ollivier, J. Salaün, A. Brandi, *J. Am. Chem. Soc.* **2000**, *122*, 8075−8076.
[13] [13a] J. Salaün, M. S. Baird, *Curr. Med. Chem.* **1995**, *2*, 511−542. [13b] J. Salaün, *Top. Curr. Chem.* **2000**, *207*, 1−67.
[14] J. Salaün, J. M. Conia, *Tetrahedron Lett.* **1972**, 2849−2852.
[15] J. Salaün, *Chem. Rev.* **1983**, *83*, 619−632.
[16] J. Salaün, *J. Chem. Rev.* **1989**, *89*, 1247−1270.
[17] [17a] O. G. Kulinkovich, S. V. Sviridov, D. A. Vasilevskii, T. S. Prityts kaya, *Zh. Org. Khim.* **1989**, *25*, 2245−2246. [17b] O. G. Kulinkovich, S. V. Sviridov, D. A. Vasilevskii, T. S. Prityts kaya, *Synthesis* **1991**, 234−235. [17c] O. G. Kulinkovich, S. V. Sviridov, D. A. Vasilevskii, A. I. Savchenko, T. S. Prityts kaya, *Zh. Org. Khim.* **1991**, *27*, 294−298. [17d] O. G. Kulinkovich, A. de Meijere, *Chem. Rev.* **2000**, *100*, 2789−2834 and references cited therein.[17e] O. G. Kulinkovich, *Pure Appl. Chem.* **2000**, *72*, 1715−1719 and references cited therein. [17f] A. I. Savchenko, O. G. Kulinkovich, *Zh. Org. Khim.* **1997**, *33*, 913−915.
[18] [18a] F. Sato, H. Urabe, S. Otamoto, *Synlett* **2000**, 753−775 and references cited therein. [18b] O. L. Epstein, A. I. Savchenko, O. G. Kulinkovich, *Tetrahedron Lett.* **1999**, *40*, 5935−5938 and references cited therein.
[19] V. Chaplinski, Dissertation, University of Göttingen, **1996**.
[20] F. Huet, G. Emptoz, A. Jubier, *Tetrahedron* **1973**, *29*, 479−485.
[21] J. Salaün, J. Ollivier, *Nouv. J. Chim.* **1981**, *5*, 587−594.
[22] J. Salaün, F. Bennani, J. C. Compain, A. Fadel, J. Ollivier, *J. Org. Chem.* **1980**, *45*, 4129−4135.
[23] J. Ollivier, P. P. Piras, A. Stolle, P. Aufranc, A. de Meijere, J. Salaün, *Tetrahedron Lett.* **1992**, *33*, 3307−3310.
[24] [24a] S. Racouchot, J. Ollivier, J. Salaün, *Synlett* **2000**, 1729−1732. [24b] O. G. Kulinkovich, O. L. Epstein, V. E. Isakov, E. A. Khmel′nitskaya, *Synlett* **2001**, 49−52.
[25] M. V. Raiman, N. A. Il′ina, O. G. Kulinkovich, *Synlett* **1999**, 1053−1054.
[26] S. Y. Cho, J. K. Cha, *Org. Lett.* **2000**, *2*, 1337−1339.
[27] J. Salaün, Y. Almirantis, *Tetrahedron* **1983**, *39*, 2421−2428.
[28] E. J. Corey, S. A. Rao, M. S. Noe, *J. Am. Chem. Soc.* **1994**, *116*, 9345−9346.
[29] O. G. Kulinkovich, A. I. Savchencko, S. V. Sviridov, D. A. Vasilevski, *Mendeleev Commun.* **1993**, 230−231.
[30] I. Müller, J. Ollivier, J. Salaün, unpublished.
[31] Y. Kozyrkov, A. Pukin, O. G. Kulinkovich, J. Ollivier, J. Salaün, *Tetrahedron Lett.* **2000**, *41*, 6399−6402.
[32] [32a] B. Achmatowicz, P. Jankowski, J. Wicha, *Tetrahedron Lett.* **1996**, *37*, 5589−5592. [32b] A. Pukin, O. G. Kulinkovich, J. Ollivier, J. Salaün, unpublished.
[33] [33a] S. V. Sviridov, D. A. Vasilevskii, O. Kulinkovich, *Zh. Org. Khim.* **1991**, *27*, 1431−1433. [33b] S. V. Sviridov, D. A. Vasilevskii, O. Kulinkovich, *J. Org. Chem. USRR [Engl. Transl.]* **1991**, *27*, 1251−1253.
[34] I. Sylvestre, J. Ollivier, J. Salaün, *Tetrahedron Lett.* **2001**, *42*, 4991−4994.
[35] A. Esposito, M. Taddei, *J. Org. Chem.* **2000**, *65*, 9245−9248.
[36] [36a] O. Grummitt, E. I. Becker, *Org. Synth.* **1963**, Coll. Vol. 4, 771−775. [36b] C. M. Utermoehlen, M. Singh, R. E. Lehr, *J. Org. Chem.* **1987**, *52*, 5574−5582.
[37] M. A. Tius, X. Gu, J. W. Truesdell, S. Savariar, P. P. Crooker, *Synthesis* **1988**, 36−40.
[38] A. Boutros, J. Y. Legros, J. C. Fiaud, *Tetrahedron* **2000**, *56*, 2239−2242.
[39] N. Ragoussis, *Tetrahedron Lett.* **1987**, *28*, 93−96.
[40] H. M. S. Kuman, B. V. S. Reddy, E. J. Reddy, J. S. Yadav, *Tetrahedron Lett.* **1999**, *40*, 2401−2404.
[41] A. Kasatkin, F. Sato, *Tetrahedron Lett.* **1995**, *36*, 6079−6082.
[42] L. Lombardo, *Tetrahedron Lett.* **1985**, *26*, 381−384.
[43] Formation of **52a** [de: 86%] was reported previously, see ref.[41]
[44] S. Racouchot, PhD Thesis, University of Paris-Sud, Orsay, **2001**.
[45] [45a] M. Braun, *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 519−522. [45b] K. Narasaka, N. Iwasawa, M. Inone, T. Yamada, N. Nakashima, T. Suginori, *J. Am. Chem. Soc.* **1989**, *111*, 5340−5345.
[46] L. Levêque, M. Leblanc, R. Pastor, *Tetrahedron Lett.* **2000**, *41*, 5043−5046.
[47] [47a] G. E. Heck, X.-Y. Li, D. Krishamurthy, *J. Org. Chem.* **1995**, *60*, 5998−5999. [47b] S. Matsukawa, K. Mikami, *Tetrahedron: Asymmetry* **1997**, *8*, 815−816; **1995**, *6*, 2571−2574.
[48] K. Mikami, S. Matsukawa, T. Volk, M. Terada, *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2768−2771.
[49] Y.-D. Wu, Z-X. Yu, *J. Am. Chem. Soc.* **2001**, *123*, 5777−5786.
[50] [50a] C. A. Stammer, *Tetrahedron* **1990**, *46*, 2231−2254 [50b] A. Alami, M. Calmes, J. Dannis, R. Jacquier, *Bull. Soc. Chim. Fr.* **1993**, *130*, 5−24. [50c] K. Burgess, H. Ho, D. Moye-Sherman, *Synlett* **1994**, 575−583.
[51] P. Aufranc, J. Ollivier, A. Stolle, C. Bremer, M. Es-Sayed, A. de Meijere, J. Salaün, *Tetrahedron Lett.* **1993**, *34*, 4193−4196.
[52] O. Zschage, D. Hoppe, *Tetrahedron* **1992**, *48*, 8389−8392.
[53] P. Dorizon, G. Su, G. Ludvig, L. Nikitina, R. Paugam, J. Ollivier, J. Salaün, *J. Org. Chem.* **1999**, *64*, 4712−4724.
[54] J. E. Baldwin, R. M. Adlington, B. J. Rawlings, R. H. Jones, *Tetrahedron Lett.* **1985**, *26*, 485−488.
[55] S. Boudjabi, G. Dewynter, N. Voyer, L. Toupet, J. L. Monters, *Eur. J. Org. Chem.* **1999**, *9*, 2275−2283.
[56] T. Hiyama, M. Kai, *Tetrahedron Lett.* **1982**, *23*, 2103−2106.
[57] [57a] J. A. Marshall, A. W. Garofalo, R. C. Sedrani, *Synlett* **1992**, 643−645. [57b] J. A. Marshall, A. W. Garofalo, *J. Org. Chem.* **1993**, *58*, 3675−3680.
[58] [58a] A. Wei, A. Haudrechy, C. Audin, H.-S. Jun, N. Haudrechy-Bretel, Y. Kishi, *J. Org. Chem.* **1995**, *60*, 2160−2169 [58b] B. O. Lindgren, T. Nilsson, *Acta Chem. Scand.* **1973**, *27*, 888−890.
[59] H. H. Wasserman, R. E. Cochoy, M. S. Baird, *J. Am. Chem. Soc.* **1969**, *91*, 2375−2376.
[60] B. Laber, K. P. Gerbling, C. Harde, K. H. Neff, E. Nordhoff, H. D. Pohlenz, *Biochemistry* **1994**, *33*, 3413−3423.
[61] J. M. Jiménez, R. M. Ortuno, *Tetrahedron: Asymmetry* **1996**, *7*, 3203−3208
[62] M. S. Dappen, R. Pelliciari, B. Natalini, J. B. Monahan, C. Chiorri, A. A. Cordi, *J. Med. Chem.* **1991**, *34*, 161−168.
[63] P. J. Joyce, PCT Int. Appl. WO 86 03,944; *Chem. Abstr.* **1987**, *106:* 31592.
[64] C. R. Johnson, D. S. Dhanoa, S. Daljit, *J. Org. Chem.* **1986**, *52*, 1885−1888.
[65] [65a] A. Gaucher, J. Ollivier, J. Marguerite, R. Paugam, J. Salaün, *Can. J. Chem.* **1994**, *72*, 1312−1327. [65b] R. M. Williams, G. J. Fegley, *J. Am. Chem. Soc.* **1991**, *113*, 8796−8806.

Received January 7, 2002
[O02005]