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Diastereoselectivity Control in Formal Nucleophilic Substitution of Bromocyclopropanes with Oxygen- and Sulfur-Based Nucleophiles

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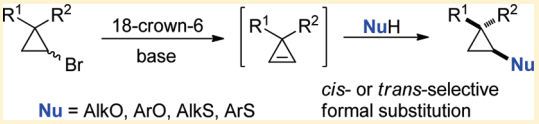
Supporting Information

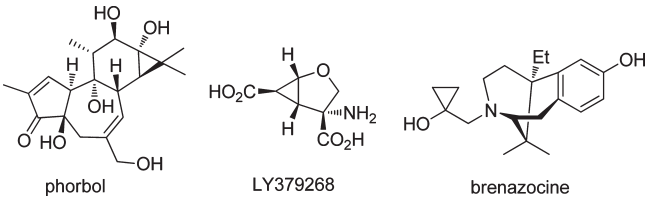
ABSTRACT: A diastereoconvergent formal nucleophilic substitution of bromocyclopropanes with oxygen- and sulfur-based nucleophiles is described. The reaction proceeds via in situ formation of a highly reactive cyclopropene intermediate and subsequent diastereoselective addition of a nucleophile across the strained C=C bond. Three alternative means of controlling the diastereoselectivity of addition have been demonstrated: (1) thermodynamically driven epimerization of enolizable carboxamides, (2) steric control by bulky substituents, and (3) directing effect of carboxamide or carboxylate functions.



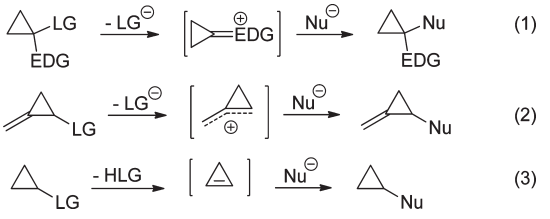
INTRODUCTION

Cyclopropanol derivatives are omnipresent among biologically active natural products[1] and synthetic medicinal agents[2] such as phorbol,[3] brenazocine,[4] and LY379268[5] (Scheme 1). The characteristic reactivity involving a facile Lewis acid- or transition metal-assisted ring-opening makes these compounds versatile building blocks for organic synthesis.[6,7] A number of powerful methods to access cyclopropanols and cyclopropyl ethers have been developed,[6] the most important being the cyclopropanation of enolates,[8] cyclopropanations of olefins with alkoxycarbene equivalents,[9,10] and the Kulinkovich reaction.[11] We envisioned an attractive alternative approach to cyclopropyl ethers via a direct reaction between appropriate oxygen-based nucleophiles and cyclopropyl halides. While it is well-recognized that the classical nucleophilic substitution in strained carbocycles is highly disfavored, it does occur in the substrates possessing strongly electron-donating geminal substituents (Scheme 2, eq 1),[12] as well as in methylenecyclopropanes, assisted by the formation of an allylic carbocation (Scheme 2, eq 2).[13] Alternatively, formal nucleophilic substitution can also be achieved via a 1,2-elimination to generate a cyclopropene intermediate, followed by addition of a nucleophile across the strained double bond (Scheme 2, eq 3). This transformation proceeds readily in the presence of vicinal electron-withdrawing groups.[14] Unsubstituted cyclopropyl halides have been shown to undergo this reaction as well, producing useful cyclopropanol derivatives.[15] However, the majority of the known reactions of this type (Scheme 2, eq 3) are either nonselective due to harsh reaction conditions or have no potential selectivity issue, with only a handful of examples showing good site or facial differentiation in polycyclic substrates, where selectivity of addition is imparted by excessive rigidity and bulk.[16] The same challenge exists[17,18] in the formal substitution of cyclopropyl halides with thiolates en route to stereochemically defined cyclopropyl sulfides.[19] Herein, we report a full account on the formal nucleophilic substitution of bromocyclopropanes applicable to a wide range of oxygen- and sulfur-based nucleophiles, with efficient selectivity control achieved by three alternative means: sterics, directing effect, and thermodynamic equilibrium.[20]

Scheme 1



Scheme 2



RESULTS AND DISCUSSION

Stereoselectivity Control via Thermodynamically Driven Epimerization. The most prominent example showcasing successful selectivity control was the pioneering work by Wiberg,

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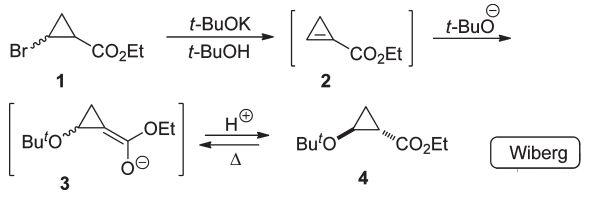
who demonstrated that bromocyclopropane **1** upon dehydrobromination with *t*-BuOK in *t*-BuOH produced a highly unstable intermediate **2**. The latter once formed, immediately reacted with *t*-BuO$^-$ nucleophile to afford trans-adduct **4** (Scheme 3).[21] This protocol, however, proved limited to bulky tertiary alkoxides and the most reactive conjugate double bonds. Thus, our attempt to carry out the reaction of ester **1** with NaOEt in ethanol led to quick decomposition of the starting material and formation of a dark resin. In situ generation of cyclopropene intermediate **6** possessing a less reactive nonconjugate double bond upon treatment of ester **5** with various alkoxides (*t*-BuOK, *i*-PrONa, EtONa, MeONa) in the presence of catalytic amounts of 18-crown-6 ether[22] afforded no detectable monomeric products (Scheme 4).[23] We have also attempted the intramolecular version of this reaction by trapping the tethered alkoxide with the cyclopropene intermediate generated in situ from ester **7**. However, the expected formation of dioxacanone **10** via 8-*exo-trig* cyclization did not take place; instead an intramolecular nucleophilic attack of an alkoxide to the carboxyl function took place, ultimately leading to ring cleavage and formation of the cyclic ester enolate **11** in moderate yield, accompanied by polymeric byproducts (Scheme 5).

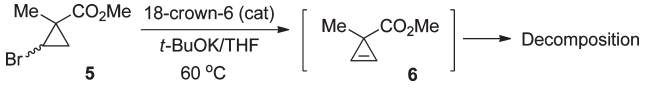
To address this issue we substituted the ester function with a more electron-rich carboxamide functionality. We have previously shown that 2-bromocyclopropylcarboxamides can be readily converted into the corresponding cyclopropenes in the presence of nucleophilic reagents with complete preservation of the amide function.[24] As a proof of concept, amide **12a** was treated with *t*-BuOK in the presence of catalytic 18-crown-6 ether.[22] Gratifyingly, the corresponding trans-diastereomer of *tert*-butyl ether **13aa** was obtained in good yield and high diastereoselectivity (Scheme 6, eq 4). To test the possibility of a ring-retentive addition of more nucleophilic primary and secondary alkoxides, we carried out the same reaction in the presence of external nucleophilic sources (ROH = *n*-PrOH, *i*-PrOH, and PhOH) and excess *t*-BuOK. The addition of *tert*-butoxide species was strongly suppressed under these conditions providing the corresponding *n*-propyl (**13ab**), isopropyl (**13ac**), and phenyl (**16aa**) ethers as major products with complete preservation of the small cycle. Nonetheless, small amounts of unwanted *tert*-butoxide adduct **13aa** were also observed in these cases (Scheme 6, eq 5).

To address the chemoselectivity issue, we tested a series of alternative non-nucleophilic bases in this reaction; however, most of them (such as NaH, LDA, and LiHMDS) failed to generate the requisite cyclopropene intermediate. After substantial experimentation, it was found that powdered KOH allowed for smooth 1,2-elimination, without subsequent addition of the hydroxide species to the cyclopropene double bond (Scheme 7). Indeed, even after prolonged heating at 110 °C, cyclopropene **15**,[24b] generated from bromocyclopropane **25a** in the presence of KOH and 18-crown-6, did not show any traces of hydroxide

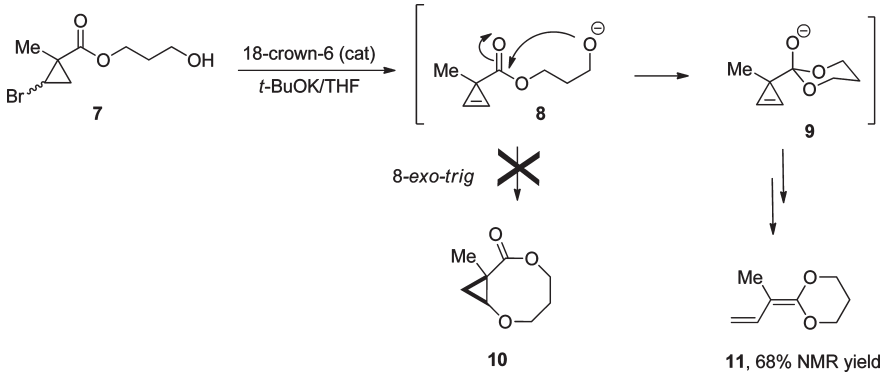
Scheme 3



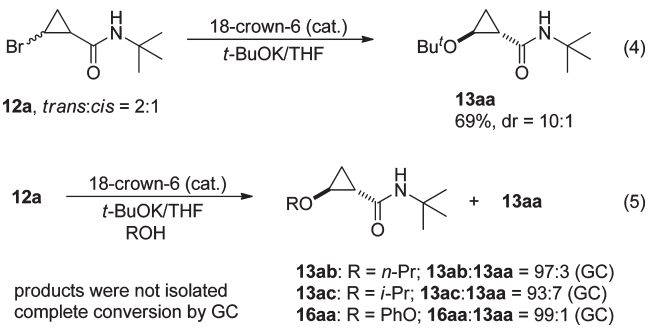
Scheme 4



Scheme 5



Scheme 6



Scheme 7

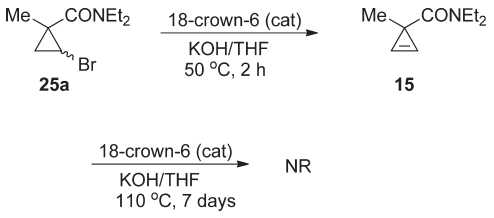


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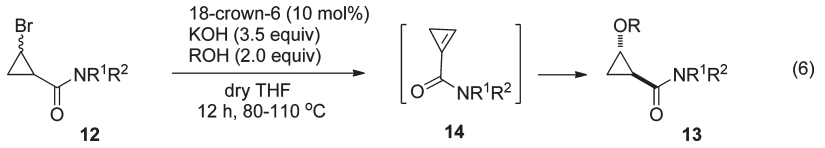
Table 1. Formal Nucleophilic Substitution of Bromocyclopropanes with Alkoxides[a]



entry	R^1, R^2	RO	product	yield, %[b]	dr[c]	dr upgraded[d]
1	*t*-Bu, H (**12a**)	*n*-PrO	**13ab**	71	9:1	39:1 (100)
2	*t*-Bu, H (**12a**)	$MeOCH_2CH_2O$	**13ad**	97	8:1	19:1 (97)
3	Et, Et (**12b**)	$MeOCH_2CH_2O$	**13bd**	87	16:1	
4	*t*-Bu, H (**12a**)	$CH_2{=}CH(CH_2)_3O$	**13ae**	85	7:1	19:1 (95)
5	morph[e] (**12c**)	$CH_2{=}CH(CH_2)_3O$	**13ce**	84	12:1	
6	*t*-Bu, H (**12a**)	*m*-$NO_2C_6H_4CH_2O$	**13af**	81	8:1	24:1 (98)
7	Et, Et (**12b**)	*m*-$NO_2C_6H_4CH_2O$	**13bf**	93	7:1	22:1 (97)
8	Et, Et (**12b**)	$PhCH_2O$	**13bg**	87[f]	6:1	>50:1 (100)
9	*t*-Bu, H (**12a**)	*c*-$HexNH(CH_2)_3O$	**13ah**	78	14:1	
10	piper[g] (**12d**)	$CH_2{=}CHCH_2O$	**13di**	95[h]	15:1	
11	piper[g] (**12d**)	$PhCH{=}CHCH_2O$	**13dj**	81[i]	19:1	
12	*t*-Bu, H (**12a**)	$HC{\equiv}C{-}CH_2O$	**13ak**	78[h]	10:1	
13	*t*-Bu, H (**12a**)	*i*-PrO	**13ac**	71	8:1	16:1 (96)
14	*t*-Bu, H (**12a**)	$HC{\equiv}C{-}CMe_2O$	**13a*l***	59	10:1	
15	*t*-Bu, H (**12a**)	Ph_3CO	**13am**	50	25:1	
16	Me, MeO	$PhCH_2O$	**13eg**	44[j]	>25:1	

[a] Reactions performed in 0.3−0.5 mmol scale unless specified otherwise. [b] Isolated yields of diastereomeric mixtures. [c] dr (trans:cis) determined by GC or ^{1}H NMR analysis of crude reaction mixtures prior to the diastereoselectivity upgrade. [d] dr (trans:cis) determined by GC or ^{1}H NMR analysis of crude reaction mixtures after the diastereoselectivity upgrade, material balance (%) is given in parentheses. [e] morph = morpholine derivative, R^1R^2 = $(CH_2CH_2)_2O$. [f] Reaction performed in 8 mmol scale. [g] piper = piperidine derivative, R^1R^2 = $(CH_2)_5$. [h] Reaction carried out at 50 °C. [i] Reaction mixture was stirred for 3 h at 60 °C. [j] *t*-BuOK (2.5 equiv) was employed as base, the reaction was performed at rt.

addition or decomposition (Scheme 7). Although such extremely low nucleophilicity of hydroxide species in the described transformation is puzzling, it was a long-sought solution that allowed for combining the 1,2-elimination reaction and addition of an alkoxide, generated in situ from an appropriate alcohol pronucleophile, in a sequential chemoselective transformation (eq 6, Table 1).

The scope of this transformation was investigated with respect to the *N*-substituents and the oxygen nucleophile. Thus, the reaction of bromocyclopropane **12a** with KOH in the presence of *n*-propanol proceeded smoothly affording *trans*-*n*-propoxide adduct **13ab** in good yield and high diastereoselectivity (eq 6, Table 1, entry 1). Other primary alkoxides possessing functional groups, such as methyl ether or an isolated C=C double bond, were added very efficiently, providing the corresponding cyclopropanol ethers **13ad**, **13bd**, **13ae**, and **13ce** in high yields (entries 2−5). *m*-Nitrobenzyl-protected cyclopropanols **13af** and **13bf** were also obtained in very good yields from the corresponding benzyl alcohol (entries 6 and 7). The reaction with benzyl alcohol was easily scaled up to 8 mmol scale: product **13bg** was obtained after vacuum distillation in 87% yield (entry 8). Notably, a very selective attack of a bifunctional pronucleophile by the *O*-terminus was observed in the reaction of bromocyclopropane **12a** with 3-cyclohexylaminopropanol, affording cyclopropyl ether **13ah** in high yield (entry 9). The high chemoselectivity observed in this case was rationalized by a selective deprotonation of the more acidic alcohol function, which renders this moiety more nucleophilic as compared to a less acidic 2° amine.[25] Formal substitution with alkoxides generated from allyl and cinnamyl alcohols also proceeded smoothly, affording the corresponding ethers **13di** and **13dj** (entries 10 and 11). Similarly, a reaction carried out in the presence of propargyl alcohol readily afforded propargyl ether **13ak** (entry 12). It should be mentioned that the latter reaction must be performed at temperatures <60 °C and monitored closely to prevent a base-assisted 1,3-prototropic rearrangement of allyl and propargyl ether moieties into enol and allenyl ether functions, respectively. A much less nucleophilic alkoxide generated from a bulky tertiary propargyl alcohol was also efficiently intercepted with the cyclopropene intermediate, affording product **13a*l***, albeit in a somewhat lower yield (entry 14). Remarkably, no addition of the acetylide species was observed under the described reaction conditions.[26] Furthermore, an extremely sterically hindered trityl ether **13am** was prepared successfully by the reaction of **12a** with triphenylmethanol (entry 15). Attempted addition of benzyl alcohol to Weinreb amide **12e** in the presence of powdered KOH provided a complex mixture of products. However, the analogous reaction performed in the presence of *t*-BuOK proceeded smoothly at room temperature, affording the corresponding cyclopropyl ether **13eg** in moderate yield but with perfect diastereoselectivity (entry 16).

Having met success with the addition of alkoxides, we attempted to extend this methodology to the addition of aryloxide species.[27] We rationalized that the aptitude toward addition of these nucleophiles to the soft conjugate double bond of cyclopropene intermediate **12** should be sufficiently high (Scheme 6, eq 5). To our delight, these expectations were fully realized. Thus, the reaction between phenol and cyclopropyl

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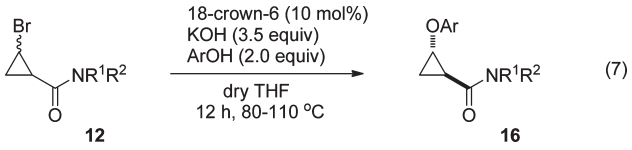
Table 2. Formal Nucleophilic Substitution of Bromocyclopropanes with Aryloxides[a]



entry	R^1, R^2	ArO	product	yield, %[b]	dr[c]	dr upgraded[d]
1	*t*-Bu, H (**12a**)	PhO	**16aa**	79	6:1	>50:1 (96)
2	*t*-Bu, H (**12a**)	*p*-$MeOC_6H_4O$	**16ab**	75	7:1	>50:1 (97)
3	*t*-Bu, H (**12a**)	*p*-BrC_6H_4O	**16ac**	86	8:1	46:1 (100)
4	*t*-Bu, H (**12a**)	*p*-IC_6H_4O	**16ad**	80	10:1	
5	*t*-Bu, H (**12a**)	*p*-$PhCOC_6H_4O$	**16ae**	90	10:1	
6	*t*-Bu, H (**12a**)	*p*-NCC_6H_4O	**16af**	74	10:1	42:1 (96)
7	*t*-Bu, H (**12a**)	*o*-FC_6H_4O	**16ag**	89	12:1	
8	*t*-Bu, H (**12a**)	*o*-$CF_3OC_6H_4O$	**16ah**	84	15:1	
9	Et, Et (**12b**)	*o*-FC_6H_4O	**16bg**	82	12:1	
10	*t*-Bu, H (**12a**)	3,5-$(CH_3)_2C_6H_3O$	**16ai**	95	13:1	
11	morph[e] (**12c**)	3,5-$(CH_3)_2C_6H_3O$	**16ci**	87	20:1	
12	*t*-Bu, H (**12a**)	3,5-$(CF_3)_2C_6H_3O$	**16aj**	85	17:1	
13	*t*-Bu, H (**12a**)	2,4-$(t\text{-Bu})_2C_6H_3O$	**16ak**	95	15:1	
14	morph[e] (**12c**)	2,6-$(CH_3)_2C_6H_3O$	**16cl**	83	25:1	
15	piper[f] (**12d**)	quinolin-8-olate	**16dm**	97	single	

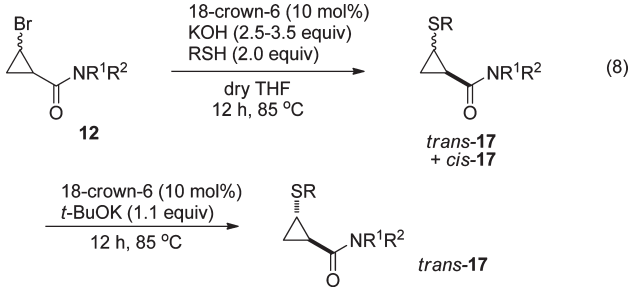
[a] Reactions performed in 0.3−0.5 mmol scale unless specified otherwise. [b] Isolated yields of diastereomeric mixtures. [c] dr (trans:cis) determined by GC or ^{1}H NMR analysis of crude reaction mixtures. [d] dr (trans:cis) determined by GC or ^{1}H NMR analysis of crude reaction mixtures after diastereoselectivity upgrade; material balance (%) is given in parentheses. [e] morph = morpholine derivative, $R^1R^2 = (CH_2CH_2)_2O$. [f] piper = piperidine derivative, $R^1R^2 = (CH_2)_5$.

bromide **12a** provided phenyl ether **16aa** in good isolated yield and high diastereoselectivity (Table 2, entry 1). Electronically diverse para-substituted aryloxides also reacted smoothly producing the corresponding aryl cyclopropyl ethers (**16ab**, **16ac**, **16ad**, **16ae**, **16af**) in high yields (entries 2−6). Similarly, excellent reactivity was demonstrated in the addition of ortho-substituted phenoxides (entries 7−9). Both electron-rich and electron-poor 3,5-disubstituted phenoxides reacted smoothly to produce aryloxycyclopropanes **16ai**, **16bi**, and **16aj** (entries 10−12). Remarkably, highly sterically encumbered phenoxides derived from 2,4-di-*tert*-butylphenol, 2,6-dimethylphenol, and 8-hydroxyquinoline provided the corresponding adducts **16ak**, **16cl**, and **16dm** in high yields and excellent diastereoselectivities (entries 13−15).

It should be mentioned that, regardless of the nucleophile source, all above-described additions of alkoxides and aryloxides provided *trans*-cyclopropyl ethers as major products (Tables 1 and 2). However, in some cases, the relatively low basicity of the non-nucleophlic hydroxide led to an incomplete epimerization of the minor cis-isomers of products **13** and **16** into the thermodynamically more favorable trans-isomers (for example, Table 1, entry 8; Table 2, entry 1). Neither the addition of excess KOH to the reaction mixture nor prolonged reaction times improved the selectivity of these reactions. To address this issue, the isolated mixtures of trans- and cis-products were additionally treated with *t*-BuOK in the presence of catalytic 18-crown-6 in dry THF at elevated temperatures. This allowed for a significant improvement of the diastereomeric ratios for all tested compounds, without notable decomposition of the products (Tables 1 and 2, column 7).

An analogous challenge was stumbled upon as we explored the addition of thiolates to bromocyclopropanes **12** (Table 3, eq 8). These reactions were carried out under general conditions in the presence of alkylthiol pronucleophiles to afford the

Table 3. Formal Nucleophilic Substitution of Bromocyclopropanes with Thiolates and Thiophenols[a]



entry	R^1, R^2	RS	product	yield, %[b]	dr[c]	dr upgraded[d]
1	Bu, H (**12f**)	*n*-$C_{12}H_{25}S$	**17fa**	95	1:1	16:1
2	morph[e] (**12c**)	$PhCH_2S$	**17cb**	92	2:1	>30:1
3	$PhCH_2$, H (**12g**)	$PhCH_2S(CH_2)_3S$	**17gc**	87	2:1	>30:1
4	*t*-Bu, H (**12a**)	$HOCH_2CH_2S$	**17ad**	97	10:1	
5	Ph, H (**12h**)	$HOCH_2CH_2S$	**17hd**	85	>30:1	
6	Bu, H (**12f**)	$PhNHCH_2CH_2S$	**17fe**	94	2:1	>30:1
7	Bu, H (**12f**)	PhS	**17ff**	98	2:1	>30:1

[a] Reactions performed in 0.5 mmol scale unless specified otherwise. [b] Isolated yields of diastereomeric mixtures after the diastereoselectivity upgrade. [c] dr (trans:cis) determined by GC or ^{1}H NMR analysis of crude reaction mixtures prior to the upgrade. [d] dr (trans:cis) determined by GC or ^{1}H NMR analysis of crude reaction mixtures after the diastereoselectivity upgrade. [e] morph = morpholine derivative, $R^1R^2 = (CH_2CH_2)_2O$.

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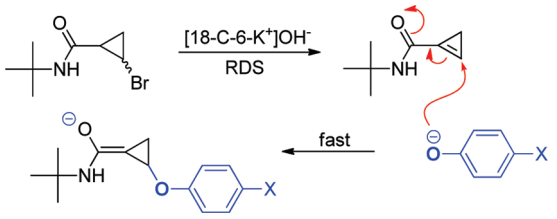
corresponding cyclopropyl sulfides **17fa**, **17cb**, and **17gc** in high yields but with only marginal diastereoselectivity. However, the selectivity was substantially improved upon treatment of the crude products with a stronger base (entries 1−3). The chemoselectivity in the reaction with bifunctional nucleophiles 2-mercaptoethanol and 2-(benzylamino)ethanethiol was investigated (entries 4−6). Expectedly, the less reactive alkoxide and the 2° amine moieties were completely outcompeted by the much more nucleophilic thiolate species, leading to the exclusive formation of cyclopropyl sulfides **17ad**, **17hd**, and **17fe** (entries 4−6). Interestingly, the reactions with 2-mercaptoethanol were sufficiently stereoselective for preparative purpose, therefore no further diastereoselectivity upgrade was necessary (entries 4 and 5). Finally, the reaction with thiophenol provided the corresponding adduct **17ff** in high yield and poor diastereoselectivity, which was routinely upgraded after treatment of the crude reaction mixture with potassium *tert*-butoxide (Table 3, entry 7).



It also deserves noting that the formal substitution with phenoxides and thiolates proceeded much slower and required higher temperatures to achieve complete conversion, as compared to analogous reactions with alkoxides. This disparity in the reactivity can be explained in terms of increased acidity of phenols (and thiols), which readily produce phenoxides (thiolates) and water via a stoichiometric reaction with KOH. As a result, formation of the hydroxide−phenoxide (or hydroxide−thiolate) "buffer" lowers the effective basicity of the system. This, in turn, results in significant deceleration of the dehydrobromination step. The later process is a rate-determining step in this reaction, which was confirmed by the fact that the overall kinetic rate of the transformation did not depend on electronic properties of the phenoxide species. The Swain−Lupton LFER parameters obtained from a series of competing parallel reactions reveal a profound negative *F*-value, indicating the diminution of the negative charge in the anionic phenoxide reagent as a result of addition to an electrophilic double bond (Figure 1).

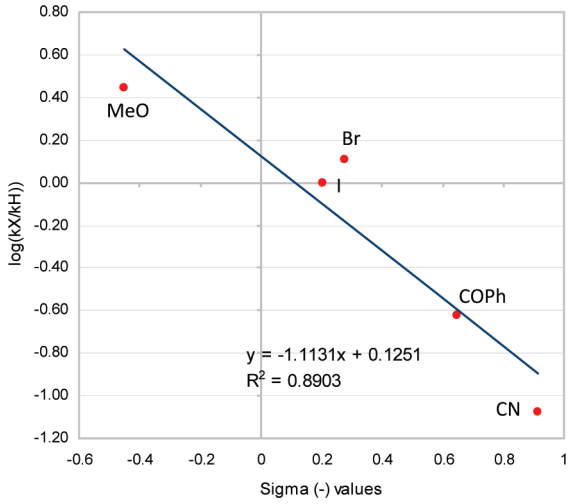
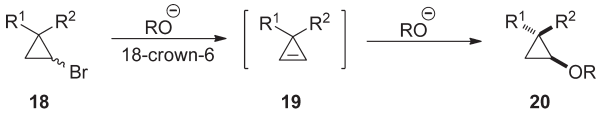


Figure 1. Swain−Lupton LFER studies of the formal nucleophilic substitution of bromocyclopropane **4a** with aryloxides.[28]

We also questioned whether the thermodynamic control of the diastereoselectivity is realized via an epimerization of the tertiary carbon atom adjacent to the amide functionality, or via a reversible addition of a nucleophilic species. To clarify the mechanism, we performed a crossover experiment employing a pair of 2-alkoxycyclopropane carboxamides **13ad** and **13bf**, bearing different alkoxide and amide groups. A mixture of **13ad** and **13bf** was subjected to the typical reaction conditions in the presence of either KOH or *t*-BuOK as a base. In both cases no formation of crossover products **13af** and **13bd** was detected by GC analysis of the crude reaction mixtures (Scheme 8). These results strongly support irreversibility of the nucleophilic addition which, in turn, suggests that thermodynamic control of the diastereoselectivity in this reaction is realized solely via a base-assisted epimerization of the α-CH group.

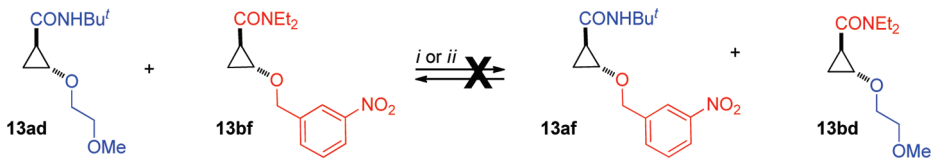
Stereoselectivity Controlled by Steric Effect. As mentioned above, a base-assisted 1,2-dehydrohalogenation of 2,2-disubstituted bromocyclopropanes **18** produces 3,3-disubstituted cyclopropenes **19** possessing a nonconjugate strained double bond (Scheme 9).[29] The corresponding products are relatively stable, readily isolable, and storable, which makes them very attractive synthons[30] for stereoselective additions of various organometallic entities.[31] At the same time, additions of oxygen-based nucleophiles to 3,3-disubstituted cyclopropenes are scarce. All reported examples of this transformation were performed on C_{2v}-symmetric substrates (**19**, $R^1 = R^2$), and thus did not have a stereoselectivity issue.[32] We envisioned that the facial selectivity of the nucleophilic addition to these substrates could be

Scheme 9



18a, **20aa**: R^1 = Ph, R^2 = Me, RO = *t*-BuO; yield 93%, dr >25:1
18b, **20ba**: R^1 = Ph, R^2 = Et, RO = *t*-BuO; yield 85%, dr >25:1

Scheme 8. Test on Reversibility of the Nucleophilic Addition of Alkoxide Species[a]



[a] Conditions i: **13ad** (50 μmol), **13bf** (50 μmol), 18-crown-6 (5 μmol), KOH (175 μmol), THF (500 μL), 85 °C, 48 h. Conditions ii: Same as above, but with *t*-BuOK (175 μmol) in place of KOH.

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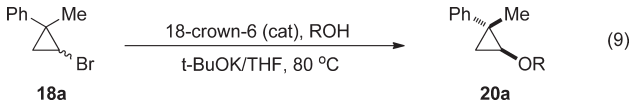
Table 4. Steric Control of Diastereoselectivity in the Formal Nucleophilic Substitution of Bromocyclopropane 18a with Alkoxides[a]

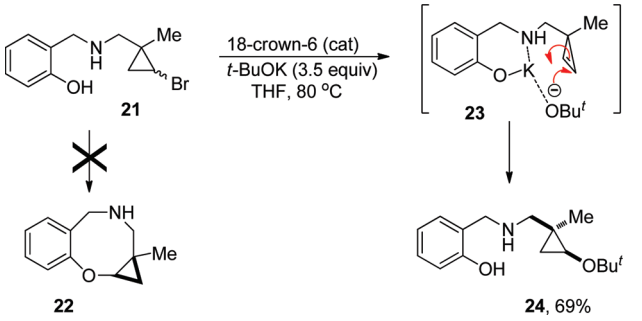


entry	RO	product	yield, %[b]	dr (trans:cis)[c]
1	*n*-PrO	**20ab**	99	16:1
2	*i*-PrO	**20ac**	96	18:1
3	$PhCH_2O$	**20ad**	75	>25:1
4	$Me_2NCH_2CH_2O$	**20ae**	83	11:1
5	*n*-$HexNHCH_2CH_2CH_2O$	**20af**	92	11:1
6	$PhCH_2NHCH_2CH_2CH_2O$	**20ag**	90	12:1
7	2-$FuCH_2NHCH_2CH_2CH_2O$	**20ah**	80	7:1
8	*n*-$BuNHCH_2CH_2OCH_2CH_2O$	**20ai**	82	15:1
9	$H_2NCH_2CH_2CH_2O$	**20aj**	81	13:1
10	*E*-MeCH=CHO	**20ak**[d]	98	>25:1
11	CH=C=CH—O	**20al**[e]	82	>25:1
12	*p*-MeC_6H_4O	**20aa**	70[f]	>25:1

[a] Reactions performed in 0.5 mmol scale unless specified otherwise. [b] Isolated yields of diastereomeric mixtures. [c] dr (trans:cis) determined by GC or ^1H NMR analysis of crude reaction mixtures. [d] Allyl alcohol was used as pronucleophile. [e] Propargyl alcohol was used as pronucleophile. [f] Only trace amounts of 1-methoxy-4-((1*S**,2*R**)-2-methyl-2-phenylcyclopropoxy)benzene (**20am**) were detected by GC analysis of the crude mixture.

efficiently controlled by steric factors. This effect was observed in the previously reported additions of metallic entities to cyclopropenes bearing substituents at C3, which are significantly different in size.[31a,d] It was also believed that generation of the strained intermediate **19** in situ would eliminate the olefin isolation step and thus expand the range of applicable substrates to the most sensitive cyclopropenes. To test this idea, we carried out the reaction of 2-bromo-1-methyl-1-phenylcyclopropane (**18a**) with excess *t*-BuOK (2.0 equiv) in the presence of catalytic 18-crown-6 ether (10 mol %) at various temperatures. It was found that at 50 °C bromocyclopropane **18a** was transformed completely into 3-methyl-3-phenyl cyclopropene (**19a**) along with trace amounts of *tert*-butoxide adduct **20aa**. However, **20aa** was obtained as the sole product in excellent yield when the reaction was allowed to run overnight at 80 °C. Remarkably, the addition proceeded with very high facial selectivity, producing a single trans-diastereomer. Similarly, the reaction of bromocyclopropane **18b**, bearing an ethyl substituent at C3, provided *tert*-butyl ether **20ba** in high yield and excellent diastereoselectivity, thus confirming the efficient steric control (Scheme 9). Inspired by this result, we tested a series of more nucleophilic primary and secondary alkoxides in the addition reaction with **18a** in the presence of 1.5 equiv of *t*-BuOK (Table 4, eq 9). We were pleased to find that both *n*-propoxide and isopropoxide underwent efficient addition, providing the corresponding cyclopropyl ethers **20ab** and **20ac** as sole products in high yields and excellent diastereoselectivities (Table 4, entries 1 and 2). Benzyl-protected[33] cyclopropanol **20ad** was also obtained in good yield in the reaction carried out in the presence of benzylic alcohol (entry 3). *O*-Nucleophiles bearing additional functional groups were also successfully employed in this transformation. Thus,

Scheme 10



2-(dimethylamino)ethanol reacted uneventfully affording **20ae** in high yield (entry 4). Alkoxides possessing a secondary amine functionality reacted chemoselectively producing cyclopropyl ethers **20af**, **20ag**, **20ah**, and **20ai** (entries 5−8) with no corresponding cyclopropylamine derivatives detected. Likewise, the reaction of **18a** with amino alcohol bearing a primary amine function afforded cyclopropyl ether **20aj** as the sole product (entry 9). Apparently, the observed chemoselectivity follows the same trend as the above-described addition of amino alcohols to conjugate cyclopropene intermediates (Table 1, entry 9). However, in contrast to the conjugate additions, the reactions of **18a** with allylic and propargylic alcohols were accompanied with a base-assisted migration of the π-bond, selectively producing the corresponding alkenyl (**20ak**) and allenyl ethers (**20al**), respectively, in excellent yields (Table 4, entries 10 and 11). Considering the relatively high reactivity of phenoxides in the conjugate addition (Table 2) we also attempted the reaction between *p*-methoxyphenol and **18a**. Surprisingly, only traces of 1-methoxy-4-((1*S**,2*R**)-2-methyl-2-phenylcyclopropoxy)benzene (**20am**) were detected in the crude reaction mixture; instead *tert*-butyl ether **20aa** was obtained as the major product (entry 12), while use of KOH instead of *t*-BuOK resulted in no reaction. The inferior reactivity of aryloxides compared to *tert*-butoxide is opposite to that observed in the conjugate addition. Although this phenomenon is not yet completely understood, the non-conjugate strained double bond of cyclopropene **19** apparently behaves as a relatively hard electrophile as opposed to the soft conjugate double bond in the 1-cyclopropene carboxamides described above (eq 5).

Stereoselectivity Controlled by Directing Effect. An attempt to facilitate the addition of an aryloxide species was made by carrying out the reaction in an intramolecular fashion. Bromocyclopropane **21** possessing a tethered phenol was treated with a base under the standard reaction conditions (Scheme 10). Nonetheless, no benzoxazacine product **22** was formed; the intermolecular addition of *tert*-butoxide took place instead, providing **24** as a sole product. Remarkably, the cis-diastereomer of **24** was obtained exclusively, controlled by a strong chelating effect of the 2-(aminomethyl)phenolate moiety in intermediate **23** (Scheme 10).

Accordingly, we probed the ability of other functional groups to coordinate to a potassium cation and direct the addition of alkoxides to the more sterically hindered face. Gratifyingly, it was found that carboxamide moieties can serve as excellent directing groups, governing the addition of nucleophiles to the more hindered face. Thus, reactions of tertiary amide **25a** and

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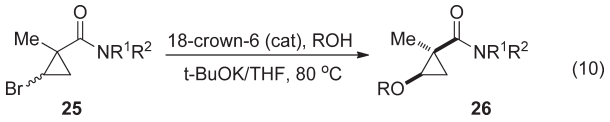
Table 5. Directing Control of Diastereoselectivity in Formal Nucleophilic Substitution of Bromocyclopropyl Carboxamides with Alkoxides[a]

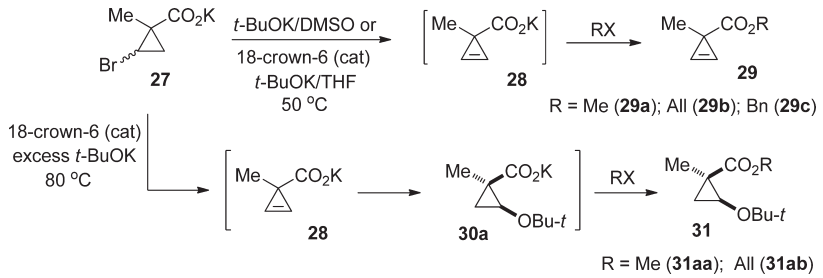


(10)

entry	R^1, R^2	RO	product	yield, %[b]	dr[c]
1	Et, Et (**25a**)	*t*-BuO	**26aa**	87	20:1
2	*t*-Bu, H (**25b**)	*t*-BuO	**26ba**	92	>25:1
3	$CHPh_2$, H (**25c**)	*t*-BuO	**26ca**	75	>25:1
4	Et, Et (**25a**)	*n*-PrO	**26ab**	94	14:1
5	Et, Et (**25a**)	*n*-BuO	**26ac**	91	14:1
6	*n*-Oct, H (**25d**)	*n*-PrO	**26db**	94	>25:1
7	*n*-Hex, H (**25e**)	*i*-PrO	**26ed**	94	14:1
8	Et, Et (**25a**)	$PhCH_2O$	**26ae**	95	>25:1
9	Et, Et (**25a**)	$MeOCH_2CH_2O$	**26af**	89	>25:1
10	Et, Et (**25a**)	$Me_2NCH_2CH_2O$	**26ag**	80	>25:1
11	Et, Et (**25a**)	$CH_2{=}CH(CH_2)_3O$	**26ah**	89	>25:1
12	$-(CH_2)_4-$ (**25f**)	$CH_2{=}CH(CH_2)_3O$	**26fh**	92	20:1
13	$-(CH_2)_5-$ (**25g**)	$CH_2{=}CHCH_2O$	**26gi**	91[d]	>25:1
14	morph[e] (**25h**)	$CH_2{=}CHCH_2O$	**26hi**	88[d]	>25:1
15	Me, Me (**25i**)	$CH_2{=}CHCH_2O$	**26ii**	91[d]	>25:1
16	*n*-Hex, H (**25e**)	$CH_2{=}CHCH_2O$	**26ei**	82[d]	>25:1
17	Me, Me (**25i**)	$Me_2C{=}CHCH_2O$	**26ij**	93[d]	>25:1
18	Me, Me (**25i**)	$Me_2C{=}CHCH2CH_2C(Me){=}CHCH_2O$	**26ik**	89[d]	>25:1

[a] Reactions performed in 0.3−1.0 mmol scale. [b] Isolated yields of diastereomeric mixtures. [c] dr (trans:cis) determined by GC or ^{1}H NMR analysis of crude reaction mixtures. [d] The reaction was performed at 50 °C. [e] morph = morpholine derivative, $R^1R^2 = (CH_2CH_2)_2O$.

Scheme 11



secondary amide **25b** with excess *t*-BuOK afforded the corresponding *tert*-butyl ethers **26aa** and **26ba** in high yield and excellent cis-selectivity (Table 5, entries 1 and 2). Analogously, high facial selectivity was observed in the reaction of a sterically hindered secondary amide **25c** (entry 3). Additions carried out in the presence of competing alkoxides, including primary (**26ab**, **26ac**, and **26ae**, entries 4, 5, and 8) and secondary (**26db** and **26ed**, entries 6 and 7) species, revealed both very high diastereo- and chemoselectivity. Finally, cis-adducts of 2-methoxyethanol (**26af**), 2-(dimethylamino)ethanol (**26ag**), and 4-pentenol (**26ah** and **26fh**) were obtained in high yields (entries 9−12), once again highlighting the excellent functional group compatibility of this transformation.

It should be mentioned that the reaction of **25g** with allylic alcohol carried out at 80 °C afforded allyl ether **26gi** contaminated with the corresponding *E*-prop-1-enyl ether. The latter product has resulted from a thermodynamically driven base-assisted prototropic migration of the double bond into a conjugate position, analogous to the isomerization described above for the addition of allylic and propargylic alkoxides with bromocyclopropane **18a** (Table 4, entries 10 and 11). However, migration proceeded much slower in the case of carboxamides, and could be prevented by lowering the reaction temperature to 50 °C (Table 5, entry 13). Thus, bromocyclopropanes **25e**,**g**−**i** underwent efficient formal substitution to produce the corresponding allylic ethers **25ei**,**gi**,**hi**,**ii** (entries 13−16). Similarly, reaction of **25i** with prenyl and geranyl alcohols proceeded uneventfully to give ethers **26ij** and **26ik**, respectively (entries 17 and 18).

As mentioned above, the strongly nucleophilic reaction conditions did not permit employment of ester-containing substrates

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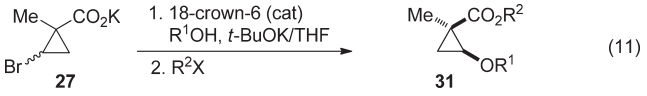
Table 6. Directing Control of Diastereoselectivity in Formal Nucleophilic Substitution of Bromocyclopropyl Carboxylates with Alkoxides[a]



(11)

entry	R^1O	R^2X	product	yield, %[b]	dr[c]
1	*t*-BuO	MeI	**31aa**	79	>50:1
2	*t*-BuO	CH_2=$CHCH_2Br$	**31ab**	81	>50:1
3	*n*-PrO	MeI	**31ba**	83	>50:1
4	*i*-PrO	CH_2=$CHCH_2Br$	**31cb**	76	>50:1
5	$PhCH_2O$	MeI	**31da**	82	>50:1
6	CH_2=$CH(CH_2)_3O$	MeI	**31ea**	72	>50:1
7	CH_2=$CH(CH_2)_3O$	CH_2=$CHCH_2Br$	**31eb**	68	>50:1
8	*E*-CH_3CH=CH [d]	MeI	**31fa**	84	>50:1

[a] Reactions performed in 0.5 mmol scale unless specified otherwise. [b] Isolated yields. [c] dr (trans:cis) determined by GC or ^{1}H NMR analysis of crude reaction mixtures; in most cases, the minor product was not detected above the threshold limit of the analytical method. [d] Allyl alcohol was used as a pronucleophile.

(Schemes 4 and 5).[24a] It was found, however, that the corresponding diastereomeric potassium 1-methyl-2-bromocyclopropylcarboxylates (**27**) could be efficiently used instead of cyclopropyl esters. Thus, it was previously demonstrated that treatment of **27** with *t*-BuOK in dry DMSO at 50 °C effects 1,2-dehydroboromination to produce cyclopropene-3-carboxylic salt **28**. The latter upon trapping in situ with an S_N2-active alkyl halide affords the corresponding ester **29**.[23,31b,e] We observed very similar reactivity when carboxylate **27** was treated with base in the presence of catalytic 18-crown-6 in a THF solution at 50 °C (Scheme 11). The corresponding cyclopropenylesters **29a** (R = Me), **29b** (R = Allyl), and **29c** (R = Bn) were produced cleanly, as judged by GC/MS and ^{1}H NMR analyses of the crude reaction mixtures. In contrast, dehydrobromination of **27** carried out at 80 °C with excess *t*-BuOK resulted in exclusive formation of salt **30a**, which after subsequent treatment with methyl iodide or allyl bromide afforded the corresponding cis-esters **31aa** or **31ab** as sole products in high yield (Scheme 11, Table 6, entires 1 and 2). Remarkably, similarly to the carboxamide function, the carboxylate moiety in intermediate **28** served as an effective directing group for the diastereoselective nucleophilic attack.

Thus, directed additions of *n*-propoxide and isopropoxide nucleophiles gave rise to cis-esters **31ba** and **31cb** in good overall yields and excellent cis-selectivities (Table 6, entires 3 and 4). Benzyl-protected *cis*-cyclopropanol **31da** was readily produced in the presence of benzyl alcohol (entry 5). Employment of pent-4-enyl alcohol as a pronucleophile allowed for efficient preparation of cyclopropyl ethers **31ea** and **31eb** possessing a terminal olefin moiety in the side chain (entries 6 and 7). In contrast to the above-described nucleophilic attack of allylic alkoxides on carboxamides (Table 5, entries 13−18), the analogous addition to carboxylates was accompanied by a facile base-assisted 1,2-migration of the double bond to afford, after electrophilic quench, *E*-propenyl ether **31fa** (Table 6, entry 8). Such different reactivity can be attributed to a higher kinetic acidity of the *cis*-allyloxide moiety, as a result of lower sterical hindrance exerted by the carboxylic moiety compared to a more bulky carboxamide functionality.

CONCLUSIONS

An efficient formal nucleophilic substitution of bromocyclopropanes with *O*- and *S*-based nucleophiles has been developed. This transformation proceeds via a stereoconvergent dehydrobromination, followed by diastereoselective addition of a nucleophilic species across the strained C=C bond of a cyclopropene intermediate. Both potentially isolable cyclopropene intermediates and the extremely unstable, monosubstituted strained cyclic species have been efficiently intercepted with various alkoxides. The use of KOH as a base in the case of disubstituted cyclopropanes allowed for expanding the range of applicable nucleophiles, encompassing both hard and soft species, such as alkoxides, phenoxides, and thiolates. In addition, by taking advantage of a fine balance between the pronucleophiles' acidity and nucleophilicity, a highly chemoselective addition of bifunctional pronucleophiles was achieved without the need for protecting groups. A conjugate addition of nucleophiles to the unstable monosubstituted cyclopropenes generated in situ from disubstituted cyclopropanes provided trans-products via a thermodynamically controlled epimerization. On the other hand, the nonconjugate addition can be efficiently controlled by either sterics or a directing effect of appropriate functional groups, such as carboxamides or carboxylic salts.

EXPERIMENTAL SECTION

General Information. NMR spectra were recorded on a 400 MHz instrument, equipped with a quadruple-band gradient probe (H/C/P/F QNP) or a 500 MHz instrument with a dual carbon/proton cryoprobe (CPDUL). ^{13}C NMR spectra were registered with broad-band decoupling. The (+) and (−) designations represent positive and negative intensities of signals in ^{13}C DEPT-135 experiments. GC/MS analyses were performed with a 30 m × 0.25 mm × 0.25 μm capillary column (polydimethylsiloxane, 5% Ph). Helium (99.96%), additionally purified by passing consecutively through an oxygen/moisture/hydrocarbon trap and oxygen/moisture trap, was used as a carrier gas. High-resolution mass spectra were obtained by using electrospray ionization and time-of-flight detection techniques. Glassware employed in moisture-free syntheses was flame-dried under vacuum prior to use. Water was purified by dual stage deionization, followed by dual stage reverse osmosis. Anhydrous THF was obtained by passing degassed commercially available HPLC-grade inhibitor-free solvent consecutively through two columns filled with activated alumina. Anhydrous triethylamine was obtained by distillation of ACS-grade commercially available materials over calcium hydride in a nitrogen atmosphere. All other commercially available reagents were used as received. Bromocyclopropanes **5**,[31c] **12a**,[20b,34] **12b**,[34] **12c**,[20b,34] **12d**,[34] **12e**,[34] **18a**,[29b] **18b**,[20a] **21**,[20a] **25a**,[20a,24a] **25b**,[20a] **25c**,[20a] **25d**,[20a] **25e**,[20a,24a] **25f**,[20a] **25g**,[24a] **25h**,[24a] and **27**[31b,e] were prepared according to previously published procedures. Cyclopropenes **15**,[24a] **29a**,[31b,e] and **29b,c**[31e] are known compounds, and their physical properties and spectral data were described in our previous publications. Preparative procedures and characterization data for compounds obtained under thermodynamically driven stereoselectivity control (alkoxide adducts **13aa**, **13ab**, **13ac**, **13ad**, **13bd**, **13ae**, **13ce**, **13af**, **13bf**, **13bg**, **13al**, and **13am** as well as for aryloxide adducts **16aa**, **16ab**, **16ac**, **16ad**, **16ae**, and **16af**) were described in the Supporting Information of the corresponding preliminary communication.[20b] Synthesis and properties of several compounds obtained under stereoselectivity control governed by sterics

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(alkoxide adducts **20aa**, **20ba**, **20ab**, **20ac**, **20ad**, **20ae**, and **20ak**) also were previously described in our preliminary report.[20a] The same communication referenced synthetic protocols and characteristics of selected compounds obtained under directed control (alkoxide adducts **24**, **26aa**, **26ba**, **26ca**, **26ab**, **26ac**, **26db**, **26ed**, **26fh**, **31aa**, **31ab**, and **31ba**).[20a] 2-Bromocyclopropanecarbonyl chloride[34] and 2-bromo-1-methylcyclopropanecarbonyl chloride[20a,24a] were prepared according to published procedures. Synthesis, physical properties, and spectral data of all new compounds obtained in the frame of these studies are described below.

Preparation of Starting Materials. 3-Cyclohexylamino-1-propanol:[35]**.** A three-necked, round-bottomed flask (250 mL) equipped with a reflux condenser, a thermometer, and an addition funnel (100 mL) was charged with $LiAlH_4$ (1.30 g, 38.4 mmol, 1.50 equiv) and anhydrous THF (30 mL). The resulting suspension was stirred at 0 °C and a solution of methyl 3-(cyclohexylamino)propanoate[36] (4.40 g, 23.2 mmol, 1.00 equiv) in dry THF (50 mL) was added dropwise over 30 min. Once addition was complete the mixture was stirred at reflux overnight, then quenched at 0 °C consecutively with water (20 mL) and a concentrated aqueous solution of NaOH (5.0 g in 5 mL of water). The resulting suspension was diluted with water (30 mL) and THF (50 mL) and filtered through a fritted funnel. The filter cake was washed with THF (3 × 20 mL), and the washing liquids were combined with the filtrate. The resulting solution was saturated with NaCl and extracted with THF (3 × 20 mL). The combined organic phases were dried with Na_2SO_4, filtered, and concentrated. The crude product was purified by vacuum distillation (bp 60 °C at 15 Torr) to afford the titled compound as a colorless oil, solidifying upon standing. Yield 2.4 g (15.1 mmol, 65%). This material was identical with the known compound based on NMR spectral data. ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 3.80 (t, J = 5.2 Hz, 2H), 2.89 (t, J = 5.7 Hz, 2H), 2.41 (tt, J = 10.3 Hz, 3.6 Hz, 1H), 2.05 (br s, 2H), 1.97−1.79 (m, 2 H), 1.77−1.52 (m, 5H), 1.31−1.13 (m, 3H), 1.11−0.99 (m, 2H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 64.5 (−), 56.6 (+), 46.9 (−), 33.4 (−, 2C), 31.2 (−), 26.0 (−), 24.9 (−, 2C).

3-(Hexylamino)propan-1-ol:[37]**.** The title compound was prepared following the same protocol by reduction of 3-(hexylamino)-propanoate[38] with $LiAlH_4$ (1.50 g, 38.4 mmol, 1.5 equiv). Yield 2.80 g (15.9 mmol, 62%). This material was identical with the known compound based on NMR spectral data. ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 3.77 (t, J = 5.6 Hz, 2H), 2.84 (t, J = 5.8 Hz, 2H), 2.57 (t, J = 7.1 Hz, 2H), 1.67 (quin, J = 5.6 Hz, 2H), 1.44 (quin, J = 7.1 Hz, 2H), 1.35−1.19 (m, 6H), 0.86 (t, J = 6.5 Hz, 3H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 64.1 (−), 49.9 (−), 49.8 (−), 31.6 (−), 30.7 (−), 29.8 (−), 26.9 (−), 22.5 (−), 13.9 (+).

3-((Furan-2-ylmethyl)amino)propan-1-ol:[39]**.** To a stirred solution of furfural (5.00 g, 52.0 mmol, 1.00 equiv) in MeOH (30 mL) was added 3-aminopropan-1-ol (4.00 g, 53.3 mmol, 1.00 equiv), and the mixture was stirred for 30 min at room temperature, then cooled to 0 °C and $NaBH_4$ (2.90 g, 76.6 mmol, 1.50 equiv) was added by small portions over 10 min. The suspension was stirred for 4 h at room temperature and the solvent was removed under vacuum. An aqueous solution of KOH (5.00 g, 47.8 mmol, 1.7 equiv in 20 mL of water) was added and the solution was partitioned between EtOAC and brine. The aqueous layer was extracted with EtOAc (3 × 30 mL). The combined organic phases were dried with Na_2SO_4, filtered, and concentrated. The resulting crude oil was distilled (130 °C) to afford the title compound as a colorless viscous oil. Yield 7.50 g (48.4 mmol, 93%). This material was identical with the known compound based on NMR spectral data. ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 7.32 (dd, J = 1.8, 0.8 Hz, 1H), 6.27 (dd, J = 3.2, 1.9 Hz, 1H), 6.14 (d, J = 3.0 Hz, 1H), 3.74 (s, 2H), 3.71 (t, J = 5.6 Hz, 2H), 2.78 (t, J = 6.1 Hz, 2H), 1.66 (quin, J = 5.9 Hz, 2H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 153.2, 141.7 (+), 110.0 (+), 106.9 (+), 63.0 (−), 48.0 (−), 45.7 (−), 30.9 (−).

2-(2-(Butylamino)ethoxy)ethanol:[40]**.** A two-necked, round-bottomed flask equipped with a reflux condenser and addition fummel (30 mL) was charged with neat *n*-butylamine (7.00 g, 9.46 mL, 96.7 mmol, 3.00 equiv) and 2-(2-chloroethoxy)ethanol (4.00 g, 32.1 mmol, 1.00 equiv) in MeOH (20 mL) was added dropwise over 10 min. Once addition was complete, the mixture was heated at reflux for 18 h. The solvent was removed under vacuum; the resulting salt was washed with hexane (3 × 10 mL) and dissolved in a solution of KOH (1.89 g, 33.7 mmol) in water (10 mL). The resulting slurry was partitioned between THF (10 mL) and brine (10 mL) and extracted with THF (3 × 20 mL). The combined organic phases were dried with Na_2SO_4, filtered, and concentrated to obtain the title compound as a colorless oil, pure enough to be used in further transformation without additional purification. Yield 3.60 g (22.8 mmol, 71%). This material was identical with the known compound based on NMR spectral data. ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 3.68 (t, J = 4.6 Hz, 2H), 3.58 (t, J = 5.2 Hz, 2H), 3.55 (t, J = 4.6 Hz, 2H), 2.77 (t, J = 5.2 Hz, 2H), 2.58 (t, J = 7.3 Hz, 2H), 1.54 (quin, J = 7.3 Hz, 2H), 1.31 (sxt, J = 7.3 Hz, 2H), 0.89 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ ppm 72.6 (−), 70.1 (−), 61.5 (−), 49.5 (−), 49.3 (−), 32.0 (−), 20.4 (−), 14.0 (+).

2-(Phenylamino)ethanethiol:[41]**.** An oven-dried, 250-mL, round-bottomed flask equipped with a reflux condenser was charged with 2-(phenylamino)ethanol (686 mg, 5.00 mmol), 2,4-bis(4-methoxyphenyl)-1,3,2,4-dithiadiphosphetane-2,4-disulfide (Lawesson's reagent, 1.01 g, 2.50 mmol), and dry toluene (150 mL). The mixture was stirred at reflux for 1 h, and then filtered through a frit funnel. The filtrate was concentrated, and the crude residual oil was distilled under vacuum (Kugelrohr oven temperature 250 °C, at 2.5 Torr) to yield a colorless oil (475 mg, 3.10 mmol, 62% yield). This material was identical with the known compound based on NMR spectral data. ^{1}H NMR (500.13 MHz, $CDCl_3$) δ 7.22 (app. t, J = 8.2, 7.3 Hz, 2H), 6.77 (t, J = 7.3 Hz, 1H), 6.87 (d, J = 8.2 Hz, 2H), 3.39 (t, J = 6.3 Hz, 2H), 2.81 (q, J = 6.6 Hz, 2H), 1.44 (t, J = 6.9 Hz, 1H, 1H, suppressed after treatment with D_2O); ^{13}C NMR (125.76 MHz, $CDCl_3$) δ 147.7, 129.4 (+, 2C), 117.9 (+), 113.2 (+, 2C), 42.4 (−), 32.8 (−).

3-(Benzylthio)propane-1-thiol:[42]**.** An oven-dried, 250-mL, round-bottomed flask was charged with 1,3-propanedithiol (2.16 g, 20 mmol, 1.1 equiv) and tetrabutylammonium iodide (150 mg, 0.40 mmol, 2.2 mol %) in dry THF (100 mL). The mixture was stirred at room temperature and sodium hydride (60% suspension in mineral oil, 0.80 g, 20 mmol, 1.1 equiv) was added by portions. The resulting mixture was stirred for 30 min, then benzyl bromide (2.1 mL, 3.1 g, 18 mmol) was added dropwise. The solution was stirred for 1 h at room temperature, then filtered on a frit funnel and concentrated under vacuum. The resulting crude oil was distilled under vacuum to afford the title compound as a colorless oil, bp 135−136 °C (1.0 Torr). Yield 1.82 g (9.19 mmol, 51%). This material was identical with the known compound based on NMR spectral data. ^{1}H NMR (500.13 MHz, $CDCl_3$) δ 7.37−7.33 (m, 4H), 7.30−7.25 (m, 1H), 3.74 (s, 2H), 2.62 (dt, J = 7.9, 6.9 Hz, 2H), 2.56 (t, J = 7.1 Hz, 2H), 1.87 (quin, J = 7.1 Hz, 2H), 1.34 (t, J = 8.0 Hz, 1H, suppressed after treatment with D_2O); ^{13}C NMR (125.76 MHz, $CDCl_3$) δ 138.3, 128.8 (+, 2C), 128.4 (+, 2C), 126.9 (+), 36.2 (−), 32.9 (−), 29.5 (−), 23.3 (−); HRMS (TOF ES) found 199.0613, calcd for $C_{10}H_{15}S_2$ (M + H) 199.0615 (1.0 ppm).

3-Hydroxypropyl 2-bromo-1-methylcyclopropanecarboxylate (7): To a stirred solution of 1,3-propanediol (520 μL, 551 mg, 7.24 mmol, 5.00 equiv) in anhydrous pyridine (2 mL) was added dropwise 2-bromo-1-methylcyclopropanecarbonyl chloride (200 μL, 286 mg, 1.45 mmol). The mixture was stirred for 2 h at 0 °C, then quenched with water (20 mL) and extracted with EtOAc (3 × 10 mL). The combined organic phases were washed consecutively with 10% aqueous HCl (10 mL), saturated aqueous $NaHCO_3$ (10 mL), and brine (10 mL), dried with $MgSO_4$, filtered, and concentrated under vacuum. Preparative column chromatography of a residue (eluent hexane/EtOAc, gradient from 4:1 to

1:1) afforded two fractions. The less polar fraction (R_f 0.50, eluent hexane/EtOAc 4:1) contained a mixture of diastereomeric propane-1,3-diyl bis(2-bromo-(methyl)cyclopropanecarboxylates) as a yellowish oil, yield 115 mg (0.29 mmol, 40%). The more polar fraction (R_f 0.50, eluent hexane/EtOAc 1:1) represented a colorless oil that was identified as the title compound. Yield 200 mg (0.84 mmol, 58%). ^{1}H NMR (400.13 MHz, $CDCl_3$) δ [4.34−4.22 (m) and 4.19 (t, J = 6.3 Hz), 2H], [3.69 (t, J = 6.1 Hz) and 3.65 (t, J = 6.1 Hz), 2H], [3.48 (dd, J = 8.1 Hz, 5.3 Hz) and 2.94 (dd, J = 7.6 Hz, 5.6 Hz), 1H], 2.43 (br s, 1H), 1.91−1.74 (m, 3H), [1.44 (s) and 1.36 (s), 3H], [1.23 (dd, J = 7.6 Hz, 6.6 Hz) and 0.99 (app. t, J = 6.1 Hz, 5.6 Hz), 1H]; ^{13}C NMR (100.67 MHz, $CDCl_3$) δ major 173.5, 62.1 (−), 58.77 (−), 31.5 (−), 28.7 (+), 25.1 (−), 23.7, 16.7 (+); minor 171.3, 62.1 (−), 58.84 (−), 31.6 (−), 26.6, 25.9 (+), 22.5 (−), 19.6 (+); FT IR (NaCl, film, cm^{-1}) 3427, 2961, 2887, 1726, 1429, 1398, 1369, 1350, 1250, 1205, 1178, 1155, 1099, 1051, 922, 905, 590; HRMS (TOF ES) found 258.9952, calcd for $C_8H_{13}BrNaO_3$ (M + Na) 258.9946 (2.3 ppm).

2-Bromo-*N*-butylcyclopropanecarboxamide (12f): To a stirred solution of butylamine (0.73 g, 10.0 mmol, 2.50 equiv) in dry THF (25 mL) was added 2-bromocyclopropanecarbonyl chloride (730 mg, 4.0 mmol). The mixture was stirred for 1 h at room temperature, then concentrated under vacuum. The residue was partitioned between 10% aqueous HCl (20 mL) and EtOAc (20 mL). The organic layer was separated and washed consecutively with 10% aqueous HCl (3 × 10 mL) and 4 N aqueous NaOH (5 mL), dried with $MgSO_4$, filtered, and concentrated. The obtained amorphous solid was pure enough to be used for the following transformations without additional purification. Yield 809 mg (3.68 mmol, 92%). ^{1}H NMR (500.13 MHz, CD_3OD) δ 3.19 (t, J = 6.9 Hz, 2H), 3.16 (td, J = 7.6, 4.7, 3.2 Hz, 1H), 2.01 (ddd, J = 9.2, 5.9, 3.2 Hz, 1H), 1.55−1.46 (m, 3H), 1.38 (sxt, J = 7.4 Hz, 2H), 1.32−1.25 (m, 1H), 0.95 (t, J = 7.3 Hz, 3H); ^{13}C NMR (125.76 MHz, CD_3OD) δ 172.7, 40.6 (−), 32.7 (−), 26.1 (+), 21.2 (−), 19.2 (+), 17.8 (−), 14.2 (+); FT IR (NaCl, film, cm^{-1}) 3302, 3092, 3065, 2959, 2932, 2872, 2419, 1634, 1462, 1223, 1020, 953, 800, 696; HRMS (TOF ES) found 220.0337, calcd for $C_8H_{15}BrNO$ (M + H) 220.0337 (0.0 ppm).

***N*-Benzyl-2-bromocyclopropanecarboxamide (12g):** The title compound was prepared by using the protocol described above for the preparation of amide **12f** employing benzylamine (1.10 g, 10.0 mmol, 2.50 equiv) and 2-bromocyclopropanecarbonyl chloride (730 mg, 4.0 mmol). Yield 910 mg (3.57 mmol, 89%). ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 7.37−7.23 (m, 5H), 6.89 (br s, 1H), 4.42−4.31 (m, 2H), 3.18 (ddd, J = 7.6, 4.7, 3.0 Hz, 1H), 1.91 (ddd, J = 9.2, 5.9, 3.0 Hz, 1H), 1.58 (dt, J = 7.6, 5.9 Hz, 1H), 1.27 (dt, J = 9.2 Hz, 5.4 Hz, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 170.2, 137.7, 128.6 (+, 2C), 127.6 (+, 2C), 127.5 (+), 43.8 (−), 25.3 (+), 19.0 (+), 17.5 (−); FT IR (NaCl, film, cm^{-1}) 3296, 3088, 3063, 2930, 1634, 1553, 1454, 1213, 1034, 746, 696, 515; HRMS (TOF ES) found 254.0176, calcd for $C_{11}H_{13}BrNO$ (M + H) 254.0181 (2.0 ppm).

2-Bromo-*N*-phenylcyclopropanecarboxamide (12h): The title compound was prepared by using the protocol described above for the preparation of amide **12f** employing aniline (930 mg, 10 mmol, 2.5 equiv) and 2-bromocyclopropanecarbonyl chloride (730 mg, 4.0 mmol). Yield 874 mg (3.64 mmol, 91%). ^{1}H NMR (500.13 MHz, $CDCl_3$) δ 7.66 (br s, 1H), 7.50 (d, J = 7.9 Hz, 2H), 7.34 (t, J = 7.7 Hz, 2H), 7.14 (t, J = 7.4 Hz, 1H), 3.34 (ddd, J = 7.7, 4.9, 3.2 Hz, 1H), 1.98 (ddd, J = 8.9, 5.8, 3.0 Hz, 1H), 1.77 (dt, J = 7.6, 6.0 Hz, 1H), 1.43 (dt, J = 9.0, 5.4 Hz, 1H); ^{13}C NMR (125.76 MHz, $CDCl_3$) δ 168.4, 137.6, 129.1 (+, 2C), 124.6 (+), 119.9 (+, 2C), 26.6 (+), 19.3 (+), 18.2 (−); FT IR (NaCl, film, cm^{-1}) 3300, 3063, 2932, 1657, 1547, 1447, 1385, 1186, 1024, 756; HRMS (TOF ES) found 261.9844, calcd for $C_{10}H_{10}BrNO$-Na (M + Na) 261.9843 (0.4 ppm).

2-Bromo-*N*,*N*,1-trimethylcyclopropanecarboxamide (25i): Dimethyl amine (40% aqueous solution, 3.25 mL, 26 mmol, 1.3 equiv) was added to a solution of NaOH (2 g, 50 mmol, 2.5 equiv) in water (25 mL). The mixture was stirred at room temperature and 2-bromo-1-methylcyclopropanecarbonyl chloride (3.94 g, 20 mmol) was added dropwise over 5 min. The mixture was stirred for 2 h; the resulting suspension was extracted with EtOAc (3 × 20 mL). The combined organic phases were washed with 5% aqueous NH_4Cl, dried with Na_2SO_4, and concentrated under vacuum. The residue was distilled under vacuum to obtain a 1:1 mixture of diastereomeric title carboxamides as a colorless oil, bp 80 °C (1 Torr). Yield 3.73 g (18.1 mmol, 90%). ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 3.18 (s, 3H), 3.18 (dd, J = 8.1, 4.8 Hz, 1H), 3.10 (br s, 3H), 2.99 (s, 3H), 2.99 (dd, J = 7.3, 4.8 Hz, 1H), 2.92 (br s, 3H), 1.70 (dd, J = 8.0, 6.7 Hz, 1H), 1.58 (dd, J = 6.8, 4.5 Hz, 1H), 1.47 (s, 3H), 1.39 (s, 3H), 1.18 (dd, J = 8.1, 6.8 Hz, 1H), 0.91 (dd, J = 6.7, 4.9 Hz, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 171.2, 169.9, 37.3 (+), 37.0 (br, +), 35.3 (+), 35.1 (br, +), 27.4, 27.2 (+), 25.5 (+), 25.4, 21.3 (−, 2C), 20.6 (+), 18.7 (+); FT IR (NaCl, film, cm^{-1}) 3043, 2932, 2876, 2806, 1643, 1508, 1493, 1381, 1312, 1277, 1213, 1126, 1094, 1034, 754, 694, 608, 503, 422; HRMS (TOF ES) found 228.0007, calcd for $C_7H_{12}BrNONa$ (M + Na) 228.0000 (3.1 ppm).

Decomposition of Esters under Conditions of the Formal Nucleophilic Substitution. Experiment A: An oven-dried, 2-mL Wheaton vial was charged with methyl 2-bromo-1-methylcyclopropane carboxylate (**5**) (19 mg, 0.10 mmol), 18-crown-6 (2.6 mg, 10 μmol, 10 mol %), *t*-BuOK (28 mg, 0.25 mmol, 2.50 equiv), *p*-xylene (10 μL, GC internal standard), and anhydrous THF (1 mL). The mixture was stirred at 60 °C, and the reaction progress was monitored by GC/MS. While relative integral intensity of two peaks corresponding to cis- and trans-diastereomers of **5** was decreasing, a chromatogram of the crude reaction mixture showed no distinct new peaks that could be attributed to an intermediate or a product. When carboxylate **5** was fully consumed (ca. 3−4 h), the mixture was filtered through a Pasteur pipet filled with Celite, partitioned, and concentrated under vacuum. The residue was dissolved in $CDCl_3$ (1 mL) and washed consecutively with water and brine, then the ^{1}H NMR spectrum was recorded, which contained a complex mixture of unidentified oligomeric and polymeric products, but no characteristic signals typical for a three-substituted cyclopropane fragment.

Experiment B: An oven-dried, 2-mL Wheaton vial was charged with 3-hydroxypropyl 2-bromo-1-methylcyclopropanecarboxylate (**7**) (36 mg, 0.15 mmol), 18-crown-6 (4 mg, 15 μmol, 10 mol %), *t*-BuOK (42 mg, 0.38 mmol, 2.50 equiv), and anhydrous THF (1.5 mL). The mixture was stirred at room temperature for 3 h, then filtered through a short plug of Celite, and concentrated under vacuum. ^{1}H NMR spectrum of the residue showed characteristic signals of a vinyl group. Also, four distinct olefinic carbon siganals were detected in the ^{13}C NMR spectrum: two quarternary carbons 157.1 and 148.8 ppm, one methine at 133.9 ppm, and one methylene at 117.6 ppm. This allowed the product to be assigned a putative structure **11**, containing 2-(but-3-en-2-ylidene) moiety. FT IR (NaCl, film, cm^1) 2972, 2930, 2858, 1651, 1632, 1454, 1431, 1412, 1371, 1296, 1277, 1238, 1207, 1151, 1126, 1086, 1026, 1001, 943, 928, 849, 401; HRMS (TOF ES) found 163.0727, calcd for $C_8H_{12}O_2Na$ (M + Na) 163.0735 (4.9 ppm). An attempt to purify this compound by column chromatography caused decomposition.

Adducts Resulting from Thermodynamically Controlled Nucleophilic Attack. (1*R,2*R**)-*N*-(*tert*-Butyl)-2-(3-(cyclohexylamino)propoxy)cyclopropanecarboxamide (13ah): Typical Procedure I:** An oven-dried, 10-mL Weaton vial was charged with 2-bromo-*N*-(*tert*-butyl)cyclopropanecarboxamide (**12a**) (110 mg, 0.5 mmol), 18-crown-6 (13 mg, 50 μmol, 10 mol %), powdered KOH (62 mg, 1.1 mmol, 2.2 equiv), *N*-cyclohexylaminopropanol (157 mg, 1.0 mmol, 2.0 equiv), and anhydrous THF (5 mL). The mixture was stirred at 85 °C for 12 h, then filtered through a fritted funnel and concentrated. The residue was purified by flash chromatography on silica gel, eluting with a mixture EtOAc/triethylamine 95:5. The title compound was isolated as a yellowish viscous oil, R_f 0.26. Yield 116 mg (0.39 mmol, 78%). ^{1}H NMR (500.13 MHz, $CDCl_3$) δ 5.68 (br s, 1H),

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3.53 (t, J = 6.1 Hz, 2H), 3.44 (ddd, J = 6.5, 4.1, 2.0 Hz, 1H), 2.73−2.62 (m, 2H), 2.43 (tt, J = 10.6, 3.6 Hz, 1H), 1.91−1.82 (m, 2H), 1.82−1.63 (m, 4H), 1.56 (dt, J = 12.5, 3.2 Hz, 1H), 1.43 (ddd, J = 9.6, 5.8, 1.9 Hz, 1H), 1.27 (s, 9H), 1.24−1.01 (m, 7H), 0.94 (ddd, J = 9.5, 5.4 Hz, 4.1 Hz, 1H); ^{13}C NMR (125.76 MHz, $CDCl_3$) δ 170.5, 69.2 (−), 59.5 (+), 57.0 (+), 51.2, 43.7 (−), 32.71 (−), 32.65 (−), 29.4 (−), 28.9 (+, 3C), 25.9 (−), 24.9 (−, 2C), 23.5 (+), 13.9 (−); FTIR (NaCl, film, cm^1) 3300, 2928, 2854, 1643, 1549, 1454, 1391, 1381, 1364, 1333, 1258, 1225, 1200, 1169, 1099, 1078, 1047, 1034, 964, 889, 802, 764, 748, 702, 405; HRMS (TOF ES) found 319.2362, calcd for $C_{17}H_{32}N_2O_2Na$ (M + Na) 319.2361 (0.3 ppm).

((1*R,2*R**)-2-(Allyloxy)cyclopropyl)(piperidin-1-yl)methanone (13di):** The title compound was prepared according to typical procedure I, employing (2-bromocyclopropyl)(piperidin-1-yl)methanone (**12d**) (70 mg, 0.3 mmol, 1.0 equiv) and allylic alcohol (19.9 mg, 0.36 mmol, 1.2 equiv). The reaction was carried out at 50 °C for 12 h. Preparative column chromatography of a residue on silica gel afforded the title compound as a colorless oil, R_f 0.40 (hexane/EtOAc 2:1). Yield 59 mg (0.29 mmol, 95%). ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 5.91 (ddt, J = 17.3, 10.4, 5.8 Hz, 1H), 5.28 (dq, J = 17.3, 1.6 Hz, 1H), 5.19 (dq, J = 10.4, 1.3 Hz, 1H), 4.07 (ddt, J = 12.6, 5.6, 1.3 Hz, 1H), 4.02 (m, J = 12.6, 5.8, 1.5 Hz, 1H), 3.63 (ddd, J = 6.3, 3.8, 2.3 Hz, 1H), 3.62−3.52 (m, 4H), 1.97 (ddd, J = 9.5, 5.9, 2.0 Hz, 1H), 1.71−1.58 (m, 4H), 1.58−1.49 (m, 2H), 1.29 (td, J = 6.3, 5.9, 5.3 Hz, 1H), 1.14 (ddd, J = 9.5, 5.3, 3.9 Hz, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 169.4, 134.0 (+), 117.5 (−), 72.0 (−), 60.2 (+), 46.7 (−), 43.1 (−), 26.6 (−), 25.5 (−), 24.6 (−), 19.3 (+), 14.9 (−); FT IR (KBr, cm^{-1}) 3081, 2935, 2854, 1632, 1454, 1445, 1352, 1250, 1225, 1169, 1136, 1128, 1094, 1053, 1014, 943, 924, 874; HRMS (TOF ES) found 210.1496, calcd for $C_{12}H_{20}NO_2$ (M + H) 210.1494 (1.0 ppm).

((1*R,2*R**)-2-(Cinnamyloxy)cyclopropyl)(piperidin-1-yl)-methanone (13dj):** The title compound was prepared according to typical procedure I, employing (2-bromocyclopropyl)(piperidin-1-yl)methanone (**12d**) (62 mg, 0.30 mmol, 1.0 equiv) and cinnamyl alcohol (44 mg, 0.36 mmol, 1.2 equiv). The reaction was carried out at 60 °C for 12 h. Preparative column chromatography of a residue on silica gel afforded the title compound as a colorless oil, R_f 0.40 (hexane/EtOAc 2:3). Yield 69 mg (0.24 mmol, 81%). ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 7.43−7.37 (m, 2H), 7.37−7.30 (m, 2H), 7.30−7.23 (m, 1H), 6.63 (d, J = 15.9 Hz, 1H), 6.30 (dt, J = 15.9, 6.2 Hz, 1H), 4.27 (ddd, J = 12.5, 5.9, 1.3 Hz, 1H), 4.20 (ddd, J = 12.4, 6.4, 1.4 Hz, 1H), 3.71 (ddd, J = 6.4, 4.0, 2.0 Hz, 1H), 3.66−3.47 (m, 4H), 2.02 (ddd, J = 9.6, 5.9 Hz, 2.1 Hz, 1H), 1.70−1.49 (m, 6H), 1.33 (ddd, J = 6.4, 5.9, 5.3 Hz, 1H), 1.19 (ddd, J = 9.5, 5.3, 3.9 Hz, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 169.5, 136.4, 132.9 (+), 128.5 (+, 2C), 127.8 (+), 126.5 (+, 2C), 125.2 (+), 71.6 (−), 60.3 (+), 46.7 (−), 43.1 (−), 26.6 (−), 25.5 (−), 24.6 (−), 19.5 (+), 14.9 (−); FT IR (KBr, cm^{-1}) 3059, 3024, 2935, 2855, 1634, 1446, 1225; HRMS (TOF ES) found 286.1801, calcd for $C_{18}H_{24}NO_2$ (M + H) 286.1807 (2.1 ppm).

(1*R,2*R**)-*N*-(*tert*-Butyl)-2-(prop-2-yn-1-yloxy)cyclopropane-carboxamide (13ak):** The title compound was prepared according to typical procedure I, employing 2-bromo-*N*-(*tert*-butyl)cyclopropanecarboxamide (**12a**) (66 mg, 0.30 mmol, 1.0 equiv) and propargyl alcohol (21 mg, 0.32 mmol, 1.2 equiv). The reaction was carried out at 60 °C for 3 h. Preparative column chromatography of a residual oil on silica gel afforded the title compound as a colorless oil, R_f 0.30 (hexane/EtOAc, 4:1). Yield 46 mg (0.23 mmol, 78%). ^{1}H NMR (500.13 MHz, $CDCl_3$) δ 5.46 (br s, 1 H), 4.24−4.19 (m, 1H), 4.19−4.14 (m, 1H), 3.71 (ddd, J = 6.4, 4.0, 2.2 Hz, 1H), 2.46 (t, J = 2.5 Hz, 1H), 1.55 (ddd, J = 9.6, 6.0, 2.0 Hz, 1H), 1.35 (s, 9H), 1.24 (q, J = 6.0 Hz, 1H), 1.10 (ddd, J = 9.5, 5.6 Hz, 4.1 Hz, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 170.0, 79.3, 74.7 (+), 59.4 (+), 58.2 (−), 51.3, 28.9 (+, 3C), 23.5 (+), 13.6 (−); FT IR (NaCl, cm^{-1}) 3308, 3078, 2968, 2930, 2870, 1724, 1643, 1549, 1537, 1479, 1454, 1394, 1364, 1331, 1256, 1227, 1202, 1153, 1097, 1061, 1043, 1026, 995, 986, 955, 926, 910, 893, 878, 764, 737, 665, 635; HRMS (TOF ES) found 196.1341, calcd for $C_{11}H_{18}NO_2$ (M + H) 196.1338 (1.5 ppm).

(1*R,1*R**)-2-(Benzyloxy)-*N*-methoxy-*N*-methylcyclopropane-carboxamide (13eg):** An oven-dried, 5-mL Wheaton vial was charged with *t*-BuOK (135 mg, 1.20 mmol, 2.5 equiv), 18-crown-6 (13 mg, 50 μmol, 10 mol %), benzyl alcohol (124 mL, 130 mg, 1.20 mmol, 2.50 equiv), and anhydrous THF (3 mL). The mixture was stirred at room temperature and bromocyclopropane **12e** (100 mg, 0.48 mmol) was injected via syringe. The resulting dark-brown mixture was stirred at room temperature for 1 h, then the formed precipitate of KBr was filtered off by using a short plug of Celite, and the filtrate was concentrated under vacuum. Flash column chromatography of a residual dark crude oil silica gel afforded the title compound as a colorless oil, R_f 0.33 (hexane/EtOAc 1:1). Yield 50 mg (0.21 mmol, 44%). ^{1}H NMR (500.13 MHz, $CDCl_3$) δ 7.38−7.24 (m, 5H), 4.60 (d, J = 11.7 Hz, 1H), 4.57 (d, J = 11.7 Hz, 1H), 3.73 (s, 3H), 3.70 (ddd, J = 6.5, 4.3, 1.9 Hz, 1H), 3.19 (s, 3H), 2.36 (br s, 1H), 1.35−1.24 (m, 2H); ^{13}C NMR (125.76 MHz, $CDCl_3$) δ 172.6, 137.3, 128.4 (+, 2C), 127.9 (+, 2C), 127.8 (+), 73.2 (−), 61.5 (+), 60.7 (+), 32.4 (+), 18.6 (+), 15.4 (−); FT IR (film, cm^{-1}) 3030, 3005, 2964, 2935, 2897, 2866, 1661, 1643, 1495, 1454, 1445, 1418, 1385, 1350, 1211, 1175, 1155, 1113, 1086, 1047, 1028, 1005, 972, 951, 897, 872, 741, 698, 611, 440; HRMS (TOF ES) found 258.1117, calcd for $C_{13}H_{17}NO_3Na$ (M + Na) 258.1106 (4.3 ppm).

(1*R,2*R**)-*N*-(*tert*-Butyl)-2-(2,4-di-*tert*-butylphenoxy)-cyclopropanecarboxamide (16ak): Typical Procedure II:** An oven-dried, 5-mL Weaton vial was charged with bromocyclopropane **12a** (110 mg, 0.5 mmol), 18-crown-6 (13.2 mg, 0.05 mmol, 10 mol %), powdered KOH (98 mg, 1.75 mmol, 3.5 equiv), 2,4-di-*tert*-butylphenol (206 mg, 1.00 mmol, 2 equiv), and anhydrous THF (3 mL). The mixture was stirred at 80 °C for 14 h. The mixture was partitioned between water (10 mL) and EtOAc (10 mL). The aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic phases were washed with brine (10 mL), dried with $MgSO_4$, filtered, and concentrated. The residue was purified by flash column chromatography on silica gel eluting first with a 10:1 mixture of hexane/EtOAc until separation of 2,4-di-*tert*-butylphenol. Then the polarity of the eluent was increased (hexane/EtOAc 4:1) and two fractions of diastereomeric products were collected, R_f 0.50 (155 mg), 0.38 (10 mg). Both compounds were white crystalline solids. Combined yield 165 mg (0.48 mmol, 95%). **16ak** (major), mp 87−88 °C: ^{1}H NMR (500.13 MHz, $CDCl_3$) δ 7.35 (d, J = 2.5 Hz, 1H), 7.21 (dd, J = 8.5, 2.5 Hz, 1H), 7.05 (d, J = 8.5 Hz, 1H), 5.69 (br s, 1H), 4.06 (ddd, J = 6.3, 4.1, 2.2 Hz, 1H), 1.61 (ddd, J = 9.5, 6.0, 2.2 Hz, 1H), 1.54 (ps q, J = 6.3, 6.0 Hz, 1H), 1.42 (s, 9H), 1.37 (s, 9H), 1.34 (s, 9H), 1.33−1.30 (m, 1H); ^{13}C NMR (125.76 MHz, $CDCl_3$) δ 170.1, 154.6, 143.2, 136.9, 123.9 (+), 123.3 (+), 112.1 (+), 56.2 (+), 51.5, 34.9, 34.3, 31.6 (+, 3C), 29.8 (+, 3C), 28.9 (+, 3C), 24.2 (+), 14.5 (−); IR (KBr, cm^{-1}) 3298, 3090, 2964, 2907, 2868, 1641, 1560, 1495, 1485, 1454, 1433, 1394, 1360, 1234, 1204, 1165, 1095; GC, R_t 13.01 min; HRMS (TOF ES) found 345.2661, calcd for $C_{22}H_{35}NO_2$ (M^+) 345.2668 (2.0 ppm). *cis*-**16ak** (minor), mp 124−125 °C: ^{1}H NMR (500.19 MHz, $CDCl_3$) δ 7.33 (d, J = 2.2 Hz, 1H), 7.19 (dd, J = 8.5, 2.2 Hz, 1H), 7.16 (d, J = 8.5 Hz, 1H), 5.50 (br s, 1H), 3.82 (td, J = 6.6, 4.4 Hz, 1H), 1.82 (dt, J = 9.5, 6.9 Hz, 1H), 1.58 (td, J = 6.3, 4.4 Hz, 1H), 1.38 (s, 9H), 1.32 (s, 9H), 1.25 (dt, J = 9.5, 6.3 Hz, 1H), 1.17 (s, 9H); ^{13}C NMR (125.76 MHz, $CDCl_3$) δ 167.2, 154.6, 143.6, 137.3, 123.9 (+), 123.1 (+), 112.6 (+), 55.2 (+), 51.1, 35.0, 34.3, 31.6 (+, 3C), 30.0 (+, 3C), 28.6 (+, 3C), 23.6 (+), 11.6 (−); GC, R_t 13.10 min; IR (KBr, cm^{-1}) 3277, 3074, 2959, 2926, 2866, 1651, 1556, 1489, 1456, 1435, 1392, 1362, 1339, 1265, 1234, 1205, 1161, 1142, 1126, 1092, 1026, 1007, 970, 932, 889, 841, 806, 787, 748, 721, 704, 644; GC, R_t 13.10 min; HRMS (TOF ES) found 346.2754, calcd for $C_{22}H_{36}NO_2$ (M + H) 346.2746 (2.3 ppm).

(1*R,2*R**)-*N*-*tert*-Butyl-2-(2-fluorophenoxy)cyclopropanecarboxamide (16ag):** The title compound was prepared according to typical procedure II, employing bromocyclopropane **12a** (110 mg, 0.5 mmol) and 2-fluorophenol (112 mg, 1.0 mmol, 2 equiv). The reaction was carried out at 110 °C for 13 h. Flash column chromatography on silica gel, eluting first with a 12:1 mixture of hexane/EtOAc to separate 2-fluorophenol (R_f 0.34), then with a 3:1 mixture of hexane/EtOAc (R_f 0.36 (major), 0.10 (minor)) afforded the title compound as a white crystalline solid, mp 80−81 °C. Yield 111 mg (0.44 mmol, 89%). ^{1}H NMR (500.13 MHz, $CDCl_3$) δ 7.13−7.20 (m, 1H), 7.03−7.10 (m, 2H), 6.90−6.96 (m, 1H), 5.70 (br s, 1H), 4.08 (ddd, J = 6.3, 3.9, 2.0 Hz, 1H), 1.70 (ddd, J = 9.7, 6.2, 2.0 Hz, 1H), 1.49 (ddd, J = 6.3, 6.2, 5.8 Hz, 1H), 1.37 (s, 9H), 1.28 (ddd, J = 9.7, 5.8, 3.8 Hz, 1H); ^{13}C NMR (125.76 MHz, $CDCl_3$) δ 169.6, 152.1 (d, $^1J_{CF}$ = 245.6 Hz), 146.2 (d, $^2J_{CF}$ = 10.1 Hz), 124.3 (d, $^3J_{CF}$ = 3.8 Hz, +), 121.6 (d, $^3J_{CF}$ = 6.8 Hz, +), 116.1 (d, $^2J_{CF}$ = 18.3 Hz, +), 115.0 (+), 57.3 (+), 51.5, 28.8 (+, 3C), 23.7 (+), 14.2 (−); ^{19}F NMR (376.50 MHz, $CDCl_3$) δ −135.2; IR (KBr, cm^{-1}) 3294, 3090, 3074, 2993, 2962, 1638, 1560, 1502, 1400, 1340, 1279, 1254, 1205, 1111, 1080, 974, 928, 912, 773, 739; GC 10.86 min (major), 11.00 min (minor); HRMS (TOF ES) found 258.1490, calcd for $C_{14}H_{18}FNO_2Li$ (M + Li) 258.1481 (3.5 ppm).

(1*R,2*R**)-*N*-*tert*-Butyl-2-((2-trifluoromethoxy)phenoxy)-cyclopropanecarboxamide (16ah):** The title compound was prepared according to typical procedure II, employing bromocyclopropane **12a** (110 mg, 0.5 mmol) and 2-(trifluoromethoxy)phenol (178 mg, 1.0 mmol, 2 equiv). The reaction was carried out at 105 °C for 4 h. Flash column chromatography on silica gel eluting with 1:1 hexane/EtOAc (R_f 0.49 (major), 0.30 (minor)) afforded the title compound as a white crystalline solid, mp 122−123 °C. Yield 133 mg (0.42 mmol, 84%). ^{1}H NMR (500.13 MHz, $CDCl_3$) δ 7.28 (ddd, J = 8.5, 7.3, 1.6 Hz, 1H), 7.21−7.25 (m, 2 H), 6.99 (ddd, J = 7.9, 7.6, 1.6 Hz, 1H), 5.69 (br s, 1H), 4.11 (ddd, J = 6.3, 3.9, 2.0 Hz, 1H), 1.69 (ddd, J = 9.7, 6.2, 2.0 Hz, 1H), 1.50 (ddd, J = 6.3, 6.2, 5.8 Hz, 1H), 1.39 (s, 9H), 1.26 (ddd, J = 9.7, 5.8, 3.8 Hz, 1H); ^{13}C NMR (125.76 MHz, $CDCl_3$) δ 169.5, 150.8, 137.8, 127.9 (+), 123.0 (+), 121.4 (+), 120.6 (q, $^1J_{CF}$ = 257.5 Hz), 114.7 (+), 57.1 (+), 51.5, 28.8 (+, 3C), 23.8 (+), 14.4 (−); ^{19}F NMR (376.50 MHz, $CDCl_3$) δ −58.3; IR (KBr, cm^{-1}) 3300, 3092, 2968, 2930, 2908, 2872, 1639, 1607, 1564, 1501, 1456, 1435, 1396, 1362, 1339, 1302, 1285, 1269, 1225, 1196, 1161, 1150, 1115, 978, 750, 403; GC 10.49 min (major), 10.68 min (minor); HRMS (TOF ES) found 340.1127, calcd for $C_{15}H_{18}F_3NO_3Na$ (M + Na) 340.1136 (2.6 ppm).

(1*R,2*R**)-*N*-*tert*-Butyl-2-(3,5-dimethylphenoxy)cyclopropanecarboxamide (16ai):** The title compound was prepared according to typical procedure II, employing bromocyclopropane **12a** (110 mg, 0.5 mmol) and 3,5-dimethylphenol (122 mg, 1.00 mmol, 2 equiv). The reaction was carried out at 100 °C for 13 h. Flash column chromatography on silica gel (eluent hexane/EtOAc 3:1, R_f 0.56 (major), 0.13 (minor)) afforded the title compound as a colorless crystalline solid, mp 111−112 °C. Yield 124 mg (0.47 mmol, 95%). ^{1}H NMR (500.13 MHz, $CDCl_3$) δ 6.67 (s, 1H), 6.63 (s, 2H), 5.56 (br s, 1H), 4.00−3.98 (m, 1H), 2.31 (s, 6H), 1.56−1.50 (m, 2H), 1.41 (s, 9H), 1.30−1.26 (m, 1H); ^{13}C NMR (125.76 MHz, $CDCl_3$) δ 169.9, 158.3, 139.3 (2C), 123.1 (+), 112.5 (+, 2C), 56.6 (+), 51.5, 28.9 (+, 3C), 24.2 (+), 21.4 (+), 14.2 (−); IR (KBr, cm^{-1}) 3300, 3207, 3092, 2966, 2918, 2870, 1641, 1614, 1595, 1564, 1474, 1458, 1433, 1396, 1364, 1342, 1317, 1296, 1261, 1231, 1205, 1167, 1144, 1097, 982, 891, 831; GC R_t 11.66 min (major), 11.83 min (minor); HRMS (TOF ES) found 262.1805, calcd for $C_{16}H_{24}NO_2$ (M + H) 262.1807 (0.8 ppm).

(1*R,2*R**)-2-(3,5-Bis(trifluoromethyl)phenoxy)-*N*-*tert*-butylcyclopropanecarboxamide (16aj):** The title compound was prepared according to typical procedure II, employing bromocyclopropane **12a** (110 mg, 0.5 mmol) and 3,5-bis(trifluoromethyl)phenol (230 mg, 1.0 mmol, 2 equiv). The reaction was carried out at 100 °C for 6.5 h. Flash column chromatography on silica gel, eluting first with a 10:1 hexane/EtOAc mixture, then after separation of the residual phenol (R_f 0.25) with a 3:1 hexane/EtOAc mixture (R_f 0.43 (major), 0.40 (minor)) afforded the title compound as a white crystalline solid, mp 158−160 °C. Yield 157 mg (0.43 mmol, 85%). ^{1}H NMR (500.13 MHz, $CDCl_3$) δ 7.53 (s, 1H), 7.42 (s, 2H), 5.62 (br s, 1H), 4.11−4.07 (m, 1H), 1.64−1.58 (m, 2H), 1.41 (s, 9H), 1.37−1.34 (m, 1H); ^{13}C NMR (125.76 MHz, $CDCl_3$) δ 168.9, 159.0, 133.0 (q, $^2J_{CF}$ = 33.0 Hz, 2C), 123.1 (q, $^1J_{CF}$ = 272.2 Hz, 2C), 115.3 (q, $^3J_{CF}$ = 3.7 Hz, 2C), 115.0 (septet, $^3J_{CF}$ = 4.1 Hz), 57.4 (+), 51.8, 28.8 (+, 3C), 23.9 (+), 14.1 (−); ^{19}F NMR (376.50 MHz, $CDCl_3$) δ −63.1; IR (KBr, cm^{-1}) 3306, 3097, 2989, 2974, 2939, 1637, 1560, 1464, 1400, 1377, 1342, 1321, 1277, 1231, 1188, 1128, 1092, 959; GC 10.03 min (major), 9.99 min (minor); HRMS (TOF ES) found 392.1055, calcd for $C_{16}H_{17}F_6NO_2Na$ (M + Na) 392.1061 (1.5 ppm).

(1*R,2*R**)-*N*,*N*-Diethyl-2-(2-fluorophenoxy)cyclopropanecarboxamide (16bg):** The title compound was prepared according to typical procedure II, employing bromocyclopropane **12b** (110 mg, 0.50 mmol) and 2-fluorophenol (112 mg, 1.00 mmol, 2.00 equiv). The reaction was carried out at 110 °C for 14 h. Flash column chromatography on silica gel (eluent hexane/EtOAc 12:1, R_f 2-fluorophenol 0.34, major 0.11, minor 0.03) after elution of 2-fluorophenol where the eluent polarity was increased (hexane/EtOAc 3:1, R_f 0.19 (major), 0.06 (minor)) afforded the title compound as a colorless oil. Yield 103 mg (0.41 mmol, 82%). ^{1}H NMR (500.13 MHz, $CDCl_3$) δ 7.18 (td, J = 8.1, 1.4 Hz, 1H), 7.07 (t, J = 9.1 Hz, 2H), 6.96−6.90 (m, 1H), 4.20 (ddd, J = 6.4, 3.9, 2.0 Hz, 1H), 3.50−3.39 (m, 4H), 2.09 (ddd, J = 9.7, 6.2, 2.0 Hz, 1H), 1.53 (ddd, J = 6.4, 6.2, 5.8 Hz, 1H), 1.40 (ddd, J = 9.7, 5.8, 3.8 Hz, 1H), 1.21 (t, J = 7.3 Hz, 3H), 1.14 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125.76 MHz, $CDCl_3$) δ 169.6, 152.3 (d, $^1J_{CF}$ = 245.6 Hz), 146.3 (d, $^2J_{CF}$ = 11.0 Hz), 124.3 (d, J_{CF} = 4.6 Hz, +), 121.7 (d, J_{CF} = 7.3 Hz, +), 116.2 (d, $^3J_{CF}$ = 17.4 Hz, +), 115.4 (+), 58.3 (+), 42.2 (−), 40.8 (−), 19.9 (+), 15.5 (−), 14.8 (+), 13.2 (+); GC 11.18 min (major), 11.34 min (minor); FTIR (NaCl, film, cm^{-1}) 2976, 2934, 1634, 1504, 1458, 1265, 1254, 1209, 1136, 748; HRMS (TOF ES) found 252.1398, calcd for $C_{14}H_{19}FNO_2$ (M + H) 252.1400 (0.8 ppm).

((1*R,2*R**)-2-(3,5-Dimethylphenoxy)cyclopropyl)(4-morpholino)methanone (16ci):** The title compound was prepared according to typical procedure II, employing bromocyclopropane **12c** (117 mg, 0.50 mmol), 3,5-dimethylphenol (122 mg, 1.00 mmol, 2.00 equiv), and anhydrous THF (5 mL). The reaction was carried out at 100 °C for 13 h. Flash column chromatography on a silica gel (eluent hexane/EtOAc 3:1, R_f 0.16) afforded the title compound as a colorless viscous oil. Yield 120 mg (0.44 mmol, 87%). ^{1}H NMR (500.13 MHz, $CDCl_3$) δ 6.67 (s, 1H), 6.62 (s, 2H), 4.08 (ddd, J = 6.5, 3.9, 2.2 Hz, 1H), 3.82−3.58 (m, 8H), 2.32 (s, 6H), 2.02 (ddd, J = 9.5, 6.2, 2.2 Hz, 1H), 1.61 (ddd, J = 6.5, 6.2, 5.4 Hz, 1H), 1.38 (ddd, J = 9.5, 5.4, 3.9 Hz, 1H); ^{13}C NMR (125.76 MHz, $CDCl_3$) δ 169.5, 158.2, 139.3 (2C), 123.3 (+), 112.5 (+, 2C), 66.9 (−), 66.8 (−), 57.4 (+), 46.1 (−), 42.5 (−), 21.4 (+), 19.6 (+), 15.4 (−); GC 13.27 min (major), 13.42 min (minor); FTIR (NaCl, film, cm^1) 2961, 2918, 2854, 1639, 1443, 1319, 1294, 1117, 1032, 835, 689; HRMS (TOF ES) found 276.1612, calcd for $C_{16}H_{22}NO_3$ (M + H) 276.1600 (4.3 ppm).

((1*R,2*R**)-2-(2,6-Dimethylphenoxy)cyclopropyl)(morpholino)methanone (16cl):** The title compound was prepared according to typical procedure II, employing bromocyclopropane **12c** (117 mg, 0.50 mmol), and 2,6-dimethylphenol (122 mg, 1.00 mmol, 2.0 equiv). The reaction was carried out at 90 °C for 14 h. Flash column chromatography on silica gel afforded the title compound as a colorless oil, R_f 0.17 (eluent hexane/EtOAc 3:1). Yield 114 mg (0.42 mmol, 83%). ^{1}H NMR (500.13 MHz, $CDCl_3$) δ 6.94 (d, J = 7.6 Hz, 2H), 6.86 (dd, J = 8.2, 6.6 Hz, 1H), 3.99 (ddd, J = 6.5, 3.9, 2.2 Hz, 1H), 3.66−3.49 (m, 4H), 3.48−3.30 (m, 4H), 2.20 (s, 6H), 2.02 (ddd, J = 9.6, 6.1, 2.2 Hz, 1H), 1.40 (ddd, J = 6.5, 6.2, 5.6 Hz, 1H), 1.31 (ddd, J = 9.5, 5.6, 4.1 Hz, 1H); ^{13}C NMR (125.76 MHz, $CDCl_3$) δ 169.4, 155.0, 130.3 (2C),

128.9 (+, 2C), 124.1 (+), 66.7 (−), 66.6 (−), 62.1 (+), 45.9 (−), 42.3 (−), 19.4 (+), 17.0 (+, 2C), 15.1 (−); FTIR (NaCl, film, cm^1) 2961, 2920, 2854, 1643, 1443, 1371, 1265, 1236, 1211, 1188, 1117, 932, 851; HRMS (TOF ES) found 275.1524, calcd for $C_{16}H_{21}NO_3$ (M^+) 275.1521 (1.1 ppm).

Piperidin-1-yl((1*R,2*R**)-2-(quinolin-8-yloxy)cyclopropyl)-methanone (16dm):** The title compound was prepared according to typical procedure II, employing bromocyclopropane **12d** (116 mg, 0.50 mmol) and 8-hydroxyquinoline (145 mg, 1.00 mmol, 2.00 equiv). Flash column chromatography on silica gel (eluent EtOAc, R_f 0.73 (8-hydroxyquinoline), 0.23 (title product)) afforded a colorless viscous oil. Yield 144 mg (0.49 mmol, 97%). ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 8.95 (dd, J = 4.0, 1.8 Hz, 1H), 8.16 (dd, J = 8.2, 1.6 Hz, 1H), 7.53−7.41 (m, 4H), 4.37 (ddd, J = 6.3, 4.6, 2.3 Hz, 1H), 3.75−3.55 (m, 4H), 2.34 (ddd, J = 9.3, 6.9, 2.3 Hz, 1H), 1.79−1.56 (m, 8H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 168.9, 154.2, 149.4 (+), 139.7, 135.9 (+), 129.3, 126.6 (+), 121.6 (+), 120.3 (+), 110.1 (+), 58.0 (+), 46.8 (−), 43.1 (−), 26.5 (−), 25.5 (−), 24.5 (−), 19.6 (+), 15.5 (−); FT IR (NaCl, film, cm^{-1}) 3007, 2935, 2854, 1628, 150, 1470, 1375, 1247, 1209, 1184, 1103, 1022, 825, 792; HRMS (TOF ES) found 297.1603, calcd for $C_{18}H_{21}N_2O_2$ (M + H) 297.1603 (0.0 ppm).

(1*S,2*R**)-*N*-Butyl-2-(phenylthio)cyclopropanecarboxamide (17ff): Typical Procedure III:** An oven-dried, 10-mL Weaton vial was charged with bromocyclopropane **12f** (110 mg, 0.5 mmol, 1 equiv), 18-crown-6 (13.2 mg, 0.05 mmol, 10 mol %), KOH (98 mg, 1.75 mmol, 3.5 equiv), thiophenol (110 mg, 1 mmol, 2 equiv), and anhydrous THF (5 mL). The mixture was stirred at 85 °C for 12 h. The crude mixture was filtered through a fritted funnel and the filtrate was concentrated under vacuum. The residual crude material, containing a mixture of diastereomeric cyclopropylsulfides (trans:cis = 2:1) was combined with potassium *tert*-butoxide (168 mg, 1.50 mmol, 3.0 equiv) in a 10-mL Weaton vial, then the mixture was dissolved in dry THF (total volume of 8 mL) and heated at 85 °C for 6 h. The resulting mixture was filtered through a fritted funnel into an evaporating flask, and the filtrate was concentrated under vacuum. The residue was purified by flash column chromatography on silica gel to obtain the individual trans-isomer of the title compound as a white solid, mp 95−97 °C, R_f 0.29 (eluent hexane/EtOAc 3:1). Yield 121 mg (0.483 mmol, 97%). ^{1}H NMR (500.13 MHz, $CDCl_3$) δ 7.33−7.27 (m, 4H), 7.21−7.15 (m, 1H), 5.82 (br s, 1H), 3.42−3.21 (m, 2H), 2.76 (ddd, J = 8.2, 5.4, 3.5 Hz, 1H), 1.70 (dt, J = 8.2, 5.0 Hz, 1H), 1.59 (ddd, J = 8.5, 5.2, 3.6 Hz, 1H), 1.57−1.47 (m, 2H), 1.39 (dq, J = 14.9, 7.4 Hz, 2H), 1.16 (ddd, J = 8.5, 5.4, 4.7 Hz, 1H), 0.96 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125.76 MHz, $CDCl_3$) δ 170.6, 137.5, 128.8 (+, 2C), 126.6 (+, 2C), 125.3 (+), 39.6 (−), 31.7 (−), 26.2 (+), 20.7 (+), 20.0 (−), 16.3 (−), 13.7 (+); IR (NaCl, cm^{-1}) 3296, 3223, 3202, 3196, 3084, 3055, 2955, 2922, 2851, 2826, 1636, 1583, 1558, 1479, 1466, 1456, 1439, 1423, 1396; HRMS (TOF ES) found 250.1268, calcd for $C_{14}H_{20}NOS$ (M + H) 250.1266 (0.8 ppm).

(1*S,2*S**)-*N*-Butyl-2-(phenylthio)cyclopropanecarboxamide (*cis*-17ff):** The title compound was isolated as a reference sample in a separate experiment by column chromatography of the crude reaction mixture prior to re-equilibration with *t*-BuOK, R_f 0.15 (eluent hexane/EtOAc 3:1). Yield 37 mg (0.15 mmol, 30%). ^{1}H NMR (500.13 MHz, $CDCl_3$) δ 7.37 (d, J = 7.3 Hz, 2H), 7.32−7.27 (m, 2H), 7.20−7.15 (m, 1H), 5.81 (br s, 1H), 3.24−3.16 (m, 2H), 2.64 (td, J = 8.0, 6.3 Hz, 1H), 2.09 (td, J = 8.0, 6.6 Hz, 1H), 1.47 (td, J = 8.4, 5.4 Hz, 1H), 1.40 (q, J = 6.3 Hz, 1H), 1.35−1.27 (m, 2H), 1.26−1.17 (m, 2H), 0.84 (t, J = 7.3 Hz, 3H); ^{13}C NMR (125.76 MHz, $CDCl_3$) δ 168.5, 137.2, 128.8 (+, 2C), 127.3 (+, 2C), 125.6 (+), 39.5 (−), 31.5 (−), 23.5 (+), 20.7 (+), 19.9 (−), 13.7 (+), 12.9 (−); HRMS (TOF ES) found 250.1270, calcd for $C_{14}H_{20}NOS$ (M + H) 250.1266 (1.6 ppm).

((1*S,2*R**)-2-(Benzylthio)cyclopropyl)(morpholino)methanone (17cb):** The reaction was performed according to typical procedure III, employing bromocyclopropane **12c** (117 mg, 0.50 mmol) and benzylmercaptan (124 mg, 1.00 mmol) to produce the title compound as a yellow oil, R_f 0.28 (eluent hexane/EtOAc 1:1, yield 128 mg (0.46 mmol, 92%)). Initial dr 2:1, after equilibration was upgraded to >30:1. ^{1}H NMR (500.13 MHz, $CDCl_3$) δ 7.33−7.30 (m, 4H), 7.29−7.24 (m, 1H), 3.82 (d, J = 13.6 Hz, 1H), 3.77 (d, J = 13.6 Hz, 1H), 3.72−3.58 (m, 5H), 3.56−3.34 (m, 3H), 2.44 (ddd, J = 8.4, 5.3, 3.6 Hz, 1H), 1.66 (ddd, J = 8.7, 5.2, 3.5 Hz, 1H), 1.43 (dt, J = 8.2, 5.2, 4.5 Hz, 1H), 0.97 (ddd, J = 8.4, 5.3, 4.8 Hz, 1H); ^{13}C NMR (125.76 MHz, $CDCl_3$) δ 169.8, 138.5, 128.7 (+, 2C), 128.4 (+, 2C), 126.9 (+), 66.7 (−), 66.5 (−), 45.7 (−), 42.3 (−), 37.9 (−), 22.1 (+), 22.0 (+), 16.2 (−); IR (NaCl, cm^{-1}) 3001, 2961, 2918, 2899, 2854, 1637, 1603, 1495, 1454, 1439, 1389, 1362, 1329, 1300, 1273, 1231, 1194, 1115, 1070, 1041, 1026, 966, 918, 868, 845, 771, 744, 702, 667, 642, 567, 440, 419; HRMS (TOF ES) found 300.1033, calcd for $C_{15}H_{19}NO_2SNa$ (M + Na) 300.1034 (0.3 ppm).

((1*S,2*S**)-2-(Benzylthio)cyclopropyl)(morpholino)methanone (*cis*-17cb):** The title compound was isolated as a reference sample in a separate experiment by column chromatography of the crude reaction micture prior to re-equilibration with *t*-BuOK, R_f 0.15 (eluent hexane/EtOAc 1:1). Yield 42 mg (0.15 mmol, 30%). ^{1}H NMR (500.13 MHz, $CDCl_3$) δ 7.36−7.31 (m, 4H), 7.30−7.25 (m, 1H), 3.86 (ddd, J = 13.2, 5.4, 3.2 Hz, 1H), 3.77 (s, 2H), 3.76−3.62 (m, 5H), 3.58 (ddd, J = 13.2, 6.9, 3.8 Hz, 1H), 3.52 (ddd, J = 13.4, 7.4, 3.2 Hz, 1H), 2.20 (td, J = 8.0, 6.0 Hz, 1H), 2.02 (td, J = 8.3, 6.1 Hz, 1H), 1.45 (q, J = 5.8 Hz, 1H), 1.25 (td, J = 8.0, 5.2 Hz, 1H); ^{13}C NMR (125.76 MHz, $CDCl_3$) δ 167.1, 138.2, 128.8 (+, 2C), 128.5 (+, 2C), 127.0 (+), 66.9 (−), 66.8 (−), 45.9 (−), 42.5 (−), 37.8 (−), 21.8 (+), 19.8 (+), 13.1 (−); HRMS (TOF ES) found 278.1219, calcd for $C_{15}H_{20}NO_2S$ (M + H) 278.1215 (1.4 ppm).

(1*S,2*R**)-*N*-Butyl-2-(dodecylthio)cyclopropanecarboxamide (17fa):** The reaction was performed according to typical procedure III, employing bromocyclopropane **12f** (110 mg, 0.50 mmol) and dodecanethiol (202 mg, 1.00 mmol) to produce the title compound as a white solid, mp 50−52 °C, R_f 0.23 (eluent hexane/EtOAc 3:1). Yield 162 mg (0.48 mmol, 95%). Initial dr 1:1, after equilibration was upgraded to 16:1. ^{1}H NMR (500.13 MHz, $CDCl_3$) δ 5.84 (br s, 1H), 3.32−3.22 (m, 2H), 2.64−2.52 (m, 2H), 2.45−2.36 (m, 1H), 1.69−1.56 (m, 2H), 1.55−1.44 (m, 4H), 1.42−1.33 (m, 4H), 1.44−1.20 (m, 16H), 1.02−0.96 (m, 1H), 0.94 (t, J = 7.4 Hz, 3H), 0.89 (t, J = 6.9 Hz, 3H); ^{13}C NMR (125.76 MHz, $CDCl_3$) δ 171.1, 39.5 (−), 33.4 (−), 31.9 (−), 31.7 (−), 29.62 (−), 29.60 (−), 29.58 (−), 29.57 (−), 29.5 (−), 29.3 (−), 29.2 (−), 28.8 (−), 25.9 (+), 22.6 (−), 21.4 (+), 20.0 (−), 16.3 (−), 14.1 (+), 13.7 (+); IR (KBr, cm^{-1}) 3271, 2955, 2918, 2849, 1636, 1558, 1456, 1277, 1232, 746, 719, 658, 501, 403; HRMS (TOF ES) found 342.2833, calcd for $C_{20}H_{40}NOS$ (M + H) 342.2831 (0.6 ppm).

(1*S,2*R**)-*N*-Butyl-2-((2-(phenylamino)ethyl)thio)cyclopropanecarboxamide (17fe):** This compound was prepared according to typical procedure III starting from bromocyclopropane **12f** (55 mg, 0.25 mmol) and 2-anilinoethanthiol (78 mg, 0.50 mmol, 2.0 equiv). The product was isolated by column chromatography on silica gel (eluent hexane/EtOAc 3:1, gradually changed to 1:1) as a yiellowish oil, R_f 0.28 (hexane/EtOAc, 1:1). Yield 128 mg (0.46 mmol, 92%). Initial dr 2:1, after equilibration was upgraded to >30:1. ^{1}H NMR (500.13 MHz, $CDCl_3$) δ 7.23 (t, J = 7.9 Hz, 2H), 6.77 (t, J = 7.3 Hz, 1H), 6.67 (d, J = 8.5 Hz, 2H), 5.40 (br s, 1H), 4.12 (br s, 1H), 3.40 (t, J = 6.3 Hz, 2H), 3.25 (dq, J = 13.4, 6.8 Hz, 1H), 3.15 (dq, J = 12.6, 6.9 Hz, 1H), 2.95 (dt, J = 13.6, 6.0 Hz, 1H), 2.85 (dt, J = 13.6, 6.6 Hz, 1H), 2.39 (ddd, J = 8.4, 5.3, 3.6 Hz, 1H), 1.49 (dt, J = 8.2, 4.7 Hz, 1H), 1.44 (dq, J = 15.4, 6.9 Hz, 2H), 1.40 (ddd, J = 8.5, 5.0, 3.5 Hz, 1H), 1.33 (dq, J = 14.9, 7.2 Hz, 2H), 0.99 (dt, J = 8.4, 5.0 Hz, 1H), 0.94 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125.76 MHz, $CDCl_3$) δ 170.6, 147.7, 129.4 (+, 2C), 117.8 (+), 113.1 (+, 2C), 42.3 (−), 39.5 (−), 32.8 (−), 31.7 (−), 26.4 (+), 20.9 (+), 20.0 (−), 15.6 (−), 13.7 (+); IR (KBr, cm^{-1}) 3304, 2957, 2930, 1641, 1603, 1556, 1506, 1466, 1433, 1394, 1373, 1323, 1288, 1261, 1225, 1196, 1180, 1153, 1113, 1095, 1072, 1030, 989, 962, 920, 868, 852, 804, 748, 692, 652, 617, 554, 538, 511;

HRMS (TOF ES) found 293.1685, calcd for $C_{16}H_{25}N_2OS$ (M + H) 293.1688 (1.0 ppm).

(1*S,2*R**)-*N*-Benzyl-2-((3-(benzylthio)propyl)thio)cyclopropanecarboxamide (17gc):** The reaction was performed according to typical procedure III employing bromocyclopropane **12g** (127 mg, 0.50 mmol) and 3-(benzylthio)propane-1-thiol (198 mg, 1.00 mmol, 2.0 equiv) to produce the title compound as a white solid, mp 78−80 °C, R_f 0.40 (hexane/EtOAc, 3:1). Yield 107 mg (0.44 mmol, 87%). Initial dr 2:1, after equilibration was upgraded to >30:1. ^{1}H NMR (500.13 MHz, $CDCl_3$) δ 7.40−7.24 (m, 10H), 6.00 (br s, 1H), 4.52−4.41 (m, 2H), 3.71 (s, 2H), 2.74−2.61 (m, 2H), 2.60−2.49 (m, 2H), 2.43 (ddd, J = 8.2, 5.7, 3.8 Hz, 1H), 1.94−1.85 (m, 2H), 1.55 (dt, J = 8.2, 4.7 Hz, 1H), 1.47 (ddd, J = 8.5, 5.0, 3.5 Hz, 1H), 1.02 (ddd, J = 8.5, 5.7, 4.4 Hz, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 170.9, 138.3, 138.0, 128.8 (+, 2C), 128.7 (+, 2C), 128.5 (+, 2C), 127.8 (+, 2C), 127.5 (+), 127.0 (+), 43.9 (−), 36.2 (−), 32.2 (−), 29.9 (−), 28.6 (−), 25.9 (+), 21.5 (+), 16.2 (−); FT IR (NaCl, film, cm^{-1}) 3290, 3061, 3028, 2918, 1641, 1603, 1551, 1495, 1452, 1423, 1394, 1356, 1298, 1273, 1227, 1196, 1157, 1109, 1082, 1070, 1040, 1028, 1003, 966, 918, 860, 841, 802, 768, 731, 698, 656, 621, 600, 565, 538, 509, 474, 447, 432; HRMS (TOF ES) found 371.1374, calcd for $C_{21}H_{25}NOS_2$ (M^+) 371.1374 (1.1 ppm);

(1*S,2*R**)-*N*-*tert*-Butyl-2-(2-hydroxyethylthio)cyclopropanecarboxamide (17ad): Typical Procedure IV:** An oven-dried, 5-mL Weaton vial was charged with bromocyclopropane **12a** (110 mg, 0.50 mmol), 18-crown-6 (13 mg, 0.05 mmol, 10%), powdered KOH (140 mg, 2.5 mmol, 5.0 equiv), 2-mercaptoethanol (70 μL, 78 mg, 1.00 mmol, 2.0 equiv), and anhydrous THF (5 mL). The mixture was stirred at 85 °C for 12 h, then filtered through a fritted funnel and concentrated. The residue was purified by flash chromatography on silica gel (eluent hexane/EtOAc 1:1) to afford the title compound as a colorless oil, R_f 0.40 (hexane/EtOAc 1:3). Yield 108 mg (0.49 mmol, 97%). ^{1}H NMR (500.13 MHz, $CDCl_3$) δ 5.59 (br s, 1H), 3.82 (t, J = 6.0 Hz, 2H), 2.89−2.75 (m, 2H), 2.43−2.33 (m, 1H), 2.22 (br s, 1H), 1.50−1.43 (m, 2H), 1.37 (s, 9H), 1.03−0.93 (m, 1H); ^{13}C NMR (125.76 MHz, $CDCl_3$) δ 170.0, 60.4 (−), 51.5, 36.4 (−), 28.8 (+, 3C), 26.5 (+), 20.4 (+), 16.1 (−); IR (KBr, cm^{-1}) 3315, 2966, 2928, 1651, 1553, 1456, 1425, 1393, 1364, 1283, 1244, 1225, 1196, 1047, 1016; HRMS (TOF ES) found 240.1031, calcd for $C_{10}H_{19}NO_2SNa$ (M + Na) 240.1034 (1.2 ppm).

(1*S,2*R**)-2-((2-Hydroxyethyl)thio)-*N*-phenylcyclopropanecarboxamide (17hd):** The title compound was prepared according to typical procedure IV, employing bromocyclopropane **12h** (120 mg, 0.50 mmol). The reaction was carried out at 60 °C for 14 h. Flash column chromatography on silica gel afforded th title compound as colorless crystals, mp 87−88 °C, R_f 0.38 (hexane/EtOAc 1:3). Yield 101 mg (0.43 mmol, 85%). ^{1}H NMR (400.13 MHz, CD_3CN) δ 8.78 (br s, 1H), 7.58 (d, J = 8.1 Hz, 2H), 7.33 (t, J = 8.0 Hz, 2H), 7.10 (t, J = 7.5 Hz, 1H), 3.72 (q, J = 6.3 Hz, 2H), 3.10 (t, J = 5.7 Hz, 1H), 2.77 (t, J = 6.6 Hz, 2H), 2.44 (ddd, J = 8.3, 5.3, 3.5 Hz, 1H), 1.84 (ddd, J = 8.5, 5.2, 3.5 Hz, 1H), 1.47 (dt, J = 8.3, 4.8 Hz, 1H), 1.08 (ddd, J = 8.6, 5.6, 4.6 Hz, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 169.4, 137.8, 129.0 (+, 2C), 124.3 (+), 119.8 (+, 2C), 60.5 (−), 36.5 (−), 27.1 (+), 21.8 (+), 16.8 (−); FT IR (NaCl, film, cm^{-1}) 3286, 2922, 2872, 1655, 1601, 1549, 1447, 1393, 1313, 1190, 1036, 756, 692; HRMS (TOF ES) found 260.0714, calcd for $C_{12}H_{15}NO_2SNa$ (M + Na) 260.0721 (2.7 ppm).

***N*-Benzyl-3-((1*R**,2*S**)-2-Methyl-2-phenylcyclopropoxy)propan-1-amine (20ag): Typical Procedure V:** To a stirred suspension of *t*-BuOK (141 mg, 1.26 mmol, 2.50 equiv) and 18-crown-6 (13 mg, 50 μmol, 10 mol %) in anhydrous THF (1 mL) was added (2-bromo-1-methylcyclopropyl)benzene (**18a**) (106 mg, 0.503 mmol, 1.00 equiv), followed by 3-(benzylamino)propan-1-ol (125 mg, 0.76 mmol, 1.51 equiv). The mixture was stirred at 80 °C for 18 h. Then, the KBr precipitate was filtered off on a fritted funnel and the filtrate was concentrated under vacuum. Preparative column chromatography of a residue on silica gel doped with triethylamine afforded the title compound as a light orange oil, R_f 0.30 (EtOAc). Yield 134 mg (0.45 mmol, 90%). ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 7.48−7.21 (m, 10H), 3.88 (s, 2H), 3.78−3.69 (m, 2H), 3.41 (dd, J = 7.1, 3.5 Hz, 1H), 2.85 (t, J = 6.9 Hz, 2H), 1.93 (quin, J = 6.6 Hz, 2H), 1.57 (s, 3H), 1.21 (t, J = 6.4 Hz, 1H), 0.90 (dd, J = 5.8, 3.8 Hz, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 145.7, 140.2, 128.2 (+, 2C), 128.2 (+, 2C), 128.0 (+, 2C), 126.72 (+), 126.68 (+, 2C), 125.6 (+), 69.5 (−), 64.4 (+), 53.9 (−), 46.6 (−), 30.0 (−), 25.9, 20.3 (−), 18.7 (+); FT IR (cm^{-1}, film) 3338, 3061, 3026, 2951, 2828, 2870, 1589, 1495, 1454, 1447, 1360, 1169, 1119, 1092, 1028, 827, 760, 743, 698; HRMS (TOF ES) found 318.1838, calcd for $C_{20}H_{25}NONa$ (M + Na) 318.1834 (1.3 ppm).

***N*-(3-((1*R**,2*S**)-2-Methyl-2-phenylcyclopropoxy)propyl)-hexan-1-amine (20af):** The title compound was prepared according to typical procedure V, employing (2-bromo-1-methylcyclopropyl) benzene (**18a**) (111 mg, 0.52 mmol, 1.0 equiv) and 3-(hexylamino)-propanol (110 mg, 0.69 mmol, 1.3 equiv). Preparative column chromatography on silica gel doped with triethylamine afforded the title compound as a yellowish oil, R_f 0.50 (hexane/EtOAc 8:1). Yield 139 mg (0.48 mmol, 92%). ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 7.34−7.27 (m, 2H), 7.26−7.16 (m, 3H), 3.71−3.61 (m, 2H), 3.35 (dd, J = 6.9, 3.7 Hz, 1H), 2.74 (t, J = 6.9 Hz, 2H), 2.62 (t, J = 7.2 Hz, 2H), 1.89−1.80 (m, 2H), 1.50 (s, 3H), 1.53−1.45 (m, 2H), 1.38−1.25 (m, 7H), 1.15 (t, J = 6.6 Hz, 1H), 0.93−0.87 (m, 3H), 0.84 (dd, J = 5.9, 3.7 Hz, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 145.9, 128.3 (+, 2C), 126.8 (+, 2C), 125.7 (+), 69.8 (−), 64.5 (+), 50.1 (−), 47.4 (−), 31.8 (−), 30.2 (−), 30.1 (−), 27.1, 26.1 (−), 22.6 (−), 20.4 (−), 18.8 (+), 14.0 (+); FT IR (cm^{-1}, film) 3319, 2955, 2928, 2870, 2856, 2816, 1497, 1458, 1447, 1364, 1292, 1240, 1171, 1132, 1090, 1070, 1028, 1013, 997, 933, 891, 827, 762, 744, 727, 698, 534; HRMS (TOF ES) found 312.2305, calcd for $C_{19}H_{31}NONa$ (M + Na) 312.2303 (0.6 ppm).

***N*-(Furan-2-ylmethyl)-3-((1*R**,2*S**)-2-methyl-2-phenylcyclopropoxy)propan-1-amine (20ah):** The title compound was prepared according to typical procedure V, employing (2-bromo-1-methylcyclopropyl)benzene (**18a**) (110 mg, 0.52 mmol, 1.0 equiv) followed by 3-((furan-2-ylmethyl)amino)propan-1-ol (124 mg, 0.80 mmol, 1.5 equiv). Preparative column chromatography of the residue on silica gel doped with triethylamine afforded the title compound as a light orange oil, R_f 0.50 (Hex/EtOAc 5:1). Yield 119 mg (0.42 mmol, 80%). ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 7.38 (dd, J = 1.8, 0.8 Hz, 1H), 7.35−7.27 (m, 2H), 7.26−7.17 (m, 3H), 6.33 (dd, J = 3.2, 1.9 Hz, 1H), 6.20 (d, J = 2.8 Hz, 1H), 3.82 (s, 2H), 3.66 (td, J = 6.2, 2.5 Hz, 2H), 3.35 (dd, J = 7.1, 3.8 Hz, 1H), 2.77 (t, J = 6.9 Hz, 2H), 1.86 (quin, J = 6.6 Hz, 2H), 1.57 (quin, J = 6.4 Hz, 1H), 1.50 (s, 3H), 1.16 (t, J = 6.4 Hz, 1H), 0.84 (dd, J = 5.8, 3.8 Hz, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 154.0, 145.9, 141.8 (+), 128.4 (+, 2C), 126.9 (+, 2C), 125.8 (+), 110.1 (+), 106.8 (+), 69.7 (−), 64.6 (+), 46.6 (−), 46.3 (−), 30.1 (−), 26.1, 20.4 (−), 18.8 (+); FT IR (KBr, cm^{-1}) 3105, 3086, 3072, 2951, 2928, 2868, 1161, 1148, 1117, 1092, 1072, 1028, 762, 733, 700; HRMS (TOF ES) found 286.1802, calcd for $C_{18}H_{24}NO_2$ (M + H) 286.1807 (1.7 ppm).

***N*-(2-(2-((1*R**,2*S**)-2-Methyl-2-phenylcyclopropoxy)ethoxy)-ethyl)butan-1-amine (20ai):** The title compound was prepared according to typical procedure V, employing (2-bromo-1-methylcyclopropyl)-benzene (**18a**) (106 mg, 0.50 mmol, 1.0 equiv) and 2-(2-(butylamino)-ethoxy)ethanol (99 mg, 0.62 mmol, 1.3 equiv). Preparative column chromatography of the residue on silica gel doped with triethylamine afforded the title compound as a yiellow oil, R_f 0.50 (EtOAc/MeOH 20:1). Yield 120 mg (0.41 mmol, 82%). ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 7.34−7.26 (m, 2H), 7.25−7.16 (m, 3H), 3.79−3.74 (m, 2H), 3.71−3.66 (m, 2H), 3.63 (t, J = 5.3 Hz, 2H), 3.43 (dd, J = 7.1, 3.5 Hz, 1H), 3.41−3.33 (m, 1H), 2.84−2.79 (m, 2H), 2.66−2.60 (m, 2H), 1.89 (br s, 1H), 1.52 (s, 3H), 1.54−1.43 (m, 1H), 1.41−1.30 (m, 2H), 1.16 (t, J = 6.6 Hz, 1H), 0.93 (t, J = 7.3 Hz, 3H), 0.88 (dd, J = 5.8, 3.8 Hz, 1H); ^{13}C NMR (100.67 MHz,

$CDCl_3$) δ 145.8, 128.3 (+, 2C), 126.8 (+, 2C), 125.7 (+), 70.6 (−), 70.4 (−), 70.1 (−), 64.8 (+), 49.6 (−), 49.3 (−), 32.2 (−), 26.2, 20.43 (−), 20.41 (−), 18.7 (+), 14.0 (+); FT IR (cm^{-1}, film) 3321, 3059, 3024, 2957, 2928, 2872, 1670, 1603, 1578, 1541, 1497, 1458, 1447, 1377, 1348, 1323, 1292, 1246, 1173, 1121, 1095, 1055, 1028, 1013, 995, 951, 920, 872, 827, 762, 748, 698, 669, 650, 596, 534, 473, 409; HRMS (TOF ES) found 292.2271, calcd for $C_{18}H_{30}NO_2$ (M + H) 292.2277 (2.1 ppm).

3-((1*R,2*S**)-2-Methyl-2-phenylcyclopropoxy)propan-1-amine (20aj):** The title compound was prepared according to typical procedure V, employing (2-bromo-1-methylcyclopropyl)benzene (**18a**) (102 mg, 0.49 mmol, 1.0 equiv) and 3-aminopropan-1-ol (66 mg, 0.88 mmol, 1.7 equiv). Preparative column chromatography on silica gel doped with triethylamine afforded the title compound as a pale orange oil, R_f 0.50 (EtOAc/MeOH 1:1). Yield 80 mg (0.39 mmol, 81%). ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 7.33−7.28 (m, 2H), 7.24−7.18 (m, 3H), 3.71−3.66 (m, 2H), 3.70 (br s, 2H), 3.36 (dd, J = 6.9, 3.7 Hz, 1H), 2.94 (t, J = 6.6 Hz, 1H), 2.03−1.96 (m, 2H), 1.88 (quin, J = 6.5 Hz, 1H), 1.50 (s, 3H), 1.16 (app. t, J = 6.9, 6.1 Hz, 1H), 0.84 (dd, J = 6.1, 3.8 Hz, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 145.6, 128.3 (+, 2C), 126.8 (+, 2C), 125.8 (+), 68.7 (−), 64.5 (+), 38.2 (−), 30.2 (−), 26.0, 20.3 (−), 18.8 (+); FT IR (cm^{-1}, film) 3354, 3292, 3057, 3024, 2955, 2928, 2872, 1558, 1539, 1497, 1404, 1362, 1339, 1294, 1250, 1169, 1092, 1028, 1013, 955, 922, 829, 698, 650, 536; HRMS (TOF ES) found 206.1547, calcd for $C_{13}H_{20}NO$ (M + H) 206.1545 (1.0 ppm).

((1*R,2*S**)-1-Methyl-2-(propa-1,2-dien-1-yloxy)cyclopropyl)benzene (20al):** The title compound was prepared according to typical procedure V, employing (2-bromo-1-methylcyclopropyl)benzene (105 mg, 0.50 mmol, 1.00 equiv) and propargyl alcohol (34 mg, 0.60 mmol, 1.2 equiv). The reaction was carried out at 80 °C for 3 h. Preparative column chromatography of the residual oil on silica gel afforded the title compound as a colorless oil, R_f 0.20 (hexane). Yield 76 mg (0.41 mmol, 82%). ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 7.24−7.16 (m, 4H), 7.11 (tdd, J = 6.6, 2.5, 1.8 Hz, 1H), 6.69 (t, J = 5.9 Hz, 1H), 5.38 (dd, J = 8.3, 6.1 Hz, 1H), 5.34 (dd, J = 8.6, 6.1 Hz, 1H), 3.48 (dd, J = 7.1, 3.8 Hz, 1H), 1.40 (s, 3H), 1.16 (t, J = 6.6 Hz, 1H), 0.87 (dd, J = 6.2, 3.7 Hz, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 201.6, 145.2, 128.3 (+, 2C), 126.9 (+, 2C), 125.9 (+), 121.5 (+), 90.6 (−), 63.0 (+), 25.8, 20.4 (−), 18.9 (+); FT IR (NaCl, cm^{-1}) 3059, 2932, 2378, 2291, 2253, 1798, 1730, 1686, 1628, 1603, 1578, 1541, 1528, 1508, 1497, 1483, 1464, 1448, 1375, 1364, 1267, 1171, 1121, 1109, 1094, 1070, 1041, 1030, 1011, 918, 808, 764, 700, 588; HRMS (TOF ES) found 187.1119, calcd for $C_{13}H_{15}O$ (M + H) 187.1123 (2.1 ppm).

(1*S,2*R**)-2-(Benzyloxy)-*N*,*N*-diethyl-1-methylcyclopropanecarboxamide (26ae): Typical Procedure VI:** Bromocyclopropane **25a** (70.2 mg, 1.00 equiv, 0.30 mmol) was added to a mixture of 66.6 mg of *t*-BuOK (2.0 equiv, 0.60 mmol) and 7.8 mg of 18-crown-6 ether (10%, 30 μmol). Then 49 mg of benzyl alcohol (1.5 equiv, 0.45 mmol) was added and the reaction mixture was stirred in anhydrous THF (1 mL) overnight at 80 °C. The reaction mixture was partitioned between water (10 mL), brine, and EtOAc (3 × 20 mL). The combined organic phases were dried with Na_2SO_4, filtered, and concentrated. The residue was filtered through a short bed of silica gel (EtOAc) to afford the title compound as a colorless oil. Yield 74 mg (0.28 mmol, 95%). ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 7.36−7.24 (m, 5H), 4.58 (d, J = 12.1 Hz, 1H), 4.49 (d, J = 11.9 Hz, 1H), 3.69 (dq, J = 14.4, 7.3 Hz, 1H), 3.54−3.37 (m, 2H), 3.31 (dd, J = 5.8, 3.5 Hz, 1H), 3.31 (dq, J = 14.2, 7.1 Hz, 1H), 1.32 (dd, J = 5.8, 3.5 Hz, 1H), 1.24 (s, 3H), 1.22 (t, J = 7.3 Hz, 3H), 1.10 (t, J = 7.1 Hz, 3H), 0.66 (t, J = 5.9 Hz, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 170.7, 138.1, 128.2 (+, 2C), 127.5 (+, 2C), 127.4 (+), 72.3 (−), 62.7 (+), 41.1 (−), 38.6 (−), 27.8, 20.6 (+), 18.5 (−), 14.0 (+), 12.4 (+); FT IR (cm^{-1}, film) 2990, 2980, 1713, 1623, 1433, 1364, 1259, 1223, 1159, 1132, 1090, 1047, 1003, 910, 733, 698, 648, 530; HRMS (TOF ES) found 262.1817, calcd for $C_{16}H_{24}NO_2$ (M + H) 262.1807 (3.8 ppm).

(1*R,2*S**)-*N*,*N*-Diethyl-2-(2-methoxyethoxy)-1-methylcyclopropanecarboxamide (26af):** The title compound was prepared according to typical procedure VI, employing bromocyclopropane **25a** (117 mg, 1.00 equiv, 0.50 mmol) and ethylene glycol monomethyl ether (57 mg, 1.0 equiv, 0.5 mmol). Preparative column chromatography on silica gel afforded the title compound as a clear oil, R_f 0.40 (hexane/EtOAc 3:1). Yield 102 mg (0.44 mmol, 89%). ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 3.72−3.56 (m, 2H), 3.53 (ddd, J = 10.9, 4.9, 3.5 Hz, 1H), 3.47−3.35 (m, 4H), 3.29 (s, 3H), 3.28−3.21 (m, 2H), 1.20−1.18 (m, 1H), 1.18 (s, 3H), 1.18 (t, J = 7.2 Hz, 3H), 1.04 (t, J = 7.1 Hz, 3H), 0.59 (ps t, J = 5.9 Hz, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 170.6, 71.6 (−), 69.6 (−), 63.2 (+), 58.9 (+), 41.0 (−), 38.5 (−), 27.6 (+), 20.5, 18.2 (−), 13.9 (+), 12.2 (+); FT IR (cm^{-1}, film) 2968, 2934, 2874, 2824, 2737, 1722, 1634, 1518, 1427, 1379, 1364, 1348, 1323, 1304, 1259, 1219, 1200, 1167, 1128, 1101, 1067, 1030, 957, 920, 903, 860, 800, 760; HRMS (TOF ES) found 229.1677, calcd for $C_{12}H_{23}NO_3$ (M^+) 229.1678 (0.4 ppm);

(1*S,2*R**)-2-(2-(Dimethylamino)ethoxy)-*N*,*N*-diethyl-1-methylcyclopropanecarboxamide (26ag):** The title compound was prepared according to typical procedure VI, employing bromocyclopropane **25a** (117 mg, 1.00 equiv, 0.50 mmol) and 2-*N*,*N*-dimethylaminoethanol (67 mg 1.5 equiv, 0.75 mmol). Preparative column chromatography on silica gel to afford the titled compound as a clear oil, R_f 0.20 (EtOAc). Yield 97 mg (0.40 mmol, 80%). ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 3.62−3.53 (m, 2H), 3.52−3.39 (m, 2H), 3.37−3.21 (m, 2H), 3.15 (dd, J = 5.7, 3.7 Hz, 1H), 2.31 (t, J = 5.8 Hz, 2H), 2.11 (s, 6H), 1.11 (t, J = 7.1 Hz, 3H), 1.10 (s), 1.11−1.09 (m, 1H), 0.97 (t, J = 7.1 Hz, 3H), 0.49 (t, J = 5.9 Hz, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 170.6, 68.7 (−), 63.1 (+), 58.2 (−), 45.7 (+, 2C), 41.0 (−), 38.5 (−), 27.4, 20.4 (+), 18.1 (−), 13.9 (+), 12.3 (+); FT IR (cm^{-1}, film) 2970, 2934, 2874, 1637, 1462, 1427, 1381, 1364, 1348, 1323, 1304, 1219, 1200, 1167, 1128, 1101, 1067, 1030, 957, 903, 473; HRMS (TOF ES) found 243.2080, calcd for $C_{13}H_{27}N_2O_2$ (M + H) 243.2073 (2.9 ppm).

(1*S,2*R**)-*N*,*N*-Diethyl-1-methyl-2-(pent-4-enyloxy)cyclopropanecarboxamide (26ah:).** The title compound was prepared according to typical procedure VI, employing bromocyclopropane **25a** (117 mg 1.00 equiv, 0.50 mmol) and 4-pentene-1-ol (87 mg, 1.00 equiv, 0.50 mmol). Preparative column chromatography on silica gel to afford the titled compound as a yellowish oil, R_f 0.50 (hexane/EtOAc 2:1). Yield 117 mg (0.49 mmol, 89%). ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 5.75 (ddt, J = 17.2, 10.1, 6.6 Hz, 1H), 4.97 (dq, J = 17.2, 1.7 Hz, 1H), 4.92 (ddt, J = 10.1, 2.0, 1.3 Hz, 1H), 3.63 (dq, J = 14.3, 7.1 Hz, 1H), 3.50−3.33 (m, 4H), 3.24 (dq, J = 13.6, 7.1 Hz, 1H), 3.20 (dd, J = 5.6, 3.5 Hz, 1H), 2.06−1.98 (m, 2H), 1.60−1.50 (m, 2H), 1.20 (t, J = 7.1 Hz, 3H), 1.19 (s, 3H), 1.17 (dd, J = 5.8, 3.5 Hz, 1H), 1.07 (t, J = 7.1 Hz, 3H), 0.57 (t, J = 5.8 Hz, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 170.7, 138.2 (+), 114.6 (−), 69.4 (−), 62.9 (+), 40.9 (−), 38.5 (−), 30.2 (−), 28.6 (−), 27.4, 20.5 (+), 18.3 (−), 14.0 (+), 12.3 (+); FT IR (cm^{-1}, film) 3078, 2970, 2935, 2872, 1641, 1462, 1443, 1425, 1258, 1219, 1165, 1128, 1090, 1005, 960, 912, 636; HRMS (TOF ES) found 262.1774, calcd for $C_{14}H_{25}NO_2Na$ (M + Na) 262.1783 (3.4 ppm).

((1*S,2*R**)-1-Methyl-2-(pent-4-enyloxy)cyclopropyl)(pyrrolidin-1-yl)methanone (26fh):** The title compound was prepared according to typical procedure VI, employing (2-bromo-1-methylcyclopropyl)(pyrrolidin-1-yl)methanone (**25f**) (250 mg, 1.07 mmol) and pent-4-en-1-ol (138 mg, 1.61 mmol, 1.50 equiv). Preparative column chromatography of a residue on silica gel afforded the title compound as a yellow oil, R_f 0.30 (hexane/EtOAc 2:3). Yield 219 mg (0.98 mmol, 92%). ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 5.76 (ddt, J = 17.0, 10.3 Hz, 6.7 Hz, 1H), 4.97 (ddt, J = 17.2, 1.8, 1.5 Hz, 1H), 4.92 (ddt, J = 10.4, 2.2, 1.2 Hz, 1H), 3.83 (ddd, J = 10.1, 6.2, 3.7 Hz, 1H), 3.50−3.36 (m, 5H), 3.17 (dd, J = 5.8, 3.5 Hz, 1H), 2.02 (q, J = 7.3 Hz, 2H), 1.96−1.74 (m, 4H), 1.56 (quin, J = 7.0 Hz, 2H), 1.23 (s, 3H), 1.19 (dd, J = 6.1, 3.5 Hz, 1H), 0.57 (dd, J = 6.1, 5.8 Hz, 1H); ^{13}C NMR (100.67 MHz,

$CDCl_3$) δ 170.0, 138.2 (+), 114.6 (−), 69.4 (−), 62.2 (+), 46.3 (−), 45.9 (−), 30.2 (−), 28.6 (−), 28.2, 26.2 (−), 24.1 (−), 19.3 (+), 17.7 (−); FT IR (cm^{-1}, film) 3076, 2937, 2874, 1774, 1726, 1614, 1529, 1344, 1252, 1157, 1090, 1040, 912, 874, 731, 644, 503; HRMS (TOF ES) found 238.1815, calcd for $C_{14}H_{24}NO_2$ (M + H) 238.1807 (3.4 ppm).

(1*S,2*R**)-2-(Allyloxy)-*N*-hexyl-1-methylcyclopropanecarboxamide (26ei):** The title compound was prepared according to typical procedure VI, employing 2-bromo-*N*-hexyl-1-methylcyclopropanecarboxamide (**25e**) (79 mg, 0.30 mmol) and allylic alcohol (35 mg, 0.60 mmol, 2.0 equiv). The reaction was carried out at 60 °C for 12 h. Preparative column chromatography of a residue on silica gel afforded the title compound as a colorless oil, R_f 0.25 (hexane−EtOAc 5:1). Yield 59 mg (0.25 mmol, 82%). ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 6.37 (br s, 1H), 5.91 (ddt, J = 17.2, 10.4, 5.8 Hz, 1H), 5.30 (dq, J = 17.2, 1.5 Hz, 1H), 5.23 (dq, J = 10.4, 1.3 Hz, 1H), 4.12−3.99 (m, 2H), 3.36 (dd, J = 6.6, 4.0 Hz, 1H), 3.25−3.16 (m, 2H), 1.50−1.39 (m, 2H), 1.34−1.22 (m, 6H), 1.20 (s, 3H), 1.16 (dd, J = 6.3, 4.3 Hz, 1H), 0.94 (t, J = 6.6, 6.3 Hz, 1H), 0.87 (t, J = 6.7 Hz, 3H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 173.2, 133.3 (+), 117.9 (−), 72.3 (−), 64.5 (+), 39.3 (−), 31.5 (−), 29.5 (−), 26.7 (−), 25.2, 22.5 (−), 22.1 (−), 20.0 (+), 14.0 (+); FT IR (NaCl, film, cm^{-1}) 3360, 3080, 2957, 2930, 2858, 1645, 1537, 1462, 1445, 1344, 1331, 1211, 1169, 1101, 1043, 991, 922; HRMS (TOF ES) found 240.1969, calcd for $C_{14}H_{26}NO_2$ (M + H) 240.1964 (2.1 ppm).

((1*S,2*R**)-2-(Allyloxy)-1-methylcyclopropyl)(piperidin-1-yl)methanone (26gi):** The title compound was prepared according to typical procedure VI, employing (2-bromo-1-methylcyclopropyl)-(piperidin-1-yl)methanone (**25g**) (79 mg, 0.30 mmol) and allylic alcohol (35 mg, 0.60 mmol, 2.0 equiv). The reaction was carried out at 60 °C for 12 h. Preparative column chromatography of a residue on silica gel afforded the title compound as a colorless oil, R_f 0.20 (hexane−EtOAc 3:1). Yield 61 mg (0.27 mmol, 91%). ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 5.87 (dddd, J = 17.2, 10.4, 5.9, 5.1 Hz, 1H), 5.23 (dq, J = 17.2, 1.8 Hz, 1H), 5.14 (dq, J = 10.4, 1.5 Hz, 1H), 4.03 (ddt, J = 13.1, 5.1, 1.8 Hz, 1 H), 3.96 (ddt, J = 13.1, 5.9, 1.3 Hz, 1H), 3.68−3.54 (m, 3H), 3.54−3.43 (m, 1H), 3.30 (dd, J = 5.8, 3.5 Hz, 1H), 1.69−1.51 (m, 6H), 1.23 (s, 3H), 1.20 (dd, J = 6.1, 3.5 Hz, 1H), 0.63 (app. t, J = 6.1, 5.8 Hz, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 169.9, 134.5 (+), 116.4 (−), 71.2 (−), 62.9 (+), 46.7 (−), 43.0 (−), 27.3, 24.7 (−), 20.5 (−), 18.0 (+); FT IR (NaCl, film, cm^{-1}) 3080, 2999, 2934, 2854, 1730, 1643, 1516, 1439, 1350, 1310, 1277, 1256, 1236, 1209, 1163, 1132, 1126, 1090, 1043, 1014, 989, 955, 924, 854, 758, 689, 604, 532, 507, 417; HRMS (TOF ES) found 224.1653, calcd for $C_{13}H_{22}NO_2$ (M + H) 224.1651 (0.8 ppm).

((1*S,2*R**)-2-(Allyloxy)-1-methylcyclopropyl)(morpholino)-methanone (26hi):** The title compound was prepared according to typical procedure VI, employing (2-bromo-1-methylcyclopropyl)-(morpholino)methanone (**25h**) (74 mg, 0.30 mmol) and allylic alcohol (35 mg, 0.60 mmol, 2.0 equiv). The reaction was carried out at 60 °C for 12 h. Preparative column chromatography of a residue on silica gel afforded the title compound as a colorless oil, R_f 0.23 (hexane−EtOAc 1:1). Yield 59 mg (0.26 mmol, 88%). ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 5.85 (dddd, J = 17.2, 10.4, 5.8, 5.1 Hz, 1H), 5.23 (dq, J = 17.2, 1.7 Hz, 1H), 5.15 (dq, J = 10.4, 1.4 Hz, 1H), 4.03 (ddt, J = 12.6, 5.1, 1.5 Hz, 1H), 3.95 (ddt, J = 12.6, 5.8, 1.3 Hz, 1 H), 3.79−3.53 (m, 7H), 3.41−3.31 (m, 1H), 3.29 (dd, J = 5.8, 3.5 Hz, 1H), 1.23 (s, 3H), 1.21 (dd, J = 6.1, 3.5 Hz, 1H), 0.65 (app. t, J = 6.1, 5.8 Hz, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 170.0, 134.2 (+), 116.8 (−), 71.3 (−), 67.3 (−), 66.9 (−), 62.5 (+), 46.3 (−), 42.5 (−), 26.8, 20.2 (+), 17.7 (−); FT IR (KBr, film, cm^{-1}) 3269, 3182, 3080, 2962, 2926, 2899, 2858, 2359, 2125, 1732, 1614, 1514, 1429, 1358, 1310, 1242, 1204, 1198, 1161, 1113, 1068, 1034, 991, 945, 926, 858, 847, 804, 690, 621, 559, 515; HRMS (TOF ES) found 226.1438, calcd for $C_{12}H_{20}NO_3$ (M + H) 226.1443 (2.2 ppm).

(1*S,2*R**)-2-(Allyloxy)-*N*,*N*,1-trimethylcyclopropanecarboxamide (26ii):** The title compound was prepared according to typical procedure VI, employing 2-bromo-*N*,*N*,1-trimethylcyclopropanecarboxamide (**25i**) (103 mg, 0.50 mmol) and allylic alcohol (35 mg, 0.60 mmol, 2.0 equiv). The reaction was carried out at 50 °C for 12 h. Preparative column chromatography of a residue on silica gel afforded the title compound as a colorless oil, R_f 0.35 (hexane−EtOAc 2:1). Yield 93.8 mg (0.46 mmol, 91%). ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 5.84 (dddd, J = 17.3, 10.4, 5.8, 5.1 Hz, 1H), 5.19 (dq, J = 17.3, 1.6 Hz, 1H), 5.11 (dq, J = 10.4, 1.5 Hz, 1H), 4.01 (ddt, J = 13.1, 5.1, 1.5 Hz, 1H), 3.94 (ddt, J = 13.1, 5.8, 1.3 Hz, 1H), 3.27 (dd, J = 5.8, 3.5 Hz, 1H), 3.13 (s, 3H), 2.92 (s, 3H), 1.22 (s, 3H), 1.16 (dd, J = 6.1, 3.5 Hz, 1H), 0.60 (app. t, J = 6.1, 5.8 Hz, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 171.4, 134.4 (+), 116.3 (−), 71.2 (−), 62.5 (+), 37.1 (+), 35.4 (+), 27.2, 20.0 (+), 17.9 (−); FT IR (NaCl, film, cm^{-1}) 3547, 3464, 3080, 3001, 2959, 2934, 2872, 1643, 1634, 1497, 1454, 1396, 1379, 1350, 1265, 1167, 1124, 1101, 1086, 1059, 1043, 991, 964, 926, 858, 704, 606, 575, 569, 517, 492; HRMS (TOF ES) found 206.1156, calcd for $C_{10}H_{17}NO_2Na$ (M + Na) 206.1157 (0.5 ppm).

(1*S,2*R**)-*N*,*N*,1-Trimethyl-2-((3-methylbut-2-en-1-yl)oxy)-cyclopropanecarboxamide (26ij):** The title compound was prepared according to typical procedure VI, employing 2-bromo-*N*,*N*,1-trimethylcyclopropanecarboxamide (**25i**) (62 mg, 0.30 mmol) and 3-methylbut-2-en-1-ol (28 mg, 0.33 mmol, 1.1 equiv). The reaction was carried out at 60 °C for 12 h. Preparative column chromatography of a residue on silica gel afforded the title compound as a colorless oil, R_f 0.40 (hexane−EtOAc 2:3). Yield 59 mg (0.28 mmol, 93%). ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 5.25 (t sept, J = 6.9, 1.3 Hz, 1H), 4.03−3.91 (m, 2H), 3.22 (dd, J = 5.8, 3.5 Hz, 1H), 3.11 (s, 3H), 2.92 (s, 3H), 1.71 (s, 3H), 1.64 (s, 3H), 1.21 (s, 3H), 1.16 (dd, J = 5.8, 3.5 Hz, 1H), 0.59 (t, J = 5.8 Hz, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 171.5, 136.5, 120.8 (+), 66.9 (−), 62.2 (+), 37.2 (+), 35.4 (+), 27.2, 25.7 (+), 20.1 (+), 17.97 (−), 17.96 (+); FT IR (NaCl, film, cm^{-1}) 3082, 2962, 2932, 1643, 1448, 1394, 1157, 1126; HRMS (TOF ES) found 212.1653, calcd for $C_{12}H_{22}NO_2$ (M + H) 212.1651 (0.9 ppm).

(1*S,2*R**)-2-(((*E*)-3,7-Dimethylocta-2,6-dien-1-yl)oxy)-*N*,*N*,1-trimethylcyclopropanecarboxamide (26ik):** The title compound was prepared according to typical procedure VI, employing 2-bromo-*N*,*N*,1-trimethylcyclopropanecarboxamide (**25i**) (102 mg, 0.60 mmol) and geraniol (93 mg, 0.66 mmol, 1.1 equiv). The reaction was carried out at 60 °C for 12 h. Preparative column chromatography of a residue on silica gel afforded the title compound as a colorless oil, R_f 0.40 (hexane−EtOAc 2:3). Yield 149 mg (0.53 mmol, 89%). ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 5.31−5.22 (m, 1H), 5.11−5.03 (m, 1H), 4.00 (d, J = 6.8 Hz, 2H), 3.23 (dd, J = 5.8, 3.5 Hz, 1H), 3.12 (s, 3H), 2.92 (s, 3H), 2.13−1.97 (m, 4H), 1.67 (s, 3H), 1.64 (s, 3H), 1.59 (s, 3H), 1.21 (s, 3H), 1.17 (dd, J = 5.8, 3.5 Hz, 1H), 0.59 (t, J = 5.8 Hz, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 171.5, 139.8, 131.5, 123.9 (+), 120.6 (+), 66.9 (−), 62.2 (+), 39.5 (−), 37.2 (+), 35.4 (+), 27.2, 26.2 (−), 25.6 (+), 20.1 (+), 18.0 (−), 17.6 (+), 16.3 (+); FT IR (KBr, cm^{-1}) 2964, 2928, 2872, 2858, 1645, 1495, 1450, 1394, 1360, 1126, 1101, 1084, 1041, 986; HRMS (TOF ES) found 302.2084, calcd for $C_{17}H_{29}NO_2Na$ (M + Na) 302.2096 (4.0 ppm).

(1*S,2*R**)-Allyl 2-isopropoxy-1-methylcyclopropanecarboxylate (31cb): Typical Procedure VII:** A mixture of *t*-BuOK (64.5 mg, 1.25 mmol, 2.50 equiv), 18-crown-6 (13 mg, 50 μmol), and potassium 1-methyl-2-bromocyclopropane carboxylate (**27**) (109 mg, 0.50 mmol) in anhydrous THF (2 mL) was stirred at room temperature, and isopropanol (59 μL, 46 mg, 0.75 mmol, 1.5 equiv) was added. The reaction was stirred at 80 °C for 12 h, then cooled to room temperature and quenched with allyl bromide (130 μL, 182 mg, 1.50 mmol, 3.00 equiv). The resulting mixture was stirred for 1 h, then filtered through a fritted funnel and concentrated. Preparative column chromatography of a residue on silica gel afforded the title compound as a clear oil, R_f 0.30 (hexane/EtOAc 20:1). Yield 76.0 mg (0.38 mmol, 76%). ^{1}H NMR (500.13 MHz, $CDCl_3$) δ ppm 5.94 (dddd, J = 17.3, 10.4, 5.9, 5.7 Hz, 1H), 5.34 (dq, J = 17.3, 1.6 Hz, 1H), 5.22 (dq, J = 10.5, 1.3 Hz, 1H), 4.60

(dt, J = 5.6, 1.3 Hz, 2H), 3.63 (spt, J = 6.1 Hz, 1H), 3.31 (dd, J = 6.6, 4.7 Hz, 1H), 1.77 (dd, J = 6.0, 4.7 Hz, 1H), 1.27 (s, 3H), 1.18 (d, J = 6.0 Hz, 3H), 1.09 (d, J = 6.0 Hz, 3H), 0.87 (dd, J = 6.9, 6.0 Hz, 2H); ^{13}C NMR (125.76 MHz, $CDCl_3$) δ 171.7, 132.4 (+), 117.7 (−), 72.6 (+), 65.2 (−), 64.3 (+), 26.1, 22.0 (+), 21.6 (+), 20.4 (−), 18.9 (+); IR (film, cm^{-1}) 2972, 2934, 2876, 1730, 1717, 1456, 1321, 1159, 989, 932; HRMS (TOF ES) found 205.1420, calcd for $C_{11}H_{18}O_3Li$ (M + Li) 205.1416 (1.9 ppm).

(1*S,2*R**)-Methyl 2-(benzyloxy)-1-methylcyclopropanecarboxylate (31da):** The title compound was prepared according to typical procedure VII employing benzyl alcohol (83 mg, 0.77 mmol, 1.5 equiv) and MeI (93 μL, 213 mg, 1.50 mmol, 3.00 equiv). Preparative column chromatography on silica gel afforded the title compound as a clear oil, R_f 0.40 (hexane/EtOAc 10:1). Yield 100 mg (0.41 mmol, 82%). ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 7.39−7.30 (m, 5H), 4.53 (d, J = 11.6 Hz, 1H), 4.48 (d, J = 11.6 Hz, 1H), 3.71 (s, 3H), 3.36 (dd, J = 6.6, 4.5 Hz, 1H), 1.85 (dd, J = 5.9, 4.7 Hz, 1H), 1.27 (s, 3H), 0.90 (t, J = 6.6, 5.9 Hz, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 172.4, 137.1, 128.4 (+, 2C), 128.1 (+, 2C), 127.9 (+), 73.4 (−), 65.6 (+), 52.0 (+), 26.1, 20.7 (−), 19.0 (+); FT IR (film, cm^{-1}) 3088, 3030, 3005, 2907, 2872, 1960, 1880, 1728, 1497, 1454, 1437, 1385, 1356, 1329, 1286, 1269, 1254, 1194, 1155, 1107, 1045, 1028, 993, 943, 903, 866, 833, 795, 737, 698, 606, 554, 490, 451; HRMS (TOF ES) found 221.1188, calcd for $C_{13}H_{17}O_3$ (M + H) 221.1178 (4.5 ppm).

(1*S,2*R**)-Methyl 1-methyl-2-(pent-4-en-1-yloxy)cyclopropanecarboxylate (31ea):** The title compound was prepared according to typical procedure VII employing pent-4-en-1-ol (64.5 mg, 0.75 mmol, 1.5 equiv) and MeI (93 μL, 213 mg, 1.50 mmol, 3.00 equiv) was added dropwise. Preparative column chromatography of a residue on silica gel afforded the title compound as a colorless oil, R_f 0.40 (hexane/EtOAc 20:1). Yield 71 mg (0.36 mmol, 72%). ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 5.81 (ddt, J = 17.1, 10.3, 6.7 Hz, 1H), 5.03 (dq, J = 17.1, 1.7 Hz, 1H), 4.97 (ddt, J = 10.2, 2.1, 1.2 Hz, 1H), 3.72 (s, 3H), 3.51 (dt, J = 9.3, 6.6 Hz, 1H), 3.38 (dt, J = 9.3, 6.4 Hz, 1H), 3.28 (dd, J = 6.8, 4.5 Hz, 1H), 2.16−2.01 (m, 2H), 1.77 (dd, J = 5.9, 4.7 Hz, 1H), 1.64 (quin, J = 7.0 Hz, 2H), 1.27 (s, 3H), 0.87 (app. t, J = 6.8, 5.9 Hz, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 172.5, 138.1 (+), 114.8 (−), 70.7 (−), 66.1 (+), 51.9 (+), 30.2 (−), 28.6 (−), 25.9, 20.6 (−), 19.1 (+); FT IR (cm^{-1}, film) 3081, 2949, 2939, 1734, 1437, 1364, 1352, 1329, 1194, 1157, 1107, 1043, 995, 945, 912, 858, 557, 444; HRMS (TOF ES) found 221.1164, calcd for $C_{11}H_{18}O_3Na$ (M + Na) 221.1154 (4.5 ppm).

(1*S,2*R**)-Allyl 1-methyl-2-(pent-4-en-1-yloxy)cyclopropanecarboxylate (31eb):** The title compound was prepared according to typical procedure VII employing pent-4-en-1-ol (65 mg, 0.75 mmol, 1.5 equiv) and allyl bromide (130 μL, 182 mg, 1.50 mmol, 3.00 equiv). Preparative column chromatography of a residual oil on silica gel afforded the title compound as a clear oil, R_f 0.40 (hexane/EtOAc 20:1). Yield 76 mg (0.34 mmol, 68%). ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 5.94 (dddd, J = 17.0, 10.5, 6.6, 5.6 Hz, 1H), 5.79 (ddt, J = 17.0, 10.3, 6.7 Hz, 1H), 5.35 (dq, J = 17.3, 1.6 Hz, 1H), 5.23 (dq, J = 10.5, 1.4 Hz, 1H), 5.02 (ddt, J = 17.2, 2.0, 1.5 Hz, 1H), 4.96 (ddt, J = 10.2, 2.0, 1.4 Hz, 1H), 4.62 (dt, J = 5.6, 1.4 Hz, 2H), 3.50 (dt, J = 9.1, 6.6 Hz, 1H), 3.38 (dt, J = 9.4, 6.6 Hz, 1H), 3.29 (dd, J = 6.6, 4.5 Hz, 1H), 2.12−2.03 (m, 2H), 1.78 (dd, J = 5.8 , 4.6 Hz, 1H), 1.63 (quin, J = 6.9 Hz, 2H), 1.28 (s, 3H), 0.87 (t, J = 6.5 Hz, 2H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 171.6, 138.0 (+), 132.3 (+), 117.9 (−), 114.7 (−), 70.7 (−), 66.2 (+), 65.3 (−), 30.1 (−), 28.6 (−), 25.9, 20.6 (−), 19.0 (+); FT IR (film, cm^{-1}) 3078, 3005, 2962, 2937, 2874, 1730, 1641, 1462, 1441, 1385, 1364, 1321, 1261, 1155, 1105, 1043, 1032, 989, 914, 858, 795, 768, 635, 557, 505; HRMS (TOF ES) found 247.1304, calcd for $C_{13}H_{20}O_3Na$ (M + Na) 247.1310 (2.4 ppm).

(1*R,2*S**)-Methyl 1-methyl-2-((*E*)-prop-1-enyloxy)cyclopropanecarboxylate (31fa):** The title compound was prepared according to typical procedure VII employing allyl alcohol (51 μL, 44 mg, 0.75 mmol, 1.5 equiv) and MeI (93 μL, 213 mg, 1.50 mmol, 3.00 equiv). Preparative column chromatography of a residue on silica gel afforded the title compound as a colorless oil, R_f 0.38 (hexane/EtOAc 20:1). Yield 71 mg (0.42 mmol, 84%). ^{1}H NMR (500.13 MHz, $CDCl_3$) δ 5.96 (dq, J = 6.0, 1.6 Hz, 1H), 4.45 (ps quintet, J = 6.9, 6.0 Hz, 1H), 3.67 (s, 3H), 3.54 (dd, J = 6.6, 4.4 Hz, 1H), 1.85 (dd, J = 6.0, 4.4 Hz, 1H), 1.51 (dd, J = 6.9, 1.6 Hz, 3H), 1.27 (s, 3H), 0.91 (ps t, J = 6.6, 6.0 Hz, 1H); ^{13}C NMR (125.76 MHz, $CDCl_3$) δ 171.7, 144.0 (+), 103.2 (+), 65.5 (+), 51.9 (+), 25.9, 20.0 (−), 18.8 (+), 9.0 (+); FT IR (NaCl, film, cm^{-1}) 2949, 2873, 1729, 1641, 1462, 1437, 1362, 1329, 1261, 1194, 1157, 1107, 1045, 995, 945, 912, 858, 793, 528; HRMS (TOF ES) found 171.1016, calcd for $C_9H_{15}O_3$ (M + H) 171.1021 (2.9 ppm).

■ ASSOCIATED CONTENT

Supporting Information. ^{1}H and ^{13}C NMR spectral charts for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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