Tetrahedron: *Asymmetry* 25 (2014) 1537–1549

Contents lists available at ScienceDirect

Tetrahedron: *Asymmetry*

journal homepage: www.elsevier.com/locate/tetasy

Preparative resolution of bromocyclopropylcarboxylic acids

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ARTICLE INFO

Article history:
Received 5 October 2014
Accepted 27 October 2014

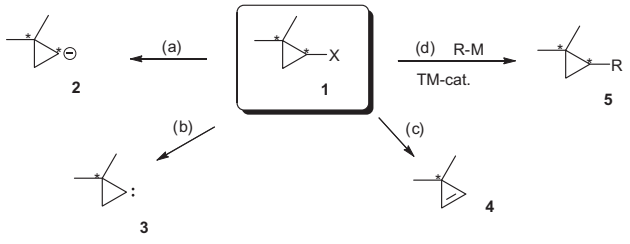
ABSTRACT

A general and efficient method for the preparative resolution of α- and β-bromocyclopropylcarboxylic acids has been developed. This protocol involves a sequence of two crystallizations with pseudo-enantiomeric amines, cinchonine, and cinchonidine, which yield both enantiomers of the acid in highly enriched form. Both alkaloids can be easily recovered and reused multiple times without any loss of efficacy.

1. Introduction

Chiral halocyclopropanes are useful building blocks and convenient precursors for chiral cyclopropyl anions **2** (Scheme 1, path a),[1] cyclopropylidenes **3** (path b),[2] and cyclopropenes **4** (path c).[3] They can also be engaged in transition-metal catalyzed cross-coupling reactions (path d).[4] These synthons are also important for the assembly of cyclopropane-containing targets.[2,5,6] Their ability to participate in highly stereoselective ring-opening transformations[7] may be advantageously employed in the installation of stereodefined three carbon atom fragments.

In continuation of our long-standing interests in additions across strained C=C bonds of cyclopropenes[8,9] and the formal nucleophilic substitution of halocyclopropanes, we have recently reported on a new mode for the highly diastereoselective formal nucleophilic substitution of chiral cyclopropylbromides **6** with alkoxides.[10] This reaction involves dual control of selectivity, in which steric factors at the quaternary stereogenic center of cyclopropene intermediate **7** dictate the configuration of the newly installed stereocenter at C-1. The stereochemistry of the third stereogenic center at C-3 is set by a thermodynamically driven epimerization of enolate **8** (Scheme 2).[10] This strategy allows for rapid access to densely functionalized chiral cyclopropanes **9** with three contiguous stereogenic centers; however, the poor availability of the corresponding enantiomerically enriched precursors **6**, derivatives of bromocyclopropylcarboxylic acids (BCCA), has been the bottleneck of this methodology.



Scheme 1.

The most efficient known approach to chiral β-BCCAs **10** is the catalytic asymmetric [2+1]-cycloaddition of diazoacetates **12** to vinylbromides **11** (Scheme 3, Mode I). This strategy, however, has only been successfully employed for intramolecular cyclopropanations,[11] since the lowered π-density in the vinyl bromide makes the intermolecular version of this reaction rather ineffective. Cyclopropanation of olefins **14** via carbenoid transfer from 2-bromo-2-diazoacetates **15** by Hansen[12] permits access to racemic α-BCCA derivatives **13**; an asymmetric version of this methodology, however, is still to be developed (Scheme 3, Mode II). It has also been shown that enantiomerically enriched derivatives of β-BCCA **18** can be obtained via the transition metal-catalyzed asymmetric hydro- and carbometallation of cyclopropenes **16** followed by metal–halogen exchange (Scheme 4).[13,14] Several examples of diastereoselective cyclopropanations of homochiral olefins with halo- and dihalocarbenes have also been reported.[15] All of these strategies, however, have not found significant synthetic applications, mainly due to substrate or catalyst limitations.

The lack of suitable enantio- and diastereoselective syntheses and cost-prohibitive or non-scalable preparative enzymatic[16] and chromatographic methods[5,17] have prompted us to develop a new approach for the resolution of racemic bromocyclopropylcarboxylic acids via crystallization of diastereomeric salts with pseudo-enantiomeric bases, cinchonine, and cinchonidine. This method

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http://dx.doi.org/10.1016/j.tetasy.2014.10.017
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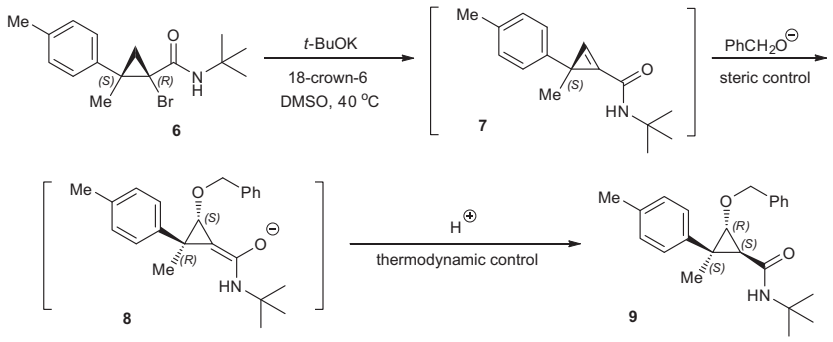
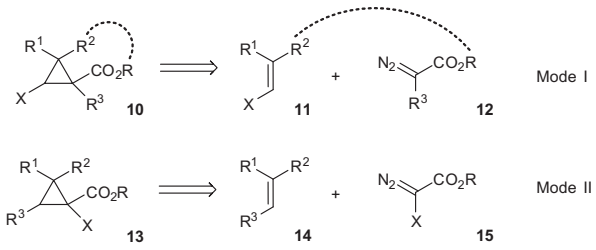
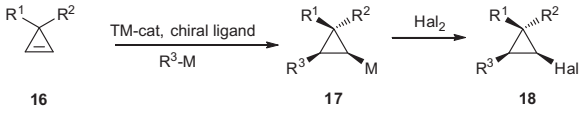


Scheme 2.



Scheme 3.



Scheme 4.

provides high yields of both enantiomers of the acid in nearly enantiopure form after a single recrystallization with the corresponding base, which can be easily recycled and reused.

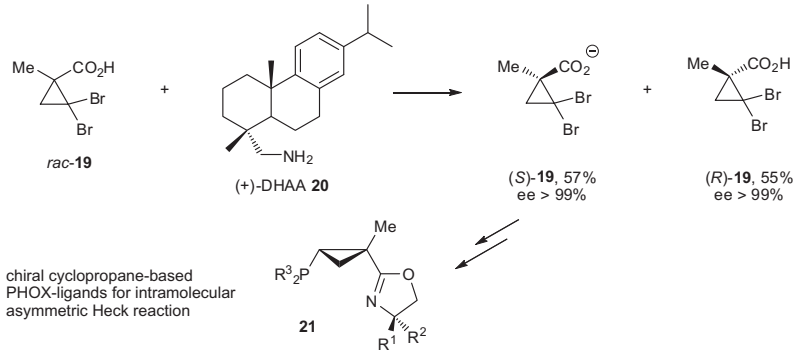
2. Results and discussion

Successful known attempts at the resolution of halocyclopropylcarboxylic acids via the crystallization of diastereomeric salts include the use of (+)-dehydroabietylamine **20** (DHAA)[18,19] and brucine[20] for β- and α-BCCA, respectively. We have previously employed crystallization with (+)-DHAA in a scale-up preparation of both individual enantiomers of 2,2-dibromo-1-methylcyclopropanecarboxylic acid **19** in the synthesis of chiral cyclopropylphosphine ligands **21** (Scheme 5).[6,21] Our experience with amine **20** revealed several disadvantages of this reagent. The main issue was the relatively poor stability of the free amine. Commercially available technical grade amine **20** has only 60% assay, and must be purified prior to use. The purified product in a free form has a limited shelf live, but can be stored in the form of hydrochloride or acetate, which adds steps to the resolution routine. Freshly purified amine can be recycled and reused but every successive cycle gives a lower purity material and eventually requires re-purification therefore increasing the cost of this already expensive reagent. It should also be mentioned that (+)-DHAA is very substrate specific and can only be used for the efficient separation of 2,2-dibromocyclopropanecarboxylic acids. Other types of cyclopropylcarboxylic acids tested with (+)-DHAA provided inferior results. We therefore carried out a search for alternative, efficient, and more stable resolving agents that would allow for a multigram-scale preparation of a variety of enantiomerically pure BCCAs.

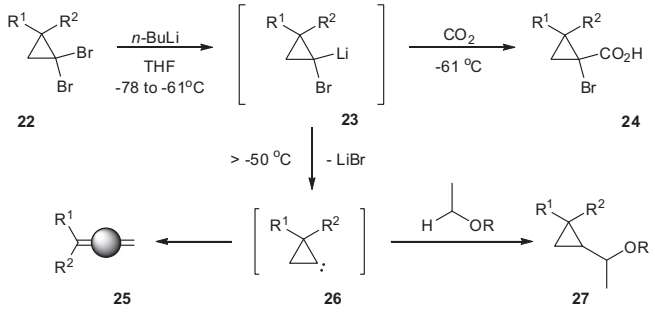
2.1. Preparation of racemic acids

A straightforward approach to racemic BCCA **24** was envisioned via Hoffman's[22] mono-lithiation of *gem*-dibromocyclopropanes **22** with *n*-BuLi, followed by trapping with CO_2 (Scheme 6). To this end, a multigram synthesis of the starting geminal dibromides **22**, was carried out via the addition of dibromocarbene to styrenes **28** under phase-transfer catalytic conditions according to our previously published procedure[23] (Table 1).

With a series of geminal dibromocyclopropanes **22** in hand, we evaluated the scalability of Hoffman's mono-lithiation procedure. Although the preparation of α-bromocyclopropane carboxylic acids **24** via this protocol was previously used in synthesis,[24] most of the reported examples were carried out on a relatively small scale and provided marginal yields. The main challenge in achieving high selectivity in the mono-lithiation was the accurate monitoring of the reaction temperature, which must be maintained within a narrow range between −60 and −65 °C. Lowering the

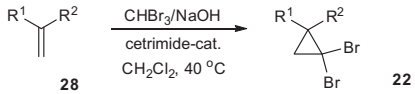


Scheme 5.



Scheme 6.

Table 1
Synthesis of dibromocyclopropanes **22** via [2+1] cycloaddition of dibromocarbene to styrenes



	28	R^1	R^2	Scale (mmol)	22	Yield[a] (%)
1	**28a**	Me	Ph	500	**22a**	80
2	**28b**	Me	4-MeC_6H_4	117	**22b**	73
3	**28c**	Et	Ph	88	**22c**	69
4	**28d**	Me	2-Naphthyl	110	**22d**	66
5	**28e**	Me	4-$MeOC_6H_4$	67	**22e**	74
6	**28f**	H	Ph	500	**22f**	88
7	**28g**	Me	3-MeC_6H_4	116	**22g**	68
8	**28h**	Me	3,4-$Me_2C_6H_4$	120	**22h**	78
9	**28i**	Me	4-EtC_6H_4	128	**22i**	71
10	**28j**	Ph	Ph	55	**22j**	66

[a] Isolated yields of purified dibromocyclopropanes.

temperature reduces the efficiency of the lithium–halogen exchange and the subsequent electrophilic trapping of species **23**, whereas increasing it beyond these limits may trigger α-elimination to cyclopropylidene species **26**. The latter can subsequently rearrange into allene **25**[25] or undergo C–H insertion to afford cyclopropane derivatives **27**[26] (Scheme 6).

Having studied several different solvents and temperature regimens, we found that the recently reported Carlier's method for the preparation of diphenyl derivative **24j**[20] reproduced well upon scale-up and afforded good yields for all *gem*-dibromides (Table 2).

It should be pointed out that in most cases, the corresponding acids were obtained as individual diastereomers (Table 2, entries 1, 2 and 6–9), or with high *trans*-diastereoselectivity (Table 2, entries 3 and 4). When necessary, a single crystallization was performed to obtain a diastereomerically pure product. The high *trans*-selectivity has been attributed[27] to the thermodynamically more favored *trans*-α-halocyclopropyl lithium species **23**, in which the bromide and the bulky aromatic ring are located on the opposite sides of the small ring plane (Scheme 7). The reduced diastereoselectivity observed in the reaction of **22c** (Table 2, entry 3) can be rationalized by the increased steric demands imposed by the ethyl substituent as compared to methyl, which made facial differentiation less efficient. We believe that excessive steric hindrance of the aromatic substituent in anionic species *trans*-**23d** may reduce a relative kinetic rate of electrophilic trapping at the *syn*-phase, which could explain the observed lower dr (Table 2, entry 4). The lowest diastereoselectivity in the series obtained in the reaction of **22e** (Table 2, entry 5) could be explained by a destabilizing stereoelectronic effect of the electron-donating aromatic substituent. Apparently, this effect could only be realized in the *trans*-**23** anionic species, in which the dihedral angle Ar-C-C-Li is close to 0°. In *cis*-**23** species this angle approaches 120°, which does not allow for efficient orbital overlap.

Table 2
Synthesis of racemic α-bromocyclopropylcarboxylic acids **24** via mono-lithiation of *gem*-dibromocyclopropanes **22**

#	22	R^1	R^2	Scale (mmol)	24	dr[a]	Yield[b] (%)
1	**22a**	Me	Ph	70	**24a**	100:0	90
2	**22b**	Me	4-MeC_6H_4	70	**24b**	100:0	75
3	**22c**	Et	Ph	56	**24c**	89:11	76
4	**22d**	Me	2-Naphthyl	70	**24d**	86:14	42
5	**22e**	Me	4-$MeOC_6H_4$	49	**24e**	67:33	88[c]
6	**22f**	H	Ph	70	**24f**	100:0	56
7	**22g**	Me	3-MeC_6H_4	79	**24g**	100:0	76
8	**22h**	Me	3,4-$Me_2C_6H_4$	75	**24h**	100:0	71
9	**22i**	Me	4-EtC_6H_4	70	**24i**	100:0	46
10	**22j**	Ph	Ph	34	**24j**	–	84[d]

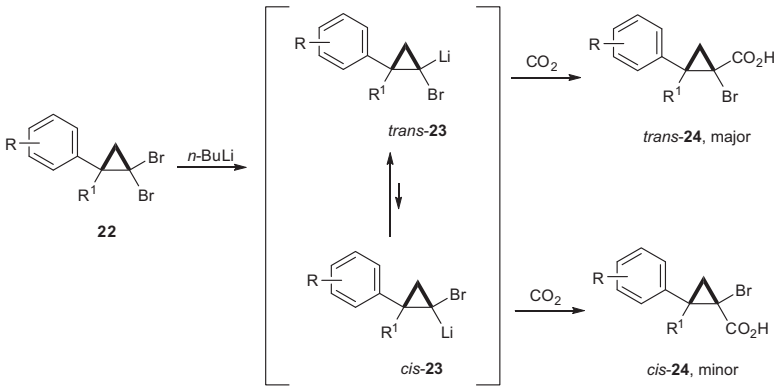
[a] Ratio of *trans*/*cis* was determined in the crude reaction mixture.
[b] Isolated yields of purified *trans*-diastereomer, unless specified otherwise.
[c] Isolated yields of a mixture of diastereomers.
[d] Isolated yield of purified product **24j**.

2.2. Resolution of α-BCCAs

We first attempted the resolution of acid **24a** by employing (+)-DHAA **20**.[26] Taking into account the reported tendency of the latter to form acidic salts with cyclopropylcarboxylic acids, several crystallizations of diastereomeric salts have been probed using 4:1, 2:1, and 1:1 acid-to-amine ratios. However in all cases, the samples of acid recovered by extraction from acidified solutions of the corresponding crystalline crops were racemic (Table 3, entries 1–3). Carlier's method for the resolution of acid **24j** with brucine **29** proved to be efficient,[20] however, analogous treatment of methyl-substituted acid **24a** gave racemic product (Table 3, entries 4 and 5), thus confirming that brucine is also a very substrate-sensitive resolving agent.

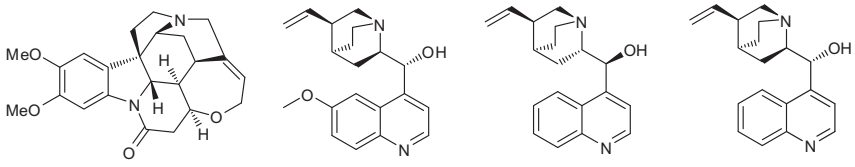
Having achieved no success with the above established literature protocols, we began screening alternative chiral amine-based resolving agents. Our attention was drawn to the cinchona alkaloids, currently one of the most powerful and versatile chirality-inducing agents for synthetic[28,29] and analytical[30] applications. These chiral amines are very inexpensive and readily available in both pseudo-enantiomeric forms. Initial attempts at crystallization of quinine salts produced marginal results: employment of 0.5 and 1.0 equiv of chiral base afforded acid (−)-**24a** in 16% and 33% ee, respectively (Table 3, entries 6 and 7). A second crystallization with 1.0 equiv of quinine allowed for an improved enantiomeric purity up to 55% (Table 3, entry 8), but was still inadequate for preparative method development. Another problem associated with using quinine **30** as a resolving agent was the relatively high solubility of both diastereomeric salts, which produced poorly separable, loose, and flaky crystalline crops. In contrast, crystallization of the corresponding salts with cinchonine **31** afforded a visibly dense and much less soluble needle-like crystalline precipitate. The enantiomeric purity of dextrorotatory acid **24a**, isolated after a single crystallization, exceeded 95% (Table 3, entry 9). Re-crystallization of the acid recovered from the mother liquor with cinchonidine **32** afforded a second crystalline crop, acidic digestion and extraction of which provided the levorotatory enantiomer with high enantiomeric purity (Table 3, entry 10).

With a pair of powerful resolving reagents in hand, we focused on the development of a preparative resolution protocol that would allow for material recycling and reuse (Scheme 8). The optimized routine involves dissolving equimolar amounts of racemic acid **24a** and cinchonine **31** in the minimal amount of boiling acetone, hot filtration, after which the hot solution was allowed to cool to room temperature, and then further chilled to +4 °C. The crystalline precipitate obtained provided, after routine acid–



Scheme 7.

Table 3
Resolution of **24a**: optimization of resolving agent



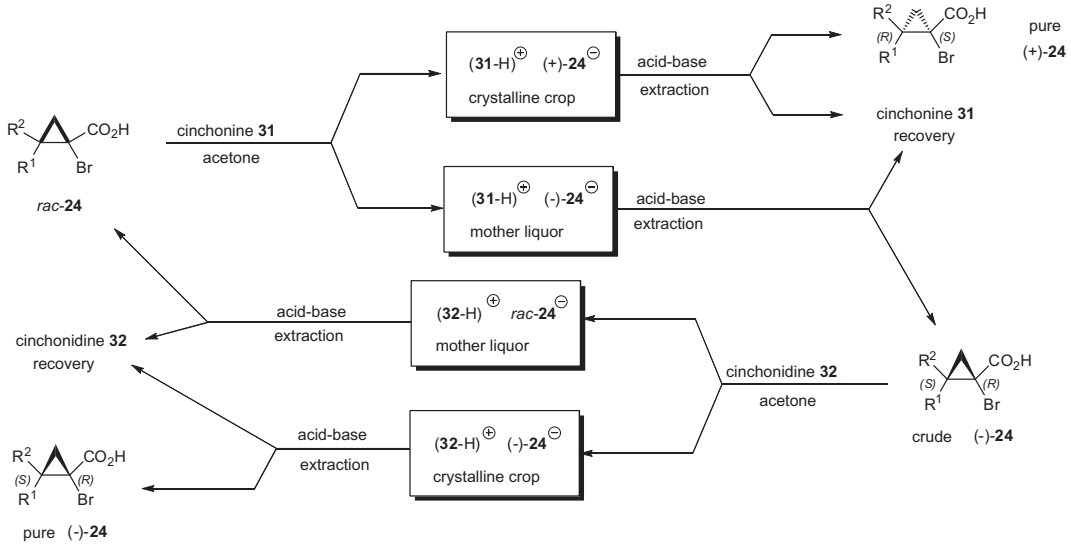
	Resolving agent	Equivalents[a]	Enantiomer[b]	ee[c] (%)
1	(+)-DHHA **20**	0.25	—	0
2	**20**	0.5	—	0
3	**20**	1.0	—	0
4	Brucine **29**	0.5	—	0
5	**29**	1.0	—	0
6	Quinine **30**	0.5	(−)	16
7	**30**	1.0	(−)	33
8	**30**	1.0	(−)	55[d]
9	Cinchonine **31**	1.0	(+)	98
10	Cinchonidine **32**	1.0	(−)	91[e]

[a] Amine to acid ratios. All of the test experiments were performed on a 500 mg scale.
[b] Signs of the specific rotation of the recovered enantiomer **24a** obtained after acid–base extraction.
[c] Determined by chiral GC of the corresponding methyl esters.
[d] Second crystallization of the acid (33% ee), obtained in entry 7.
[e] Re-crystallization of acid **24a** recovered from the mother liquor obtained in the experiment shown in entry 9.

base extraction, enantiomerically pure (+)-**24a** and recovered cinchonine. Acid base extraction of the concentrated mother liquor afforded an additional amount of recovered cinchonine along with partially enriched crude acid (−)-**24a**. The latter was next re-crystallized from hot acetone with an equimolar amount of cinchonidine **32**. The crystalline precipitate formed upon cooling of the hot acetone solution was digested with aqueous acid followed by acid–base extraction to provide enantiomerically pure (−)-**24a** and recovered cinchonidine **32**. The mother liquor from this crystallization was also subjected to acid base-extraction to provide an additional amount of alkaloid **32** and a small amount of nearly racemic **24a** (Scheme 8, see Section 4 for details). Overall, the described protocol afforded a good material balance of acid and allowed for the recovery of both alkaloids in a purity sufficient enough for further reuse without additional purification. Thus, in the frame of this project, the same 25 g of each alkaloid was reused multiple times to obtain all of the described enantiomerically enriched carboxylic acids. Furthermore, in many cases it was found that the amount of the resolving agent could be reduced down to 0.7–0.5 equiv without deterioration of the resolution efficiency (see Table 4 and Section 4 for details).

The optimized protocol was applied to the preparation of various enantiomerically enriched α-bromocyclopropanecarboxylic acids. Acid **24a** was successfully resolved on a 13 g scale, providing more than 4 g of each enantiomer. Swapping the order in which the alkaloids were applied did not affect the efficacy of the separation. When cinchonidine **32** was used first, the corresponding (−)-enantiomer was afforded with 91% ee. Subsequent crystallization with cinchonine **31** provided (+)-**30a** with 98% ee. When alkaloid **31** was used first, followed by **32**, the corresponding enantiomers (+)-**24a** and (−)-**24a** were also obtained with 98% and 91% ee, respectively (Table 3, entries 9 and 10; Table 4, entries 1 and 2).

The introduction of a small substituent at the *para*- or *meta*-position of the phenyl ring (substituent R^2) in acid **24** improved the resolution efficiency. Both enantiomers of acids bearing *p*-tolyl **24b** (entries 3 and 4), *m*-tolyl **24g** (entries 11 and 12), or *p*-ethylphenyl **24i** (entries 15 and 16) substituents were obtained in pure form according to the described protocol. At the same time, the resolution of acids possessing a large R^2 group with cinchonidine **32** was found to be rather problematic. Thus, the purity of levorotatory acids (−)-**24d** (R^2 = 2-naphthyl, entry 8) and (−)-**24h** (R^2 = 3,4-$Me_2C_6H_3$, entry 14) barely exceeded 50%, while the corresponding dextrorotatory acids (+)-**24d** and (+)-**24h** were obtained in enantiomerically pure form after crystallization with cinchonine **31** (entries 7 and 13). Increased steric hindrance of R^1 (*trans*-substituent with respect to the carboxylic function) improved the



Scheme 8.

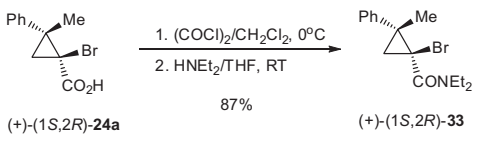
Table 4
Chiral resolution of α-bromocyclopropanecarboxylic acids[a]

	R^1, R^2	Resolving agent	RA (equiv)	**24**	Yield[b] (%) (ee, %)[c]
1	Me, Ph	Cinchonine **31**	1.0	(+)-**24a**	62 (98)[d]
2	Me, Ph	Cinchonidine **32**	0.70	(−)-**24a**	53 (91)
3	Me, *p*-MeC_6H_4	Cinchonine **31**	1.0	(+)-**24b**	50 (>99)
4	Me, *p*-MeC_6H_4	Cinchonidine **32**	1.0	(−)-**24b**	34 (>99)
5	Et, Ph	Cinchonine **31**	1.0	(+)-**24c**	57 (>99)
6	Et, Ph	Cinchonidine **32**	1.0	(−)-**24c**	40 (>99)
7	Me, 2-Napthyl	Cinchonine **31**	1.0	(+)-**24d**	51 (99)
8	Me, 2-Napthyl	Cinchonidine **32**	1.0	(−)-**24d**	73 (54)
9	H, Ph	Cinchonine **31**	1.0	(+)-**24f**	32 (>99)
10	H, Ph	Cinchonidine **32**	1.0	(−)-**24f**	70 (90)
11	Me, 3-MeC_6H_4	Cinchonine **31**	1.0	(+)-**24g**	23 (>99)
12	Me, 3-MeC_6H_4	Cinchonidine **32**	0.5	(−)-**24g**	11 (>99)
13	Me, 3,4-$Me_2C_6H_3$	Cinchonine **31**	1.0	(+)-**24h**	34 (92)
14	Me, 3,4-$Me_2C_6H_3$	Cinchonidine **32**	0.6	(−)-**24h**	66 (52)
15	Me, 4-EtC_6H_4	Cinchonine **31**	0.5	(+)-**24i**	33 (99)
16	Me, 4-EtC_6H_4	Cinchonidine **32**	0.5	(−)-**24i**	35 (>99)
17	Ph, Ph	Cinchonine **31**	0.75	(+)-**24j**	22 (99)
18	Ph, Ph	Cinchonidine **32**	0.75	(−)-**24j**	19 (98)

[a] Resolutions were performed on a 4–5 g scale unless specified otherwise.
[b] Isolated yields of enantiomerically enriched acid, obtained in a single crystalline crop.
[c] Enantiomeric excesses determined by chiral GC or HPLC techniques after conversion of the carboxylic acids into the corresponding methyl esters, see Table 5.
[d] Resolution was performed on a 13 g scale.

resulting ee in both cinchonidine (entries 6 and 18) and cinchonine (entries 1, 5, 9, and 17) with crystallizations up to 98–99%.

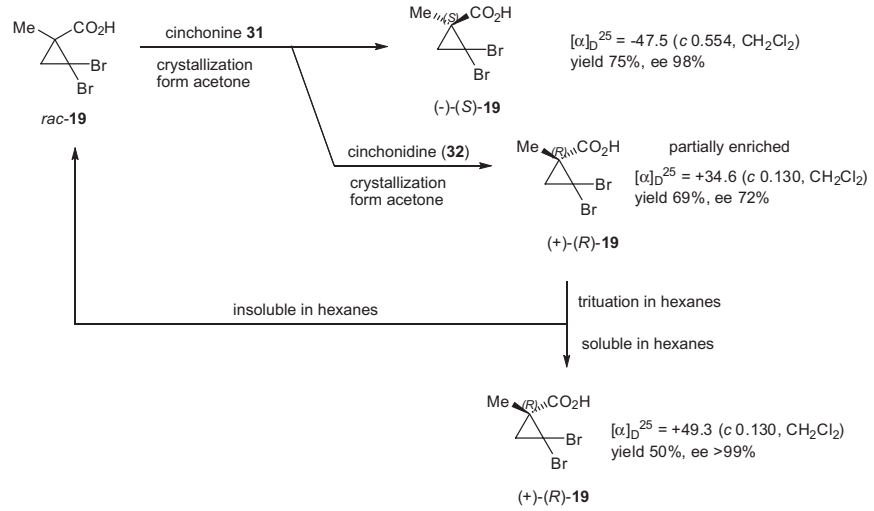
The absolute configurations of both enantiomers of compound **24a** were unambiguously assigned by single crystal X-ray crystallography. (−)-(1*R*,2*S*)-**24a** and (+)-(1*S*,2*R*)-**24a** were characterized in a form of cinchonidine salt and diethylamide (+)-(1*S*,2*R*)-**33**, respectively. The latter derivative was obtained as depicted in Scheme 9 upon sequential treatment of the parent acid with oxalyl chloride and diethylamine.



Scheme 9.

2.3. Resolution of β-BCCA

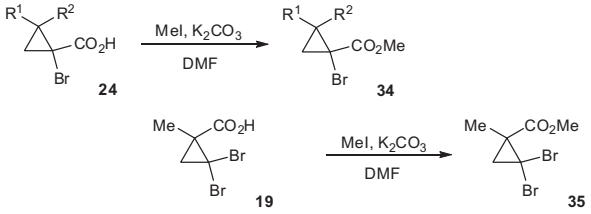
The described above general protocol was also applied toward the resolution of 2,2-dibromo-1-methylcyclopropanecarboxylic acid **19**. First crystallization of *rac*-**19** with cinchonine **31** afforded (−)-(*S*)-**19** in high yield and with excellent enantiomeric purity (Scheme 10). The absolute configuration of this enantiomer was established by X-ray analysis of the corresponding cinchonine salt. Subsequent single crystallization of the crude, partially enriched (+)-acid recovered from the mother liquor, with cinchonidine **32** provided (+)-(*R*)-**19** in good isolated yield and with 72% ee (Scheme 10). Trituration of the partially enriched (+)-(*R*)-**19** (in a free acid form) in hexane at rt allowed for nearly quantitative precipitation of a hardly soluble acid *rac*-**19**, whereas the more soluble (+)-enantiomer remained in the solution and was recovered upon concentration to give (+)-(*R*)-**19** in 50% overall yield and with ee >99%.



Scheme 10.

2.4. Synthesis of cyclopropylcarboxylates

For analytical and characterization purposes, all of the synthesized racemic and enantiomerically enriched carboxylic acids were converted into the corresponding methyl esters with preservation of their stereoconfiguration by treatment of the carboxylic acids with methyl iodide in DMF in the presence of K_2CO_3 (Scheme 11). Chiral GC analyses of the esters were used to determine the enantiomeric purities of the parent carboxylic acids, and the overall efficiency of the featured resolution routine. Chemical yields and chiral GC data are summarized in Table 5.



Scheme 11.

3. Conclusion

In conclusion, we have developed a highly efficient protocol for the resolution of α- and β-BCCAs employing two consecutive crystallizations of racemic materials with cinchonine and cinchonidine. A single crystallization with each of the resolving agents was required to afford both enantiomers of the acids with high enantiomeric purity. It was demonstrated that both alkaloids employed as resolving agents could be cleanly recovered and reused multiple times, which makes this approach very cost-efficient. The described method is also more general with respect to substitution patterns in bromocyclopropylcarboxylic acids as compared to previously reported procedures.

4. Experimental

4.1. General

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 analyses

Table 5
Synthesis of methyl carboxylates from carboxylic acids

	R^1, R^2	Acid	Ester	Yield[a] (%)	R_t, min[b] (T)	$[\alpha]_D^{25}$ (c)[c]
1	Me, Ph	*rac*-**24a**	*rac*-**34a**	71		
		(+)-**24a**	(+)-**34a**	70	49.72 (120)	+34.6 (0.220)
		(−)-**24a**	(−)-**34a**	71	50.57 (120)	−32.3 (0.820)
2	Me, *p*-MeC_6H_4	*rac*-**24b**	*rac*-**34b**	80		
		(+)-**24b**	(+)-**34b**	80	45.08 (131)	+42.6 (0.620)
		(−)-**24b**	(−)-**34b**	80	45.62 (131)	−38.3 (0.300)
3	Et, Ph	*rac*-**24c**	*rac*-**34c**	91		
		(+)-**24c**	(+)-**34c**	90	34.64 (134)	+29.3 (0.244)
		(−)-**24c**	(−)-**34c**	91	34.97 (134)	−30.9 (0.800)
4	Me, 2-Naphthyl	*rac*-**24d**	*rac*-**34d**	71		
		(+)-**24d**	(+)-**34d**	75	14.40[d]	+90.0 (0.600)
		(−)-**24d**	(−)-**34d**	73	16.29[d]	−39.8 (0.560)
5	H, Ph	*rac*-**24f**	*rac*-**34f**	90		
		(+)-**24f**	(+)-**34f**	91	12.23 (150)	+122.4 (0.840)
		(−)-**24f**	(−)-**34f**	89	12.76 (150)	−109.4 (0.900)
6	Me, *m*-MeC_6H_4	*rac*-**24g**	*rac*-**34g**	65		
		(+)-**24g**	(+)-**34g**	65	52.91 (125)	+29.3 (0.820)
		(−)-**24g**	(−)-**34g**	65	53.99 (125)	−30.2 (0.420)
7	Me, 3,4-$Me_2C_6H_3$	*rac*-**24h**	*rac*-**34h**	85		
		(+)-**24h**	(+)-**34h**	85	8.87[d]	+35.4 (0.820)
		(−)-**24h**	(−)-**34h**	89	10.66[d]	−20.4 (0.940)
8	Me, *p*-EtC_6H_4	*rac*-**24i**	*rac*-**34i**	73		
		(+)-**24i**	(+)-**34i**	73	71.88 (131)	+42.6 (0.660)
		(−)-**24i**	(−)-**34i**	80	72.69 (131)	−40.3 (0.340)
9	Ph, Ph	*rac*-**24j**	*rac*-**34j**	84		
		(+)-**24j**	(+)-**34j**	77	19.79[d]	+85.6 (0.820)
		(−)-**24j**	(−)-**34j**	75	23.27[d]	−85.4 (0.900)
10		*rac*-**19**	*rac*-**35**	–[e]		
		(+)-**19**	(+)-**35**	69	28.51 (120)	+45.1 (0.500)
		(−)-**19**	(−)-**35**	75	27.79 (120)	−62.0 (0.512)

[a] Isolated yields of purified esters.
[b] Retention times from chiral GC analyses, unless specified otherwise. Temperatures of GC oven in °C are provided in parentheses. For partially enriched compounds the R_t value of the major component is provided.
[c] Concentrations in CH_2Cl_2 in g/100 mL are provided in parentheses.
[d] Retention times from Chiral HPLC analyses.
[e] Authentic sample of *rac*-**35** was obtained according to the previously reported procedure.[32]

were performed using 30 m × 0.25 mm × 0.25 μm capillary column (polydimethylsiloxane, 5% Ph, helium carrier gas, 1 mL/min). CYCLODEX-B 30 m × 0.25 mm × 0.25 μm column was used for chiral GC-chromatography (hydrogen carrier gas, 1 mL/min). Helium (99.96%) or hydrogen (99.99%) additionally purified by passing consecutively through oxygen/moisture/hydrocarbon traps and oxygen/moisture traps, were used as a carrier gases. Chiral HPLC was performed employing 30 mm × 5 mm Chiralcel OD-H column and UV-detector tuned for 254 nm band. High resolution mass-spectra were obtained using electrospray ionization and time of flight detection techniques. Glassware employed in moisture-free syntheses was flame-dried in 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. Dibromocyclopropanes **28** were synthesized according to the general procedure, as described in our earlier reports.[23] Physical and spectroscopic properties of compounds **22a**,**b**,**e**,**g**,[23a] **22c**,[9f] **22d**,[23b] and **22f**,**j**[31] were identical to those previously reported in the literature. Syntheses of carboxylic acids *rac*-**24a**, *rac*-**24b**, and *rac*-**24c** were described in our preliminary communication.[10] Syntheses of acids *rac*-**24j**[20] and *rac*-**19**[31] were also previously reported. Physical and spectroscopic properties of chiral acids (+)-**19** and (−)-**19**[6] as well as their methyl esters (+)-**35** and (−)-**35**[18] were identical to those previously reported in the literature.

4.2. 1,2-Dimethyl-4-(prop-1-en-2-yl)benzene 28h

A solution of potassium *tert*-butoxide (7.71 g, 68.7 mmol, 0.955 equiv) in dry THF (75 mL) was added dropwise to a stirred suspension of methyltriphenylphosphonium bromide (41.16 g, 115.2 mmol, 1.6 equiv) in dry THF (175 mL) at 0 °C. The resulting yellow mixture was stirred for one hour at 0 °C and then a solution of 3′,4′-dimethylacetophenone (10.7 g, 10.7 mL, 72.0 mmol, 1.0 equiv) in THF was added dropwise and stirred overnight. The mixture was then quenched with saturated aqueous NH_4Cl and partitioned between water (25 mL) and diethyl ether (3 × 75 mL). The combined ether phases were washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by short column chromatography using silica gel and a hexane mobile phase to afford the title compound as a clear oil. Yield 8.6 g (59 mmol, 82%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.18–7.01 (m, 3H), 5.25 (s, 1H), 4.94 (s, 1H), 2.20 (s, 3H), 2.18 (s, 3H), 2.06 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 143.4, 139.0, 136.4, 136.0, 129.6 (−), 126.9 (−), 123.1 (−), 111.6 (+), 22.0 (−), 20.1 (−), 19.6 (−); FTIR (KBr, cm^{-1}): 3084, 3020, 2970, 2941, 2918, 2887, 2862, 1630, 1566, 1504, 1450, 1371, 1020, 995, 881, 822, 733; HRMS (TOF ES): Found 153.1253, calcd for $C_{11}H_{14}Li$ (M+Li) 153.1256 (2.0 ppm).

4.3. (2,2-Dibromo-1methylcyclopropyl)-1,2-dimethylbenzene 22h

To a vigorously stirred mixture of styrene **28h** (17.48 g, 119.5 mmol), bromoform (45.2 g, 15.6 mL, 179 mmol, 1.50 equiv), tetradecyltrimethylammonium bromide (TDTAB) (750 mg, 2.23 mmol, 1.9 mol %), and dichloromethane (200 mL) was added dropwise 50% aqueous solution of sodium hydroxide (12 g NaOH in 12 mL H_2O). The mixture was stirred at 900–1100 rpm overnight at 30–35 °C. When GC analysis indicated full conversion of the olefin, the mixture was quenched with water (300 mL) and extracted with dichloromethane (3 × 50 mL). The combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash column chromatography on silica gel with hexanes as the mobile phase to afford (2,2-dibromo-1methylcyclopropyl)-1,2-dimethylbenzene as a light yellow oil. Yield 29.7 g (93.3 mmol, 78%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.18–7.01 (m, 3H), 2.29 (s, 3H), 2.27 (s, 3H), 2.15 (d, J = 7.5 Hz, 1H), 1.76 (d, J = 7.5 Hz, 1H), 1.71 (s, 3H); ^{13}C (126 MHz, $CDCl_3$): δ 139.9, 136.7, 135.7, 129.8 (+), 129.7 (+), 125.9 (+), 37.4 (−), 35.6, 33.8, 28.0 (+), 20.0 (+), 19.7 (+); FTIR (KBr, cm^{-1}): 2980, 2966, 2924, 2864, 2359, 1504, 1447, 1427, 1062, 1022, 822, 692; HRMS (TOF ES): Found 314.9389, calcd for $C_{12}H_{13}Br_2$ (M−H) 314.9384 (1.6 ppm).

4.4. (2,2-Dibromo-1-methylcyclopropyl)-4-ethylbenzene 22i

Compound was obtained via the same procedure using 1-ethyl-4-(prop-1-en-2-yl)benzene **28i** (18.68 g, 127.7 mmol, 1.0 equiv) as the starting material. The tiled compound was obtained as a clear oil in a yield of 31.1 g (97.9 mmol, 77%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25–7.18 (m, 4H), 2.66 (q, J = 7.6 Hz, 2H), 2.15 (d, J = 7.5 Hz, 1H), 1.77 (d, J = 7.5 Hz, 1H), 1.71 (s, 3H), 1.26 (t, J = 7.6 Hz, 3H); ^{13}C (126 MHz, $CDCl_3$): 143.3, 139.7, 128.5 (+, 2C), 128.0 (+, 2C), 37.3, 35.6, 33.8 (−), 28.6 (−), 27.9 (+), 15.5 (+); FTIR (KBr, cm^{-1}): 3022, 2962, 2928, 2893, 2870, 1512, 1445, 1427, 1377, 1082, 1063, 1051, 1018, 831, 692, 573; HRMS (TOF ES): Found 314.9386, calcd for $C_{12}H_{13}Br_2$ (M−H) 314.9384 (0.6 ppm).

4.5. (1*R**,2*S**)-1-Bromo-2-(3,4-dimethylphenyl)-2-methylcyclopropanecarboxylic acid *rac*-24h, typical procedure

A solution of (2,2-dibromo-1methylcyclopropyl)-1,2-dimethylbenzene **22h** (23.7 g, 74.5 mmol, 1.0 equiv) in dry THF (200 mL) was placed under a nitrogen atmosphere into a 500 mL oven dried two neck flask. The solution was cooled to −78 °C and 2.5 M solution of *n*-BuLi (28.3 ml, 70.8 mmol, 0.950 equiv) in hexane was added dropwise over the course of 15 min. Immediately following the addition of *n*-BuLi, the reaction mixture was warmed to −61 °C and stirred for 20 min. The mixture was then cannulated into a 1 L three neck flask containing freshly condensed dry carbon dioxide and allowed to warm to room temperature with moderate stirring while a constant flow of dry CO_2 gas was maintained. The mixture was partitioned between water (140 mL) and chloroform (100 mL) and acidified with 4 M HCl (210 mL). The aqueous layer was extracted with chloroform (3 × 40 mL). The combined organic phases were then extracted with saturated sodium bicarbonate (3 × 40 mL). The remaining aqueous solution was washed with 20 mL of chloroform. The combined aqueous phases were then acidified to pH < 1 and extracted with chloroform (3 × 40 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated to afford the product as light yellow crystals, mp 127–129 °C. Yield 14.2 g (50.1 mmol, 71%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.05–6.86 (m, 3H), 2.42 (d, J = 6.3 Hz, 1H), 2.21 (s, 3H), 2.20 (s, 3H), 1.70 (s, 3H), 1.36 (d, J = 6.3 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 174.0, 137.5, 136.7, 135.6, 129.8 (+), 129.1 (+), 125.2 (+), 39.6, 36.9, 28.8 (−), 28.0 (+), 19.8 (+), 19.6 (+); FTIR (KBr, cm^{-1}): 3084, 3015, 2982, 2968, 2924, 2885, 2866, 2652, 1699, 1445, 1418, 1302, 1281, 1250, 1221, 1061, 878, 820, 696; HRMS (TOF ES): Found 281.0179, calcd for $C_{13}H_{14}BrO_2$ (M−H) 281.0177 (0.7 ppm).

4.6. (1*R**,2*S**)-1-Bromo-2-methyl-2(naphthalene-2-yl)cyclopropanecarboxylic acid *rac*-24d

This compound was obtained as a dark brown highly viscous oil via the typical procedure starting from 2-(2,2-dibromo-1-methylcyclopropyl)naphthalene **22d** (23.8 g, 70.0 mmol). Yield 9.06 g

(29.7 mmol, 45%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.80–7.13 (m, 7H), 2.46 (d, J = 6.4 Hz, 1H), 1.70 (s, 3H), 1.38 (d, J = 6.4 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 172.6, 137.7, 133.4, 132.6, 128.4 (+), 127.9 (+), 127.8 (+), 126.9 (+), 126.3 (+), 126.1 (+), 126.0 (+), 39.5, 37.3, 29.0 (−), 27.9 (+); FTIR (KBr, cm^{-1}): 3053, 2359, 2341, 1697, 1420, 1292, 1231, 1061, 856, 818, 748, 681, 444, 424, 411; HRMS (TOF ES): Found 303.0027, calcd for $C_{15}H_{12}BrO_2$ (M−H) 303.0021 (2.0 ppm).

4.7. (1*R**,2*S**)- and (1*R**,2*R**)-1-bromo-2-(4-methoxyphenyl)-2-methylcyclopropanecarboxylic acid *rac*-24e

This compound was obtained as a dark brown highly viscous oil via the typical procedure starting from (2,2-dibromo-1-methylcyclopropyl)-4-methoxybenzene (15.8 g, 49.4 mmol, 1.0 equiv). Yield 10.7 g (43.5 mmol, 88%) as a mixture of two inseparable diastereomers, 2:1. The unfavorable diastereomeric ratio in combination with high light sensitivity leading to decomposition prohibited further use of this material for resolution. Major: ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.13 (d, J = 8.8 Hz, 2H), 6.79 (d, J = 8.8 Hz, 2H), 3.78 (s, 3H), 2.45 (d, J = 6.4 Hz, 1H), 1.71 (s, 3H), 1.38 (d, J = 6.4 Hz, 1H); ^{13}C (126 MHz, $CDCl_3$): δ 173.7, 158.7, 132.1, 129.1 (+, 2C), 114.0 (+, 2C), 55.4 (+), 39.5, 36.4, 28.7 (−), 27.8 (+). Minor: ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.22–7.16 (m, 2H), 6.93–6.86 (m, 2H), 3.81 (s, 3H), 2.05 (d, J = 6.6 Hz, 1H), 1.74 (d, J = 6.6 Hz, 1H), 1.50 (s, 3H); ^{13}C (126 MHz, CDCl3): δ 174.9, 158.8, 134.6, 130.0 (+, 2C), 113.8 (+, 2C), 55.4 (+), 37.9, 36.5, 28.5 (−), 22.2 (+). HRMS (TOF ES): Found 282.9986, calcd for $C_{12}H_{12}BrO_3$ (M−H) 282.9975 (3.9 ppm).

4.8. (1*R**,2*S**)-1-Bromo-2-phenylcyclopropanecarboxylic acid *rac*-24f

This compound was obtained as light yellow crystals (mp 100–102 °C) via the typical procedure starting from (2,2-dibromocyclopropyl)benzene **22f** (19.3 g, 70.0 mmol). Yield 6.04 g (25.1 mmol, 38%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35–7.17 (m, 5H), 3.15 (dd, J = 10.0, 8.8 Hz, 1H), 2.35 (dd, J = 8.8, 6.6 Hz, 1H), 1.83 (dd, J = 10.0, 6.6 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 173.1, 133.8, 128.9 (+, 2C), 128.4 (+, 2C), 127.7 (+), 38.3 (+), 30.8, 23.2 (−); FTIR (KBr, cm^{-1}): 3088, 3061, 3028, 2903, 2876, 1697, 1448, 1425, 1306, 1225, 1184, 1126, 957, 935, 870, 849, 783, 725, 696, 525; HRMS (TOF ES): Found 238.9700, calcd for $C_{10}H_8BrO_2$ (M−H) 238.9708 (3.3 ppm).

4.9. (1*R**,2*S**)-1-Bromo-2-methyl-2-(*m*-tolyl)cyclopropanecarboxylic acid *rac*-24g

This compound was obtained as a yellow oil via the typical procedure starting from 1-(2,2-dibromo-1-methylcyclopropyl)-3-methylbenzene **22g** (23.9 g, 78.5 mmol). Yield 15.2 g (56.4 mmol, 76%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.18–6.93 (m, 4H), 2.44 (d, J = 6.3 Hz, 1H), 2.30 (s, 3H), 1.71 (s, 3H), 1.38 (d, J = 6.4 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 172.7, 140.1, 138.2, 128.7 (+), 128.5 (+), 128.2 (+), 125.0 (+), 39.5, 37.1, 28.8 (−), 27.9 (+), 21.5 (+); FTIR (KBr, cm^{-1}): 3400, 3364, 3225, 3180, 3101, 3020, 2984, 2964, 2926, 2864, 1699, 1418, 1379, 1298, 1248, 1200, 1049, 947, 876, 787, 706, 671; HRMS (TOF ES): Found 269.0184, calcd for $C_{12}H_{14}BrO_2$ (M+H) 269.0177 (2.6 ppm).

4.10. (1*R**,2*S**)-1-Bromo-2-(4-ethylphenyl)-2-methylcyclopropanecarboxylic acid *rac*-24i

This compound was obtained as light brown crystals (mp 109–111 °C) via the typical procedure starting from 1-(2,2-dibromo-1-methylcyclopropyl)-4-ethyl benzene **22i** (22.4 g, 70.4 mmol). Yield 8.57 g (30.3 mmol, 46%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.15–7.03 (m, 4H), 2.61 (q, J = 7.6 Hz, 2H), 2.44 (d, J = 6.4 Hz, 1H), 1.71 (s, 3H), 1.37 (d, J = 6.4 Hz, 1H), 1.22 (t, J = 7.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 173.7, 143.3, 137.3, 128.0 (+, 2C), 127.9 (+, 2C), 39.5, 37.0, 28.8 (−), 28.6 (−), 27.8 (+), 15.6 (+); FTIR (KBr, cm^{-1}): 3090, 3049, 3022, 2964, 2928, 2895, 2872, 1701, 1516, 1421, 1377, 1298, 1286, 1250, 1119, 1080, 1063, 1045, 941, 885, 862, 833, 696, 569; HRMS (TOF ES): Found 283.0328, calcd for $C_{13}H_{16}BrO_2$ (M+H) 283.0334 (2.1 ppm).

4.11. (+)-(1*S*,2*R*)-(+)-24a, and (−)-(1*R*,2*S*)-1-bromo-2-methyl-2-phenylcyclopropanecarboxylic acids (−)-24a, typical procedure

At first, *rac*-**24a** (13.5 g, 52.9 mmol, 1.00 equiv) and cinchonine **31** (15.9 g, 53.8 mmol, 1.00 equiv) were dissolved in the minimum amount of hot acetone (~300 mL) with stirring. The solution was stirred for 20 min and then filtered while hot into a thermal-insulated Erlenmeyer flask. The flask was capped and the mixture was allowed to cool to room temperature over two hours. The capped flask was then placed in the fridge at +3 °C and left overnight. The recovered crystalline cinchonine salt, $[\alpha]_D^{25}$ = +109.1 (*c* 0.502, MeOH) was isolated by suction filtration and dissolved in ethyl acetate (100 mL). The organic phase was added to water and acidified to pH 2 using 6 M hydrochloric acid. The product was extracted using ethyl acetate (3 × 50 mL), dried, filtered, and concentrated. Individual acid (+)-**30** was obtained as a light yellow oil, $[\alpha]_D^{25}$ = +56.5 (*c* 0.200, CH_2Cl_2). Yield 4.20 g (16.5 mmol, 62%, ee 98%). Basification of the aqueous phase to pH 10 followed by extraction with EtOAc (3 × 50 mL) afforded a first portion of recovered alkaloid **31**.

Concentration of the mother liquor, obtained after the first crystallization, followed by aqueous treatment and acid–base extraction, identical to the one described above afforded an additional portion of recovered **31** and crude partially enriched (−)-**24a** (9.0 g). This acid was re-crystallized with cinchonidine **32** (7.47 g, 25.3 mmol, 0.72 equiv) from hot acetone (~250 mL). A crystalline crop of cinchonidine salt, $[\alpha]_D^{25}$ = −102.2 (*c* 0.360, MeOH) was isolated by suction filtration, then digested and subjected to acid–base extraction in the same manner as was described above for cinchonine salt. Acid (−)-**24a** was obtained as a light yellow oil, $[\alpha]_D^{25}$ = −49.4 (*c* 0.172, CH_2Cl_2). Yield 3.8 g, (14.1 mmol, 53%, ee 91%). NMR properties of both enantiomerically enriched acids were identical to those previously reported for *rac*-**24a**.[10]

4.12. (+)-(1*S*,2*R*)-(+)-24b and (−)-(1*R*,2*S*)-1-bromo-2-methyl-2-(*p*-tolyl)cyclopropanecarboxylic acids (−)-24b

These compounds were obtained according to the typical procedure by recrystallization of *rac*-**24b** (5.25 g, 19.5 mmol, 1.0 equiv), with cinchonine (5.75 g, 19.5 mmol, 1.0 equiv) from hot acetone (~300 mL). Crystalline crop of cinchonine salt, $[\alpha]_D^{25}$ = +103.9 (*c* 0.640, MeOH) was digested to afford (+)-**24b** a light yellow oil, $[\alpha]_D^{25}$ = +66.0 (*c* 0.106, CH_2Cl_2). Yield 1.3 g (4.8 mmol, 50%, ee >99%). Crystalline crop of cinchonidine salt, $[\alpha]_D^{25}$ = −139.3 (*c* 0.600, MeOH) was digested to afford (−)-**24b** as a cream-colored oil, $[\alpha]_D^{25}$ = −61.0 (*c* 0.100, CH_2Cl_2). Yield 0.879 g (3.27 mmol, 34%, ee >99%). NMR properties of both enantiomerically enriched acids were identical to those previously reported for *rac*-**24b**.[10]

4.13. (+)-(1*S*,2*R*)-(+)-24c and (−)-(1*R*,2*S*)-1-bromo-2-ethyl-2-phenylcyclopropanecarboxylic acids (−)-24c

These compounds were obtained according to the typical procedure by recrystallization of *rac*-**24c** (5.39 g, 20.0 mmol, 1.0 equiv) with cinchonine (5.89 g, 20.0 mmol, 1.0 equiv) from hot acetone (~300 mL). Crystalline crop of cinchonine salt, $[\alpha]_D^{25}$ = +93.5

(*c* 0.306, MeOH) was digested to afford (+)-**24b** as a cream colored solid, mp 75–76.5 °C, $[\alpha]_D^{25}$ = +69.5 (*c* 0.118, CH_2Cl_2). Yield 1.53 g (5.68 mmol 57%, ee >99%). Crystalline crop of cinchonidine salt, $[\alpha]_D^{25}$ = −74.4 (*c* 0.418, MeOH) was digested to afford (−)-**24c** as a cream-colored solid, mp 72.5–73.4 °C, $[\alpha]_D^{25}$ = −43.1 (*c* 0.144, CH_2Cl_2). Yield 1.06 g (3.94 mmol, 40%, ee >99%). NMR properties of both enantiomerically enriched acids were identical to those previously reported for *rac*-**24c**.[10]

4.14. (+)-(1*S*,2*R*)-(+)-24d and (−)-(1*R*,2*S*)-1-bromo-2-methyl-2-(naphthalen-2-yl)cyclopropanecarboxylic acids (−)-24d

These compounds were obtained according to the typical procedure by recrystallization of *rac*-**24d** (4.68 g, 14.6 mmol, 1.0 equiv) with cinchonine (4.30 g, 14.6 mmol, 1.0 equiv) from hot acetone (∼300 mL). Crystalline crop of cinchonine salt, $[\alpha]_D^{25}$ = +112.0 (*c* 0.382, MeOH) was digested to afford (+)-**30d** as a light brown solid, mp 121.5–123.5 °C, $[\alpha]_D^{25}$ = +108.2 (*c* 0.122, CH_2Cl_2). Yield 1.19 g (3.72 mmol, 51%, ee 99%). Crystalline crop of cinchonidine salt, $[\alpha]_D^{25}$ = −96.1 (*c* 0.382, MeOH) was digested to afford (−)-**24d** as dark-brown oil, $[\alpha]_D^{25}$ = −57.4 (*c* 0.162, CH_2Cl_2). Yield 1.70 g (5.30 mmol, 73%, ee 54%). NMR properties of both enantiomerically enriched acids were identical to those listed above for *rac*-**24d**.

4.15. (+)-(1*S*,2*R*)-(+)-24f and (−)-(1*R*,2*S*)-1-bromo-2-phenylcyclopropanecarboxylic acids (−)-24f

These compounds were obtained according to the typical procedure by recrystallization of *rac*-**24f** (4.61 g, 18.0 mmol, 1.0 equiv) with cinchonine (5.29 g, 18.0 mmol, 1.0 equiv) from acetone (∼300 mL). Crystalline crop of cinchonine salt, $[\alpha]_D^{25}$ = +117.7 (*c* 0.430, MeOH) was digested to afford (+)-**30f** as a light-brown solid, mp 78.8–79.9 °C, $[\alpha]_D^{25}$ = +166.0 (*c* 0.106, CH_2Cl_2). Yield 0.72 g (2.8 mmol, 32%, ee >99%). Crystalline crop of cinchonidine salt, $[\alpha]_D^{25}$ = −130.5 (*c* 0.430, MeOH) was digested to afford (−)-**24f** as a light brown solid, mp 68–69.4 °C, $[\alpha]_D^{25}$ = −131.2 (*c* 0.138, CH_2Cl_2). Yield 1.62 g (6.33 mmol, 70%, ee 90%). NMR properties of both enantiomerically enriched acids were identical to those listed above for *rac*-**24f**.

4.16. (+)-(1*S*,2*R*)-(+)-24g and (−)-(1*R*,2*S*)-1-bromo-2-methyl-2-(*m*-tolyl)cyclopropanecarboxylic acids (−)-24g

These compounds were obtained according to the typical procedure by recrystallization of *rac*-**24g** (4.78 g, 17.6 mmol, 1.0 equiv) with cinchonine (5.17 g, 17.6 mmol, 1.0 equiv) from hot acetone (∼300 mL). Crystalline crop of cinchonine salt, $[\alpha]_D^{25}$ = +113.9 (*c* 0.418, MeOH) was digested to afford (+)-**24g** as cream colored crystals, mp 92.0–93.4 °C, $[\alpha]_D^{25}$ = +77.5 (*c* 0.102, CH_2Cl_2). Yield 550 mg, (2.0 mmol, 23%, ee >99%). Crystalline crop of cinchonidine salt, $[\alpha]_D^{25}$ = −93.5 (*c* 0.184, MeOH) was digested to afford (−)-**24g** as gray oil, $[\alpha]_D^{25}$ = −74.6 (*c* 0.114, CH_2Cl_2). Yield 270 mg (1.00 mmol, 11%, ee >99%). NMR properties of both enantiomerically enriched acids were identical to those listed above for *rac*-**24g**.

4.17. (+)-(1*S*,2*R*)-(+)-24h and (−)-(1*R*,2*S*)-1-bromo-2-(3,4-dimethylphenyl)-2-methylcyclopropanecarboxylic acids (−)-24h

These compounds were obtained according to the typical procedure by recrystallization of *rac*-**24g** (5.00 g, 17.7 mmol, 1.0 equiv) with cinchonine (5.00 g, 16.9 mmol, 0.96 equiv) from hot acetone (∼300 mL). Crystalline crop of cinchonine salt, $[\alpha]_D^{25}$ = +94.1 (*c* 0.408, MeOH) was digested to afford (+)-**24g** as a light yellow oil, $[\alpha]_D^{25}$ = +54.7 (*c* 0.172, CH_2Cl_2). Yield 850 mg (3.00 mmol, 34%, ee 92%). Crystalline crop of cinchonidine salt, $[\alpha]_D^{25}$ = −67.4 (*c* 0.328, MeOH) was digested to afford (−)-**24h** as a light yellow oil, $[\alpha]_D^{25}$ = −31.6 (*c* 0.190, CH_2Cl_2). Yield 1.65 g (5.83 mmol, 66%, ee 52%). NMR properties of both enantiomerically enriched acids were identical to those listed above for *rac*-**24h**.

4.18. (+)-(1*S*,2*R*)-(+)-24i and (−)-(1*R*,2*S*)-1-bromo-2-(4-ethylphenyl)-2-methylcyclopropanecarboxylic acids (−)-24i

These compounds were obtained according to the typical procedure by recrystallization of *rac*-**24i** (5.01 g, 17.7 mmol, 1.0 equiv) with cinchonine (2.5 g, 8.5 mmol, 0.48 equiv) from hot acetone (∼300 mL). Crystalline crop of cinchonine salt, $[\alpha]_D^{25}$ = +109.4 (*c* 0.170, MeOH) was digested to afford (+)-**24i** as a yellowish brown solid, mp 72.8–74.8 °C, $[\alpha]_D^{25}$ = +69.8 (*c* 0.116, CH_2Cl_2). Yield 820 mg (2.9 mmol, 33%, ee >99%). Crystalline crop of cinchonidine salt, $[\alpha]_D^{25}$ = −70.2 (*c* 0.124, MeOH), was digested to afford (−)-**24i** as a yellowish-brown solid, mp 71.0–73.2 °C, $[\alpha]_D^{25}$ = +55.4 (*c* 0.130, CH_2Cl_2). Yield 870 mg (3.1 mmol, 35%, ee >99%). NMR properties of both enantiomerically enriched acids were identical to those listed above for *rac*-**24i**.

4.19. (+)-(*S*)-(+)-24j and (−)-(*R*)-1-bromo-2,2-diphenylcyclopropanecarboxylic acids (−)-24j

These compounds were obtained according to the typical procedure by recrystallization of *rac*-**24j** (5.03 g, 15.8 mmol, 1.00 equiv) with cinchonine (3.48 g, 11.8 mmol, 0.75 equiv) from hot acetone (∼300 mL). Crystalline crop of cinchonine salt, $[\alpha]_D^{25}$ = +133.3 (*c* 0.198, MeOH) was digested to afford (+)-**24j** as a colorless solid, mp: 168–169.8 °C, $[\alpha]_D^{25}$ = +110.3 (*c* 0.204, CH_2Cl_2). Yield 570 mg, 2.14 mmol, 22%, ee 99%). Crystalline crop of cinchonidine salt, $[\alpha]_D^{25}$ = −111.8 (*c* 0.386, MeOH), was digested to afford (−)-**24j** as a colorless solid, mp 182.0–183.0 °C, $[\alpha]_D^{25}$ = −106.1 (*c* 0.198, CH_2Cl_2). Yield 478 mg (1.5 mmol, 19%, ee >99%). NMR properties of both enantiomerically enriched acids were identical to those reported for *rac*-**24j**.[20]

4.20. (1*S*,2*R*)-1-Bromo-*N*,*N*-diethyl-2-methyl-2-phenylcyclopropane-1-carboxamide (+)-(1*S*,2*R*)-33

A flame dried 100 mL round bottom flask equipped with a drying tube and magnetic stirrer bar was charged with acid (+)-**24a** (1.28 g, 5.00 mmol), anhydrous CH_2Cl_2 (40 mL), and dry DMF (10 drops). The mixture was stirred at 0 °C and oxalyl chloride (0.65 mL, 7.5 mmol, 1.5 equiv) was added dropwise. Stirring was continued for 15 min, then the mixture was warmed up to rt and stirred for an additional 2 h. The solvent was removed in vacuum and the crude acyl chloride was dissolved in anhydrous THF (20 mL), followed by the addition of diethylamine (1.55 mL, 15.0 mmol, 3.0 equiv) solution in dry THF (20 mL). The resulting mixture was stirred overnight, then the solvent was removed in vacuum and the residue was partitioned between water (25 mL) and EtOAc (25 mL). The organic phase was separated, and the aqueous layer was extracted with EtOAc (2 × 25 mL). The combined organic phases were dried ($MgSO_4$), filtered, and concentrated. Chromatographic purification afforded the title compound as a yellowish solid, R_f 0.34 (hexane/EtOAc 10:1). Yield 1.34 g (4.35 mmol, 87%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.56–7.04 (m, 5H), 3.48 (dt, *J* = 14.2, 7.1 Hz, 1H), 3.37 (dq, *J* = 14.2, 7.1 Hz, 1H), 2.71 (dq, *J* = 14.0, 7.1 Hz, 1H), 2.65 (d, *J* = 7.3 Hz, 1H), 2.58 (dq, *J* = 14.0, 7.0 Hz, 1H), 1.85 (s, 3H), 1.33 (d, *J* = 7.3 Hz, 1H), 1.00 (t, 7.1 Hz, 3H), 0.47 (t, 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 165.8, 138.1, 128.1 (+, 2C), 127.0 (+, 2C), 126.7 (+), 42.4, 42.0 (−), 38.3 (−), 31.0, 26.9 (−), 24.3 (+), 12.6 (+), 11.1 (+); FTIR (KBr, cm^{-1}): 2977, 2933, 1643, 1639, 1498, 1456, 1433, 1380, 1282,

1219, 1064, 719, 696, 582; HRMS (TOF ES): Found 309.0724, calcd for $C_{15}H_{20}BrNO$ (M^+) 309.0728 (1.3 ppm); $[\alpha]_D^{25}$ = +17.0 (*c* 0.194, CH_2Cl_2).

4.21. (1*R**,2*S**)-Methyl 1-bromo-2-methyl-2-phenylcyclopropanecarboxylate *rac*-34a (typical procedure)

A mixture of (1*R**,2*S**)-1-bromo-2-methyl-2-phenylcyclopropanecarboxylic acid *rac*-**24a** (255 mg, 0.947 mmol), potassium carbonate (276 mg, 2.00 mmol, 2.0 equiv), and methyl iodide (280 mg, 123 μL, 1.97 mmol, 2.0 equiv) was vigorously stirred in dimethyl formamide (10 mL) for 12 h at rt. Then, the mixture was quenched with water (5 mL) and extracted with dichloromethane (3 × 10 mL). The combined organic phases were dried ($MgSO_4$), filtered, and concentrated in vacuum. The crude material was purified by silica gel chromatography to afford the title compound as a light yellow oil, R_f 0.22 (hexanes/EtOAc 50:1). Yield 181 mg (0.672 mmol, 71%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.56–7.01 (m, 5H), 3.34 (s, 3H), 2.55 (d, *J* = 6.4 Hz, 1H), 1.75 (s, 3H), 1.40 (d, *J* = 6.5 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 168.5, 140.7, 128.5 (+, 2C), 128.1 (+, 2C), 127.2 (+), 52.9 (+), 40.4, 35.9, 27.9 (−), 27.5 (+); FTIR (KBr, cm^{-1}): 3026, 2986, 2951, 1732, 1603, 1497, 1434, 1379, 1325, 1298, 1285, 1234, 1115, 1094, 1061, 1026, 982, 876, 775, 758, 721, 700, 559, 542; HRMS (TOF ES): Found 269.0177, calcd for $C_{12}H_{14}BrO_2$ (M+H) 269.0177 (0.0 ppm). Chiral GC: R_t (120 °C isotherm) 49.72 min (50%), 50.57 min (50%).

4.22. (1*S*,2*R*)-Methyl 1-bromo-2-methyl-2-phenylcyclopropanecarboxylate (+)-34a

This ester was obtained according to the typical procedure employing acid (+)-**24a** (50 mg, 0.20 mmol), potassium carbonate (55 mg, 0.40 mmol, 2.0 equiv), methyl iodide (56.8 mg, 25 μL, 0.400 mmol, 2.0 equiv), and DMF (5 mL). The title compound was obtained as a light yellow oil, with TLC and spectroscopic properties identical to those listed above for *rac*-**34a**. Yield 37.7 mg (0.140 mmol, 70%). Chiral GC: R_t (120 °C isotherm), 49.72 min; $[\alpha]_D^{25}$ = +34.6 (*c* 0.220, CH_2Cl_2).

4.23. (1*R*,2*S*)-Methyl 1-bromo-2-methyl-2-phenylcyclopropanecarboxylate (−)-34a

This ester was obtained according to the typical procedure employing acid (−)-**24a** (48 mg, 0.19 mmol), potassium carbonate (51 mg, 0.37 mmol, 2.0 equiv), methyl iodide (52.8 mg, 23 μL, 0.38 mmol, 2.0 equiv), and DMF (5 mL). The title compound was obtained as a light yellow oil, with TLC and spectroscopic properties identical to those listed above for *rac*-**34a**. Yield 36.3 mg (0.135 mmol, 71%). Chiral GC: R_t (120 °C isotherm), 50.57 min; $[\alpha]_D^{25}$ = +32.3 (*c* 0.820, CH_2Cl_2).

4.24. (1*R**,2*S**)-Methyl 1-bromo-2-methyl-2-(*p*-tolyl)cyclopropanecarboxylate *rac*-34b

This ester was obtained according to the typical procedure employing acid *rac*-**24b** (300 mg, 1.11 mmol, 1.0 equiv), potassium carbonate (307 mg, 2.22 mmol, 2.0 equiv), and methyl iodide (315 mg, 138 μL, 2.22 mmol, 2.0 equiv) in dimethyl formamide (10 mL). The title compound was obtained as a light yellow oil, R_f 0.22 (hexanes/EtOAc 50:1). Yield 251 mg (0.888 mmol, 80%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.14–7.04 (m, 4H), 3.36 (s, 3H), 2.50 (d, *J* = 6.4 Hz, 1H), 2.30 (s, 3H), 1.71 (s, 3H), 1.35 (d, *J* = 6.4 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 168.6, 137.6, 136.8, 129.2 (+, 2C), 127.9 (+, 2C), 53.0 (+), 40.3, 35.6, 27.9 (−), 27.5 (+), 21.2 (+); FTIR (KBr, cm^{-1}): 2984, 2951, 2926, 1732, 1516, 1435, 1377, 1325, 1300, 1281, 1232, 1113, 1094, 1063, 1047, 820, 719, 557; HRMS (TOF ES): Found 283.0335, calcd for $C_{13}H_{16}BrO_2$ (M+H) 283.0334 (0.4 ppm); Chiral GC: R_t (131 °C isotherm), 45.10 min (50%), 45.64 min (50%).

4.25. (1*S*,2*R*)-Methyl 1-bromo-2-methyl-2-(*p*-tolyl)cyclopropanecarboxylate (+)-34b

This ester was obtained according to the typical procedure employing acid (+)-**24b** (54 mg, 0.20 mmol, 1.0 equiv), potassium carbonate (55 mg, 0.40 mmol, 2.0 equiv), and methyl iodide (57 mg, 25 μL, 0.40 mmol, 2.0 equiv) in DMF (5 mL). The title compound was obtained as a light yellow oil, with TLC and spectroscopic properties identical to those listed above for *rac*-**34b**. Yield 44 mg (0.16 mmol, 80%). Chiral GC: R_t (131 °C isotherm), 45.08 min; $[\alpha]_D^{25}$ = +42.6 (*c* 0.620, CH_2Cl_2).

4.26. (1*R*,2*S*)-Methyl 1-bromo-2-methyl-2-(*p*-tolyl)cyclopropanecarboxylate (−)-34b

This ester was obtained according to the typical procedure employing acid (−)-**24b** (300 mg, 1.11 mmol, 1.0 equiv), potassium carbonate (306 mg, 2.22 mmol, 2.0 equiv), and methyl iodide (315 mg, 138 μL, 2.22 mmol, 2.0 equiv) in DMF (10 mL). The title compound was obtained as a light yellow oil, with TLC and spectroscopic properties identical to those listed above for *rac*-**34b**. Yield 251 mg (0.88 mmol, 80%). Chiral GC: R_t (131 °C isotherm), 45.62 min; $[\alpha]_D^{25}$ = −38.3 (*c* 0.300, CH_2Cl_2).

4.27. (1*R**,2*S**)-Methyl 1-bromo-2-ethyl-2-phenylcyclopropanecarboxylate *rac*-34c

This ester was obtained according to the typical procedure employing acid *rac*-**24c** (100 mg, 0.372 mmol, 1.0 equiv), potassium carbonate (103 mg, 0.744 mmol, 2.0 equiv), and methyl iodide (106 mg, 46 μL, 0.745 mmol, 2.0 equiv) in DMF (5 mL). The title compound was obtained as a light yellow oil, R_f 0.22 (hexane/EtOAc 50:1). Yield 95.7 mg (0.338 mmol, 91%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.33–7.17 (m, 5H), 3.34 (s, 3H), 2.45 (d, *J* = 6.4 Hz, 1H), 2.11 (dtd, *J* = 14.6, 7.3, 1.5 Hz, 1H), 1.92 (dq, *J* = 13.7, 7.4 Hz, 1H), 1.35 (d, *J* = 6.3 Hz, 1H), 0.89 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 168.6, 138.7, 129.1 (+, 2C), 128.3 (+, 2C), 127.3 (+), 52.9 (+), 40.9, 40.9, 33.4 (−), 26.9 (−), 11.2 (+); FTIR (KBr, cm^{-1}): 3026, 2970, 2951, 2934, 1732, 1495, 1435, 1377, 1300, 1286, 1225, 1118, 1090, 1067, 989, 881, 795, 756, 721, 702, 592; HRMS (TOF ES): Found 282.0257, calcd for $C_{13}H_{15}BrO_2$ (M+) 282.0255 (0.7 ppm). Chiral GC: R_t (134 °C isotherm) 34.64 min (50%), 34.97 min (50%).

4.28. (+)-(1*S*,2*R*)-Methyl 1-bromo-2-ethyl-2-phenylcyclopropanecarboxylate (+)-34c

This ester was obtained according to the typical procedure employing acid (+)-**24c** (50 mg, 0.19 mmol, 1.0 equiv), potassium carbonate (51 mg, 0.37 mmol, 2.0 equiv), and methyl iodide (53 mg, 23 μL, 0.37 mmol, 2.0 equiv) in DMF (5 mL). The title compound was obtained as a light yellow oil with TLC and spectroscopic properties identical to those listed above for *rac*-**34c**. Yield 48 mg (0.171 mmol, 90%). $[\alpha]_D^{25}$ = +29.3 (*c* 0.244, CH_2Cl_2); Chiral GC: R_t (134 °C isotherm) 34.64 min.

4.29. (−)-(1*R*,2*S*)-Methyl 1-bromo-2-ethyl-2-phenylcyclopropanecarboxylate (−)-34c

This ester was obtained according to the typical procedure employing acid (+)-**24c** (50.0 mg, 0.19 mmol, 1.0 equiv), potassium carbonate (51 mg, 0.37 mmol, 2.0 equiv), and methyl iodide

(53 mg, 23 μL, 0.37 mmol, 2.0 equiv) in DMF (5 mL). The title compound was obtained as a light yellow oil with TLC and spectroscopic properties identical to those listed above for *rac*-**34c**. Yield 49 mg (0.17 mmol, 91% yield). $[\alpha]_D^{25} = -30.9$ (*c* 0.800, CH_2Cl_2); Chiral GC: R_t (134 °C isotherm) 34.97 min.

4.30. (1*R**,2*S**)-Methyl 1-bromo-2-methyl-2-(naphthalen-2-yl) cyclopropanecarboxylate *rac*-34d

This ester was obtained according to the typical procedure employing acid *rac*-**24d** (50 mg, 0.16 mmol, 1.0 equiv), potassium carbonate (45 mg, 0.33 mmol, 2.0 equiv), and methyl iodide (46 mg, 20 μL, 0.33 mmol, 2.0 equiv) in DMF (5 mL). The title compound was obtained as a light brown oil, R_f 0.22 (hexanes/EtOAc 50:1). Yield 38 mg (0.12 mmol, 71%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.94–7.33 (m, 7H), 3.26 (s, 3H), 2.66 (d, J = 6.5 Hz, 1H), 1.81 (s, 3H), 1.47 (d, J = 6.5 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): 168.5, 138.2, 133.4, 132.6, 128.3 (+), 127.9 (+), 127.8 (+), 126.9 (+), 126.3 (+), 126.1 (+), 126.0 (+), 53.0 (+), 40.4, 36.1, 28.1 (−), 27.5 (+); FTIR (KBr, cm^{-1}): 2984, 2949, 1734, 1435, 1325, 1294, 1271, 1246, 1227, 1196, 1134, 1101, 1063, 982, 955, 895, 858, 820, 746, 717; HRMS (TOF ES): Found 319.0331, calcd for $C_{16}H_{16}BrO_2$ (M+H) 319.0334 (0.9 ppm). Chiral HPLC: (isocratic 99.5% hexane, 0.5% isopropanol, 0.7 mL/min) 14.40 min (50%), 16.29 min (50%).

4.31. (+)-(1*S*,2*R*)-Methyl 1-bromo-2-methyl-2-(naphthalen-2yl) cyclopropanecarboxylate (+)-34d

This ester was obtained according to the typical procedure employing acid (+)-**24d** (50 mg, 0.16 mmol, 1.0 equiv), potassium carbonate (45 mg, 0.33 mmol, 2.0 equiv), and methyl iodide (46 mg, 20 μL, 0.33 mmol, 2.0 equiv) in DMF (5 mL). The title compound was obtained as a light brown oil with TLC and spectroscopic properties identical to those listed above for *rac*-**34d**. Yield 38 mg (0.12 mmol, 75%). $[\alpha]_D^{25} = +90.0$ (*c* 0.600, CH_2Cl_2); Chiral HPLC: (isocratic 99.5% hexane, 0.5% isopropanol, 0.7 mL/min) 14.40 min (>99%).

4.32. (−)-(1*R*,2*S*)-Methyl 1-bromo-2-methyl-2-(naphthalen-2-yl) cyclopropanecarboxylate (−)-34d

This ester was obtained according to the typical procedure employing acid (−)-**24d** (50 mg, 0.16 mmol, 1.0 equiv), potassium carbonate (45 mg, 0.33 mmol, 2.0 equiv), and methyl iodide (46 mg, 20 μL, 0.33 mmol, 2.0 equiv) in DMF (5 mL). The title compound was obtained as a light yellow oil with TLC and spectroscopic properties identical to those listed above for *rac*-**34d**. Yield 37 mg (0.12 mmol, 73%). $[\alpha]_D^{25} = -39.8$ (*c* 0.560, CH_2Cl_2); Chiral HPLC: (isocratic 99.5% hexane, 0.5% isopropanol, 0.7 mL/min) 14.40 min (23%), 16.29 min (77%).

4.33. (1*R**,2*S**)-Methyl 1-bromo-2-phenylcyclopropanecarboxylate *rac*-34f

This compound was obtained according to the same procedure in 90% yield. All physical and spectroscopic properties of this material were identical to those previously reported in the literature.[24c] Chiral GC: R_t (150 °C isotherm) 12.23 min (50%), 12.76 min (50%).

4.34. (+)-(1*S*,2*R*)-Methyl 1-bromo-2-phenylcyclopropanecarboxylate (+)-34f

This ester was obtained according to the typical procedure employing acid (+)-**24f** (50 mg, 0.21 mmol, 1.0 equiv), potassium carbonate (57 mg, 0.41 mmol, 2.0 equiv), and methyl iodide (59 mg, 26 μL, 0.41 mmol, 2.0 equiv) in DMF (5 mL). The title compound was obtained as a light yellow oil with spectroscopic properties identical to those reported in the literature for *rac*-**34f**.[24c] Yield 48 mg (0.19 mmol, 91%). $[\alpha]_D^{25} = +122.4$ (*c* 0.840, CH_2Cl_2); Chiral GC: R_t (150 °C isotherm) 12.23 min.

4.35. (−)-(1*R*,2*S*)-Methyl 1-bromo-2-phenylcyclopropanecarboxylate (−)-34f

This ester was obtained according to the typical procedure employing acid (−)-**24f** (50 mg, 0.21 mmol, 1.0 equiv), potassium carbonate (57 mg, 0.41 mmol, 2.0 equiv), and methyl iodide (59 mg, 26 μL, 0.41 mmol, 2.0 equiv) in DMF (5 mL). The title compound was obtained as a light yellow oil with spectroscopic properties identical to those reported in the literature for *rac*-**34f**.[24c] Yield 47 mg (0.18 mmol, 89%). $[\alpha]_D^{25} = -109.4$ (*c* 0.900, CH_2Cl_2); Chiral GC: R_t (150 °C isotherm) 12.76 min.

4.36. (1*R**,2*S**)-Methyl 1-bromo-2-methyl-2-(*m*-tolyl)cyclopropanecarboxylate *rac*-34g

This ester was obtained according to the typical procedure employing acid *rac*-**24g** (50 mg, 0.19 mmol, 1.0 equiv), potassium carbonate (51 mg, 0.37 mmol, 2.0 equiv), and methyl iodide (53 mg, 23 μL, 0.37 mmol, 2.0 equiv) in DMF (5 mL). The title compound was obtained as a light yellow oil. Yield 35 mg (0.12 mmol, 65%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.19–6.98 (m, 4H), 3.34 (s, 3H), 2.50 (d, J = 6.4 Hz, 1H), 2.31 (s, 3H), 1.71 (s, 3H), 1.36 (d, J = 6.4 Hz, 1H); ^{13}C (126 MHz, $CDCl_3$): δ 168.6, 140.7, 138.1, 128.8 (+), 128.4 (+), 128.0 (+), 125.1 (+), 52.9 (+), 40.4, 35.9, 28.0 (−), 27.6 (+), 21.5 (+); FTIR (KBr, cm^{-1}): 2984, 2951, 2926, 1732, 1607, 1489, 1435, 1377, 1329, 1302, 1279, 1242, 1200, 1117, 1094, 1063, 872, 789, 706; HRMS (TOF ES): Found 282.0248, calcd for $C_{13}H_{15}BrO_2$ (M+) 282.0255 (2.5 ppm). Chiral GC: R_t (125 °C isotherm) 52.91 min (50%), 53.99 min (50%).

4.37. (+)-(1*S*,2*R*)-Methyl 1-bromo-2-methyl-2-(*m*-tolyl)cyclopropanecarboxylate (+)-34g

This ester was obtained according to the typical procedure employing acid (+)-**24g** (50 mg, 0.19 mmol, 1.0 equiv), potassium carbonate (51 mg, 0.37 mmol, 2.0 equiv), and methyl iodide (53 mg, 23 μL, 0.37 mmol, 2.0 equiv) in DMF (5 mL). The title compound was obtained as a light yellow oil with spectroscopic properties identical to those listed above for *rac*-**34g**. Yield 35 mg (0.12 mmol, 65%). $[\alpha]_D^{25} = +29.3$ (*c* 0.820, CH_2Cl_2); Chiral GC: R_t (125 °C isotherm) 52.91 min.

4.38. (−)-(1*S*,2*R*)-Methyl 1-bromo-2-methyl-2-(*m*-tolyl)cyclopropanecarboxylate (−)-34g

This ester was obtained according to the typical procedure employing acid (+)-**24g** (50 mg, 0.19 mmol, 1.0 equiv), potassium carbonate (51 mg, 0.37 mmol, 2.0 equiv), and methyl iodide (53 mg, 23 μL, 0.37 mmol, 2.0 equiv) in DMF (5 mL). The title compound was obtained as a light yellow oil with spectroscopic properties identical to those listed above for *rac*-**34g**. Yield 34 mg (0.12 mmol, 65%). $[\alpha]_D^{25} = -30.2$ (*c* 0.420, CH_2Cl_2); Chiral GC: R_t (125 °C isotherm) 53.99 min.

4.39. (1*R**,2*S**)-Methyl 1-bromo-2-(3,4-dimethylphenyl)-2-methylcyclopropanecarboxylate *rac*-34h

This ester was obtained according to the typical procedure employing acid *rac*-**24h** (50 mg, 0.18 mmol, 1.0 equiv), potassium carbonate (49 mg, 0.36 mmol, 2.0 equiv), and methyl iodide (50 mg, 22 μL, 0.36 mmol, 2.0 equiv) in DMF (5 mL). The title com-

pound was obtained as a light yellow oil. Yield 45.5 mg (0.15 mmol, 85%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.08–6.90 (m, 3H), 3.38 (s, 3H), 2.48 (d, J = 6.4 Hz, 1H), 2.22 (s, 3H), 2.21 (s, 3H), 1.71 (s, 3H), 1.34 (d, J = 6.3 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 168.6, 138.1, 136.6, 135.5, 129.7 (+), 129.2 (+), 125.4 (+), 53.0 (+), 40.3, 35.6, 27.9 (−), 27.6 (+), 19.9 (+), 19.6 (+); FTIR (KBr, cm^{-1}): 2982, 2949, 2924, 1732, 1506, 1435, 1377, 1306, 1283, 1236, 1221, 1095, 1063, 874, 822, 717, 600; HRMS (TOF ES): Found 296.0412, calcd for $C_{14}H_{17}BrO_2$ (M+) 296.0412 (0.0 ppm). Chiral HPLC: (isocratic 99.5% hexane, 0.5% isopropanol, 0.7 mL/min) 8.87 min (50%), 10.66 min (50%).

4.40. (+)-(1*S*,2*R*)-Methyl 1-bromo-2-(3,4-dimethylphenyl)-2-methylcyclopropanecarboxylate (+)-34h

This ester was obtained according to the typical procedure employing acid (+)-**24h** (50 mg, 0.18 mmol, 1.0 equiv), potassium carbonate (49 mg, 0.36 mmol, 2.0 equiv), and methyl iodide (50 mg, 22 μL, 0.36 mmol, 2.0 equiv) in DMF (5 mL). The title compound was obtained as a light yellow oil with spectroscopic properties identical to those listed above for *rac*-**34h**. Yield 45 mg (0.15 mmol, 85%). $[\alpha]_D^{25}$ = +35.4 (*c* 0.820, CH_2Cl_2); Chiral HPLC: (isocratic 99.5% hexane, 0.5% isopropanol, 0.7 mL/min) 8.87 min.

4.41. (−)-(1*R*,2*S*)-Methyl 1-bromo-2-(3,4-dimethylphenyl)-2-methylcyclopropanecarboxylate (−)-34h

This ester was obtained according to the typical procedure employing acid (−)-**24h** (50 mg, 0.18 mmol, 1.0 equiv), potassium carbonate (49 mg, 0.36 mmol, 2.0 equiv), and methyl iodide (50 mg, 22 μL, 0.36 mmol, 2.0 equiv) in DMF (5 mL). The title compound was obtained as a light yellow oil with spectroscopic properties identical to those listed above for *rac*-**34h**. Yield 47 mg (0.16 mmol, 89%). $[\alpha]_D^{25}$ = −20.4 (*c* 0.940, CH_2Cl_2); Chiral HPLC: (isocratic 99.5% hexane, 0.5% isopropanol, 0.7 mL/min) 10.66 min.

4.42. (1*R**,2*S**)-Methyl 1-bromo-2-(4-ethylphenyl)-2-methylcyclopropanecarboxylate *rac*-34i

This ester was obtained according to the typical procedure employing acid *rac*-**24i** (50 mg, 0.18 mmol, 1.0 equiv), potassium carbonate (49 mg, 0.35 mmol, 2.0 equiv) and methyl iodide (50 mg, 22 μL, 0.35 mmol, 2.0 equiv) in DMF (5 mL). The title compound was obtained as a light yellow oil. Yield 39 mg (0.13 mmol, 73%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.16–7.07 (m, 4H), 3.33 (s, 3H), 2.60 (q, J = 7.6 Hz, 2H), 2.50 (d, J = 6.5 Hz, 1H), 1.71 (s, 3H), 1.35 (d, J = 6.4 Hz, 1H), 1.20 (t, J = 7.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 168.6, 143.2, 137.8, 128.0 (+, 2C), 127.9 (+, 2C), 52.9 (+), 40.4, 35.5, 28.6 (−), 27.8 (−), 27.5 (+), 15.6 (+); FTIR (KBr, cm^{-1}): 3022, 2962, 2978, 2872, 1732, 1514, 1435, 1377, 1327, 1300, 1286, 1232, 1113, 1094, 1063, 1045, 982, 833, 716, 571; HRMS (TOF ES): Found 295.0334, calcd for $C_{14}H_{16}BrO_2$ (M−H) 295.0334, 0.0 ppm; Chiral GC: R_t (131 °C isotherm) 71.89 min (50%), 72.69 min (50%).

4.43. (+)-(1*S*,2*R*)-Methyl 1-bromo-2-(4-ethylphenyl)-2-methylcyclopropanecarboxylate (+)-34i

This ester was obtained according to the typical procedure employing acid (+)-**24i** (50 mg, 0.18 mmol, 1.0 equiv), potassium carbonate (49 mg, 0.35 mmol, 2.0 equiv), and methyl iodide (50 mg, 22 μL, 0.35 mmol, 2.0 equiv) in DMF (5 mL). The title compound was obtained as a light yellow oil with spectroscopic properties identical to those listed above for *rac*-**34i**. Yield 38.0 mg (0.13 mmol, 73%). $[\alpha]_D^{25}$ = +42.6 (*c* 0.660, CH_2Cl_2); Chiral GC: R_t (131 °C isotherm) 71.89 min.

4.44. (−)-(1*R*,2*S*)-Methyl 1-bromo-2-(4-ethylphenyl)-2-methylcyclopropanecarboxylate (−)-34i

This ester was obtained according to the typical procedure employing acid (−)-**24i** (50 mg, 0.18 mmol, 1.0 equiv), potassium carbonate (49 mg, 0.35 mmol, 2.0 equiv), and methyl iodide (50 mg, 22 μL, 0.35 mmol, 2.0 equiv) in DMF (5 mL). The title compound was obtained as a light yellow oil with spectroscopic properties identical to those listed above for *rac*-**34i**. Yield 43 mg (0.14 mmol, 80%). $[\alpha]_D^{25}$ = −40.3 (*c* 0.340, CH_2Cl_2); Chiral GC: R_t (131 °C isotherm) 72.69 min.

4.45. Methyl 1-bromo-2,2-diphenylcyclopropanecarboxylate *rac*-34j

This ester was obtained in 84% yield according to the typical procedure employing acid *rac*-**24j**. All physical and spectroscopic properties of this material were identical to those previously reported in the literature.[20] ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.07–6.92 (m, 10H), 3.51 (s, 3H), 2.82 (d, J = 6.5 Hz, 1H), 2.10 (d, J = 6.5 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 168.4, 141.4, 140.5, 129.5 (+, 2C), 128.6 (+, 2C), 128.4 (+, 2C), 128.4 (+, 2C), 127.4 (+), 127.3 (+), 53.1 (+), 45.2, 38.7, 27.7 (−); FTIR (KBr, cm^{-1}): 3057, 3026, 2949, 1732, 1599, 1493, 1448, 1435, 1323, 1310, 1279, 1250, 1190, 1153, 1099, 1067, 1014, 951, 798, 762, 748, 706, 694, 669, 623, 604, 592; HRMS (TOF ES): Found 330.0255, calcd for $C_{17}H_{15}BrO_2$ (M+) 330.0255 (0.0 ppm); Chiral HPLC: (isocratic 99.5% hexane, 0.5% isopropanol, 0.7 mL/min) 19.79 min (50%), 23.27 min (50%).

4.46. (+)-(*S*)-Methyl 1-bromo-2,2-diphenylcyclopropanecarboxylate (+)-34j

This ester was obtained according to the typical procedure employing acid (+)-**24j** (50 mg, 0.16 mmol, 1.0 equiv), potassium carbonate (44 mg, 0.32 mmol, 2.0 equiv), and methyl iodide (45 mg, 20 μL, 0.32 mmol, 2.0 equiv) in DMF (∼5 mL). The title compound was obtained as a colorless solid with spectroscopic properties identical to those listed above for *rac*-**34j**. Yield 41 mg (0.12 mmol, 77%). $[\alpha]_D^{25}$ = +85.6 (*c* 0.820, CH_2Cl_2); Chiral HPLC: (isocratic 99.5% hexane, 0.5% isopropanol, 0.7 mL/min) 19.79 min.

4.47. (−)-(*R*)-Methyl 1-bromo-2,2-diphenylcyclopropanecarboxylate (−)-34j

This ester was obtained according to the typical procedure employing acid (−)-**24j** (50 mg, 0.16 mmol, 1.0 equiv), potassium carbonate (44 mg, 0.32 mmol, 2.0 equiv), and methyl iodide (45 mg, 20 μL, 0.32 mmol, 2.0 equiv) in DMF (∼5 mL). The title compound was obtained as a colorless solid with spectroscopic properties identical to those listed above for *rac*-**34j**. Yield 40 mg (0.12 mmol, 75%). $[\alpha]_D^{25}$ = −85.4 (*c* 0.900, CH_2Cl_2); Chiral HPLC: (isocratic 99.5% hexane, 0.5% isopropanol, 0.7 mL/min) 23.27 min.

Acknowledgments

Financial support from Center for Environmentally Beneficial Catalysis (Lawrence, K.S.) and from Russian Ministry of Science and Education (in a frame of MIG Grant (International Investigative Groups) at Perm State University, Russia and 'New Innovation Laboratory' support program at Ural Federal University) is gratefully acknowledged. We are also grateful to Dr. Maxim Dmitriev (Perm State University, Russia) and to Prof. Nikolay Gerasimchuk (Missouri State University, Springfiled, MO, USA) for their assistance with X-ray crystallography.

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