Practical and Highly Enantioselective Ring Opening of Cyclic *Meso*-Anhydrides Mediated by Cinchona Alkaloids

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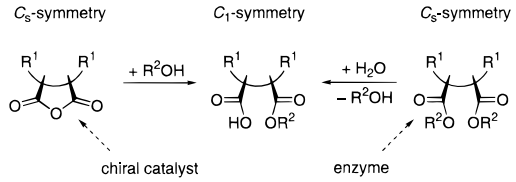
The cinchona alkaloid-mediated opening of prochiral cyclic anhydrides in the presence of methanol leading to optically active hemiesters is described. Very structurally diverse anhydrides are converted into their corresponding methyl monoesters, and either enantiomer can be obtained with up to 99% ee by using quinine or quinidine as directing additive. After the reaction, the alkaloids can be recovered almost quantitatively and reused without loss of enantioselectivity. Additionally, a catalytic protocol which permits the substoichiometric use of quinidine in the presence of easily accessible pentamethylpiperidine (pempidine) is presented.

Introduction

Desymmetrization of *meso*-compounds is an efficient strategy in asymmetric synthesis, because it allows to control the generation of multiple stereogenic centers in a single step.[1] For example, starting from symmetrically substituted diesters or anhydrides, desymmetrization with the help of enzymes[2] or chiral reagents provides dicarboxylic acid monoesters[3] which are easily transferred to other versatile chiral building blocks for numerous synthetic applications (Scheme 1).[4]

The enantioselectivity in enzyme-catalyzed hydrolyses is often very high, even on a 100-mol scale in some cases, and for example with pig liver esterase several hundred successful transformations have been described in the literature as yet.[2d,e] A disadvantage of this enzymatic approach is that most of the time only one enantiomer of the product can be obtained directly. In contrast, anhydride openings with chiral nucleophiles are usually not limited by this restriction, because often both enantiomers of the chiral reagent are available and thus several methods for the preparation of diastereomerically and enantiomerically enriched monoesters or monoamides have been reported.[5] Nevertheless, practical procedures are still quite rare and often limited to only a few examples. Unlike methods which give ring-opened products with covalently linked chiral auxiliaries,[1,5] the Seebach system, using a slight excess of diisopropoxytitanium-TADDOLates, delivers directly enantiomerically enriched isopropyl monoesters of bi- and tricyclic anhydrides with uniformly high ee and yield.[6] This concept of an alkoxide transfer from the chiral ligand sphere to the Lewis acid-activated substrate[7] permitted even the de-

Scheme 1



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velopment of a catalytic version though on the expense of longer reaction times.[6c]

In the late 1980s, Aitken[8] and Oda[9] independently reported on a particularly interesting metal-free asymmetric anhydride opening utilizing readily available alkaloids as catalysts. Here, we now describe an improvement of the existing procedure and the development of a simple and highly enantioselective methanolysis of cyclic *meso*-anhydrides giving a broad variety of hemiesters with up to 99% ee. Inexpensive and quantitatively recoverable cinchona alkaloids serve as directing additives and methanol as nucleophile.[10] In addition, we found a new catalytic version of this process, using 10 mol % of alkaloid in the presence of stoichiometric amounts of a sterically hindered achiral base.

Results and Discussion

Ring-Opening Reaction Using a Stoichiometric Amount of Cinchona Alkaloid. Beside ephedrine and other chiral amino alcohols, cinchona alkaloids have commonly been used for the resolution of racemic dicarboxylic acid monoesters through their corresponding ammonium salts.[11] It was as early as 1929 when use of quinine led to the isolation of the (−)-monomethyl ester of *cis*-cyclohexane dicarboxylic acid.[12] On the basis of these observations and given the findings of Aitken[8] and Oda,[9] we decided to test a variety of chiral amines on their ability to catalyze asymmetric anhydride openings in order to develop a highly practical route to products with uniformly high enantiomeric excesses.[13] First, the effect of the amine structure and the type of nucleophile on the enantioselectivity was investigated. Using anhydride **1** as model substrate and performing the reactions in toluene at ambient temperature, the best results were obtained with combinations of commercially available quinidine as chiral additive (1.1 equiv) and methanol as nucleophile (78% ee). Increasing the alkaloid amount did not lead to an improvement of enantioselectivity. Use of derivatives of quinidine with protected hydroxyl or modified vinyl groups gave lower asymmetric induction. Both sterically more hindered alcohols such as ethanol or 2-propanol as well as thiols and primary or secondary amines resulted in decreased reaction rates and lower enantioselectivities.

Scheme 2

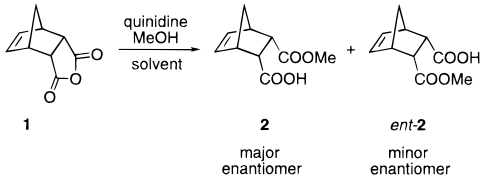

Table 1. Influence of the Solvent on the Quinidine-Mediated Opening of Anhydride 1[a]

entry	solvent	polarity (ϵ_r)[b]	ee (%)[c]	yield of **2** (%)
1	acetone	20.56	49	73
2	THF	7.58	72	79
3	diethyl ether	4.20	75	87
4	di-*n*-butyl ether	3.08 (20 °C)	79	83
5	toluene	2.38	78	82
6	mesitylene	2.30	72	78
7	*p*-xylene	2.27 (20 °C)	80	85
8	benzene	2.27	83	77
9	CCl_4	2.23	86	84
10	*n*-pentane	1.84 (20 °C)	61	76
11	toluene/CCl_4	-	83	83

[a] All reactions were performed at ambient temperature for 24 h using 1.1 equiv of quinidine and 3.0 equiv of methanol in a 0.05 M solution relative to anhydride. [b] Relative permittivity (dielectric constant)[14] for the pure liquid at 25 °C (other temperatures are given in parentheses). [c] Determined by HPLC-analysis of the corresponding *p*-bromophenyl methyl diester.

To optimize the reaction outlined in Scheme 2 further, the influence of the solvent and its polarity on the enantioselectivity was investigated. The most representative results are summarized in Table 1.

In solvents of low polarity the highest enantioselectivities were observed (Table 1). As an exception, *n*-pentane deviated clearly and led to a decreased selectivity (entry 10). The best asymmetric inductions were achieved when the desymmetrizations were performed in benzene or tetrachloromethane (entries 8 and 9). However, due to the relatively high melting points of these solvents, they were unsuitable for reactions at lower temperature. Therefore, further studies were performed in a solvent system consisting of toluene and CCl_4 in a 1:1-ratio, which also afforded the product with high enantiomeric excess (entry 11). In reactions at −55 °C a considerable increase in enantioselectivity was observed, which unfortunately was accompanied by longer reaction times (from 24 to 60 h). Finally, under optimized conditions use of 1.1 equiv of quinidine in toluene/CCl_4 (0.2 M with respect to the anhydride) at −55 °C led to the formation of methyl monoester **2** with 99% ee in excellent yield. Diastereomeric quinine, which can be considered as pseudo-enantiomer of quinidine, generated *ent*-**2** with the same enantiomeric excess. In this case, the reaction mixture had to be more dilute due to solubility reasons (0.05 M with respect to the anhydride). Besides the excellent enantioselectivity in the formation of either enantiomer of **2**, the ease of workup is noteworthy. After completion of the methanolysis, simple acidic extraction of the reaction mixture afforded the product in pure form and no additional purification of the methyl monoester by chromatography or recrystallization was required. The cinchona alkaloids were easily recovered almost quanti-

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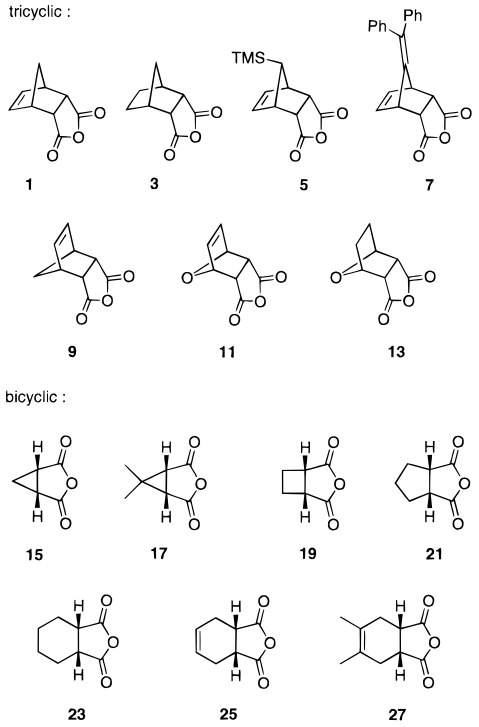
Table 2. Quinidine- and Quinine-Mediated Methanolysis of Various *Meso*-anhydrides[a]

		quinidine-mediated			quinine-mediated		
entry	anhydride	hemi-ester	ee (%)[b]	yield (%)	hemi-ester	ee (%)[b]	yield (%)
1	**1**	**2**	99	98	*ent*-**2**	99	92
2	**3**	**4**	94[c]	84	*ent*-**4**	94[c]	86
3	**5**	**6**	96[c]	99	*ent*-**6**	98[c]	98
4	**7**	**8**	95[c]	95	*ent*-**8**	92[c]	96
5	**9**	**10**	96	96	*ent*-**10**	93[d]	94
6	**11**	**12**	93	61	*ent*-**12**	75	71
7	**13**	**14**	94	69	*ent*-**14**	93	79
8	**15**	**16**	85[e]	96	*ent*-**16**	85[e]	95
9	**17**	**18**	90	97	*ent*-**18**	84[d]	96
10	**19**	**20**	94	99	*ent*-**20**	87	93
11	**21**	**22**	95	97	*ent*-**22**	93	99
12	**23**	**24**	93	98	*ent*-**24**	87	91
13	**25**	**26**	95	93	*ent*-**26**	93	99
14	**27**	**28**	97	96	*ent*-**28**	94	97

[a] All reactions were performed at −55 °C for 60 h using 1.1 equiv of alkaloid and 3.0 equiv of methanol in a toluene/CCl_4-mixture (1:1); for quinidine: 0.2 M with respect to the anhydride, for quinine: 0.05 M. [b] Determined by GC-analysis of the corresponding lactones using a chiral stationary phase. [c] Determined by HPLC-analysis of the corresponding *p*-bromophenyl methyl diester. [d] Recrystallization furnished an increase on >99% ee. [e] Determined by GC-analysis of the corresponding isopropyl methyl diester.

tatively as their hydrochloride salts and after basic work up reused without loss of selectivity (tested in three sequential reactions).



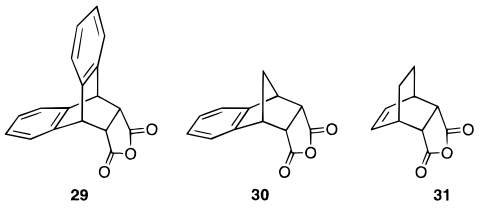
Scope and Limitations. Next, we evaluated the scope of the reaction and found that under the optimized conditions, a large variety of bicyclic- and tricyclic anhydrides could be opened with very high enantioselectivities and excellent yields (Table 2).

In general, quinidine-mediated ring openings furnished monoesters with slightly higher or equal enantiomeric excesses in comparison to the quinine reactions. The moderate yields in the conversion of the two oxatricyclic compounds **11** and **13** (Table 2, entries 6 and 7) are probably due to, first, the considerable higher water solubility of the monoesters, which results in loss of product during the aqueous workup, and second, a certain instability of the oxygen bridge toward basic reagents. Recrystallization of the esters obtained from **9** and **17** led to an enantiomer enrichment of >99% ee (entries 5 and 9). The alkaloid-mediated methanolysis is also applicable to monocyclic substrates, such as, for example, *meso*-dimethylsuccinic anhydride. However, in this case the appropriate methyl-monoester was obtained as an unseparable mixture with ca. 14% of the epimerization product.[15] Presumably due to steric reasons anhydrides **29**−**31** did not react at all (see below).

Table 3. Quinidine-Mediated Opening of *Meso*-Anhydrides in Toluene as Solvent[a]

entry	anhydride	ester	ee (%)[b]	yield, %
1	**1**	**2**	96[c]	85
2	**5**	**6**	94[d]	97
3	**11**	**12**	86	70
4	**17**	**18**	87[c]	94
5	**19**	**20**	94	96
6	**21**	**22**	95	93
7	**25**	**26**	94	91
8	**27**	**28**	96	96

[a] All reactions were performed at −55 °C for 60 h using 1.1 equiv of alkaloid and 3.0 equiv of methanol in a 0.1 M solution related to anhydride. [b] Determined by GC-analysis of the corresponding lactones using a chiral stationary phase. [c] Recrystallization furnished an increase on >99% ee. [d] Determined by HPLC-analysis of the corresponding *p*-bromophenyl methyl diester.

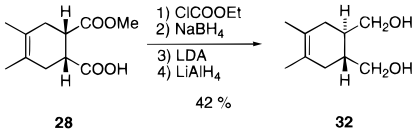


As discussed above, the best solvent system for the low-temperature reactions consisted of a 1:1 mixture of toluene and CCl_4. Various attempts to replace the toxic CCl_4 by less harmful solvents of comparable polarity and solution characteristics resulted in a decrease of asymmetric induction and reaction rate. Finally we found that by performing the quinidine-mediated methanolysis at lower concentration in pure toluene (0.1 M with respect to the anhydride), the use of CCl_4 could be avoided completely. Thus, with the only exception of **11**, the anhydride openings occurred with almost the same enantioselectivities and yields under these modified conditions (Table 3).

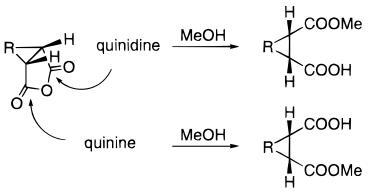
Determination of the Absolute Configurations. Apart from the products derived from the ring opening of the anhydrides **5**, **7**, and **27**, the absolute configurations of the monoesters were determined by comparison of their senses of optical rotation with those reported in the literature. For esters **10** and **14** the configuration was verified additionally via the known lactones,[16] which were obtained by selective reduction of the methyl ester group with $LiBEt_3H$ followed by catalyzed lactonization.[6c] Fi-

(14) Reichardt, C. *Solvents and Solvent Effects in Organic Chemistry*, 2nd ed.; VCH: Weinheim; 1990; p 407.
(15) As determined by GC-MS and NMR analysis.
(16) (a) Lok, K. P.; Jakovac, I. J.; Jones, J. B. *J. Am. Chem. Soc.* **1985**, *107*, 2521. (b) Bloch, R.; Guibe-Jampel, E.; Girad, C. *Tetrahedron Lett.* **1985**, *26*, 4087.

Scheme 3



Scheme 4



nally, the hemiesters from **1** and **11** were hydrogenated, and the products were compared with their saturated analogues. The absolute configuration of **28**, which was obtained by quinidine opening of **27**, was assigned by correlation with the known *trans*-diol **32** (Scheme 3).

In all cases the stereochemical outcome of the reaction was uniform: the quinidine-mediated ring opening of anhydrides generated the ester function always at the carbonyl group indicated in Scheme 4. For the anhydrides containing unsubstituted all-carbon backbones, this is the *si*-carbonyl group; due to the reversal of the CIP-priorities it is the *re*-carbonyl group of anhydrides **11**, **13**, and **17**. In the same consequence quinine always exhibited the opposite selectivity. In view of the fact that this rule is strictly kept over a wide range of substrates, we deduce that the absolute configuration of the products derived from anhydrides **5** and **7** follows accordingly although this fact has not been proven rigorously.

The differentiation between the enantiotopic carbonyl groups by the alkaloids must be based on the recognition of certain structural components in the anhydride morphology. Due to the high degree of conformational freedom of the alkaloid it is difficult to develop a simple hypothesis, which describes the cause of this differentiation. The solvent influence outlined in Table 1 suggests that a certain alkaloid conformation is mainly responsible for the asymmetric induction in the opening reaction and that a less-pronounced stabilization of this particular conformation by another solvent leads to the observed reduced selectivity. In this context Bürgi and Baiker recently described NMR and ab initio studies on the conformational behavior of cinchonidine[17] and found that, with respect to the dielectric constant of the solvent, the proportion of the energetically most favorable conformation of the alkaloid in solution (the so-called open(3)-form) goes in parallel with the enantiomeric excess achieved in the asymmetric hydrogenation of ketopantolactone over cinchonidine-modified Pt.[18] According to their investigation, the open(3)-conformation is stabilized by nonpolar solvents wherein it is present at room temperature to 60−70%. Polar solvents reduce the energetic difference to closed structures which causes the drastic selectivity reduction when using solvents with higher polarity. Since Wynberg and co-workers have postulated similar conformations for quinidine or dihydroquinidine,[19] the trend observable in Table 1 appears consistent with these results.

With respect to the mechanism we assume that an acylammonium-type intermediate is formed by nucleophilic attack of the alkaloid on the less-hindered front face of the anhydride. This intermediate is then converted to the product by a rear side attack of methanol to give the desired monoester.[20] If the carbonyls are sterically blocked, no reaction can take place. This assumption is confirmed by the experiments using anhydrides **29**−**31**, which all did not react even at elevated temperature (up to 100 °C).[21]

Catalytic Use of the Alkaloid. Next, we focused on the development of a process which required less alkaloid but retained the high enantioselectivity. The following scenario was assumed: After the anhydride opening, the resulting acid transfers its proton to the alkaloid[8b] which then becomes prone to form aggregates with the carboxylate of the former anhydride. Such acid−base complexes have previously been described by Baiker and co-workers, who found a stable 2:1 acid−alkaloid complex in a study of the molecular interactions between cinchonidine and acetic acid.[22] In the context of the mechanistic path of the asymmetric anhydride opening it is important to note that this protonated alkaloid also adopted the open(3)-conformation and that Aiken et al. demonstrated that species of such type could be catalytically active but that the enantioselectivities were rather low.[8] To render the asymmetric anhydride opening catalytically more efficient, we wondered about the possibility to remove the ammonium proton with the help of a sterically hindered base in order to liberate the alkaloid. The latter could then take part in further catalytic cycles which would allow a more economic alkaloid application for openings on larger scale.

As reference for the development of the catalytic version, the methanolysis reaction of anhydride **1** presented in Scheme 2 was selected, using only 10 mol % of quinidine. Under the optimized conditions, a conversion of 50% was observed, and ester **2** was obtained with an enantiomeric excess of 35% (Table 4, entry 1). Addition of the nonnucleophilic base DBU (**33**) or the proton sponge 1,8-bis(dimethylamino)naphthalene (**34**) remained unsuccessful, whereas reactions in the presence of Hünig's base (**35**) indicated the potential of this concept. Use of the sterically more-hindered triisopropylamine (**36**) led to a decrease in enantioselectivity (entries 5 and 6). As a consequence, amines with one unbranched alkyl group next to two sterically demanding substituents were tested (entries 7−11). The highest asymmetric induction was obtained using pempidine (**40**) as auxiliary base. Thus, at full substrate conversion ester **2** was isolated in 98% yield having an enantiomeric excess of 90% (entry 10). Unfortunately, this catalytic protocol now required an

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Table 4. Substoichiometric Use of Quinidine for the Ring Opening of Anhydride 1[a]

entry	added amine	time (d)	conversion (%)[b]	ee (%)[c]
1	none	2.5	50	35
2	DBU (**33**)	2.5	93	0
3	proton sponge **34**	2.5	95	23
4	Hünig's base (**35**)	2.5	94	79
5	**36**	3	76	60
6	**36**	6	84	67
7	**37**	6	94	72
8	**38**	6	95	84
9	**39**	6	93	73
10	**40**	6	100[d]	90
11	**41**	7	89	52

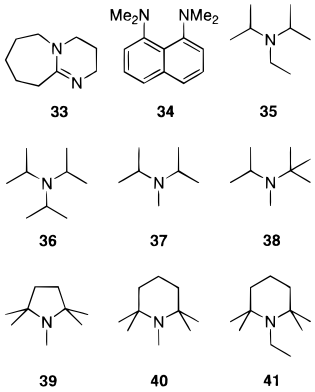
[a] All reactions were performed in a toluene/CCl_4 mixture (1:1) at −55 °C using 0.1 equiv of quinidine, 1.0 equiv of the tertiary amine, and 3.0 equiv of methanol (0.2 M solution related to anhydride). [b] Determined by GC-analysis. [c] Determined by GC-analysis of the corresponding lactone using a chiral stationary phase. [d] A yield of 98% was obtained.

Table 5. Catalytic Use of Quinidine in the Presence of Pempidine (40) in the Asymmetric Anhydride Opening of Various Substrates[a]

entry	anhydride	ester	ee (%)[b]	yield (%)
1	**1**	**2**	90	98
2	**9**	**10**	91	94
3	**17**	**18**	74	98
4	**19**	**20**	81	97
5	**21**	**22**	89	96
6	**27**	**28**	92	96

[a] All reactions were performed at −55 °C for 6 d using 0.1 equiv of quinidine, 1.0 equiv of pempidine (**40**), and 3.0 equiv of methanol (0.2 M solution related to anhydride) in a toluene/CCl_4 mixture (1:1). [b] Determined by GC-analysis of the corresponding lactones using a chiral stationary phase.

extended reaction time and complete conversion was only achieved after 6 days.



Changing the concentration as well as the amount of auxiliary base and methanol did not result in higher asymmetric induction. Doubling of the catalyst loading (20 mol %) gave only a slight increase to 93% ee.

To ensure that this new protocol involving catalytic amounts of the alkaloid was suitable for other substrates also, we selected a number of respresentative anhydrides and investigated their asymmetric openings again. The results of this study are summarized in Table 5.

As in the opening of **1**, the enantioselectivities in reactions with anhydrides **9**, **21**, and **27** were only slightly lower compared to the ones achieved in the stoichiometric version ($\Delta ee = 5-6\%$). In contrast, compounds **17** and **19** behaved differently, and the corresponding products were obtained with significantly lower enantiomeric excesses. Presumably, the higher ring strain due to the smaller carbocyclic backbones in these molecules leads to an increased reactivity, and with the help of the achiral auxiliary base an unselective anhydride opening occurs in parallel which as a consequence leads to a lower enantiomeric excess of the product.

Finally, we investigated the reuse of the reagents in the catalytic version. Thus the asymmetric anhydride opening of **1** with recovered quinidine (washed with diethyl ether followed by drying in vaccuo) and fresh pempidine gave identical results as before (comp.: Table 4, entry 10). When both bases, quinidine and pempidine, were recovered and reused, the conversion of **1** (94%) and the enantiomeric excess of the resulting **2** (84% ee) were only slighly lower, demonstrating the potential of the catalytic process for multiple use of all reagents.

Conclusion and Outlook. The desymmetrization of easily accessible *meso*-anhydrides by cinchona alkaloid-mediated methanolysis is applicable to a variety of structurally very different substrates and leads to the corresponding optically active hemiesters with high enantioselectivities (up to 99% ee). A simple reaction protocol was developed which allows synthesis of either enantiomer selectively. Extension of this study led to the introduction of a new process using stoichiometric quantities of an achiral base which only requires catalytic alkaloid amounts and gives ester **2** with up to 90% ee. Currently, we are focusing our efforts on the application of this transformation toward the synthesis of bioactive substances and new ligands for asymmetric catalysis.

Experimental Section

General. Unless otherwise specified, all reagents were purchased from commercial suppliers and used without further purification. Toluene and THF were distilled from sodium benzophenone ketyl radical under argon. All other solvents were reagent grade and used as received. Unless otherwise noted, all reactions were carried out under argon using standard Schlenk and vacuum line techniques. The anhydrides **15**, **23**, **25**, and **31** as well as the amines **33**−**35** and **37** were commercially available. Compounds **1**, **11**, and **27** were prepared by Diels−Alder reactions of maleic anhydride and the corresponding dienes. Eschweiler−Clarke methylation of commercially available isopropyl-*tert*-butylamine gave amine **38**. Substrate **19** was obtained from the corresponding diacid by refluxing in acetic anhydride. Hydrogenation of the double bond (H_2/Rh−Al_2O_3, ethyl acetate) of **1** and **11** delivered anhydrides **3** and **13**. The anhydrides **5**,[23] **7**,[24] **9**,[25] **17**,[11c] **21**,[26] **29**,[27] and **30**[28] as well as the amines **36**,[29] **39**,[30] **40**,[31] and **41**[32]

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were prepared according to literature procedures. The enantiomeric ratios of the opening products were determined as follows: (a) the methyl monoesters were transformed with 2-propanol or *p*-bromophenol to the corresponding diesters by DCC-coupling, which were then analyzed by GC or HPLC, or (b) the hemiesters were reduced with $LiBEt_3H$ and cyclized to the lactones,[6c] which were then analyzed by GC. Capillary gas chromatograms were obtained using the following columns and temperature programs: (a) Lipodex A: 2,3,6-*O*-Tripentyl-α-CD. Column head pressure: 1.0 bar H_2; 80 °C (30 min), heating rate 0.5 °C/min up to 100 °C (30 min). (b) Lipodex B: 2,6-*O*-Dipentyl-3-*O*-actyl-α-CD. Column head pressure: 0.6 bar N_2; Conditioning of the column: 70 °C, heating rate 1.0 °C/min up to 100 °C (10 min), heating rate 3.0 °C/min up to 160 °C (20 min); Sample: 120 °C (15 min), heating rate 2.0 °C/min up to 160 °C (10 min). (c) Lipodex E: 2,6-*O*-Dipentyl-3-*O*-butyryl-γ-CD. Column head pressure: 1.0 bar N_2; 100 °C (50 min), heating rate 3.0 °C/min up to 180 °C (60 min). Injector temperature 200 °C, detector temperature 250 °C. HPLC-analysis was performed using a Chiracel OD or a Chiracel OD-H (Daicel), 4.6 × 250 mm, $\lambda = 254$ nm. ^{1}H NMR and ^{13}C NMR spectra were recorded relative to TMS as internal standard. GCMS spectra were measured on a column HP-5 MS, 30 m × 0.25 mm × 0.25 μm. Melting Points were determined in open glass capillaries and are uncorrected. Optical rotations were measured at room temperature (ca. 20 °C) using HPLC-grade solvents. All microanalyses were conducted at the Institut für Organische Chemie der RWTH Aachen.

General Procedure for the Alkaloid-Mediated Ring Opening of Cyclic *Meso*-Anhydrides. (GP-A) Using Stoichiometric Alkaloid Amounts. Methanol (0.122 mL, 3.0 mmol) was added dropwise to a stirred suspension of the anhydride (1.0 mmol) and the alkaloid (0.357 g, 1.1 mmol) in a 1:1-mixture of toluene and tetrachloromethane (5 mL in the case of quinidine, 20 mL in the case of quinine) at −55 °C under argon. The reaction mixture was stirred at this temperature for 60 h. During this period, the material gradually dissolved. Subsequently, the resulting clear solution was concentrated in vacuo to dryness, and the resulting residue was then dissolved in ethyl acetate. The solution was washed with 2 N HCl, and after phase separation, followed by extraction of the aqueous phases with ethyl acetate, the organic layer was dried over $MgSO_4$, filtered, and concentrated providing the corresponding hemiester.

Analogously, the quinidine-mediated methanolysis was executed in pure toluene using 10 mL/mmol anhydride. To recover the alkaloid, the acidic aqueous phase was neutralized with Na_2CO_3 and extracted with CH_2Cl_2. The combined organic phases were dried over $MgSO_4$ and filtered. Evaporation of the solvent yielded the alkaloid almost quantitatively.

(2*R*,3*S*)-3-*endo*-Methoxycarbonyl-bicyclo[2.2.1]hept-5-ene-2-*endo*-carboxylic acid (2) was obtained from the quinidine opening of anhydride **1** in 98% yield as a white solid: mp 74 °C (rac), 75−78 °C (en), lit.[33] mp 74−76 °C (rac); $[\alpha]^{rt}_D = +7.8$ ($c = 4.23$, CCl_4), lit.[33] $[\alpha]^{20}_D = +7.9$ ($c = 4.8$, CCl_4); ee = 99% [GC-analysis of the lactone: Lipodex E, $t_1 = 80.7$, $t_2 = 81.1$ (major) or HPLC-analysis of the methyl-4-bromophenyl diester: Chiralcel OD-H at room temperature, *n*-heptane/2-propanol = 98:2, 0.5 mL/min, 254 nm, $t_1 = 20.3$, $t_2 = 23.2$ (major)]; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.32−1.36 (m, 1H), 1.50 (dd, $J = 1.8$, 8.9 Hz, 1H), 3.17−3.22 (m, 2H), 3.29−3.32 (m, 2H), 3.60 (s, 3H), 6.32 (dd, $J = 3.0$, 4.9 Hz, 1H), 11.12 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 46.1, 46.6, 47.9, 48.2, 48.8, 51.6, 134.4, 135.6, 173.1, 177.8. For IR and MS data, see the literature.[33]

(2*S*,3*R*)-3-*endo*-Methoxycarbonyl-bicyclo[2.2.1]hept-5-ene-2-*endo*-carboxylic acid (*ent*-2) was obtained from the quinine opening of anhydride **1** in 92% yield as a white solid: $[\alpha]^{rt}_D = -7.8$ ($c = 4.76$, CCl_4), lit.[33] $[\alpha]^{20}_D = -7.9$ ($c = 4.9$, CCl_4); ee = 99% [GC-analysis of the lactone: Lipodex E, $t_1 = 80.7$ (major), $t_2 = 81.1$ or HPLC-analysis of the methyl-4-bromophenyl diester: Chiralcel OD-H at room temperature, *n*-heptane/2-propanol = 98:2, 0.5 mL/min, 254 nm, $t_1 = 20.3$ (major), $t_2 = 23.2$].

(2*R*,3*S*)-3-*endo*-Methoxycarbonyl-bicyclo[2.2.1]heptane-2-*endo*-carboxylic acid (4) was obtained from the quinidine opening of anhydride **3** in 84% yield: mp 75−76 °C (rac), colorless oil (en), lit.[34] mp 77−79 °C (rac); $[\alpha]^{rt}_D = +16.9$ ($c = 1.59$, MeOH), lit.[5g] $[\alpha]^{23}_D = +17.1$ ($c = 2.06$, MeOH); ee = 94% [HPLC-analysis of the methyl-4-bromophenyl diester: Chiracel OD-H at room temperature, *n*-heptane/2-propanol = 98:2, 0.5 mL/min, 254 nm, $t_1 = 15.4$, $t_2 = 18.8$ (major)]; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.37−1.58 (m, 4H), 1.74−1.84 (m, 2H), 2.49−2.62 (m, 2H), 2.92−3.07 (m, 2H), 3.63 (s, 3H), 10.70 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 24.0, 24.2, 39.9, 40.2, 40.4, 46.7, 47.2, 51.3, 173.2, 178.3. For IR[5g] and MS[35] data see the literature.

(2*S*,3*R*)-3-*endo*-Methoxycarbonyl-bicyclo[2.2.1]heptane-2-*endo*-carboxylic acid (*ent*-4) was obtained from the quinine opening of anhydride **3** in 86% yield as a colorless oil: $[\alpha]^{rt}_D = -16.4$ ($c = 2.11$, MeOH), lit.[5g] $[\alpha]^{24}_D = -17.4$ ($c = 2.05$, MeOH); ee = 94% [HPLC-analysis of the methyl-4-bromophenyl diester: Chiracel OD-H at room temperature, *n*-heptane/2-propanol = 98:2, 0.5 mL/min, 254 nm, $t_1 = 15.4$ (major), $t_2 = 18.8$].

(2*S*,3*R*,7*S*)-7-*anti*-Trimethylsilyl-3-*endo*-methoxycarbonyl-bicyclo[2.2.1]hept-5-ene-2-*endo*-carboxylic acid (6) was obtained from the quinidine opening of anhydride **5** in 99% yield as a white solid: mp 103 °C (rac), 78−79 °C (en); $[\alpha]^{rt}_D = +11.0$ ($c = 4.21$, MeOH), $[\alpha]^{rt}_D = -5.1$ ($c = 4.03$, CH_2Cl_2); ee = 96% [HPLC-analysis of the methyl-4-bromophenyl diester: Chiracel OD at room temperature, *n*-heptane/2-propanol = 99:1, 0.5 mL/min, 254 nm, $t_1 = 11.3$, $t_2 = 12.7$ (major)]; ^{1}H NMR (400 MHz, acetone-d_6): δ −0.05 (s, 9H), 1.09 (s, 1H), 3.15−3.18 (m, 1H), 3.21−3.24 (m, 1H), 3.30 (dd, $J = 3.3$, 10.2 Hz, 1H), 3.39 (dd, $J = 3.3$, 10.2 Hz, 1H), 3.49 (s, 3H), 6.02 (dd, $J = 3.0$, 5.5 Hz, 1H), 6.14 (dd, $J = 3.0$, 5.2 Hz, 1H). ^{13}C NMR (100 MHz, acetone-d^6): δ −0.1, 49.5, 50.1, 50.8, 50.9, 51.1, 51.5, 134.3, 135.6, 172.9, 173.3. Anal. Calcd for $C_{13}H_{20}O_4Si$ (268.23): C, 58.18; H, 7.51. Found: C, 58.39; H, 7.56. For IR and MS data see Supporting Information.

(2*R*,3*S*,7*R*)-7-*anti*-Trimethylsilyl-3-*endo*-methoxycarbonyl-bicyclo[2.2.1]hept-5-ene-2-*endo*-carboxylic acid (*ent*-6) was obtained from the quinine opening of anhydride **5** in 98% yield as a white solid: $[\alpha]^{rt}_D = -5.2$ ($c = 4.75$, CH_2Cl_2), ee = 98% [HPLC-analysis of the methyl-4-bromophenyl diester: Chiracel OD at room temperature, *n*-heptane/2-propanol = 99:1, 0.5 mL/min, 254 nm, $t_1 = 11.3$ (major), $t_2 = 12.7$].

(2*R*,3*S*)-7-Benzhydrylidene-3-*endo*-methoxycarbonyl-bicyclo[2.2.1]hept-5-ene-2-*endo*-carboxylic acid (8) was obtained from the quinidine opening of anhydride **7** in 95% yield as a white solid: mp 158 °C (rac), 160 °C (en), lit.[24] mp 158 °C (rac); $[\alpha]^{rt}_D = +4.6$ ($c = 3.43$, MeOH); ee = 95% [HPLC-analysis of the methyl-4-bromophenyl diester: Chiracel OD-H at room temperature, *n*-heptane/2-propanol = 98:2, 0.7 mL/min, 254 nm, $t_1 = 11.0$, $t_2 = 17.1$ (major)]; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.46−3.55 (m, 2H), 3.59 (s, 3H), 3.67−3.73 (m, 2H), 6.44 (dd, $J = 3.0$, 5.71 Hz, 1H), 6.51 (dd, $J = 3.0$, 6.0 Hz, 1H), 7.03−7.09 (m, 4H), 7.20−7.32 (m, 6H), 9.60 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 47.7, 47.9, 51.7, 122.6, 127.0, 128.1, 129.5, 134.8, 135.6, 140.4, 149.4, 172.0, 177.5. Anal. Calcd for $C_{23}H_{20}O_4$ (360.41): C, 76.65; H, 5.59. Found: C, 76.29; H, 5.97. For IR and MS data see Supporting Information.

(2*S*,3*R*)-7-Benzhydrylidene-3-*endo*-methoxycarbonyl-bicyclo[2.2.1]hept-5-ene-2-*endo*-carboxylic acid (*ent*-8) was obtained from the quinine opening of anhydride **7** in 96% yield as a white solid: $[\alpha]^{rt}_D = -4.3$ ($c = 5.49$, MeOH), ee = 92% [HPLC-analysis of the methyl-4-bromophenyl diester:

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(35) Casas, R.; Ibarzo, J.; Jimenez, J. M.; Ortuno, R. M. *Tetrahedron: Asymmetry* **1993**, *4*, 669.

Chiracel OD-H at room temperature, *n*-heptane/2-propanol = 98:2, 0.7 mL/min, 254 nm, t_1 = 11.0 (major), t_2 = 17.1].

(2*R*,3*S*)-3-*exo*-Methoxycarbonyl-bicyclo[2.2.1]hept-5-ene-2-*exo*-carboxylic acid (10) was obtained from the quinidine opening of anhydride **9** in 96% yield as a white solid: mp 66 °C (rac), 61 °C (en); $[\alpha]^{rt}_D$ = +6.0 (*c* = 1.11, $CHCl_3$), $[\alpha]^{rt}_D$ = −1.7 (*c* = 1.31, MeOH); ee = 96% [GC-analysis of the lactone: Lipodex E, t_1 = 73.8, t_2 = 74.8 (major)]; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 1.50 (dp, *J* = 1.7, 9.1 Hz, 1H), 2.10 (dtr, *J* = 1.7, 9.1 Hz, 1H), 2.65 (d, *J* = 1.9 Hz, 2H), 3.11−3.14 (m, 2H), 3.66 (s, 3H), 6.22 (br tr, *J* = 1.9 Hz, 2H), 11.02 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 45.7, 46.1, 47.7, 47.8, 52.1, 138.1, 138.3, 174.0, 180.2. Anal. Calcd for $C_{10}H_{12}O_4$ (196.20): C, 61.22; H, 6.16. Found: C, 61.40; H, 6.28. For IR and MS data see Supporting Information.

(2*S*,3*R*)-3-*exo*-Methoxycarbonyl-bicyclo[2.2.1]hept-5-ene-2-*exo*-carboxylic acid (*ent*-10) was obtained from the quinine opening of anhydride **9** in 94% yield as a white solid: $[\alpha]^{rt}_D$ = −5.8 (*c* = 1.65, $CHCl_3$); ee = 93% (99.9% after recrystallization from hexanes, ethyl acetate) [GC-analysis of the lactone: Lipodex E, t_1 = 73.8 (major), t_2 = 74.8].

(2*S*,3*R*)-3-*exo*-Methoxycarbonyl-7-oxabicyclo[2.2.1]hept-5-ene-2-*exo*-carboxylic acid (12) was obtained from the quinidine opening of anhydride **11** in 61% yield as a white solid: mp 105 °C (rac), 111 °C (en) lit.[16b] mp 110 °C (en); $[\alpha]^{rt}_D$ = −9.7 (*c* = 2.37, MeOH), lit.[16b] $[\alpha]^{20}_D$ = −10.6 (*c* = 2, MeOH); ee = 93% [GC-analysis of the hydrogenated lactone:[6c] Lipodex E, t_1 = 95.9, t_2 = 98.7 (major)]; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 2.87 (AB-system, *J* = 9.1 Hz, 2H), 3.71 (s, 3H), 5.28 (br s, 1H), 5.31 (br s, 1H), 5.45−5.46 (m, 2H), 10.29 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 46.8, 47.2, 52.3, 80.2, 80.5, 136.2, 136.6, 171.6, 177.2. Anal. Calcd for $C_9H_{10}O_5$ (198.17): C, 54.55; H, 5.09. Found: C, 54.54; H, 5.15. For IR and MS data see Supporting Information.

(2*R*,3*S*)-3-*exo*-Methoxycarbonyl-7-oxabicyclo[2.2.1]hept-5-ene-2-*exo*-carboxylic acid (*ent*-12) was obtained from the quinine opening of anhydride **11** in 71% yield as a white solid: $[\alpha]^{rt}_D$ = +8.0 (*c* = 2.11, MeOH); ee = 75% [GC-analysis of the hydrogenated lactone:[6c] Lipodex E, t_1 = 95.9 (major), t_2 = 98.7].

(2*S*,3*R*)-3-*exo*-Methoxycarbonyl-7-oxabicyclo[2.2.1]-heptane-2-*exo*-carboxylic acid (14) was obtained from the quinidine opening of anhydride **13** in 69% yield as a white solid: mp 122 °C (rac), 136 °C (en) lit.[16b] mp 104 °C (en); $[\alpha]^{rt}_D$ = −4.7 (*c* = 2.08, MeOH), lit.[5g] $[\alpha]^{20}_D$ = −4.9 (*c* = 2.01, MeOH); ee = 94% [GC-analysis of the lactone: Lipodex E, t_1 = 95.9, t_2 = 98.7 (major)]; ^{1}H NMR (300 MHz, $CDCl_3$): *δ* 1.52−1.56 (m, 2H), 1.80−1.85 (m, 2H), 3.03 (AB-system, *J* = 9.5 Hz, 2H), 3.67 (s, 3H), 4.91−4.97 (m, 2H), 10.20 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): *δ* 29.6, 52.7, 58.3, 78.9, 79.2, 171.2, 177.1. For IR data see the literature.[5g,36] For MS data see Supporting Information.

(2*R*,3*S*)-3-*exo*-Methoxycarbonyl-7-oxabicyclo[2.2.1]-heptane-2-*exo*-carboxylic acid (*ent*-14) was obtained from the quinine opening of anhydride **13** in 79% yield as a white solid: $[\alpha]^{rt}_D$ = +4.7 (*c* = 2.11, MeOH), lit.[5g] $[\alpha]^{24}_D$ = +4.4 (*c* = 2.01, MeOH); ee = 93% [GC-analysis of the lactone:[6c] Lipodex E, t_1 = 95.9 (major), t_2 = 98.7].

(1*R*,2*S*)-*cis*-2-Methoxycarbonyl-cyclopropane-1-carboxylic acid (16) was obtained from the quinidine opening of anhydride **15** in 96% yield as a colorless oil: $[\alpha]^{rt}_D$ = +10.3 (*c* = 1.73, $CHCl_3$); ee = 85% [GC-analysis of the methyl-isopropyl diester: Lipodex A, t_1 = 50.9 (major), t_2 = 51.5]; ^{1}H NMR (300 MHz, $CDCl_3$): *δ* 1.29−1.37 (m, 1H), 1.66−1.72 (m, 1H), 2.05−2.20 (m, 2H), 3.71 (s, 3H), 11.37 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): *δ* 12.4, 21.2, 22.4, 52.4, 170.4, 176.0. For IR[37] and MS[38] data see the literature.

(1*S*,2*R*)-*cis*-2-Methoxycarbonyl-cyclopropane-1-carboxylic acid (*ent*-16) was obtained from the quinine opening of anhydride **15** in 95% yield as a colorless oil: $[\alpha]^{rt}_D$ = −10.2 (*c* = 1.78, $CHCl_3$), lit.[37] $[\alpha]^{25}_D$ = −13.4 (*c* = 0.97, $CHCl_3$); ee = 85% [GC-analysis of the methyl-isopropyl diester: Lipodex A, t_1 = 50.9, t_2 = 51.5 (major)].

(1*S*,2*R*)-*cis*-2-Methoxycarbonyl-3,3-dimethylcyclopropane-1-carboxylic acid (18) was obtained from the quinidine opening of anhydride **17** in 97% yield as a white solid: mp 106 °C (rac), 54 °C (en) lit.[11c] mp 54−55 °C (en); $[\alpha]^{rt}_D$ = +20.6 (*c* = 4.20, MeOH); ee = 90% [GC-analysis of the lactone: Lipodex B, t_1 = 11.9 (major), t_2 = 12.7]; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 1.27 (s, 3H), 1.40 (s, 3H), 1.97 (AB-system, *J* = 9.0 Hz, 2H), 3.72 (s, 3H), 11.05 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 15.5, 27.5, 28.3, 32.9, 33.0, 52.5, 171.2, 174.2. For IR and MS data see the literature.[39]

(1*R*,2*S*)-*cis*-2-Methoxycarbonyl-3,3-dimethylcyclopropane-1-carboxylic acid (*ent*-18) was obtained from the quinine opening of anhydride **17** in 96% yield as a white solid: $[\alpha]^{rt}_D$ = −19.0 (*c* = 4.08, MeOH), lit.[39] $[\alpha]^{22}_D$ = −19.0 (*c* = 4, MeOH); ee = 84% (99.4% ee after recrystallization from hexanes, Et_2O) [GC-analysis of the lactone: Lipodex B, t_1 = 11.9, t_2 = 12.7 (major)].

(1*R*,2*S*)-*cis*-2-Methoxycarbonyl-cyclobutane-1-carboxylic acid (20) was obtained from the quinidine opening of anhydride **19** in 99% yield as a colorless oil: $[\alpha]^{rt}_D$ = +3.4 (*c* = 2.61, $CHCl_3$); ee = 94% [GC-analysis of the lactone: Lipodex E, t_1 = 64.4 (major), t_2 = 64.9]; ^{1}H NMR (300 MHz, $CDCl_3$): *δ* 2.06−2.40 (m, 4H), 3.32−3.41 (m, 2H), 3.65 (s, 3H), 11.48 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): *δ* 21.6, 22.9, 40.8, 42.1, 51.4, 174.8, 177.8. For IR data see the literature.[37] For MS data see Supporting Information.

(1*S*,2*R*)-*cis*-2-Methoxycarbonyl-cyclopropane-1-carboxylic acid (*ent*-20) was obtained from the quinine opening of anhydride **19** in 93% yield as a colorless oil: $[\alpha]^{rt}_D$ = −3.3 (*c* = 2.3, $CHCl_3$), lit.[40] $[\alpha]^{25}_D$ = −3.6 (*c* = 2.36, $CHCl_3$); ee = 87% [GC-analysis of the lactone: Lipodex E, t_1 = 64.4, t_2 = 64.9 (major)].

(1*R*,2*S*)-*cis*-2-Methoxycarbonyl-cyclopentane-1-carboxylic acid (22) was obtained from the quinidine opening of anhydride **21** in 97% yield as a colorless oil: $[\alpha]^{rt}_D$ = +8.3 (*c* = 2.1, MeOH), $[\alpha]^{rt}_D$ = +5.68 (*c* = 0.95, $CHCl_3$), lit.[1g] $[\alpha]^{25}_D$ = +5.0 (*c* = 1.4, MeOH), lit.[37] $[\alpha]^{25}_D$ = +1.0 (*c* = 1.0, $CHCl_3$); ee = 95% [GC-analysis of the lactone: Lipodex E, t_1 = 68.6 (major), t_2 = 69.6]; ^{1}H NMR (300 MHz, $CDCl_3$): *δ* 1.58−1.73 (m, 1H), 1.82−2.13 (m, 5H), 3.03−3.12 (m, 2H), 3.66 (s, 3H), 10.50 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): *δ* 23.8, 28.7, 46.8, 46.9, 51.8, 174.4, 180.4. For IR data see the literature.[37] For MS data see Supporting Information.

(1*S*,2*R*)-*cis*-2-Methoxycarbonyl-cyclopentane-1-carboxylic acid (*ent*-22) was obtained from the quinine opening of anhydride **21** in 99% yield as a colorless oil: $[\alpha]^{rt}_D$ = −8.0 (*c* = 2.67, MeOH); ee = 93% [GC-analysis of the lactone: Lipodex E, t_1 = 68.6, t_2 = 69.6 (major)].

(1*R*,2*S*)-*cis*-2-Methoxycarbonyl-cyclohexane-1-carboxylic acid (24) was obtained from the quinidine opening of anhydride **23** in 98% yield as a colorless oil: $[\alpha]^{rt}_D$ = +4.5 (*c* = 0.98, $CHCl_3$), lit.[37] $[\alpha]^{25}_D$ = +4.7 (*c* = 0.87, $CHCl_3$); ee = 93% [GC-analysis of the lactone: Lipodex E, t_1 = 71.7 (major), t_2 = 73.1]; ^{1}H NMR (300 MHz, $CDCl_3$): *δ* 1.37−1.59 (m, 4H), 1.75−1.81 (m, 2H), 1.99−2.05 (m, 2H), 2.80−2.87 (m, 2H), 3.68 (s, 3H), 10.30 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): *δ* 24.2, 24.3, 26.5, 26.8, 42.9, 43.1, 52.3, 174.7, 180.7. For IR and MS data see the literature.[41]

(1*S*,2*R*)-*cis*-2-Methoxycarbonyl-cyclohexane-1-carboxylic acid (*ent*-24) was obtained from the quinine opening of anhydride **23** in 91% yield as a colorless oil: $[\alpha]^{rt}_D$ = −4.2 (*c* = 1.03, $CHCl_3$), lit.[41b] $[\alpha]^{20}_D$ = −1.7 (*c* = 1.08, $CHCl_3$); ee = 87% [GC-analysis of the lactone: Lipodex E, t_1 = 71.7, t_2 = 73.1 (major)].

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(1*R*,2*S*)-*cis*-2-Methoxycarbonyl-cyclohex-4-ene-1-carboxylic acid (26) was obtained from the quinidine opening of anhydride **25** in 93% yield as a colorless oil: $[\alpha]^{rt}_D = +10.4$ ($c = 1.23$, acetone), $[\alpha]^{rt}_D = +13.1$ ($c = 1.13$, EtOH), lit.[41a] $[\alpha]^{25}_D = +10.9$ ($c = 1.64$, acetone), lit.[42] $[\alpha]^{rt}_D = +14.9$ ($c = 1.49$, EtOH); ee = 95% [GC-analysis of the lactone: Lipodex E, $t_1 = 75.1$ (major), $t_2 = 75.7$]; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.32−2.42 (m, 2H), 2.55−2.63 (m, 2H), 3.02−3.09 (m, 2H), 3.70 (s, 3H), 5.68 (AB-system, $J = 1.7$ Hz, 2H), 10.52 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 26.1, 26.3, 40.0, 40.2, 52.5, 125.6, 125.7, 174.3, 180.3. For IR data see the literature.[41a] For MS data see Supporting Information.

(1*S*,2*R*)-*cis*-2-Methoxycarbonyl-cyclohex-4-ene-1-carboxylic acid (*ent*-26) was obtained from the quinine opening of anhydride **25** in 99% yield as a colorless oil: $[\alpha]^{rt}_D = -10.3$ ($c = 1.32$, acetone); ee = 93% [GC-analysis of the lactone: Lipodex E, $t_1 = 75.1$, $t_2 = 75.7$ (major)].

(1*R*,2*S*)-*cis*-2-Methoxycarbonyl-4,5-dimethylcyclohex-4-ene-1-carboxylic acid (28) was obtained from the quinidine opening of anhydride **27** in 96% yield as a white solid: mp 94−95 °C (rac), 60−61 °C (en); $[\alpha]^{rt}_D = +19.0$ ($c = 4.3$, MeOH), $[\alpha]^{rt}_D = +5.3$ ($c = 1.05$, $CHCl_3$); ee = 97% [GC-analysis of the lactone: Lipodex E, $t_1 = 76.6$ (major), $t_2 = 77.4$]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.63 (s, 6H), 2.22−2.29 (m, 2H), 2.42−2.48 (m, 2H), 2.97−3.07 (m, 2H), 3.69 (s, 3H), 11.20 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 18.9, 31.6, 31.7, 40.1, 40.3, 51.9, 123.9, 124.0, 173.9, 179.9. Anal. Calcd for $C_{11}H_{16}O_4$ (212.25): C, 62.25; H, 7.60. Found: C, 62.24; H, 7.65. For IR and MS data see Supporting Information.

(1*S*,2*R*)-*cis*-2-Methoxycarbonyl-4,5-dimethylcyclohex-4-ene-1-carboxylic acid (*ent*-28) was obtained from the quinine opening of anhydride **27** in 97% yield as a white solid: $[\alpha]^{rt}_D = -18.4$ ($c = 4.9$, MeOH); ee = 94% [GC-analysis of the lactone: Lipodex E, $t_1 = 76.6$, $t_2 = 77.4$ (major)].

(GP-B) Using Substoichiometric Amounts of Quinidine. Methanol (0.122 mL, 3.0 mmol) was added dropwise to a stirred suspension of anhydride **1** (0.164 g, 1.0 mmol), the tertiary amine (1.0 mmol), and quinidine (0.032 g, 0.1 mmol) in a 1:1-mixture of toluene and tetrachloromethane (5 mL) at −55 °C under argon. The reaction mixture was stirred at that temperature for 60−168 h. Workup and purification was carried out in accordance to the general procedure A. (2*R*,3*S*)-3-*endo*-Methoxycarbonyl-bicyclo[2.2.1]hept-5-ene-2-*endo*-carboxylic acid (**2**) was obtained as a white solid. The reaction times and the results are summarized in Table 4. The transformations of other substrates were performed in an analogous manner. The results are summarized in Table 5.

Chemoselective Transformation of Ester 28 to *Trans*-Diol 32. A solution of ester **28** (4.428 g, 21 mmol) and Et_3N (2.3 mL, 23 mmol) in THF (80 mL) was treated with ethyl chloroformate (2.2 mL, 23 mmol) at −20 °C and stirred at this temperature for 30 min. The ammonium salt which had formed was removed by filtration and washed with THF (5 mL). At −20 °C, the combined filtrates were treated with $NaBH_4$ (870 mg, 23 mmol), and then MeOH (5.8 mL) was carefully added dropwise. The resulting mixture was stirred at this temperature for 2 h, quenched with saturated aqueous NH_4Cl, and extracted with ethyl acetate. The combined extracts were dried over $MgSO_4$, filtered, and concentrated providing the corresponding hydroxy ester as a viscous oil. The product was dissolved in THF (20 mL) and added to a solution of LDA (63 mmol) in THF (200 mL) at −78 °C. After 30 min at this temperature, the reaction was quenched with saturated aqueous NH_4Cl, the phases were separated, and the aqueous phase was extracted with ethyl acetate. The combined organic layers were dried over $MgSO_4$ and filtered, and evaporation of the solvents delivered an oily residue which was purified by column chromatography [using silica gel 60 (0.040−0.063 mm), ethyl acetate:hexanes = 1:1]. A solution of the resulting product in THF (50 mL) was treated with $LiAlH_4$ (1.0 g, 26 mmol). The mixture was stirred at room temperature for 12 h and carefully quenched with saturated aqueous NH_4Cl. After phase separation, the organic layer was dried over $MgSO_4$, filtered, and concentrated providing 1.5 g (8.8 mmol, 42%) of *trans*-diol **32** as a white solid which was recrystallized from ethyl acetate/hexanes: mp 131−132 °C (en) lit.[43] mp 129−131 °C (en); $[\alpha]^{rt}_D = -90.2$ ($c = 1.31$, MeOH), lit.[44] $[\alpha]_D = -76.9$ ($c = 1.0$, MeOH); ^{1}H NMR (400 MHz, MeOH-d^4): δ 1.58 (br s, 6H), 1.63−1.69 (m, 2H), 1.76−1.85 (m, 2H), 1.91−2.00 (m, 2H), 3.46−3.55 (m, 4H), 4.86 (s, 2H). ^{13}C NMR (100 MHz, MeOH-d_4): δ 18.0, 33.7, 38.6, 64.6, 123.9. For IR data, see the literature.[45] For MS data, see Supporting Information.

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Supporting Information Available: Spectral characterization (^{1}H NMR, ^{13}C NMR, IR and MS) of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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