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Highly Enantioselective Epoxidation of 2-Methylnaphthoquinone (Vitamin K_3) Mediated by New *Cinchona* Alkaloid Phase-Transfer Catalysts

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Abstract: In the area of catalytic asymmetric epoxidation, the highly enantioselective transformation of cyclic enones and quinones is an extremely challenging target. With the aim to develop new and highly effective phase-transfer catalysts for this purpose, we conducted a systematic structural variation of PTCs based on quinine and quinidine. In the total of 15 new quaternary ammonium PTCs, modifications included, for example, the exchange of the quinine methoxy group for a free hydroxyl or other alkoxy substituents, and the introduction of additional elements of chirality through alkylation of the alkaloid quinuclidine nitrogen atom by chiral electrophiles. For example, the well-established 9-anthracenylmethyl group was exchanged for a "chiral" anthracene in the form of 9-chloromethyl-[(1,8-*S*;4,5-*R*)-1,2,3,4,5,6,7,8-octahydro-1,4:5,8-dimethanoanthracene. The asymmetric epoxidation of vitamin K_3 was used as the test reaction for our novel PTCs. The readily available PTC **10** (derived from quinine in three convenient and high-yielding steps) proved to be the most enantioselective catalyst for this purpose known to date: At a catalyst loading of only 2.50 mol%, the quinone epoxide was obtained in 76% yield and with 85% *ee* (previously: ≤34% *ee*), using commercial bleach (aqueous sodium hypochlorite) as the oxidant. To rationalize the sense of induction effected by our novel phase-transfer catalysts, a computational analysis of steric interactions in the intermediate chlorooxy enolate–PTC ion pair was conducted. Based on this analysis, the sense of induction for all 15 novel PTCs could be consistently explained.

Keywords: alkaloids · asymmetric catalysis · enones · epoxidation · phase-transfer catalysis

Introduction

Enantiomerically pure epoxides are valuable intermediates in the asymmetric synthesis of, for example, pharmaceuticals and natural products in both academic and industrial laboratories.[1] In most cases, epoxides are prepared by oxygen transfer from a terminal oxidant to a C=C-double bond, and the recent years have seen a dramatic development of various methods for the catalytic asymmetric epoxidation of olefins.[2,3] For the epoxidation of electron-deficient substrates such as enones, enoates or quinones, nucleophilic oxidants such as alkaline solutions of hydroperoxides, hydrogen peroxide (Weitz–Scheffer epoxidation) or hypohalites are often applied.[4–9] In fact, asymmetric Weitz–Scheffer-type epoxidations with chiral PTCs belong to the earliest examples of asymmetric catalysis in general: In 1978, Wynberg et al. reported the asymmetric epoxidation of chalcones **1a**,**b** (Scheme 1) using chiral quaternary ammonium salts derived from quinine (**2**) and quinidine (**3**) (Figure 1). Using the benzylquininium chloride **4a** as the PTC (Scheme 1) up to 54% *ee* of epoxide **5a** were achieved.[10–12]

Major breakthroughs in the phase-transfer catalyzed epoxidation of chalcones **1a**,**b** resulted from work by Corey et al. (PTC **4b**),[13] Lygo et al. (PTC **4b**),[14,15] Arai, Shioiri

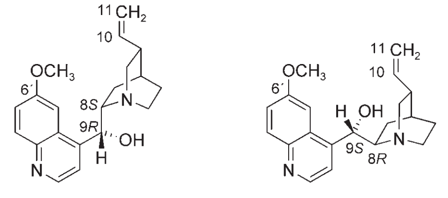

Figure 1. *Cinchona*-alkaloids quinine (**2**) and quinidine (**3**).

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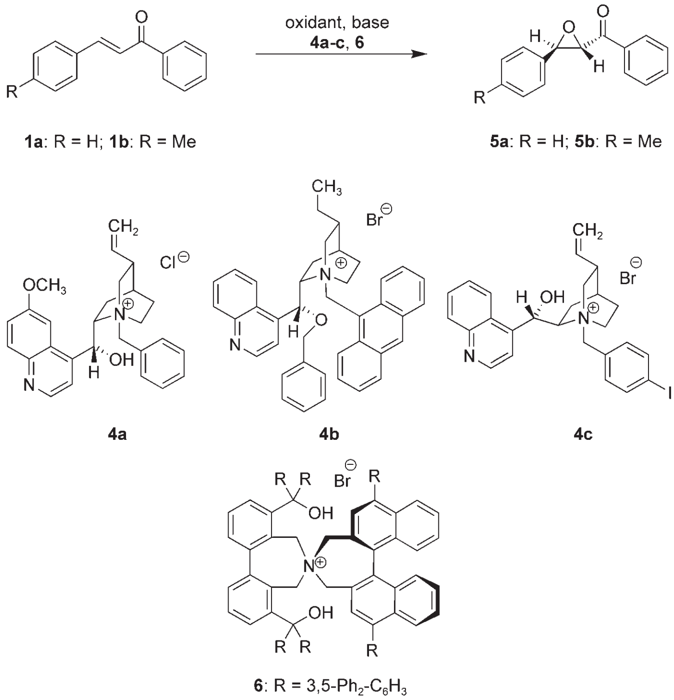
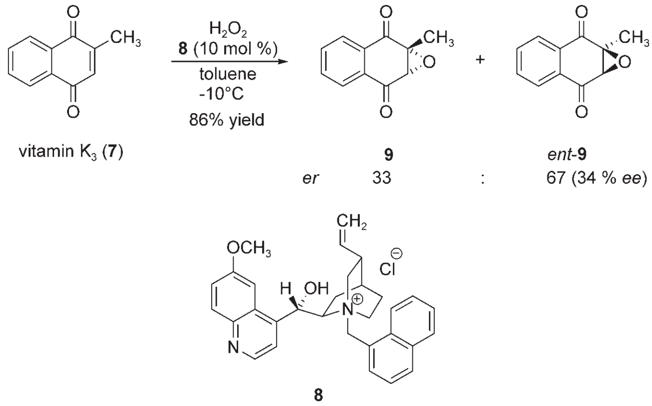
et al. (PTC **4c**)[16] and recently by Marouka et al. (PTC **6**).[9] Enantiomeric excesses up to 97% were achieved in chalcone epoxidation using the advanced PTCs **4b–c** and **6** (Scheme 1).



Scheme 1. Asymmetric epoxidation of chalcone derivatives using phase-transfer catalysts.

Despite these excellent results, few procedures for the synthesis of the epoxides of quinones and quinone acetals by asymmetric epoxidation appear to exist.[17–19] Oxiranes of the latter type are valuable building blocks for pharmaceutical and natural products. 2-Methyl-1,4-naphthoquinone (vitamin K_3 (**7**), Scheme 2) has often served as the touchstone for catalyst performance, because it is a particularly challenging substrate with respect to enantioselective epoxidation. In fact, a maximum *ee* of 78% at 32% yield was achieved by Taylor et al., using carbohydrate-derived chiral hydroperoxides as stoichiometric oxidizing agents.[18–19] As far as asymmetric phase-transfer catalysis is concerned, the best *ee* value (34%) at 86% yield was obtained by Arai, Shioiri et al. using catalyst **8** and alkaline hydrogen peroxide as the oxidant (Scheme 2).[16,20]

Therefore, a highly efficient catalytic enantioselective approach still remains a challenging task. Herein we present a detailed study regarding the catalyst and the oxidant in order to probe the catalyst structure–reactivity relationship. For catalyst optimization, our strategy is based on two main ideas. First, enhancing the catalyst–substrate interaction by additional hydrogen bonding, and second improving the asymmetric induction by introduction of further elements of chirality (Figure 2).



Scheme 2. Asymmetric epoxidation of vitamin K_3 (**7**) using hydrogen peroxide and the PTC **8**.

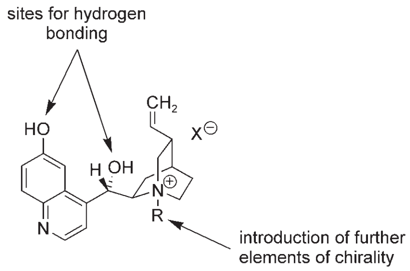
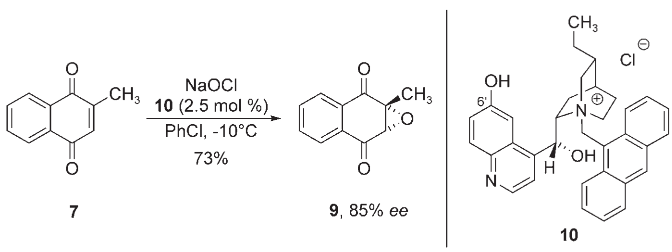


Figure 2. Schematic representation of variations on the scaffold of *cinchona*-alkaloid PTCs.

As it turned out, in particular the use of aqueous sodium hypochlorite as oxidant in combination with catalyst **10** bearing a hydroxyl group at the C6′ atom of the quinoline ring improved the enantioselectivity tremendously: up to 85% *ee* and 73% yield were achieved for the epoxide **9**, at a catalyst loading of 2.5 mol%. This value represents the best enantioselectivity reported thus far (Scheme 3).



Scheme 3. Asymmetric epoxidation of **7** with the new phase-transfer catalyst **10**.

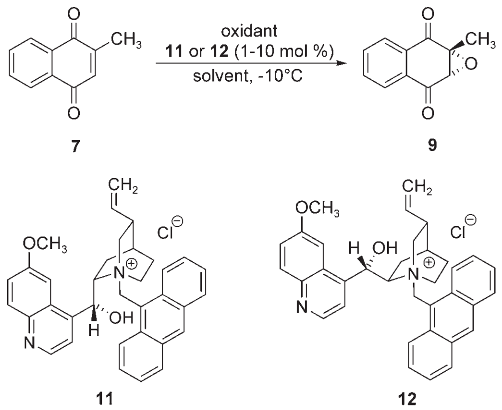
Results

Influence of the oxidant: We initially investigated the influence of several oxidants using the literature known catalysts **11** and **12** (Scheme 4).[16,21] As shown in Table 1, the epoxidation of **7** could be achieved in good yields using either hydrogen peroxide, *tert*-butyl hydroperoxide (TBHP), cumyl

Table 1. Influence of the oxidant on the asymmetric epoxidation of **7**.

Entry	PTC	mol %	Oxidant[a]	Solvent	*t* [h]	Yield [%]	Epoxide[b]	*ee* [%]
1	**11**	5	H_2O_2	$CHCl_3$	4	93	(2*R*,3*S*)	21
2	**11**	10	NaOCl	PhCl	6	90	(2*R*,3*S*)	67
3	**12**	10	NaOCl	$CHCl_3$	7	89	(2*S*,3*R*)	66
4	**12**	10	NaOCl	PhCl	8	92	(2*S*,3*R*)	72
5	**12**	1	NaOCl	PhCl	23	87	(2*S*,3*R*)	76
6	**12**	10	TBHP	PhCl	3	93	(2*S*,3*R*)	43
7	**12**	10	CHP	PhCl	5	90	(2*S*,3*R*)	36

[a] LiOH (1.6 equiv) was employed as the base when hydrogen peroxide, TBHP or CHP were used as oxidants. [b] The absolute configurations of epoxides **9** (2*R*,3*S*) and *ent*-**9** (2*S*,3*R*) were assigned by comparison with literature data.[8,13] [c] Yields and enantioselectivities were determined using GC on chiral stationary phase.



Scheme 4. Asymmetric epoxidation of **7** with different oxidants.

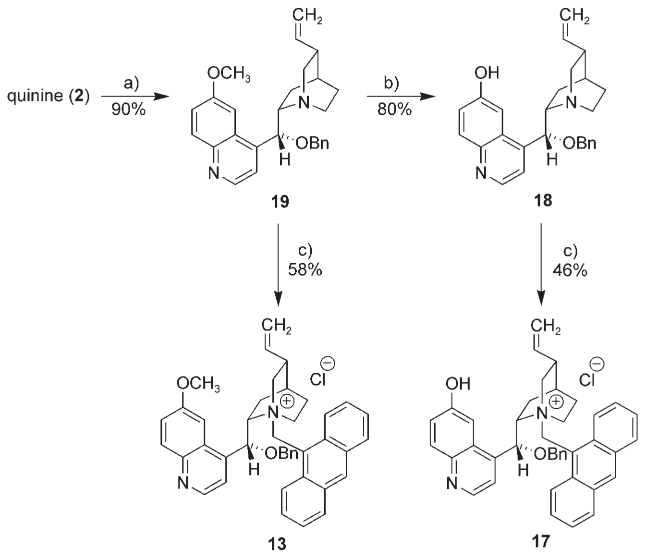
hydroperoxide (CHP) or sodium hypochlorite (Table 1, entries 1, 5 and 7).

A remarkable improvement in the enantioselectivity was found when sodium hypochlorite (commercial bleach) was used as oxidant (Table 1, entries 2–5). At a catalyst loading of 10 mol % (relative to the enone), excellent conversions and *ee* values up to 72 % were achieved in chlorobenzene at −10 °C with catalyst **12**. At lower catalyst loading (1 mol %), an epoxide *ee* of 76 % resulted (Table 1, entries 4 and 5). Chlorobenzene was chosen as solvent as it consistently provided the highest *ee* values of the product epoxide (Table 1, entries 2, 4–7). Obviously, the sense of induction is dominated by the configuration of the alkaloid moiety. Using quinine derivative **11**, epoxide enantiomer **9** is formed predominantly, whereas the pseudo-enantiomeric quinidine derivative **12** leads to epoxide *ent*-**9**, as the major enantiomer (Table 1, entries 2 and 4).

Effect of the catalyst structure

Modifications at the C9 atom: First we examined the influence of modifications at the secondary alcohol (C9) of the PTCs on the epoxidation of vitamin K_3 (**7**). Therefore, the free alcohol was converted to different ethers, leading to the novel PTCs **13**–**15** (Scheme 5 and Figure 3). Furthermore, the configuration at C9 was inverted (catalyst **16**, Figure 3). The novel PTC **17** (Scheme 5), having the secondary hydroxyl function at C9 protected as a benzyl ether, but carrying a hydroxyl group at position C6′ of the quinoline moiety, was prepared as shown in Scheme 5.

Alkylation of **2** with benzyl chloride yielded **19**, which was further converted to the phenol **18** by demethylation with sodium ethyl mercaptide using protocols developed by Deng et al. (Scheme 5).[22,23] These transformations were followed by quaternisation of **18** and **19** with 9-chloromethylanthracene to the PTCs **13** and **17**. The corresponding *O*-benzyl salt **14** (Figure 3) was prepared analogously from quinidine (**3**).



Scheme 5. Synthetic route to the catalysts **13** and **17**. a) NaH, BnCl, DMF, 110 °C, 16 h; b) NaH, EtSH, DMF, 110 °C, 16 h; c) 9-chloromethylanthracene, THF, reflux, 16 h.

The new ammonium salt **15** (Figure 3) was obtained from the literature known precursor β-isocupreidine by quaternisation with 9-chloromethylanthrancene (two steps from **3** in 35 % overall yield).[24] Starting from **2**, the known 9-*epi*-qui-

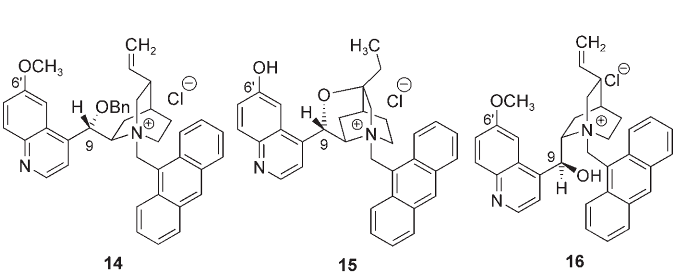


Figure 3. Structures of catalyst **14**, the β-isocupreidine salt **15** and the 9-*epi*-quinine-derived ammonium salt **16**.

nine[25] was quaternised with 9-chloromethylanthracene in 66% yield to give catalyst **16** (Figure 3). This salt exhibits the non-natural configuration at the C9 atom of the alkaloid, which was confirmed unambiguously by X-ray structural analyses.

Catalytic activity of the salts 11–17: As shown in Table 2, entries 3–7, the enantioselectivities of the novel PTCs **13**–**17** were lower compared with those achieved with the literature known catalysts **11** and **12** (Table 2, entries 1 and 2).

Table 2. Results for the asymmetric epoxidation of vitamin K_3 (**7**) with sodium hypochlorite as oxidant in chlorobenzene at −10°C with catalysts **11**–**17**.

Entry	PTC[a]	*t* [h]	Yield[b] [%]	Epoxide	*ee* [%]
1	**11**	6	90	(2*R*,3*S*)	67
2	**12**	8	92	(2*S*,3*R*)	72
3	**13**	32	82	(2*S*,3*R*)	50
4	**14**	24	81	(2*R*,3*S*)	41
5	**15**	24	79 (87)	(2*R*,3*S*)	4
6	**16**	8	40 (48)	(2*S*,3*R*)	51
7	**17**	10	60 (61)	(2*S*,3*R*)	20

[a] 10 mol% of the catalyst were used. [b] Conversion given in brackets.

As shown in Table 2 (entry 1) the quinine-derived PTC **11** forms the epoxide enantiomer **9** predominantly in the (2*R*,3*S*)-configuration. Interestingly, the introduction of a benzyl functionality at the C9 atom of the quinine-based PTC **11** switches the sense of stereoinduction: with catalyst **11** (Table 2, entry 1), 67% *ee* was obtained in favour of the epoxide **9**. However, using the catalyst **13** having the quinine scaffold and a benzyl group at C9 (Table 2, entry 3) yielded the opposite enantiomer *ent*-**9** in 50% *ee*. For the quinidine-based *O*-benzylated catalyst **14**, the same tendency was observed (Table 2, entries 2 and 4). The 9-*epi*-isomer **16** produced epoxide *ent*-**9** in 51% *ee* (Table 2, entry 6). In the case of PTC **17** (alcohol functionality at C6′ and a *O*-benzyl group at C9), the *ee* of the epoxide *ent*-**9** decreased significantly to 20% (Table 2, entry 7). Nearly no enantioselectivity was induced by the rigid PTC **15** (Table 2, entry 5).

Modifications at the quinuclidine nitrogen atom: We also investigated the possibility to enhance the enantioselectivity of the alkaloid-based catalysts by introducing further elements of chirality at the quinuclidine core. With respect to the performance of catalysts **11** and **12**, we envisaged that the combination of quinine (**2**) and quinidine (**3**) with both enantiomers of the chiral benzyl halides **20** and **21** (Scheme 6) as chiral and bulky aromatic groups would be effective in improving the enantioselectivity. Clearly, a matched–mismatched situation should result for the quaternary catalysts **22**–**27** (Figure 4).

As shown in Scheme 6, we prepared **20** and *ent*-**20** by reduction/chlorination from the corresponding aldehydes[26–28] (**28** and *ent*-**28**) in 70–80% overall yield. For the synthesis of the binaphthyl electrophile **21**, we followed the literature

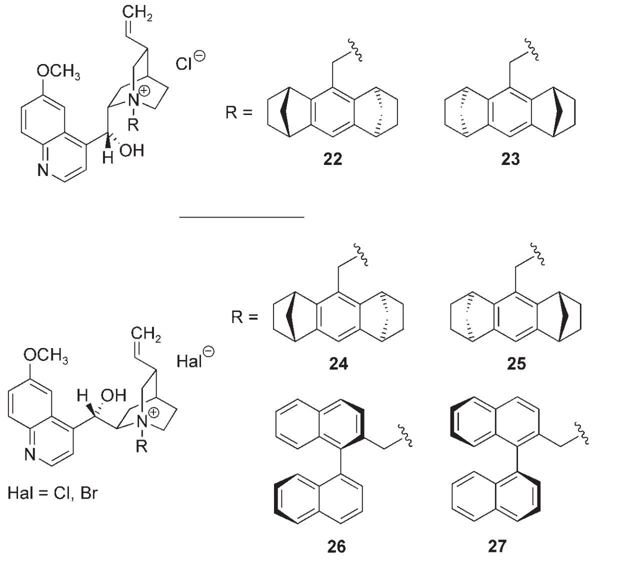
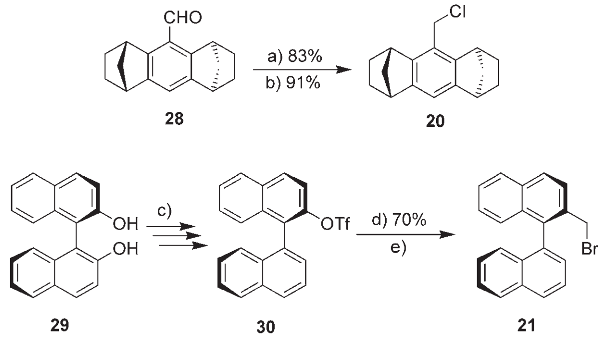


Figure 4. Structures of the novel phase-transfer catalysts **22**–**27**.

procedure by Katsuki et al. to convert (*R*)-BINOL **29** into triflate **30**.[29,30] Kumada coupling and radical bromination yielded the bromide **21**, which was used in the subsequent step without purification.[31] The bromide *ent*-**21** was synthesized analogously from (*S*)-BINOL.



Scheme 6. Synthesis of the halides **20** and **21**. a) $NaBH_4$, MeOH, 0°C, 3 h; b) PCl_5, toluene, RT, 16 h; c) $(CF_3SO_2)O$, Et_3N, CH_2Cl_2; H_2, Pd/C, Hünig base, EtOH; $(CF_3SO_2)O$, Et_3N, CH_2Cl_2;[29,30] d) MeMgCl, $[NiCl_2(PPh_3)_2]$, Et_2O, 0°C, 4 h; e) NBS, AIBN, CCl_4, reflux, 2 h.

Catalytic activity of the PTCs 22–27: With these catalysts in hand, we proceeded to evaluate their performance in the asymmetric epoxidation of vitamin K_3 (**7**). The results are summarized in Table 3.

In all cases, naphthoquinone **7** was epoxidised in good yields (up to 87%, see Table 3). The sense of stereoinduction is clearly dominated by the sense of chirality of the alkaloid moiety. Moderate enantioselectivities resulted from the use of both diastereomers of the quininium salts **22** and **23**. Clearly, **23** is the matched catalyst with a maximum of 54% *ee* (Table 3, entry 2), while the mismatched catalyst **22** yielded a mere 15% *ee* (Table 3, entry 1). Similarly pronounced effects were observed for the *N*-binaphthylmethyl

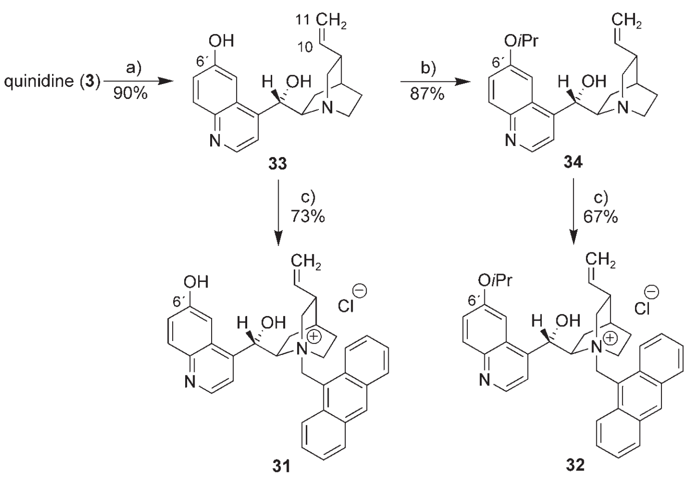
Table 3. Results for the asymmetric epoxidation of **7** with sodium hypochlorite as oxidant in chlorobenzene at −10 °C with 10 mol % of the catalysts **22**–**27**.

Entry	PTC	*t* [h]	Yield [%]	Epoxide	*ee* [%]
1	**22**	7	85	(2*R*,3*S*)	15
2	**23**	8	77 (86)[a]	(2*R*,3*S*)	54
3	**24**	8	87	(2*S*,3*R*)	76
4	**24**[b]	23	86	(2*S*,3*R*)	79
5	**25**	6	84	(2*S*,3*R*)	47
6	**26**[c]	22	83	(2*S*,3*R*)	40
7	**27**	7	85	(2*S*,3*R*)	71

[a] Conversion given in brackets. [b] 1 mol % of the catalyst was used. [c] Chloroform was used as solvent.

substituted quinidinium PTCs **26** and **27** (Table 3, entries 6 and 7): in the matched case (**27**), epoxide *ent*-**9** was obtained in 71 % *ee*, whereas its diastereomer PTC **26** generated *ent*-**9** with only 40 % *ee*. The best results were achieved with catalyst **24**. In the presence of only 1 mol % of this salt, enantioselectivities up to 79 % *ee* (Table 3, entries 3–4) were observed. In this case, the mismatched diastereomer **25** furnished the epoxide *ent*-**9** in good yield but with no more than 47 % *ee* (Table 3, entry 5).

Modifications at the C6′ atom: Another variation of the *cinchona*-alkaloid scaffold involves a modification of the ether at the C6′ position of the quinoline core. Two sets of quinidine-based PTCs were synthesized. In the first series, the PTCs maintained the "natural" double bond at C10,C11. In the second set, this position was hydrogenated. Exemplarily, the synthetic route leading to the non-hydrogenated quinidine based PTCs **31** and **32** is shown in Scheme 7. First, the methyl ether at C6′of quinidine (**3**) was cleaved to yield the phenol **33**. Further alkylation with 2-bromopropane gave the ether **34**. Subsequent quaternisation of **33** and **34** with 9-chloromethylanthracene gave salts **31** and **32** in 73 and 67 % yield, respectively.



Scheme 7. Synthetic route to the PTCs **31** and **32**. a) NaH, EtSH, DMF, 110 °C, 16 h; b) Cs_2CO_3, 2-bromopropane, DMF, 60 °C, 40 h; c) 9-chloromethylanthracene, THF, reflux, 16 h.

In analogy to the synthetic route above, the corresponding hydrogenated PTCs **10** and **35** (quinine-based) and **36** and **37** (quinidine-based) were prepared in 34–63 % overall yield (Figure 5).

Catalytic activity of PTCs 10, 31, 32 and 35–37: As summarized in Table 4, in the quinidine series (Table 4, entries 1–5), the literature known catalyst **12** (Scheme 4) with a methoxy group at the quinoline moiety (C6′) gave the best enantioselectivity of 72 % (Table 4, entry 1). Neither a free hydroxyl at C6′ (PTC **31**) nor a more bulky isopropyl substituent at this position (PTC **32**) could enhance the enantioselectivity (Table 4, entries 2 and 3).

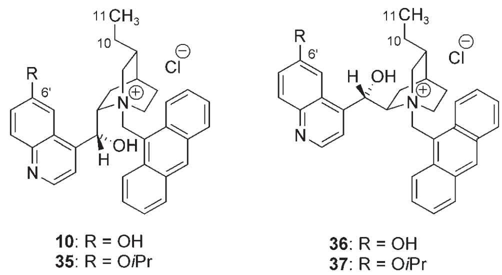


Figure 5. Structures of the catalysts **10** and **35**–**37**.

Table 4. Results for the asymmetric epoxidation of **7** with sodium hypochlorite as oxidant in chlorobenzene at −10 °C with the catalysts **10**, **12**, **31**, **32** and **35**–**37**.

Entry	PTC	mol %	*t* [h]	Yield [%]	Epoxide	*ee* [%]
1	**12**	10	8	92	(2*S*,3*R*)	72
2	**31**	5	18	89	(2*S*,3*R*)	56
3	**32**	10	2	88	(2*S*,3*R*)	59
4	**36**	2.5	28	74	(2*S*,3*R*)	67
5	**37**	10	1.5	93	(2*S*,3*R*)	60
6	**10**	2.5	25	73	(2*R*,3*S*)	85
7	**35**	10	8	89	(2*R*,3*S*)	59

Also in the case of the quinine scaffold, the effects of these modifications were studied. To our delight, PTC **10** bearing two free hydroxyl groups (C9 and C6′) and a hydrogenated double bond (C10,C11) afforded the highest enantioselectivity of 85 % *ee* with good yields (Table 4, entry 6). These values are the highest reported ever in the catalytic asymmetric epoxidation of vitamin K_3 (**7**). On the other hand, increasing the steric demand at the C6′ position by introduction of an isopropyl ether (PTC **35**), the enantioselectivity dropped to 59 % *ee* (Table 4, entry 7). Given these results, no PTCs with a sterically bulkier ether functionality at the C6′ atom of the quinoline were tested in this reaction.

Discussion

Our results show that the configuration of the major epoxide enantiomer obtained is not necessarily determined by the configuration at C8 and C9 of the alkaloid. As shown in Table 2 (entries 1 and 3), the etherification of the hydroxyl group at C9 led to a switch in the epoxide configuration.

We have presented herein that small variations at the scaffold of the *cinchona*-alkaloid PTCs may have dramatic effects on the enantioselectivity of the epoxidation. For instance, a free phenol functionality at C6′ of the quinoline core gave rise to remarkably increased enantioselectivity (**10**, 85 % *ee*; Table 4, entry 6).

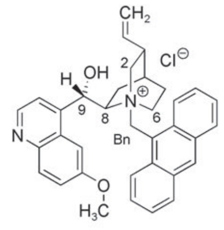
We applied Corey's approach to rationalise our observations.[32,33] Corey et al. presented a model aimed to determine the geometrical factors which are responsible for the enantioselectivity in the catalytic, asymmetric alkylation of glycine imine esters using *cinchona*-alkaloid based phase-transfer catalysts.[32]

In this approach, the nitrogen atom of the quinuclidine core is regarded as the centre of a tetrahedron. A highly enantioselective phase-transfer catalyst should be structured in a way to provide only one open tetrahedron face for interaction with the substrate. Due to the structure of the *cinchona*-alkaloids, one face is blocked by the quinuclidine ring system. In a quaternary ammonium salt (e.g. PTC **12**, Scheme 4) a second face is shielded by the 9-anthracenylmethyl moiety.[32–34] The configuration at C9 of the alkaloid determines the spatial arrangement of the quinoline moiety and this substituent blocks the third face of the tetrahedron. One face remains open for the catalyst–substrate interaction (in Figure 6, the face defined by C8, C2 and the benzylic C atom CBn).

It is assumed that the oxidation described herein is—mechanistically—an asymmetric version of the two-step Weitz–Scheffer epoxidation:[35] in this process, the first step is a reversible nucleophilic attack of the anionic oxidant (OCl^- in our case) at the Michael system to form the enolates **38** and *ent*-**38**, followed by an intramolecular nucleophilic substitution to yield the epoxides **9** and *ent*-**9** (Scheme 8). In the case of vitamin K_3 (**7**), the nucleophilic attack most likely occurs at C3, as C2 is sterically more hindered.[35]

Previous kinetic and mechanistic studies of the epoxidation of chalcone derivatives indicate a change in the rate-determining step depending on the electron density of the substrate.[36,37] Thus, for chalcones with electron-withdrawing groups attached at the β-position of the carbonyl group, the electron density at this carbon is reduced so that the attack of the oxidant (first step) is facilitated.[36,37] Likely, for electron-poor α,β-unsaturated ketones, such as vitamin K_3 (**7**), the formation of the racemic enolate **38** is fast and reversible, whereas in contrast the intramolecular ring closure to form the epoxide is assumed to determine the reaction rate (Scheme 8). In the presence of a chiral quaternary ammonium salt, one of the enolates **38** or *ent*-**38** (Scheme 8) presumably coordinates preferentially to the catalyst, impeding the reversal of the initial Michael addition, and allowing smooth formation of the epoxide.

To shed further light on our model, we carried out conformational analyses (Monte Carlo search) for the PTCs **10**–**12**,



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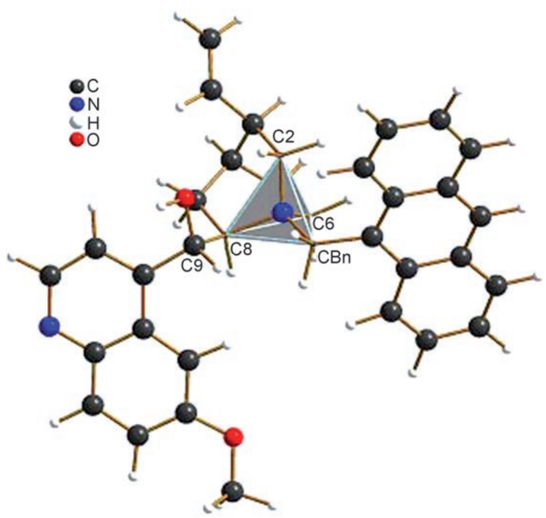
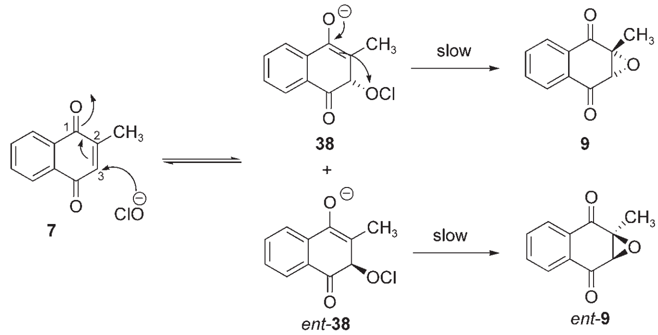


Figure 6. Structure of the PTC **12** (top) and the energy-minimized conformation of PTC **12** where the quinuclidine nitrogen atom is surrounded by a tetrahedron (bottom).



Scheme 8. Proposed mechanism of the Weitz–Scheffer epoxidation of vitamin K_3 (**7**).

14. Figures 7–10 show the minimum energy conformations of the two diastereomeric enolate–catalyst complexes for these PTCs; for better comparison the complexes with the lowest minimum energy are depicted on the top of each figure (**10a**–**12a**, **14a**). Binding of the enolate anion to the PTC cation involves i) Coulombic interaction (ion pairing); ii) hydrogen bonding between the proton of the hydroxy group at C9 of the PTC and the enolate oxygen atom (C1); and iii) π–π stacking of the anthracenyl moiety and the aromatic portion of the substrate enone. The energy values, the distances for ion pairing, hydrogen bonding and π–π stacking of the above complexes are summarized in Table 5.

Table 5. Energy values and distances for hydrogen bonding, ion pairing and π–π stacking.

Entry	PTC	Complex	E [kJ mol^{-1}]	Ion pairing [Å][a]	H Bonding (C9) [Å][b]	H Bonding (C6′) [Å][c]	π–π stacking [Å][d]
1	**12**	**12a**	546.94	4.286	1.852	–	3.778
2		**12b**	550.49	4.408	1.832	–	–
3	**11**	**11a**	545.42	4.270	1.853	–	3.578
4		**11b**	546.52	4.200	1.834	–	–
5	**14**	**14a**	640.99	4.295	–	–	3.668
6		**14b**	645.74	4.306	–	–	–
7	**10**	**10a**	372.78	4.299	1.846	1.706	3.576
8		**10b**	379.10	4.203	1.876	1.734	–

[a] Distance between the quaternary nitrogen at the quinuclidine ring and the oxygen of the enolate. [b] Distance between the alcoholic proton at C9 and the oxygen of the enolate. [c] Distance between the phenolic proton at C6′ and the oxygen of the enolate. [d] Shortest distance between an aromatic carbon atom of the substrate and a carbon atom of the anthracenyl moiety.

The resulting minimum energy conformations of PTC **12** are shown in Figure 7. As expected, both chiral enolates are arranged such that the negative charge at the oxygen atom at C1 of the substrate is stabilized by a contact ion pair with the nitrogen cation of the catalyst and by hydrogen bonding with the secondary alcohol. The aromatic part of the substrate can undergo further stabilization by π–π interaction with the anthracenyl moiety of the catalyst in the case of complex **12a** (Table 5, entries 1 and 2). The latter interactions explains the lower energy for complex **12a** (catalyst **12** coordinating to enolate *ent*-**38**) in comparison to complex **12b** (ion pair of the catalyst **12** with enolate **38**).

In Figure 8, the minimum energy conformations for the catalyst–enolate complexes of the PTC **11** are shown. Also in this case, the complex showing π–π stacking (**11a**) between catalyst and substrate has lower energy (Table 5, entry 3). This spatial arrangement leads to the epoxide enantiomer mainly observed experimentally.

For the pseudo-enantiomeric catalyst–enolate complexes **11a** (Figure 8, quinine-based) and **12a** (Figure 7, quinidine-based) it is shown that in both cases the most readily accessible tetrahedron face (C6-Bn-C8 for **11a** and C2-Bn-C8 for **12a**) is responsible for the enolate coordination. The tetrahedron face blocked by the quinoline moiety varies, depending on the catalyst scaffold, that is, (9*R*) or (9*S*). This leads to a different orientation of the enolates. In all cases, the configuration of the calculated catalyst–enolate complexes with the lowest minimum energy corresponds—without exception—to the configuration of the major epoxide enantiomer obtained experimentally. The above situation is the result of the "enantiomorphism" of the catalysts **11** and **12** around the reaction centre. Overall, they are of course pseudo-enantiomeric (diastereomeric) due to the presence of the vinyl group at the "remote" carbon atom C3. In analogy, it is clear that the (2*S*,3*R*)-epoxide configuration (Table 2, entry 6) obtained with PTC **16** (Figure 3, *epi*-quinine based) arises from the inverted configuration at C9.

Further minimized energy conformational analyses were carried out for the 9-*O*-benzylated quinidine based catalyst **14**. Due to the catalyst structure, hydrogen bonding between the catalyst and the enolate is not possible (Figure 9, Table 5, entries 5 and 6). In this case, only the ion pairing and the π–π-stacking interaction can occur. We assume that the π–π-stacking interaction in complex **14a** is again responsible for the more stable coordination and the lower energy. As shown in Figure 9, in complex **14a** the benzyl group occupies the tetrahedral face which usually accommodates the enolate. Therefore, the coordination has to take place at another tetrahedral face. The accessible site is now defined by C8, C-Bn and C6 (Figure 9, **14a** bottom). It is the same as for the pseudo-enantiomeric non-benzylated quinine catalyst **11** (Figure 8). As a result, the configuration of the major epoxide enantiomer changes. This is in accordance with the experimental results (Table 2, entry 4).

Conformational analysis of the two possible diastereomeric enolate–catalyst complexes was performed for catalyst **10** as well, and they are shown in Figure 10. This conformation suggests a further stabilizing hydrogen-bonding interaction between the phenolic proton and the carbonyl oxygen atom (C4) of the substrate (Table 5, entries 7 and 8). This additional stabilizing element in combination with the π–π-stacking present in complex **10a** could explain the excellent enantioselectivities observed using this catalyst.

Conclusion

Our study revealed the following novel aspects of the asymmetric phase-transfer catalyzed epoxidation:

i) To the best of our knowledge, aqueous sodium hypochlorite was not used before for the epoxidation of quinones. In our hands, this oxidant gave good yields and superior enantioselectivities in the epoxidation of vitamin K_3 (**7**).

ii) A number of differently modified quinine and quinidine phase-transfer catalysts were synthesized and were found to be highly effective in the epoxidation of the quinone **7**. The best results were achieved with the readily available ammonium salt **10**, carrying a hydroxyl group at the C6′ atom of the quinoline system. This catalyst afforded the highest enantioselectivity (85 % *ee* at 73 % yield for epoxide **9**) ever reported for the asymmetric epoxidation of **7**.

iii) In the mechanistic analysis presented, we successfully adopted Corey's approach, providing a rational explanation for the stereochemical course of the epoxidation observed for different catalysts.

In summary, we reported a comprehensive study of novel and established *cinchona*-based PTCs for the asymmetric epoxidation of enones, exemplified by vitamin K_3 (**7**). This

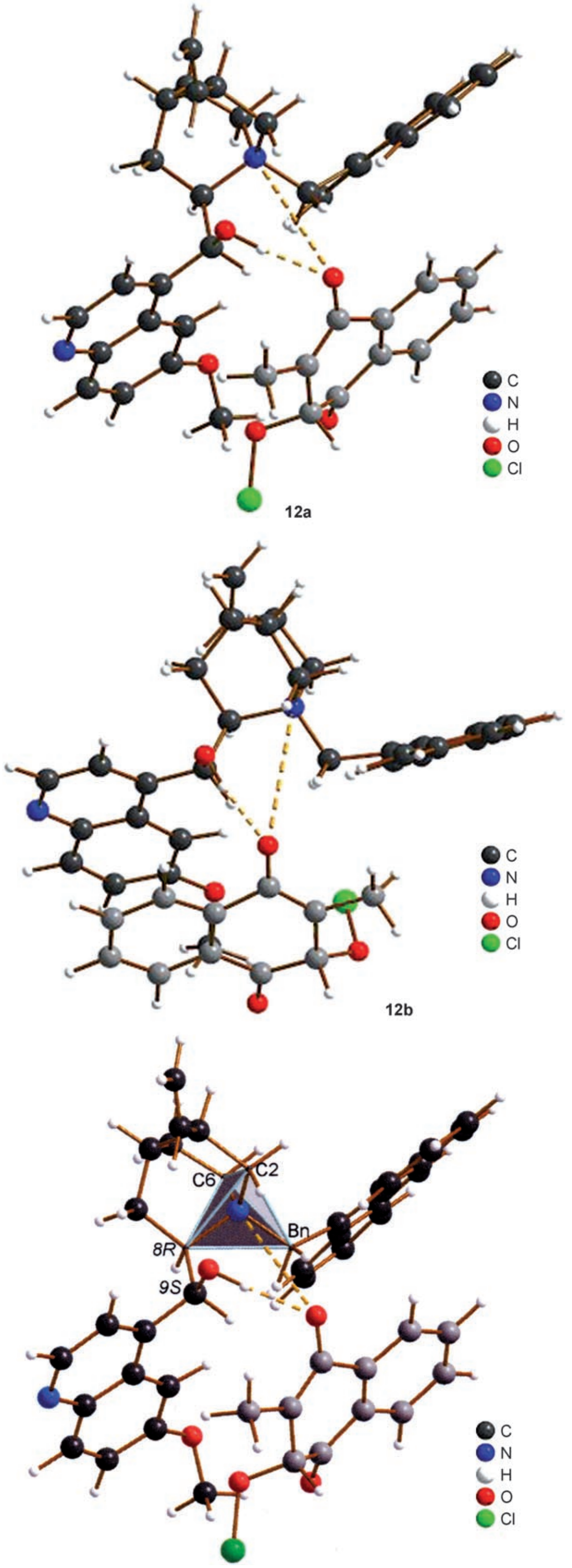


Figure 7. Top, middle: View of the diastereomeric enolate–catalyst complexes for the PTC **12**. Bottom: Illustration of the tetrahedron face (C2, CBn and C8) in complex **12a**. For the sake of clarity, the substrate C atoms are shown in light grey.

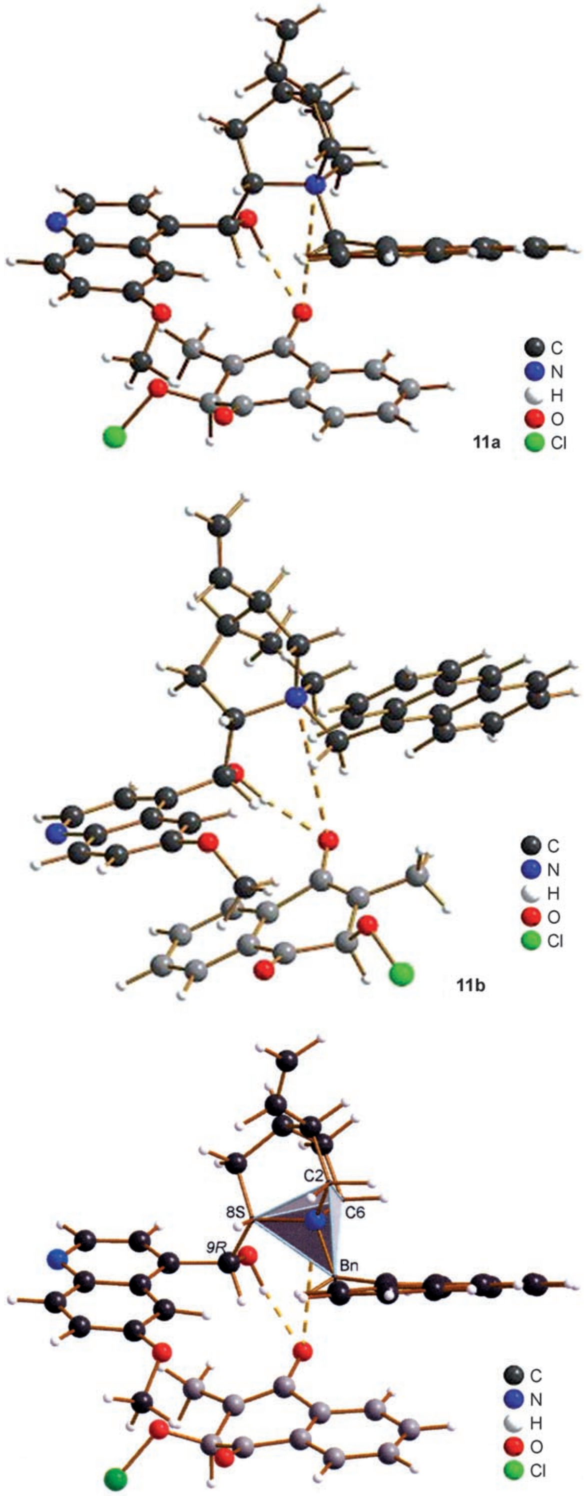


Figure 8. Top, middle: View of the diastereomeric enolate–catalyst complexes for the PTC **11**. Bottom: Illustration of the tetrahedron face (C6, CBn and C8) in complex **11a**. For the sake of clarity, the substrate C atoms are shown in light grey.

study led to the identification of the most selective catalyst for epoxidation of the quinone **7** known to date.

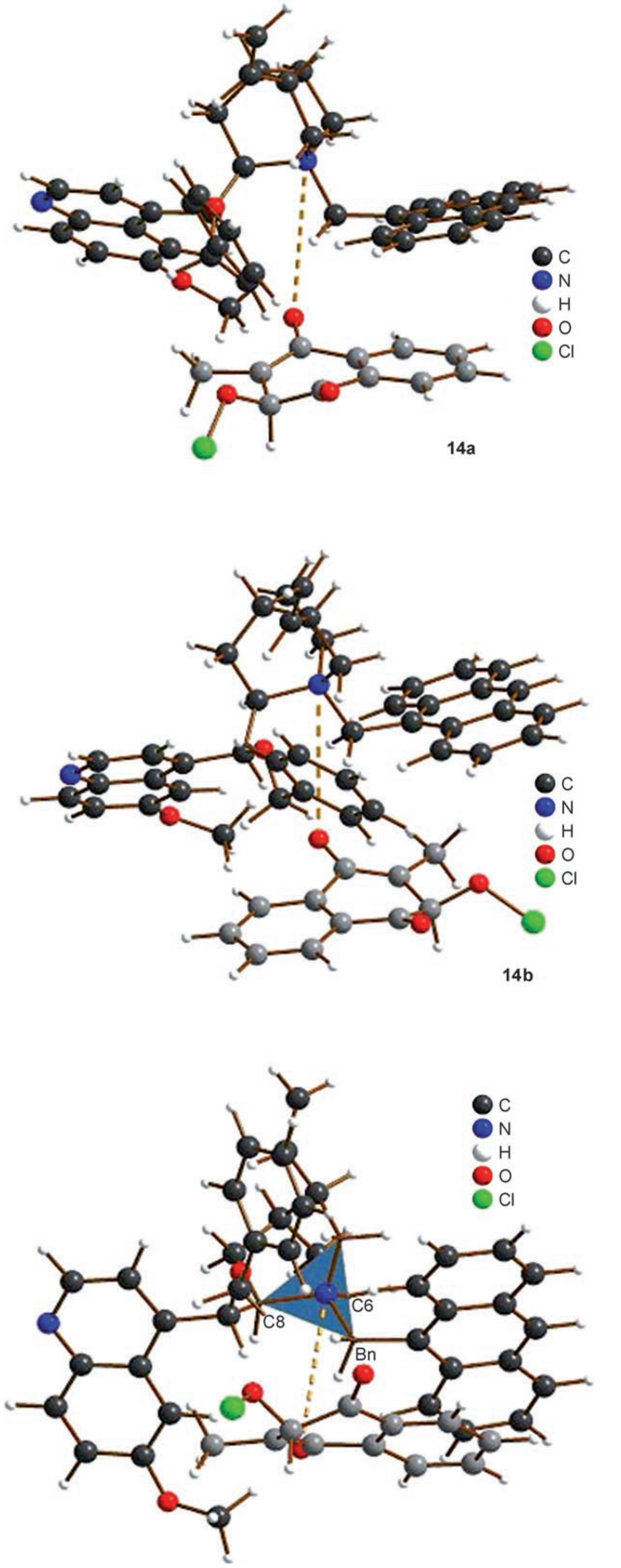


Figure 9. Top, middle: View of the diastereomeric enolate–catalyst complexes for the 9-*O*-benzylated ammonium salt **14**. Bottom: Illustration of the tetrahedron face (C6, C8 and CBn) in complex **14a**. For the sake of clarity, the substrate C atoms are shown in light grey.

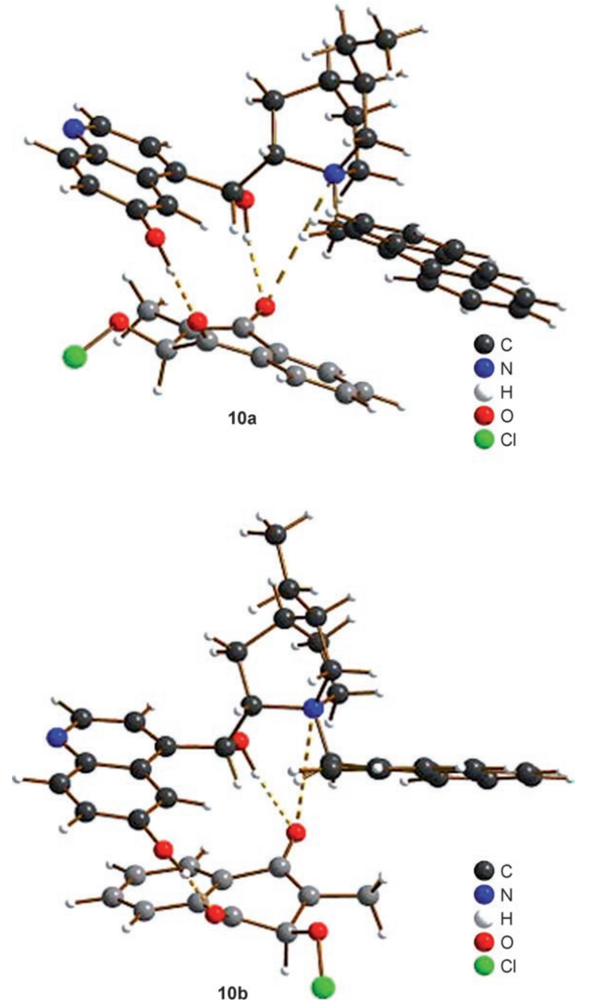


Figure 10. View of the diastereomeric enolate–catalyst complex for catalyst **10**. For the sake of clarity, the substrate C atoms are shown in light grey.

Experimental Section

General procedures: Flash chromatography was performed on silica gel (Macherey–Nagel MN-Kieselgel 60, 230–240 mesh). TLC was performed on aluminium-backed silica plates (Macherey–Nagel, Polygram SIL G/UV_{254}), which were developed by using UV fluorescence. Melting points were determined on a Büchi melting point apparatus and are uncorrected. Elemental analysis was performed on an Elementar Vario EL CHN analyzer. Infrared spectra were recorded on a Perkin–Elmer Paragon 1000 FT-IR spectrometer using the ATR technique and on a Perkin–Elmer 1600 Series FT-IR spectrometer. ^{1}H NMR spectra were recorded at 300 MHz on Bruker AC 300 and DPX 300 instruments, respectively; ^{13}C NMR spectra at 75.5 MHz. Chemical shifts (δ) are given in parts per million (ppm) referenced to TMS. Low resolution mass spectra (m/z) were recorded on an Agilent 1100 spectrometer with only molecular ions [M^+] reported. High resolution mass spectra (ESI) were recorded on a Finnigan MAT 900 ST spectrometer. Optical rotations were measured on a Perkin–Elmer 343plus polarimeter, concentrations (c) are given in g per 100 mL of solution. *ee* Values were determined by chiral GC on a Chirasil-Dex CB column (Hewlett–Packard 5890 Series II chromatograph). All commercially available chemicals were used without further purification. Anhydrous solvents were distilled from appropriate drying agents prior to use.

General procedure for the quaternisation of tertiary amines

Under an argon atmosphere, the benzyl halide (1.10 equiv) was added to a highly concentrated solution of the amine (1.00 equiv) in dry THF. The reaction mixture was heated under reflux until TLC analysis showed the complete consumption of the amine.

Work-up A: The yellow precipitate was filtered off and purified—if necessary—by flash chromatography ($CHCl_3$/MeOH 9:1) or recrystallization.

Work-up B: The solvent was removed under reduced pressure and the residue purified by flash chromatography ($CHCl_3$/MeOH 9:1).

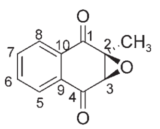
General procedure for the alkylation of phenols

Cesium carbonate (2.50 equiv) was added to a stirred solution of the alkaloid (1.00 equiv) in dry DMF (0.02 M) and stirred at RT for 10 min. The bromoalkane (2.00 equiv) was added, and the reaction mixture was stirred for 40 h at 60 °C. The solvent was removed under reduced pressure and the resulting solid was purified by flash chromatography ($CHCl_3$/MeOH 9:1). The desired product was obtained as a solid.

General procedure for the catalytic asymmetric epoxidation of 2-methyl-1,4-naphthoquinone (7) under phase-transfer-catalyzed conditions

A stock solution 0.15 M of **7** (258 mg, 1.50 mmol) and diphenyl ether (255 mg, 238 μL, 1.50 mmol, internal standard) in chlorobenzene (10 mL) was prepared. A 10 mL round bottomed flask was cooled to −10 °C and charged with the stock solution of **7** (1.5 mL, 38.7 mg, 225 μmol, 1.00 equiv) and diphenyl ether (38.3 mg, 35.7 μL, 225 μmol; internal standard). The phase-transfer catalyst (10 to 1 mol %) was added and the reaction was initiated by addition of 13 % aqueous sodium hypochlorite (500 μL, 1.09 mmol, 4.85 equiv). The mixture was vigorously stirred at −10 °C for 4 to 24 h. Samples (150 μL) of the organic layer were withdrawn periodically, diluted with toluene (1.00 mL), and added to saturated aqueous sodium thiosulfate (150 μL). The organic phase was analyzed by chiral GC (GC column: CP-Chiralsil-Dex CB, nitrogen 1.2 mL min^{-1} (constant flow modus), injector 180 °C (split modus), detector (FID) 180 °C, oven: 145 °C (20 min), 10 °C min^{-1} 160 °C (3 min)).

The retention time (τ_R) for **7** was 15.9 min, for (2*R*,3*S*)-2,3-epoxy-2-methyl-1,4-naphthoquinone (**9**) 18.2 min, for (2*S*,3*R*)-2,3-epoxy-2-methyl-1,4-naphthoquinone (*ent*-**9**) 17.1 min and for diphenyl ether 8.79 min.



ent-**9**

***ent*-9**: After epoxidation of **7** with catalyst **12** under the conditions described above, and work up, epoxide *ent*-**9** was recrystallized from ethanol and obtained in 98 % *ee*. R_f = 0.70 (hexane/ethyl acetate 5:1); m.p. 126–127 °C (ethanol) (lit:[39] 96–97 °C); $[\alpha]^{20}_{405}$ = 356 (*c* = 0.96 in chloroform, 98 % *ee*); CD: λ_{max} = 360 nm, $\Delta\varepsilon$ = +0.84 (*c* = 5.44×10^{-3} M, $CHCl_3$, 98 % *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.71 (s, 3H; CH_3), 3.83 (s, 1H; H-C3), 7.70–7.73 (m, 2H; H-C6, C7), 7.91–7.97 ppm (m, 2H; H-C5, C8); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 14.7 (CH_3), 61.3 (C3), 61.4 (C2), 126.8 (C5), 127.4 (C8), 131.9 (C9), 132.1 (C10), 134.3 (C6), 134.5 (C7), 191.8 (C=O), 191.9 ppm (C=O); IR (ATR): $\tilde{\nu}$ = 3037, 3001, 1695, 1591, 1402, 1335, 1295, 1249, 1193, 1169, 1048, 949, 853, 748, 721, 701, 629 cm^{-1}; GC-MS (capillary column HP-5MS 0.25 mm × 30 m, cross-linked 5 % PH ME siloxane 0.25 μm; He, 1 mL^{-1}; 100 °C, 5 min, 20 °C min^{-1}, 200 °C, 15 min, 20 °C min^{-1}, 280 °C, 10 min); τ_R = 10.36 min, *m*/*z*: 188, 173, 160, 131, 105, 89, 76; elemental analysis calcd (%) for $C_{11}H_8O_3$ (188.2): C 70.21, H 4.29; found: C 70.10, H 4.27.

CCDC-609372 contains the supplementary crystallographic data for compound *ent*-**9**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

The analytical data were identical with those reported.[16,39]

1-*N*-(9-Anthrylmethyl)-6′-hydroxy-10,11-dihydrocinchonidinium chloride (10): By following the general procedure for the quaternisation of tertiary amines, **10** was obtained from 6′-hydroxy-10,11-dihydrocinchonidine (**40**) (584 mg, 1.65 mmol) using work-up A as a yellow solid (665 mg, 75 %); recrystallized from dichloromethane/*n*-hexane. R_f = 0.45 (dichloromethane/methanol 9:1); m.p. > 195 °C (decomp); $[\alpha]^{20}_D$ = −413 (*c* = 1.00 in methanol); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.54 (t, *J* = 7.3 Hz, 3H; H-C11), 0.87–1.32 (m, 5H; H-C7, C3, C6, C10), 1.58–1.83 (m, 3H; H-C7, C4, C6), 2.03–2.19 (m, 1H; H-C5), 2.74–2.60 (m, 1H; H-C2), 3.36–3.45 (m, 1H; H-C2), 4.35–4.62 (m, 2H; H-C8, C5), 6.23 (d, *J* = 13.4 Hz, 1H; H-CH_2An), 6.37 (d, *J* = 13.4 Hz, 1H; H-CH_2An), 6.63–6.78 (m, 2H; H-C7′, H-C9), 6.88–6.99 (m, 1H; H-Caryl), 6.99–7.11 (m, 1H; H-Caryl), 7.20–7.29 (m, 1H; H-Caryl), 7.31–7.48 (m, 4H; H-Caryl), 7.56–7.65 (m, 1H; H-Caryl), 7.78–7.85 (m, 1H; H-C3′), 7.85–7.93 (m, 1H; OH), 8.04–8.15 (m, 1H; H-C5′), 8.25–8.38 (m, 1H; H-Caryl), 8.66–8.75 (m, 1H; H-C2′), 8.86–8.96 (m, 1H; H-Caryl), 9.15–9.31 ppm (m, 1H; OH); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 11.4 (C11), 22.6 (C7), 23.0 (C4), 26.0 (C6), 26.8 (C10), 37.0 (C3), 50.4 (C5), 54.5 (CH_2An), 64.9 (C2), 66.8 (C8), 66.8 (C9), 77.20 (Caryl), 102.9 (C5′), 116.9 (C3′), 120.5 (C7′), 124.2, 124.4, 124.5, 124.9, 126.2, 127.3, 127.7, 128.5, 128.5, 129.9, 130.3 (all Caryl), 131.0 (C8′), 131.2, 132.5), 132.6 (3 Caryl), 141.7 (C4′), 142.1 (C9′), 146.5 (C2′), 155.1 ppm (C6′); IR (ATR): $\tilde{\nu}$ = 3132, 2956, 1618, 1526, 1464, 1448, 1395, 1283, 1258, 1237, 1223, 1129, 1061, 1047, 1011, 913, 895, 859, 831, 791, 743, 705, 663, 625 cm^{-1}; HR-MS (ESI, Δm = 0.005): *m*/*z*: calcd for $C_{34}H_{35}ClN_2O_2$: 591.3011, found: 591.301 [M^+]; elemental analysis calcd (%) for $C_{35}H_{35}ClN_2O_2\cdot H_2O$ (557.12): C 73.30, H 6.69, N 5.03; found: C 73.55, H 7.01, N 4.85.

CCDC-609363 contains the supplementary crystallographic data for compound **10**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

1-*N*-(9-Anthrylmethyl)-9-*O*-benzylquininium chloride (13): By following the general procedure for the quaternisation of tertiary amines, **13** was obtained from 9-*O*-benzylquinine (**19**)[22] (953 mg, 2.30 mmol) using work-up A as a yellow solid (855 mg, 58 %). M.p. 121–122 °C; $[\alpha]^{20}_D$ = −297 (*c* = 1.00 in chloroform); ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 1.51–1.58 (m, 2H; H-C5, C7), 1.87 (brs, 1H; H-C4), 1.95–1.98 (m, 1H; H-C5), 2.33–2.38 (m, 1H; H-C3), 2.42–2.47 (m, 1H; H-C7), 2.70–2.79 (m, 1H; H-C6), 2.98–3.05 (m, 1H; H-C2), 3.95–4.01 (m, 1H; H-C2), 4.06 (s, 3H; OCH_3), 4.15–4.18 (m, 1H; H-C6), 4.75–4.79 (d, *J* = 11.0 Hz, 2H; H-CH_2Ph, C8), 4.92–4.97 (m, 2H; H-C11), 5.21–5.25 (d, *J* = 11.1 Hz, 1H; H-CH_2Ph), 5.63–5.77 (m, 2H; H-C10, H-CH_2An), 6.92–6.96 (d, *J* = 12.1 Hz, 1H; H-CH_2An), 7.44–7.77 (m, 11H; H-C9, Caryl), 7.86–7.88 (m, 2H; H-Caryl), 8.09–8.12 (d, *J* = 9.2 Hz, 1H; H-Caryl), 8.25–8.28 (m, 2H; H-Caryl), 8.51–8.54 (d, *J* = 8.2 Hz, 1H; H-Caryl), 8.92–8.98 ppm (m, 3H; H-Caryl); ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 20.7 (C5), 24.5 (C7), 25.2 (C4), 37.1 (C3), 51.8 (C6), 55.3 (OCH_3), 56.0 (CH_2An), 59.5 (C2), 68.1 (C8), 70.5 (CH_2Ph), 73.0 (C9), 102.9 (C5′), 116.5 (C11), 118.5, 120.1, 121.9, 124.5, 125.5, 125.3, 126.2, 127.0 (all Caryl), 127.6 (2 Caryl), 127.7 (2 Caryl), 128.0, 128.6, 128.6, 129.4, 129.5, 130.9, 131.0, 131.1, 132.0, 132.6, 133.1, 137.3 (all Caryl), 137.6 (C10), 139.5, 144.2 (2 Caryl), 147.3 (C2′), 157.3 ppm (C6′); IR (ATR): $\tilde{\nu}$ = 3368, 2931, 1721, 1619, 1586, 1506, 1472, 1451, 1353, 1260, 1239, 1066, 1024, 862, 826, 738, 721, 700 cm^{-1}; HR-MS (ESI, Δm = 0.005): *m*/*z*: calcd for $C_{42}H_{41}N_2O_2$: 605.3168, found: 605.317 [M^+]; elemental analysis calcd (%) for $C_{42}H_{41}ClN_2O_2.H_2O$ (659.3): C 76.52, H 6.57, N 4.25; found: C 76.67, H 6.46, N 4.13.

1-*N*-(9-Anthrylmethyl)-9-*O*-benzylquinidinium chloride (14): By following the general procedure for the quaternisation of tertiary amines, **14** was obtained from 9-*O*-benzylquinidine[22] (829 mg, 2.00 mmol) using work-up B as a yellow solid (520 mg, 41 %). R_f = 0.37 (ethyl acetate/methanol/triethylamine 8:2:0.02); m.p. 126–127 °C; $[\alpha]^{20}_D$ = 253 (*c* = 0.99 in chloroform); ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 1.25–1.27 (m, 1H; H-C7), 1.51–1.57 (m, 1H; H-C5), 1.68–1.71 (m, 1H; H-C5), 1.82 (brs, 1H; H-C4), 2.27–2.32 (m, 1H; H-C3), 2.57–3.08 (m, 2H; H-C7, C6), 3.02–3.08 (m, 1H; H-C2), 4.15–4.25 (m, 4H; H-C2, OCH_3), 4.50–4.56 (m, 1H; H-C6), 4.70–5.15 (m, 5H; H-C8, H-CH_2Ph, C11), 5.85–5.96 (m, 2H; H-C10, H-CH_2An), 6.28–6.32 (d, *J* = 13.8 Hz, 1H; H-CH_2An), 7.15–7.20 (m, 1H; H-Caryl), 7.33–7.34 (m, 1H; H-C9), 7.53–7.79 (m, 9H; H-Caryl), 7.91–8.10 (m, 4H; H-Caryl), 8.23–8.28 (m, 2H; H-Caryl), 8.93–9.01 ppm (m, 3H; H-Caryl); ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 20.7 (C7), 23.4 (C5), 25.6 (C4), 36.7 (C3), 55.1 (C2), 55.6 (CH_2Ph), 55.6 (OCH_3), 55.9 (C6), 66.6 (C8), 70.3 (CH_2Ph), 73.5 (C9), 102.9 (C5′), 116.6 (C11), 118.5, 120.3, 122.2, 123.8, 124.9, 125.2, 125.5, 126.4, 127.1, 127.7, 128.0, 128.3 (all

Caryl), 128.7 (2 Caryl), 128.7 (2 Caryl), 129.6, 129.8, 131.0, 131.1, 132.0, 132.7, 133.0 (all Caryl), 137.1 (C10), 137.3, 138.7, 144.2 (3 Caryl), 147.4 (C2′), 157.5 ppm (C6′); IR (ATR): $\tilde{\nu}$ = 2929, 2920, 1619, 1585, 1505, 1454, 1352, 1240, 1130, 1025, 925, 868, 744, 699 cm^{-1}; HR-MS (ESI, Δm = 0.005): m/z: calcd for $C_{42}H_{41}N_2O_2$: 605.3168, found: 605.318 [M^+]; elemental analysis calcd (%) for $C_{42}H_{41}ClN_2O_2{\cdot}H_2O$ (659.3): C 76.52, H 6.57, N 4.25; found: C 76.42, H 6.03, N 4.16.

(3*S*)-1-*N*-(9-Anthrylmethyl)-10,11-dihydro-3,9-epoxy-6′-hydroxycinchonium chloride (15): By following the general procedure for the quaternisation of tertiary amines, **15** was prepared from β-isocupreidine[24] (404 mg, 1.30 mmol) using work-up A as a yellow solid (500 mg, 72 %). R_f = 0.08 (chloroform/methanol 9:1); m.p. > 200 °C (decomp); $[\alpha]_D^{20}$ = −25.6 (c = 1.00 in methanol); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.74 (t, J = 7.3 Hz, 3 H; H-C11), 0.99–1.17 (m, 1 H; H-C5), 1.21–1.51 (m, 2 H; H-C10), 1.58–1.74 (m, 1 H; H-C5), 1.89–2.00 (d, J = 12.8 Hz, 1 H; H-C2), 2.15–2.42 (m, 3 H; H-C4, C7), 2.76–2.92 (m, 1 H; H-C6), 3.99 (d, J = 12.7 Hz, 1 H; H-C2), 4.65–4.86 (m, 1 H; H-C6), 5.39 (m, 1 H; H-C8), 5.93–6.03 (m, 1 H; H-Caryl), 6.27 (dd, J = 2.1, 9.1 Hz, 1 H; H-C7′), 6.36 (d, J = 14.3 Hz, 1 H; H-CH_2An), 6.47 (s, 1 H; H-C9), 6.66–6.75 (m, 1 H; H-Caryl), 6.92 (d, J = 14.3 Hz, 1 H; H-CH_2An), 7.43–7.49 (m, 1 H; H-Caryl), 7.50–7.57 (m, 1 H; H-Caryl), 7.62 (d, J = 9.1 Hz, 1 H; H-C8′), 7.66 (d, J = 4.5 Hz, 1 H; H-C3′), 7.70–7.79 (m, 1 H; H-Caryl), 7.92 (d, J = 2.2 Hz, 1 H; H-C5′), 7.97–8.04 (m, 1 H; H-Caryl), 8.22–8.31 (m, 2 H; H-C10″, Caryl), 8.77 (d, J = 4.5 Hz, 1 H; H-C2′), 8.81–8.89 (m, 1 H; H-Caryl), 10.88 ppm (br s, 1 H; OH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 6.70 (C11), 22.8 (C5), 23.1 (C7), 26.5 (C10), 32.0 (C4), 53.5 (C6), 55.8 (CH_2An), 60.9 (C2), 70.2 (C8), 71.2 (C9), 75.7 (C3), 102.4 (C5′), 118.2 (Caryl), 119.4 (C3′), 121.9 (C7′), 124.4, 124.7, 124.8, 125.4, 126.0, 126.9, 127.6, 127.9, 129.3, 130.7, 131.1 (all Caryl), 131.3 (C10″), 132.1 (C8′), 132.5, 133.1, 138.5, 142.9 (4 Caryl), 145.7 (C2′), 158.8 ppm (C6′); IR (ATR): $\tilde{\nu}$ = 2968, 1669, 1617, 1591, 1525, 1509, 1463, 1446, 1396, 1353, 1331, 1282, 1228, 1146, 1098, 1074, 1041, 1014, 981, 937, 924, 903, 892, 853, 830, 792, 746, 704, 661, 616 cm^{-1}; HR-MS (ESI, Δm = 0.005): m/z: calcd for $C_{34}H_{33}ClN_2O_2$: 501.254, found: 501.255 [M^+].

1-*N*-(9-Anthrylmethyl)-9*S*-*epi*-quininium chloride (16): By following the general procedure for the quaternisation of tertiary amines, **16** was obtained from 9*S*-*epi*-quinine[25] (811 mg, 2.50 mmol) using work-up A as a yellow solid (897 mg, 66 %); recrystallized from acetone. M.p. > 145 °C (decomp); $[\alpha]_D^{20}$ = −63.5 (c = 1.00 in chloroform); ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 1.09–1.14 (m, 1 H; H-C7), 1.78–1.84 (m, 3 H; H-C5, C4, C7), 2.08–2.11 (m, 1 H; H-C5), 2.32–2.35 (m, 1 H; H-C3), 2.92–2.98 (m, 1 H; H-C6), 3.14–3.22 (m, 1 H; H-C2), 3.81–3.88 (m, 1 H; H-C2), 4.01 (s, 3 H; OCH_3), 4.68–4.76 (m, 1 H; H-C6), 4.96–5.03 (m, 2 H; H-C11), 5.33–5.39 (m, 1 H; H-C8), 5.64–5.75 (ddd, J = 6.6, 10.5, 17.2 Hz, 1 H; H-C10), 5.86–5.91 (d, J = 14.4 Hz, 1 H; H-CH_2An), 6.23–6.28 (m, 1 H; H-C9), 6.98–7.02 (d, J = 14.4 Hz, 1 H; H-CH_2An), 7.48–7.52 (dd, J = 2.6, 9.2 Hz, 1 H; H-Caryl), 7.59–7.67 (m, 2 H; H-C7′, Caryl), 7.74–7.79 (m, 2 H; H-Caryl), 7.86–7.88 (d, J = 5.3 Hz, 1 H; OH), 7.92–7.94 (d, J = 4.5 Hz, 1 H; H-C3′), 8.02–8.07 (m, 2 H; H-C5′, Caryl), 8.22–8.25 (m, 2 H; H-C8′, Caryl), 8.86–8.95 ppm (m, 4 H; H-C2′, Caryl); ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 25.2 (C5), 25.9 (C4), 26.1 (C7), 37.5 (C3), 49.7 (C6), 60.0 (OCH_3), 59.3 (CH_2An), 59.7 (C2), 70.2 (C8), 71.2 (C9), 104.1 (C5′), 117.6 (C11), 120.8 (Caryl), 121.8 (C3′), 125.6, 125.9, 126.1, 126.2, 126.3, 128.1, 128.5, 128.7, 130.4, 130.5, 131.9, 132.0, 132.3, 132.7, 133.9, 134.2 (all Caryl), 137.9 (C10), 145.3, 145.7, 148.6 (3 Caryl), 158.6 ppm (C6′); IR (ATR): $\tilde{\nu}$ = 3051, 2954, 1722, 1619, 1588, 1506, 1474, 1446, 1359, 1257, 1223, 1126, 1026, 873, 745, 717 cm^{-1}; HR-MS (ESI, Δm = 0.005): m/z: calcd for $C_{35}H_{35}N_2O_2$: 515.2698, found: 515.270 [M^+]; elemental analysis calcd (%) for $C_{35}H_{35}ClN_2O_2{\cdot}H_2O$ (569.1): C 73.86, H 6.55, N 4.92; found: C 73.58, H 6.61, N 4.41.

CCDC-609364 contains the supplementary crystallographic data for compound **16**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

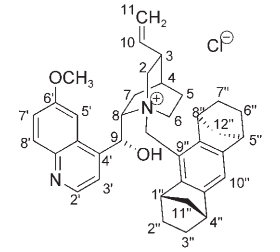
1-*N*-(9-Anthrylmethyl)-9-*O*-benzyl-6′-hydroxycinchonidinium chloride (17): By following the general procedure for the quaternisation of tertiary amines, **17** was obtained from 9-*O*-benzyl-6′-hydroxychinchonidine (**18**)[23] (1.00 g, 2.50 mmol) using work-up B as a yellow solid (713 mg, 46 %); recrystallized from acetone. R_f = 0.48 (chloroform/methanol 9:1); m.p. > 147 °C (decomp); $[\alpha]_D^{20}$ = −345 (c = 0.50 in chloroform); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.11–1.39 (m, 2 H; H-C3, H-C7), 1.72–1.94 (m, 2 H; H-C3, H-C4), 1.95–2.13 (m, 1 H; H-C7), 2.15–2.29 (m, 1 H; H-C5), 2.29–2.54 (m, 1 H; H-C8), 2.77–2.93 (m, 1 H; H-C6), 4.37–4.52 (m, 1 H; H-C8), 4.52–4.64 (m, 1 H; H-C6), 4.81–5.01 (m, 2 H; H-C2, H-C11), 5.12 (d, J = 12.6 Hz, 1 H; H-CH_2Ph), 5.24 (d, J = 16.7 Hz, 1 H; H-C11), 5.37 (d, J = 12.6 Hz, 1 H; H-CH_2Ph), 5.46–5.68 (m, 1 H; H-C10), 6.05 (d, J = 13.7 Hz, 1 H; H-CH_2An), 6.59–6.77 (m, 2 H; H-CH_2An, H-Caryl), 6.88 (d, J = 2.5 Hz, 1 H; H-C9), 6.97–7.21 (m, 3 H; H-Caryl), 7.25–7.37 (m, 2 H; H-Caryl), 7.41–7.60 (m, 4 H; H-Caryl), 7.60–7.76 (m, 3 H; H-Caryl), 7.77–8.03 (m, 3 H; H-Caryl), 8.26 (s, 1 H; OH), 8.65 (d, J = 2.2 Hz, 1 H; H-C5′), 8.69 (d, J = 4.5 Hz, 1 H; H-C2′), 9.34 ppm (d, J = 8.9 Hz, 1 H; H-C8′); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 23.3 (C7), 25.5 (C5), 25.8 (C4), 38.1 (C3), 50.5 (C6), 55.6 (CH_2An), 61.9 (C2), 66.0 (C8), 70.8 (CH_2Ph), 76.6 (C9), 105.5 (C5′), 117.8 (C11), 118.0, 118.2, 122.7, 123.4, 124.7, 125.2, 126.0 (all Caryl), 126.3 (2 Caryl), 126.7, 127.3, 127.8, 128.2, 128.4 (all Caryl), 129.0 (2 Caryl), 129.6, 130.6, 130.8, 130.9, 131.8 (all Caryl), 133.2 (Caryl), 136.2 (C9), 137.0, 137.6, 143.6 (4 Caryl), 145.8 (C2′), 157.2 ppm (C6′); IR (ATR): $\tilde{\nu}$ = 3041, 2949, 1617, 1465, 1448, 1287, 1258, 1237, 1226, 1134, 1066, 1039, 1025, 859, 831, 790, 780, 738, 706, 662, 643 cm^{-1}; HR-MS (ESI, Δm = 0.005): m/z: calcd for $C_{41}H_{39}ClN_2O_2$: 591.301, found: 591.301 [M^+]; elemental analysis calcd (%) for $C_{41}H_{39}ClN_2O_2{\cdot}2\,CDCl_3$ (868.0): C 59.50, H 4.99, N 3.23; found: C 59.54, H 4.87, N 3.13.

CCDC-609365 contains the supplementary crystallographic data for compound **17**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

9-Chloromethyl-[(1,8-*S*;4,5-*R*)-1,2,3,4,5,6,7,8-octahydro-1,4:5,8-dimethanoanthracene (20): A 250 mL round-bottomed flask with argon inlet was charged with alcohol **42** (1.55 g, 6.45 mmol, 1.00 equiv) and dry toluene (70 mL). The mixture was cooled to 0 °C and PCl_5 (2.70 g, 12.9 mmol, 2.00 equiv) was added. After stirring at room temperature overnight, saturated aqueous $NaHCO_3$ (60 mL) was added at 0 °C, and the mixture was stirred for 10 min. After separation of the phases, the aqueous layer was extracted with toluene (20 mL). The combined organic phases were washed with water (20 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by chromatography on silica gel (*n*-hexane/dichloromethane 10:1) to give chloride **20** as a colourless solid (1.52 g, 91 %). R_f = 0.81 (dichloromethane/*n*-hexane 1:2); m.p. 111–112 °C; $[\alpha]_D^{20}$ = 95.7 (c = 1.01 in chloroform); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.10–1.12 (m, 4 H; H-C2, C3, C6, C7), 1.45–1.48 (m, 2 H; H-C11, C12), 1.68–1.71 (m, 2 H; H-C11, C12), 1.84–1.86 (m, 4 H; H-C2, C3, C6, C7), 3.27 (br s, 2 H; H-C4, H-C5), 3.50 (br s, 2 H; H-C1, C8), 4.61–4.73 (q, 2 H; H-CH_2Ph), 6.93 ppm (s, 1 H; H-Caryl); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 26.6 (C2, C7), 27.2 (C3, C6), 41.2 (C1, C8), 41.2 (CH_2Ph), 44.0 (C4, C5), 49.1 (C11, C12), 111.1 (C10), 122.3 (C9), 144.2 (C4a, C10a), 145.8 ppm (C8a, C9a); IR (KBr pellet): $\tilde{\nu}$ = 2965, 2916, 2862, 1443, 1328, 1268, 1104, 942, 863, 689, 625 cm^{-1}; GC-MS (capillary column HP-5MS 0.25 mm × 30 m, cross-linked 5 % PH ME siloxane 0.25 μm; helium, 1 mL min^{-1}; 100 °C, 5 min, 20 °C min^{-1}, 200 °C, 15 min, 20 °C min^{-1}, 280 °C, 10 min) τ_R = 13.79 min, m/z: 258, 230, 202, 178, 167, 152; elemental analysis calcd (%) for $C_{17}H_{19}Cl$ (258.8): C 78.90, H 7.40; found: C 79.02, H 7.35.

9-Chloromethyl-[(1,8-*R*;4,5-*S*)-1,2,3,4,5,6,7,8-octahydro-1,4:5,8-dimethanoanthracene (*ent*-20): Compound *ent*-**20** was synthesized from the alcohol *ent*-**42** in the same manner as chloride **20** and was obtained as a colourless solid (747 mg, 87 %). The analytical data of the chloride *ent*-**20** were identical to those of chloride **20**, except for: $[\alpha]_D^{20}$ = −95.0 (c = 1.01 in chloroform); HR-MS (ESI, Δm = 0.005): m/z: calcd for $C_{17}H_{19}Cl$: 258.1175; found: 258.118 [M^+]; elemental analysis calcd (%) for $C_{17}H_{19}Cl$ (258.8): C 78.90, H 7.40; found: C 78.94, H 7.39.

1-*N*-[9-((1,8-*S*;4,5-*R*)-1,2,3,4,5,6,7,8-octahydro-1,4:5,8-dimethanoanthracenyl)methyl]quininium chloride (22): By following the general procedure for the quaternisation of tertiary amines, **22** was obtained from **2** (649 mg, 2.00 mmol) and **20** using work-up A as a colourless solid (417 mg, 36 %); recrystallized from acetone. M.p. > 201 °C (decomp); $[\alpha]_D^{20}$ = −141 (c = 0.98 in methanol); ^{1}H NMR (300 MHz,



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$[D_6]$DMSO): $\delta=0.86$–1.24 (m, 4H; H-C2″, C3″, C6″, C7″), 1.42–1.61 (m, 5H; H-C7, C11″, C12″), 1.88–1.98 (m, 6H; H-C5, C4, C2″, C3″, C6″, C7″), 2.15–2.23 (m, 2H; H-C7, C5), 2.73–2.77 (m, 1H; H-C3), 3.20–3.22 (m, 1H; H-C2), 3.48–3.55 (m, 1H; H-C2), 3.81–4.03 (m, 5H; H-C6, C1″, C8″, C4″, C5″), 4.04 (s, 3H; OCH_3), 4.29–4.34 (m, 2H; H-C8, H-C6), 4.40–4.44 (d, $J=12.9$ Hz, 1H; H-CH_2Ph), 5.00–5.09 (m, 2H; H-C11), 5.65–5.70 (d, $J=12.6$ Hz, 1H; H-CH_2Ph), 5.74–5.86 (ddd, $J=7.1$, $J=10.3$, $J=17.1$ Hz, 1H; H-C10), 6.67–6.69 (m, 1H; H-C9), 7.22–7.48 (m, 4H; H-Caryl, OH), 7.82–7.83 (d, $J=4.5$ Hz, 1H; H-Caryl), 7.99–8.02 (d, $J=9.0$ Hz, 1H; H-C8′), 8.81–8.83 ppm (d, $J=4.5$ Hz, 1H; H-C2′); ^{13}C NMR (75 MHz, $[D_6]$DMSO): $\delta=20.5$ (C7), 24.3 (C5), 25.9 (C4), 26.0 (C2″, C7″), 26.8 (C3″, C6″), 37.3 (C5), 41.1 (C1″, C8″), 43.1 (C4″, C5″), 47.6 (C11″ or C12″), 50.1 (C11″ or C12″), 51.3 (C6), 55.2 (OCH_3), 58.6 (C2), 59.7 (CH_2Ph), 63.2 (C9), 68.7 (C8), 101.9 (C5′), 114.1, 116.4 (2Caryl), 116.6 (C11), 120.4, 122.0, 125.2, 131.1 (4Caryl), 137.3 (C10), 143.6, 144.4, 147.4 (3Caryl), 147.7 (4Caryl), 157.0 ppm (C6′); IR (ATR): $\tilde{\nu}=3076$, 2957, 2866, 1620, 1589, 1506, 1471, 1456, 1429, 1330, 1254, 1238, 1224, 1179, 1111, 1027, 907, 860, 825, 730, 696 cm^{-1}; HR-MS (ESI, $\Delta m=0.005$): m/z: calcd for $C_{37}H_{43}N_2O_2$: 547.3325, found: 547.332 $[M^+]$; elemental analysis calcd (%) for $C_{37}H_{43}ClN_2O_2\cdot H_2O$ (601.2): C 73.92, H 7.54, N 4.66 found: C 73.96, H 7.55, N 4.62.

CCDC-609366 contains the supplementary crystallographic data for compound **22**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

1-*N*-[9-((1,8-*R*;4,5-*S*)-1,2,3,4,5,6,7,8-octahydro-1,4:5,8-dimethanoanthracenyl)methyl]quininium chloride (23): By following the general procedure for the quaternisation of tertiary amines, **23** was obtained from **2** (462 mg, 1.42 mmol) and *ent*-**20** using work-up A as a colourless solid (332 mg, 40%); recrystallized from acetone. M.p. > 205 °C (decomp); $[\alpha]_D^{20}=-268$ ($c=0.97$ in methanol); ^{1}H NMR (300 MHz, $[D_6]$DMSO): $\delta=1.07$–1.10 (m, 4H; H-C2″, C3″, C6″, C7″), 1.35–1.88 (m, 9H; H-C2″, C3″, C6″, C7″, C7, C4, C5), 2.00–2.01 (m, 1H; H-C3), 2.21–2.23 (m, 2H; H-C11″, C12″), 2.70–2.77 (m, 1H; H-C6), 3.29–3.33 (m, 4H; H-C1″, C8″, C4″, C5″), 3.58–3.63 (m, 2H; H-C11″, C12″), 3.77–3.86 (m, 2H; H-C2), 4.02 (s, 3H; H-OCH_3), 4.21–4.28 (m, 1H; H-C6), 4.48–4.56 (m, 1H; H-C8), 4.63–4.68 (d, $J=12.9$ Hz, 1H; H-CH_2Ph), 5.00–5.10 (m, 2H; H-C11), 5.36–5.40 (d, $J=12.9$ Hz, 1H; H-CH_2Ph), 5.73–5.84 (ddd, $J=7.1$, 10.3, 17.1 Hz, 1H; H-C10), 6.66–6.67 (m, 1H; H-C9), 7.11–7.27 (m, 2H; H-C10″, OH), 7.48–7.50 (m, 2H; H-Caryl), 7.80–7.81 (d, $J=4.5$ Hz, 1H; H-Caryl), 8.00–8.03 (d, $J=9.6$ Hz, 1H; H-C8′), 8.81–8.83 ppm (d, $J=4.5$ Hz, 1H; H-C2′); ^{13}C NMR (75 MHz, $[D_6]$DMSO): $\delta=20.5$ (C7), 24.3 (C5), 25.6 (C2″, C7″), 25.6 (C4), 26.8 (C3″, C6″), 37.3 (C3), 41.1 (C1″, C8″), 43.1 (C4″, C5″), 45.2 (C11″ or C12″), 47.0 (C11″ or C12″), 50.5 (CH_2Ph), 55.2 (OCH_3), 59.4 (C6), 59.6 (C2), 63.7 (C9), 68.1 (C8), 102.7 (C5′), 114.2 (Caryl), 114.3 (C11), 116.4 (C10″), 120.3, 121.5, 125.2, 131.2 (4Caryl), 137.2 (C10), 143.6, 144.2, 146.8 (3Caryl), 147.3 (Caryl), 157.0 ppm (C6′); IR (ATR): $\tilde{\nu}=3085$, 2954, 2860, 1619, 1589, 1507, 1470, 1430, 1330, 1238, 1224, 1110, 1026, 912, 860, 826, 730, 697 cm^{-1}; HR-MS (ESI, $\Delta m=0.005$): m/z: calcd for $C_{37}H_{43}N_2O_2$: 547.3325, found: 547.332 $[M^+]$.

CCDC-609367 contains the supplementary crystallographic data for compound **23**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

1-*N*-[9-((1,8-*S*;4,5-*R*)-1,2,3,4,5,6,7,8-octahydro-1,4:5,8-dimethanoanthracenyl)methyl]quinidinium chloride (24): By following the general procedure for the quaternisation of tertiary amines, **24** was obtained from **3** (413 mg, 1.27 mmol) and **20** using work-up A as a colourless solid (349 mg, 47%); recrystallized from acetone. $R_f=0.26$ (ethyl acetate/methanol 8:2); m.p. > 202 °C (decomp); $[\alpha]_D^{20}=286$ ($c=0.68$ in methanol); ^{1}H NMR (300 MHz, $[D_6]$DMSO): $\delta=1.02$–1.13 (m, 5H; H-C7, C2″, C3″, C6″, C7″), 1.54–1.91 (m, 11H; H-C11″, C12″, C5, C4, C2″, C3″, C6″, C7″), 2.35–2.43 (m, 1H; H-C7), 2.68–2.77 (m, 1H; H-C3), 3.02–3.12 (m, 1H; H-C6), 3.39 (brs, 2H; H-C4″, C5″), 3.50–3.80 (m, 3H; H-C2, C1″, C8″), 3.94–4.01 (m, 1H; H-C6), 4.11 (s, 3H; OCH_3), 4.14–4.21 (m, 1H; H-C8), 4.40–4.46 (m, 1H; H-C2), 4.78 (d, $J=12.9$ Hz, 1H; H-CH_2Ph), 5.11–5.27 (m, 3H; H-CH_2Ph, C11), 6.02–6.14 (ddd, $J=6.9$, $J=10.5$, $J=17.2$ Hz, 1H; H-C10), 6.61 (s, 1H; H-C9), 7.23 (s, 1H; H-C10″), 7.39–7.40 (d, $J=3.6$ Hz, 1H; OH), 7.47–7.54 (m, 2H; H-C5′, C7′), 7.80–7.82 (d, $J=4.5$ Hz, 1H; H-C3′), 8.00–8.03 (d, $J=9.0$ Hz, 1H; H-C8′), 8.81–8.82 ppm (d, $J=4.5$ Hz, 1H; H-C2′); ^{13}C NMR (75 MHz, $[D_6]$DMSO): $\delta=21.8$ (C7), 24.2 (C5), 26.9 (C4), 27.4 (C3″, C6″), 27.9 (C2″, C7″), 37.8 (C3), 43.4 (C1″, C8″), 44.8 (C4″, C5″), 48.6 (C11″ or C12″), 50.7 (C11″ or C12″), 54.9 (C2), 56.3 (OCH_3), 57.0 (C6), 59.6 (CH_2Ph), 65.9 (C9), 67.5 (C8), 103.4 (C5′), 115.1 (Caryl), 117.3 (C10″), 117.8 (C11), 121.2 (C3′), 122.4 (C7′), 126.3 (Caryl), 132.1 (C8′), 138.2 (C10), 144.6, 144.6 (2Caryl), 146.2 (2Caryl), 148.2 (2Caryl), 148.3 (C2′), 158.2 ppm (C6′); IR (CsI pellet): $\tilde{\nu}=3320$, 3175, 2964, 2870, 1623, 1509, 1474, 1432, 1332, 1243, 1227, 1113, 1029, 1004, 935, 870, 827 cm^{-1}; HR-MS (ESI, $\Delta m=0.005$): m/z: calcd for $C_{37}H_{43}N_2O_2$: 547.3325, found: 547.332 $[M^+]$; elemental analysis calcd (%) for $C_{37}H_{43}ClN_2O_2\cdot H_2O$ (601.2): C 73.92, H 7.54, N 4.66; found: C 73.75, H 7.47, N 4.58.

CCDC-609368 contains the supplementary crystallographic data for compound **24**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

1-*N*-[9-((1,8-*R*;4,5-*S*)-1,2,3,4,5,6,7,8-octahydro-1,4:5,8-dimethanoanthracenyl)methyl]quinidinium chloride (25): By following the general procedure for the quaternisation of tertiary amines, **25** was obtained from **3** (811 mg, 2.50 mmol) and *ent*-**20** using work-up A as a colourless solid (574 mg, 39%); recrystallized from methanol. M.p. > 201 °C (decomp); $[\alpha]_D^{20}=126$ ($c=0.89$ in methanol); ^{1}H NMR (300 MHz, $[D_6]$DMSO): $\delta=1.03$–1.12 (m, 5H; H-C7, C2″, C3″, C6″, C7″), 1.55–1.93 (m, 11H; H-C11″, C12″, C2″, C3″, C6″, C7″, C7, C4), 2.39–2.47 (m, 1H; H-C5), 2.71–2.79 (m, 1H; H-C3), 3.12–3.22 (m, 1H; H-C6), 3.36–3.38 (m, 2H; H-C5″, C4″), 3.44–3.51 (m, 1H; H-C2), 3.84 (brs, 2H; H-C1″, C8″), 4.12–4.18 (m, 5H; H-C6, OCH_3, C8), 4.27–4.33 (m, 1H; H-C2), 4.53–4.57 (d, $J=12.0$ Hz, 1H; H-CH_2Ph), 5.18–5.35 (m, 3H; H-CH_2Ph, C11), 6.10–6.18 (ddd, 1H; H-C10), 6.64–6.65 (m, 1H; OH), 7.22 (s, 1H; H-C10″), 7.41–7.48 (m, 3H; H-C9, C5′, C7′), 7.79–7.80 (d, $J=4.5$ Hz, 1H; H-C3′), 7.99–8.01 (d, $J=9.3$ Hz, 1H; H-C8′), 8.81–8.82 ppm (d, $J=4.5$ Hz, 1H; H-C2′);^{13}C NMR (75 MHz, $[D_6]$DMSO): $\delta=21.6$ (C7), 24.6 (C5), 26.9 (C4), 27.4 (C3″, C6″), 27.9 (C2″, C7″), 37.7 (C3), 43.2 (C1″, C8″), 44.5 (C4″, C5″), 48.6 (C11″ or C12″), 50.9 (C11″ or C12″), 55.4 (C2), 55.0 (C6), 56.1 (OCH_3), 60.2 (CH_2Ph), 65.1 (C9), 68.2 (C8), 102.6 (C5′), 115.1 (Caryl), 117.4 (C10″), 117.8 (C11), 121.1 (C3′), 122.9 (C7′), 126.2 (Caryl), 132.1 (C8′), 138.5 (C10), 144.6, 144.8 (2Caryl), 146.5 (2Caryl), 148.3 (C2′), 148.3 (2Caryl), 158.1 ppm (C6′); IR (CsI pellet): $\tilde{\nu}=3420$, 3134, 2960, 2868, 1622, 1593, 1508, 1474, 1458, 1432, 1241, 1112, 1028, 932, 862, 824, 719 cm^{-1}; HR-MS (ESI, $\Delta m=0.005$): m/z: calcd for $C_{37}H_{43}N_2O_2$: 547.3325, found: 547.332 $[M^+]$; elemental analysis calcd (%) for $C_{37}H_{43}ClN_2O_2\cdot MeOH$ (615.2): C 74.18, H 7.70, N 4.55; found: C 74.63, H 7.58, N 4.66.

1-*N*-((*R*)-Methyl-2-[1,1′]-binaphthyl)quinidinium bromide (26): A 100 mL round-bottomed flask was charged with (*S*)-2-methyl-[1,1′]-binaphthalene (*ent*-**43**; 1.50 g, 5.59 mmol, 1.00 equiv) and CCl_4 (25 mL). *N*-Bromosuccinimide (1.29 g, 6.70 mmol, 1.20 equiv) and AIBN (64.0 mg, 350 mmol, 0.07 equiv) were added to the solution. The reaction was stirred and heated to reflux for one hour. After cooling to 0 °C, the precipitates were filtered off and the filtrate was concentrated under reduced pressure to give the bromide **21**. The latter was used directly for the subsequent reaction without any purification. The crude bromide was dissolved in dry tetrahydrofuran (25 mL), quinidine (**3**, 1.06 g, 3.26 mmol, 1.00 equiv) was added, and the reaction was stirred and heated under reflux under argon atmosphere overnight. After cooling to room temperature, the solids were collected, washed with tetrahydrofuran and recrystallized from dichloromethane to give the ammonium salt **26** as a colourless solid (1.22 g, 32%). M.p. > 192 °C (decomp); $[\alpha]_D^{20}=249$ ($c=1.00$ in methanol); ^{1}H NMR (300 MHz, $[D_6]$DMSO): $\delta=0.71$–0.89 (m, 1H; H-C7), 1.60–1.79 (m, 3H; H-C5, C4), 1.89–1.97 (m, 1H; H-C7), 2.21–2.29

(m, 1H; H-C3), 2.76–2.83 (m, 1H; H-C2), 2.99–3.07 (m, 1H; H-C2), 3.37–3.41 (m, 1H; H-C6), 3.75–3.81 (m, 1H; H-C8), 3.95 (s, 3H; OCH_3), 4.09–4.11 (m, 1H; H-C6), 4.18–4.24 (d, J=17.3 Hz, 1H; H-C11), 4.75–4.81 (m, 2H; H-C11, H-CH_2Ph), 5.33–5.46 (m, 2H; H-C10, H-CH_2Ph), 6.14 (s, 1H; OH), 6.29 (s, 1H; H-C9), 7.06–7.09 (d, J=8.5 Hz, 1H; H-Caryl), 7.21–7.24 (d, J=8.5 Hz, 1H; H-Caryl), 7.29–7.39 (m, 3H; H-C5′, H-Caryl), 7.45–7.54 (m, 3H; H-C3′, Caryl), 7.60–7.65 (m, 1H; H-Caryl), 7.69–7.77 (m, 2H; H-Caryl), 7.96–7.99 (d, J=9.1 Hz, 1H; H-Caryl), 8.07–8.19 (m, 4H; H-Caryl), 8.26–8.29 (d, J=8.5 Hz, 1H; H-C8′), 8.72–8.73 ppm (d, J=4.4 Hz, 1H; H-C2′); ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ=20.6 (C7), 23.0 (C5), 25.4 (C4), 35.9 (C3), 54.2 (C2), 55.5 (OCH_3), 56.2 (C6), 60.3 (CBn), 64.9 (C9), 66.4 (C8), 102.2 (C5′), 115.6 (C11), 120.3, 121.1, 124.6 (3Caryl), 125.2 (s, Caryl), 125.9, 125.9, 126.1, 126.5, 126.8, 126.9, 127.3, 128.0, 128.2, 128.6, 128.8, 129.3, 131.2, 131.3, 132.1, 132.5, 133.1, 133.3, 133.7 (all Caryl), 136. 2 (C10), 141.7, 143.1, 143.5 (3Caryl), 147.1 (C2′), 157.2 ppm (C6′); IR (CsI pellet): $\tilde{\nu}$=3253, 3069, 2976, 2933, 2876, 1621, 1605, 1508, 1460, 1435, 1346, 1242, 1227, 1126, 1064, 1024, 935, 916, 873, 842, 806, 789, 763 cm^{-1}; HR-MS (ESI, Δm=0.005): m/z: calcd for $C_{41}H_{39}N_2O_2$: 591.3011, found: 591.301 [M^+]; elemental analysis calcd (%) for $C_{41}H_{39}BrN_2O_2{\cdot}H_2O$ (691.7): C 71.40, H 5.99, N 4.06 found: C 71.90, H 6.01, N 4.03.

CCDC-609369 contains the supplementary crystallographic data for compound **26**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

1-*N*-((*S*)-Methyl-2-[1,1′]-binaphthyl)quinidinium bromide (27): This compound was synthesized in the same manner as described for **26**, starting from (*R*)-2-methyl-[1,1′]-binaphthalene (**43**). In the case of **27**, after the reaction with **3**, the solvents were removed under reduced pressure. The crude material was dissolved in CH_2Cl_2 (5 mL) and added dropwise to diethyl ether (80 mL). The resulting precipitates were filtered off and washed with diethyl ether. The remaining solid was purified by chromatography on silica gel (ethyl acetate/methanol 8:2). Recrystallization from acetone resulted in the salt **27** as a colourless solid (187 mg, 7%). M.p. > 175°C (decomp); $[\alpha]_D^{20}$=155 (c=1.06 in methanol); ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ=0.78–0.85 (m, 1H; H-C7), 1.48–1.51 (m, 2H; H-C5), 1.73–1.74 (m, 1H; H-C4), 2.04–2.12 (m, 1H; H-C7), 2.56–2.61 (m, 1H; H-C3), 3.17–3.21 (m, 2H; H-C6), 3.72–3.90 (m, 3H; H-C2, H-C8), 4.04 (s, 3H; OCH_3), 4.97 (s, 2H; H-CH_2Ar), 5.10–5.23 (m, 2H; H-C11), 5.88–5.99 (ddd, J=6.9, 10.4, 17.3 Hz, 1H; H-C10), 6.08 (s, 1H; H-C9), 6.33 (s, 1H; OH), 7.03–7.06 (d, J=9.0 Hz, 1H; H-Caryl), 7.16–7.20 (d, 2H; H-C5′, Caryl), 7.33–7.39 (m, 2H; H-Caryl), 7.44–7.65 (m, 4H; H-Caryl), 7.70–7.73 (m, 2H; H-Caryl), 7.94–7.97 (d, J=9.0 Hz, 1H; H-Caryl), 8.05–8.19 (m, 4H; H-Caryl), 8.26–8.29 (d, J=9.0 Hz, 1H; H-C8′), 8.71–8.73 ppm (d, J=6.0 Hz, 1H; H-C2′); ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ=20.7 (C7), 22.9 (C5), 25.7 (C4), 36.6 (C3), 54.2 (C2), 55.8 (OCH_3), 56.6 (C6), 60.8 (CH_2Ar), 64.9 (C9), 66.4 (C8), 102.2 (C5′), 116.6 (C11), 120.2, 121.1, 124.3, 125.1, 125.2, 125.3, 126.0, 126.6, 126.7, 126.9, 127.3, 128.1, 128.2, 128.7, 129.1, 129.5, 131.1, 131.2, 132.1, 133.7, 133.3, 133.5, 133.9 (all Caryl), 137.3 (C10), 141.5, 143.0, 143.4 (3Caryl), 147.1 (C2′), 157.2 ppm (C6′); IR (CsI pellet): $\tilde{\nu}$=3410, 3061, 2750, 1735, 1621, 1605, 1511, 1473, 1354, 1242, 1138, 1024, 933, 833, 783, 719 cm^{-1}; HR-MS (ESI, Δm=0.005): m/z: calcd for $C_{41}H_{39}N_2O_2$: 591.3011, found: 591.3011 [M^+].

CCDC-609370 contains the supplementary crystallographic data for compound **27**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

1-*N*-(9-Anthrylmethyl)-6′-hydroxycinchoninium chloride (31): By following the general procedure for the quaternisation of tertiary amines, **31** was obtained from 6′-hydroxycinchonine (**33**)[22] (500 mg, 1.61 mmol) using work-up A as a yellow solid (633 mg, 73%). R_f=0.05 (chloroform/methanol 9:1); m.p. >170°C (decomp); $[\alpha]_D^{20}$=352 (c=1.00 in methanol); ^{1}H NMR (300 MHz, $CDCl_3$): δ=0.60–0.80 (m, 1H; H-C7), 1.35–1.53 (m, 1H; H-C5), 1.55–1.64 (m, 1H; H-C4), 1.61–1.78 (m, 2H; H-C3, C5), 1.90–2.07 (m, 1H; H-C7), 2.30–2.45 (m, 2H, H-C2, C6), 3.90–4.10 (m, 1H; H-C6), 4.24–4.39 (m, 1H; H-C2), 4.39–4.55 (m, 1H; H-C8), 4.78–4.92 (m, 1H; H-C11), 4.96–5.09 (m, 1H; H-C11), 5.45–5.68 (m, 1H; H-C10), 6.23 (d, J=13.2 Hz, 1H; H-CH_2An), 6.39 (d, J=13.2 Hz, 1H; H-CH_2An), 6.63–6.81 (m, 2H; H-C9, H-C7′), 6.89–7.01 (m, 1H; H-Caryl), 7.01–7.14 (m, 1H; H-Caryl), 7.20–7.33 (m, 1H; H-Caryl), 7.35–7.52 (m, 3H; H-Caryl, OH), 7.53 (d, J=9.1 Hz, 1H; H-C8′), 7.58–7.67 (m, 1H; H-Caryl), 7.87–7.93 (d, J=4.5 Hz, 1H; H-C3′), 7.93–8.03 (s, 1H; H-C10″), 8.06–8.23 (m, 2H; H-C5′, Caryl), 8.72 (d, J=4.5 Hz, 1H; H-C2′), 9.07 (d, J=9.1 Hz, 1H; H-C8′), 9.17 ppm (brs, 1H; OH); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=22.0 (C7), 24.1 (C5), 26.9 (C4), 37.9 (C3), 54.0 (CH_2An), 54.4 (C2), 58.1 (C6), 66.7 (C8), 67.2 (C9), 103.3 (C5′), 116.7 (C11), 117.6 (Caryl), 119.5 (C3′), 120.6 (C7′), 123.7, 124.4, 124.5, 124.9, 126.2, 127.5, 127.8, 128.5, 128.6, 129.8, 130.3 (all Caryl), 130.7 (C8′), 131.3 (C10″), 132.3, 132.6 (2Caryl), 135.1 (C10), 141.7, 141.8 (2Caryl), 146.4 (C2′), 156.1 ppm (C6′); IR (ATR): $\tilde{\nu}$=3161, 1617, 1526, 1464, 1447, 1398, 1237, 1223, 1131, 998, 924, 854, 792, 737, 707, 618 cm^{-1}; HR-MS (ESI, Δm=0.005): m/z: calcd for $C_{34}H_{33}ClN_2O_2$: 501.154, found: 501.155 [M^+]; elemental analysis calcd (%) for $C_{34}H_{33}ClN_2O_2{\cdot}H_2O$ (555.11): C 73.56, H 6.36, N 5.05; found: C 73.41, H 6.15, N 5.00.

1-*N*-(9-Anthrylmethyl)-6′-isopropoxycinchoninium chloride (32): By following the general procedure for the quaternisation of tertiary amines, **32** was obtained from 6′-isopropoxycinchonine (**34**) (200 mg, 567 µmol) using work-up B as a yellow solid (219 mg, 67%). R_f=0.16 (chloroform/methanol 9:1); m.p. >165°C (decomp); $[\alpha]_D^{20}$=368 (c=0.30 in methanol); ^{1}H NMR (300 MHz, $CDCl_3$): δ=0.89–1.04 (m, 1H; H-C5), 1.14–1.30 (m, 1H; H-C7), 1.33 (d, J=6.0 Hz, 3H; H-C13), 1.39 (d, J=6.0 Hz, 3H; H-C13), 1.56–1.64 (m, 1H; H-C4), 1.64–1.78 (m, 1H; H-C7), 1.78–1.92 (m, 1H; H-C3), 2.10–2.24 (m, 1H; H-C6), 2.25–2.39 (m, 1H; H-C5), 2.75–2.88 (m, 1H; H-C2), 3.92–4.08 (m, 1H; H-C6), 4.43–4.63 (m, 2H; H-C2, C8), 4.66–480 (sep, J=6.0 Hz, 1H; H-C12), 4.89–5.07 (m, 2H; H-C11), 5.63–5.80 (m, 1H; H-C10), 6.41–6.58 (m, 2H; H-CH_2An), 6.93–7.06 (m, 1H; H-C9), 7.19–7.27 (m, 2H; H-Caryl), 7.27–7.34 (m, 1H; H-Caryl), 7.37–7.45 (m, 2H; H-Caryl), 7.59–7.64 (m, 1H; H-Caryl), 7.66–7.75 (m, 1H; H-Caryl), 7.90–7.96 (m, 1H; H-Caryl), 7.99–8.03 (m, 1H; H-Caryl), 8.04–8.13 (m, 2H; H-Caryl), 8.17–8.28 (m, 1H; H-Caryl), 8.53–8.60 (m, 1H; H-Caryl), 8.77–8.89 ppm (m, 1H; H-Caryl); the OH proton could not be detected; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=22.2 (C13), 22.3 (C13), 22.3 (C5), 24.3 (C7), 26.3 (C4), 38.2 (C3), 54.7 (CH_2An), 54.7 (C2), 56.8 (C6), 69.0 (C8, C9), 70.6 (C12), 106.8, 117.6 (2Caryl), 118.0 (C11), 121.3, 121.7, 124.9 (3Caryl), 125.1 (Caryl), 125.4, 127.4, 127.5, 127.9, 128.8, 129.0, 130.5, 130.6 (all Caryl), 131.2 (2Caryl), 132.8, 133.0 (2Caryl), 133.5 (C10), 135.8, 143.2, 144.2, 156.0 ppm (4Caryl); IR (ATR): $\tilde{\nu}$=3152, 2972, 1669, 1616, 1505, 1505, 1457, 1372, 1310, 1275, 1238, 1200, 1108, 1048, 999, 966, 928, 866, 827, 792, 731, 699 cm^{-1}; HR-MS (ESI, Δm=0.005): m/z: calcd for $C_{37}H_{39}ClN_2O_2$: 543.301, found: 543.302 [M^+].

6′-Isopropoxycinchonine (34): By following the general procedure for the alkylation of phenols, **34** was obtained from 6′-hydroxycinchonine (**33**)[22] (1.00 g, 3.24 mmol) as a colourless solid (993 mg, 87%). R_f=0.84 (chloroform/methanol 9:1); m.p. 166°C (lit.:[40] 154°C); $[\alpha]_D^{20}$=181 (c=0.30 in chloroform); ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.00–1.15 (m, 1H; H-C7), 1.28, 1.30 (2×s, 6H; H-C13), 1.35–1.57 (m, 2H; H-C5), 1.63–1.76 (m, 1H; H-C4), 1.92–2.08 (m, 1H; H-C7), 2.10–2.28 (m, 1H; H-C3), 2.62–2.72 (m, 1H; H-C6), 2.73–2.92 (m, 2H; H-C2, C6), 2.93–3.08 (m, 1H; H-C8), 3.22–3.42 (m, 1H; H-C2), 4.58 (sep, J=6.0 Hz, 1H; H-C12), 4.94–5.08 (m, 2H; H-C11), 5.54 (d, 1H; H-C9), 5.92–6.10 (m, 1H; H-C10), 7.11–7.24 (m, 2H; C5′, C7′), 7.45 (d; J=2.6 Hz, 1H; H-C3′), 7.87 (d, J=9.1 Hz 1H; H-C8′), 8.49 ppm (d, J=4.5 Hz, 1H; H-C2′); the OH proton could not be detected; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=21.1 (C7), 21.5 (C13), 22.0 (C13), 25.4 (C5), 28.2 (C4), 40.0 (C3), 49.6 (C2), 50.2 (C6), 59.7 (C8), 70.0 (C12), 71.9 (C9), 103.5 (C5′), 114.4 (C11), 118.4 (C3′), 122.5, 126.5 (2Caryl), 131.3 (C8′), 140.6 (C10), 143.8 (Caryl), 147.3 (C2′), 147.7 (Caryl), 155.7 ppm (C6′); IR (ATR): $\tilde{\nu}$=3070, 2973, 2933, 2869, 1712, 1635, 1617, 1588, 1505, 1455, 1383, 1371, 1326, 1300, 1238, 1222, 1197, 1134, 1110, 1048, 1019, 998, 968, 909, 860, 829, 798, 761, 731, 663, 639 cm^{-1}; HR-MS (ESI, Δm=0.005): m/z: calcd for $C_{22}H_{28}N_2O_2$: 353.223, found: 353.223 [M+H$^+$].

1-*N*-(9-Anthrylmethyl)-6′-isopropoxy-10,11-dihydrocinchonidinium chloride (35): By following the general procedure for the quaternisation of tertiary amines, **35** was obtained from 6′-isopropoxy-10,11-dihydrocinchonidine (**41**) (500 mg, 1.41 mmol) using work-up B as a yellow solid

(545 mg, 66%). R_f=0.20 (chloroform/methanol 9:1); m.p. > 150°C (decomp); $[\alpha]_D^{20}=-409$ (c=1.00 in methanol); ^{1}H NMR (300 MHz, $CDCl_3$): δ=0.42 (t, J=7.2 Hz, 3H; H-C11), 0.92–1.12 (m, 2H; H-C10), 1.13–1.44 (m, 9H; H-C7, C3, C5, C13), 1.67–1.78 (m, 1H; H-C4), 2.02–2.27 (m, 2H; H-C5, C7), 2.29–2.59 (m, 2H; H-C2, OH), 2.68–2.84 (m, 1H; H-C6), 2.85–2.98 (m, 1H; H-C2), 4.08–4.22 (m, 1H; H-C8), 4.81 (sep, J=6.0 Hz, 1H; H-C12), 4.93–5.10 (m, 1H; H-C6), 5.84 (d, J=13.7 Hz, 1H; H-CH_2An), 6.84 (d, J=13.7 Hz, 1H; H-CH_2An), 6.95 (d, J=6.0 Hz, 1H; H-C9), 7.28 (dd, J=2.5, 9.2 Hz, 1H; H-C7′), 7.33–7.42 (m, 2H; H-Caryl), 7.44–7.54 (m, 1H; H-Caryl), 7.58–7.67 (m, 1H; H-Caryl), 7.73 (d, J=2.3 Hz, 1H; H-C5′), 7.75–7.84 (m, 1H; H-Caryl), 7.85–7.93 (m, 2H; H-C3′, Caryl), 7.96 (d, J=9.2 Hz, 1H; H-C8′), 7.75–7.84 (m, 2H; H-Caryl), 8.52 (d, J=4.5 Hz, 1H; H-C2′), 9.09 ppm (d, J=9.1 Hz, 1H; H-Caryl); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=11.0 (C11), 21.8, 25.8 (C7, C5), 22.1 (2×C13), 23.3 (C4), 26.3 (C10), 36.5 (C3), 52.7 (C6), 57.1 (CH_2An), 63.3 (C2), 65.7 (C9), 70.7 (C12), 71.3 (C8), 105.5 (C5′), 118.0 (Caryl), 120.1 (C3′), 121.2 (C7′), 123.6, 125.0, 125.7, 125.9, 126.5, 127.7, 128.5, 128.8, 129.9, 130.8, 131.1, 131.9 (all Caryl), 132.0 (C8′), 132.8, 133.2, 143.5, 144.0 (4Caryl), 147.6 (C2′), 156.2 ppm (C6′); IR (ATR): $\tilde{\nu}$=3050, 2961 (CH_3), 1616 (C–C), 1588, 1505, 1457 (CH_3), 1382, 1329, 1259, 1237 (C–O), 1221 (C–O), 1197, 1109, 1047, 966, 897, 860, 824, 793, 730, 699, 621 cm^{-1}; HR-MS (ESI, Δm=0.005): m/z: calcd for $C_{37}H_{41}ClN_2O_2$: 545.317, found: 345.316 [M^+]; elemental analysis calcd (%) for $C_{37}H_{41}ClN_2O_2\cdot\frac{1}{2}H_2O$ (590.2): C 75.30, H 7.17, N 4.75; found: C 74.83, H 6.97, N 4.61.

CCDC-609371 contains the supplementary crystallographic data for compound **35**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

1-(9-Anthrylmethyl)-6′-hydroxy-10,11-dihydrocinchoninium chloride (36): By following the general procedure for the quaternisation of tertiary amines, **36** was obtained from 6′-hydroxy-10,11-dihydrocinchonine (**40**) (200 mg, 640 μmol) using work-up A as a yellow solid (310 mg, 90%). R_f=0.41 (chloroform/methanol 9:1); m.p. > 195°C (decomp); $[\alpha]_D^{20}=361$ (c=0.50 in methanol); ^{1}H NMR (300 MHz, $CDCl_3$): δ=0.43 (t, J=7.3 Hz, 3H; H-C11), 0.61–0.77 (m, 1H; H-C7), 0.79–1.00 (m, 1H; H-C3), 1.06–1.42 (m, 3H; H-C5, C10), 1.44–1.57 (m, 1H; H-C4), 1.59–1.77 (m, 1H; H-C5), 1.82–2.06 (m, 1H; H-C7), 2.23–2.50 (m, 2H; H-C2, C6), 3.81–4.14 (m, 2H; H-C2, C6), 4.28–4.48 (m, 1H; H-C8), 6.07–6.24 (d, J=13.1 Hz, 1H; H-CH_2An), 6.34 (d, J=13.1 Hz, 1H; H-CH_2An), 6.59–6.82 (m, 2H; H-C7′, C9), 6.87–7.12 (m, 2H; H-Caryl), 7.17–7.32 (m, 1H; H-Caryl), 7.35–7.53 (m, 4H; H-Caryl), 7.59 (d, J=8.2 Hz, 1H; H-Caryl), 7.80–7.94 (m, 2H; H-Caryl), 8.04–8.22 (m, 2H; H-Caryl), 7.70 (d, J=4.5 Hz, 1H; H-Caryl), 9.06 (d, J=9.0 Hz, 1H; H-Caryl), 9.16 ppm (brs, 1H; OH); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=10.9 (C11), 21.9 (C7), 23.8 (C4), 24.0 (C10), 24.7 (C5), 36.0 (C3), 53.8 (CH_2An), 56.3 (C2), 58.2 (C6), 66.8 (C8), 67.3 (C9), 103.2, 116.9, 119.5, 120.8, 123.8, 124.5, 124.5, 125.0, 126.3, 127.5, 127.6, 128.5, 128.6, 129.8, 130.3, 130.5, 131.2, 132.4, 132.6, 141.4, 142.1, 146.1 (all Caryl), 156.2 ppm (C6′); IR (ATR): $\tilde{\nu}$=3087, 2956 (CH_3), 2931 (CH_2), 1618 (C–C), 1591, 1525, 1506, 1463, 1447, 1394, 1258, 1236, 1223 (O–H), 1158, 1129, 1047, 1023, 1007, 992, 961, 907, 864, 829, 791, 726, 663, 641, 623 cm^{-1}; HR-MS (ESI, Δm=0.005): m/z: calcd for $C_{34}H_{35}ClN_2O_2$: 503.2698, found: 503.269 [M^+].

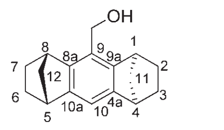
1-*N*-(9-Anthrylmethyl)-6′-isopropoxy-10,11-dihydrocinchoninium chloride (37): By following the general procedure for the quaternisation of tertiary amines, **37** was obtained from 6′-isopropoxy-10,11-dihydrocinchonine (**39**) (300 mg, 846 μmol) using work-up B as a yellow solid (329 mg, 67%). R_f=0.21 (chloroform/methanol 9:2); m.p. >150°C (decomp); $[\alpha]_D^{20}=363$ (c=1.00 in methanol); ^{1}H NMR (300 MHz, $CDCl_3$): δ=0.50 (t, J=7.3 Hz, 3H; H-C11), 0.88–1.09 (m, 2H; H-C3, C7), 1.19–1.44 (m, 9H; H-C5, C10, C13), 1.49–1.58 (m, 1H; H-C4), 1.59–1.72 (m, 1H; H-C5), 2.01–2.19 (m, 1H; H-C6), 2.20–2.37 (m, 1H; H-C7), 2.72–2.90 (m, 1H; H-C2), 3.81–3.98 (m, 1H; H-C6), 4.13–4.28 (m, 1H; H-C2), 4.39–4.52 (m, 1H; H-C8), 4.75 (sep, J=6.0 Hz, 1H; H-C12), 6.37 (d, J=13.6 Hz, 1H; CH_2An), 6.43 (d, J=13.4 Hz, 1H, CH_2An), 6.97 (brs, 1H; H-C9), 7.17–7.31 (m, 3H; H-Caryl), 7.32–7.44 (m, 2H; H-Caryl), 7.56–7.64 (m, 1H; H-Caryl), 7.64–7.72 (m, 1H; H-Caryl), 7.89–7.95 (m, 1H; H-Caryl), 7.95–8.01 (m, 1H; H-Caryl), 8.01–8.06 (m, 1H; H-Caryl), 8.12 (brm, 3H; H-Caryl, OH), 8.49–8.58 (m, 1H; H-Caryl), 8.70–8.82 ppm (m, 1H; H-Caryl); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=11.1 (C11), 22.0 (C7), 22.1 (C13), 22.4 (C13), 23.9 (C4), 24.3 (C10), 24.8 (C5), 36.2 (C3), 54.6 (CH_2An), 56.8 (C2), 56.9 (C6), 69.1 (C8), 69.5 (br; C9), 70.6 (C12), 106.7, 118.1, 121.2, 121.5, 124.9, 125.0, 125.2, 125.3, 127.4, 127.5, 127.7, 128.8, 129.0 (all Caryl), 130.6 (2Caryl), 131.2, 131.6, 132.7, 133.0, 143.1, 144.4, 147.4 (all Caryl), 155.94 ppm (C6′); IR (ATR): $\tilde{\nu}$=3062, 2968, 1706, 1670, 1616, 1588, 1457, 1382, 1238, 1222, 1200, 1109, 1047, 966, 929, 895, 866, 828, 732, 700, 618 cm^{-1}; HR-MS (ESI, Δm=0.005): m/z: calcd for $C_{37}H_{41}ClN_2O_2$: 545.617, found: 545.316 [M^+]; elemental analysis calcd (%) for $C_{37}H_{41}ClN_2O_2\cdot H_2O$ (581.2): C 74.16, H 7.23, N 4.68; found: C 74.12, H 7.68, N 4.39.

6′-Isopropoxy-10,11-dihydrocinchonine (39): By following the general procedure for the alkylation of phenols, **39** was obtained from 6′-hydroxy-10,11-dihydrocinchonine (**33**)[22] (755 mg, 2.03 mmol) as a colourless solid (720 mg, 84%). R_f=0.56 (chloroform/methanol 9:1); m.p. 177°C (lit.:[41] 181°C); $[\alpha]_D^{20}=188$ (c=2.00 in ethanol) (lit.:[41] $[\alpha]_D^{30}=206$ (c=2.00 in ethanol); ^{1}H NMR (300 MHz, $CDCl_3$): δ=0.83 (t, J=6.9 Hz, 3H; H-C11), 0.97–1.09 (m, 1H; H-C7), 1.17–1.32 (m, 6H; H-C13), 1.32–1.53 (m, 5H; H-C3, C5, C10), 1.63–1.71 (m, 1H; H-C4), 1.88–2.01 (m, 1H; H-C7), 2.59–2.93 (m, 3H; H-C2, C6), 2.94–3.06 (m, 1H; H-C8), 3.06–3.20 (m, 1H; H-C6), 4.56 (sep, J=6.0 Hz, 1H; H-C12), 5.63 (d, J=5.6 Hz, 1H; H-C9), 7.19 (dd, J=2.4, 7.6 Hz, 1H; H-C7′), 7.24 (d, J=2.6 Hz, 1H; H-C5′), 7.49 (d, J=4.4 Hz, 1H; H-C3′), 7.90 (d, J=9.1 Hz, 1H; H-C8′), 8.57 ppm (d, J=4.5 Hz, 1H; H-C2′); the OH proton could not be detected; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=10.9 (C11), 20.8 (C7), 21.6, 22.0 (C13), 25.1 (C10), 26.3 (C4), 27.1 (C5), 37.4 (C3), 50.3 (C2), 51.2 (C6), 59.7 (C8), 70.0 (C12), 71.9 (C9), 103.5 (C5′), 118.4 (C3′), 122.6 (C7′), 126.6 (Caryl), 131.3 (C8′), 143.8 (Caryl), 147.3 (C2′), 147.7 (Caryl), 155.7 ppm (C6′); IR (ATR): $\tilde{\nu}$=3156, 2929, 2869, 1711, 1616, 1588, 1503, 1454, 1382, 1371, 1328, 1237, 1221, 1198, 1135, 1111, 1047, 967, 939, 883, 859, 829, 732, 701, 639 cm^{-1}; HR-MS (ESI, Δm=0.005): m/z: calcd for $C_{22}H_{30}N_2O_2$: 355.239, found: 355.239 [$M+H^+$].

6′-Hydroxy-10,11-dihydrocinchonine (40): A solution of 10,11-dihydroquinidine[42] (419 mg, 1.28 mmol, 1.00 equiv) in dry CH_2Cl_2 (40.0 mL) was placed into a Schlenk flask at −78°C. Under vigorous stirring, BBr_3 (1.0 M in CH_2Cl_2; 5.13 mL, 5.13 mmol, 1.23 g, 4.00 equiv) was added slowly. The reaction mixture was allowed to warm up to room temperature. It was then refluxed at 40°C for 1 h and was cooled to 5°C. While stirring and maintaining the temperature, a 10% solution of aqueous sodium hydroxide (10 mL) was added. The basic aqueous solution was separated from the organic phase and washed with CH_2Cl_2 (15 mL). Hydrochloric acid (2 M) was added dropwise until a colourless solid precipitated (approx. pH 8). Extraction with chloroform, drying of the organic phase with magnesium sulfate and evaporating to dryness yielded the desired product **39** as a colourless solid (227 mg, 57%). R_f=0.21 (chloroform/methanol 9:1); m.p. 172°C (lit.:[43] 170°C); $[\alpha]_D^{20}=230$ (c=1.00 in methanol) (lit.:[44] $[\alpha]_D^{20}=243$ (c=1.00 in ethanol); ^{1}H NMR (300 MHz, $CDCl_3$): δ=0.64–0.94 (m, 4H; H-C7, C11), 1.13–1.34 (m, 3H; H-C3, C5), 1.36–1.53 (m, 2H; H-C10), 1.58–1.66 (m, 1H; H-C4), 2.12–2.36 (m, 2H; H-C2, C7), 2.40–2.61 (m, 1H; H-C2), 2.72–2.90 (m, 1H; H-C6), 2.92–3.06 (m, 1H; H-C8), 3.46–3.63 (m, 1H; H-C6), 5.94–6.09 (m, 1H; H-C9), 6.83–7.15 (brm, 2H; OH), 7.19 (d, J=8.9 Hz, 1H; H-C7′), 7.30 (s, 1H; H-C5′), 7.48 (d, J=4.9 Hz, 1H; H-C3′), 7.80 (d, J=4.5 Hz, 1H; H-C8′), 8.49 ppm (d, J=4.5 Hz, 1H; H-C2′); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=11.8 (C11), 18.1 (C7), 24.7 (C10), 25.5 (C4), 25.9 (C5), 36.5 (C3), 49.3 (C2), 50.4 (C6), 59.5 (C8), 69.9 (C9), 103.9 (C5′), 117.7 (C3′), 123.6 (C7′), 126.6 (C10), 131.4 (C8′), 142.8 (Caryl), 146.0 (C2′), 146.5 (Caryl), 158.5 ppm (C6′); IR (ATR): $\tilde{\nu}$=2948, 2928, 2869, 1615, 1585, 1463, 1329, 1227, 1113, 1079, 1051, 1024, 997, 931, 831, 734, 698, 643 cm^{-1}; HR-MS (ESI, Δm=0.005): m/z: calcd for $C_{19}H_{24}N_2O_2$: 313.192, found: 313.192 [$M+H^+$].

6′-Isopropoxy-10,11-dihydrocinchonidine (41): By following the general procedure for the alkylation of phenols, **41** was obtained from 6′-hydroxy-10,11-dihydrocinchonidine (1.10 g, 3.41 mmol) as a colourless solid (1.21 g, 97%). R_f=0.05 (chloroform/methanol 9:1); m.p. 84°C; $[\alpha]_D^{20}=-116$ (c=1.00 in ethanol); ^{1}H NMR (300 MHz, $CDCl_3$): δ=0.68 (t, J=7.2 Hz, 3H; H-C11), 1.01–1.17 (m, 2H; H-C10), 1.20–1.40 (m, 9H; H-C7, C3, C5, C13), 1.55–1.69 (m, 3H; H-C7, C4, C5), 2.17–2.30 (m, 1H; H-C2), 2.39–2.58 (m, 1H; H-C6), 2.83–3.02 (m, 2H; H-C8, C2), 3.27–3.46 (m, 1H; H-C6), 4.57 (sep, $J=6.0$ Hz, 1H; H-C12), 4.96 (brs, 1H; OH), 5.39 (d, $J=3.7$ Hz, 1H; H-C9), 7.08–7.22 (m, 2H; H-C5′, C7′), 7.35 (d, $J=4.5$ Hz, 1H; H-C3′), 7.79 (d, $J=8.9$ Hz, 1H; H-C8′), 8.38 ppm (d, $J=4.3$ Hz, 1H; H-C2′); ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta=12.0$ (C11), 21.3, 28.3 (C7, C5), 21.3 (C13), 21.5 (C13), 25.4 (C4), 27.6 (C10), 37.8 (C3), 43.3 (C6), 57.8 (C2), 59.8 (C8), 70.0 (C12), 72.0 (C9), 103.8 (C5′), 118.4 (C3′), 122.5 (C7′), 126.6 (C10), 131.2 (C8′), 143.8, 148.1 (C4′, C9′), 147.2 (C2′), 155.7 ppm (C6′); IR (ATR): $\tilde{\nu}=3172$, 2927 (CH_2), 2869 (CH_3), 1617 (C-C), 1588, 1504, 1455 (CH_3), 1381, 1375, 1328, 1237 (C−O), 1222 (C−O), 1195, 1135, 1135, 1112, 1086, 1043, 968, 880, 853, 828, 642 cm^{-1}; HR-MS (ESI, $\Delta m=0.005$): m/z: calcd for $C_{22}H_{30}N_2O_2$: 355.239, found: 355.238 [M+H$^+$].

9-Hydroxymethyl-[(1,8-*S*;4,5-*R*)-1,2,3,4,5,6,7,8-octahydro-1,4:5,8-dimethanoanthracene (42): To a suspension of $LiAlH_4$ (1.59 g, 41.9 mmol, 4.59 equiv) in dry tetrahydrofuran (30 mL), aldehyde **28**[26–28] (2.20 g, 9.23 mmol, 1.00 equiv) in dry tetrahydrofuran (20 mL) was added at 0 °C. The reaction was stirred for two hours at room temperature under argon atmosphere. After cooling to 0 °C, the remaining $LiAlH_4$ was decomposed by addition of water (70 mL). After 10 min of stirring, the reaction mixture was filtered over Celite and washed with water and tetrahydrofuran. Diethyl ether (10 mL) was added, the phases were separated and the aqueous layer was extracted with diethyl ether (2×15 mL). The combined organic phases were dried over sodium sulfate, filtered and concentrated under reduced pressure. The residue was purified by chromatography on silica gel (dichloromethane/*n*-hexane 3:1, then dichloromethane/*n*-hexane 10:1) to give alcohol **42** as a colourless solid (1.69 g, 76 %). $R_f=0.31$ (dichloromethane/*n*-hexane 10:1); m.p. 121–122 °C; $[\alpha]_D^{20}=75.1$ ($c=1.00$ in chloroform); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=1.05$–1.09 (m, 4H; H-C2, C3, C6, C7), 1.44–1.47 (m, 2H; H-C11, C12), 1.67–1.69 (m, 2H; H-C11, C12), 1.83–1.89 (m, 4H; H-C2, C3, C6, C7), 3.27 (brs, 2H; H-C4, C5), 3.53 (brs, 2H; H-C1, H-C8), 4.67–4.76 (m, 2H; H-CH_2Ph), 6.92 ppm (s, 1H; H-Caryl); the OH proton could not be detected; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=27.11$ (C2, C7), 27.2 (C3, C6), 41.2 (C1, C8), 43.9 (C4, C5), 49.1 (C11, C12), 60.4 (CH_2Ph), 113.5 (C10), 125.1 (C9), 143.9 (C4a, C10a), 145.7 ppm (C8a, C9a); IR (KBr pellet): $\tilde{\nu}=3175$, 2963, 2917, 2862, 1470, 1444, 1325, 1298, 1267, 1249, 1104, 1045, 1012, 944, 864, 719 cm^{-1}; GC-MS (capillary column HP-5MS 0.25 mm×30 m, cross-linked 5 % PH ME siloxane 0.25 µm; helium, 1 mL min^{-1}; 100 °C, 5 min, 20 °C min^{-1}, 200 °C, 15 min, 20 °C min^{-1}, 280 °C, 10 min) $\tau_R=13.99$ min, m/z: 240, 212, 184, 166, 154; HR-MS (ESI, $\Delta m=0.005$): m/z: calcd for $C_{17}H_{20}O$: 240.1514 found 240.152 [M^+]; HPLC Column: Chiralpak-AD, eluent *n*-hexane/isopropanol 100:2, flow: 1.00 mL min^{-1}; $\tau_R=15.72$ min.



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9-Hydroxymethyl-[(1,8-*R*;4,5-*S*)-1,2,3,4,5,6,7,8-octahydro-1,4:5,8-dimethanoanthracene (*ent*-42): A 100 mL round-bottomed flask with argon inlet was charged with aldehyde *ent*-**28**[26–28] (335 mg, 1.41 mmol, 1.00 equiv) and dry methanol (25 mL). The reaction mixture was cooled to 0 °C and sodium borohydride (270 mg, 7.05 mmol, 5.00 equiv) was added portionwise. After stirring at room temperature for 3 h, a 10 % HCl solution (15 mL) was added at 0 °C, and the mixture was stirred for 10 min. Dichloromethane (30 mL) was added, and the phases separated. The aqueous layer was extracted with dichloromethane (2×15 mL). The combined organic phases were dried over sodium sulfate, filtered and concentrated under reduced pressure. The residue was purified by chromatography on silica gel (dichloromethane/*n*-hexane 3:1, then dichloromethane/*n*-hexane 10:1) to give *ent*-**42** as a colourless solid (307 mg, 91 %).

The analytical data of the alcohol *ent*-**42** were identical to those of alcohol **42**, except for: $[\alpha]_D^{20}=-73.0$ ($c=0.96$ in chloroform); HR-MS (ESI, $\Delta m=0.005$): m/z: calcd for 240.1514 $C_{17}H_{20}O$: found 240.152 [M^+]; HPLC Column: Chiralpak-AD, eluent: *n*-hexane/isopropanol 100:2, flow: 1:00 mL min^{-1}; $\tau_R=13.78$ min.

(*R*)-2-Methyl-[1,1′]-binaphthalene (43):[31,45] In a 250 mL three-necked flask, equipped with an argon inlet, (*S*)-monotriflate **30**[29,30] (5.20 g, 12.9 mmol, 1.00 equiv) was dissolved in dry diethyl ether (65 mL). At 0 °C, bis(triphenylphosphine)nickel(II) dichloride (423 mg, 646 µmol, 5 mol %) was added, followed by the dropwise addition of a 3.00 M solution of MeMgCl (12.9 mL, 38.8 mmol, 3.00 equiv) in tetrahydrofuran. The reaction mixture was allowed to warm to room temperature and was stirred for 4 h. This mixture was then poured into an ice-cooled 5 % HCl solution (80 mL). The phases were separated, and the aqueous layer was extracted with diethyl ether (2×20 mL). The combined organic phases were dried over sodium sulfate, filtered and concentrated under reduced pressure. The residue was purified by chromatography on silica gel (*n*-hexane) to give methyl binaphthalene **43** as a colourless solid (2.43 g, 70 %). M.p. 132–134 °C (lit.:[31] 132–137 °C); $[\alpha]_D^{20}=-45.7$ ($c=1.00$ in chloroform) (lit.:[31] $[\alpha]_D^{20}=-43.9$ ($c=1.00$ in chloroform); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=2.11$ (s, 3H; CH_3), 7.14–7.30 (m, 4H; H-Caryl), 7.37–7.51 (m, 4H; H-Caryl), 7.59–7.64 (dd, $J=8.4$, 6.9 Hz, 1H; H-Caryl), 7.86–7.97 ppm (m, 4H; H-Caryl); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=20.5$ (CH_3), 124.8, 125.6, 125.7, 125.8, 125.9, 126.0, 126.1, 127.4, 127.5, 127.6, 127.7, 128.1, 128.5, 131.9, 132.5, 133.4, 133.7, 134.4, 136.0, 137.4 ppm (all Caryl); IR (ATR): $\tilde{\nu}=3049$, 3006, 2915, 2856, 1924, 1815, 1590, 1504, 1424, 1370, 1256, 1159, 1142, 1131, 1027, 1014, 949, 863, 802, 810, 790, 779, 772, 743, 674, 619 cm^{-1}; GC-MS (capillary column HP-5MS 0.25 mm×30 m, cross-linked 5 % PH ME siloxane 0.25 µm; He, 1 mL min^{-1}; 100 °C, 5 min, 20 °C min^{-1}, 200 °C, 15 min, 20 °C min^{-1}, 280 °C, 10 min) $\tau_R=24.32$ min, m/z: 268, 253; elemental analysis calcd (%) for $C_{21}H_{16}$ (268.4): C 93.99, H 6.01 found: C 93.69, H 6.09.

(*S*)-2-Methyl-[1,1′]-binaphthalene (*ent*-43): Compound *ent*-**43** was synthesized from the (*R*)-monotriflate *ent*-**30** in the same manner as (*R*)-2-methyl-[1,1′]-binaphthalene **43**. A colourless solid (3.76 g, 79 %) was obtained. The analytical data of this compound were identical to those of (*R*)-2-methyl-[1,1′]-binaphthalene **43**, except for: $[\alpha]_D^{20}=46.5$ ($c=1.03$ in chloroform); elemental analysis calcd (%) for $C_{21}H_{16}$ (268.4): C 93.99, H 6.01 found: C 93.70, H 5.95.

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