Asymmetric Phase-Transfer Catalysis by Quaternary Ammonium Ions Derived from *Cinchona*-Alkaloid Analogs Containing 1,1′-Binaphthalene Moieties

by **Laurent Ducry** and **François Diederich***

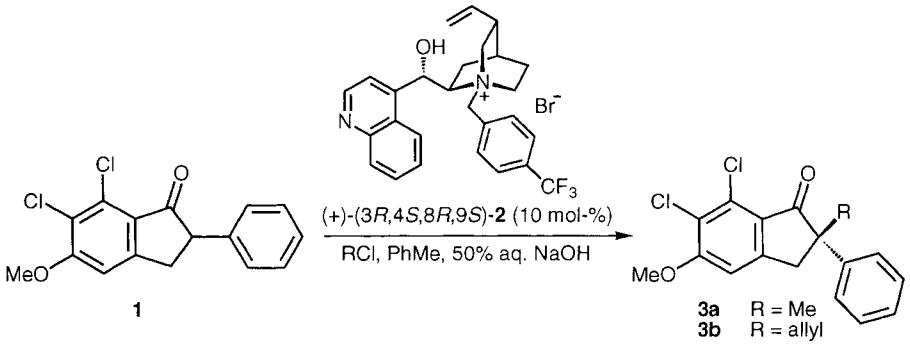
Laboratorium für Organische Chemie der Eidgenössischen Technischen Hochschule, ETH-Zentrum, Universitätstrasse 16, CH-8092 Zürich

The synthesis and catalytic properties of a new type of enantioselective phase-transfer catalysts, incorporating both the quinuclidinemethanol fragment of *Cinchona* alkaloids and a 1,1′-binaphthalene moiety, are described. Catalyst (+)-(a*S*,3*R*,4*S*,8*R*,9*S*)-**4** with the quinuclidine fragment attached to C(7′) in the major groove of the 1,1′-binaphthalene residue was predicted by computer modeling to be an efficient enantioselective catalyst for the unsymmetric alkylation of 6,7-dichloro-5-methoxy-2-phenylindanone (**1**; *Scheme 1*, *Fig. 1*). Its synthesis involved the selective oxidative cross-coupling of two differently substituted naphthalen-2-ols to afford the asymmetrically substituted 1,1′-binaphthalene derivative (±)-**17** in high yield (*Scheme 3*). Chromatographic optical resolution *via* formation of diastereoisomeric camphorsulfonyl esters and functional-group manipulation gave access to the 7-bromo-1,1′-binaphthalene derivative (−)-(a*S*)-**11** (*Scheme 4*). Nucleophilic addition of lithiated (−)-(a*S*)-**11** to the quinuclidine *Weinreb* amide (+)-(3*R*,4*S*,8*R*)-**8** afforded the two ketones (a*S*,3*R*,4*S*,8*R*)-**27** and (a*S*,3*R*,4*S*,8*S*)-**28** as an inseparable mixture of diastereoisomers (*Scheme 6*). Stereoselective reduction of this mixture with DIBAL-H (diisobutylaluminum hydride; preferred formation of the C(8)−C(9) *erythro*-pair of diastereoisomers with 18% de) or with $NaBH_4$ (preferred formation of the *threo*-pair of diastereoisomers with 50% de) afforded the four separable diastereoisomers (+)-(a*S*,3*R*,4*S*,8*S*,9*S*)-**29**, (+)-(a*S*,3*R*,4*S*,8*R*,9*R*)-**30**, (−)-(a*S*,3*R*,4*S*,8*S*,9*R*)-**31**, and (+)-(a*S*,3*R*,4*S*,8*R*,9*S*)-**32** (*Scheme 6*). A detailed conformational analysis, combining ^{1}H-NMR spectroscopy and molecular-mechanics computations, revealed that the four diastereoisomers displayed distinctly different conformational preferences (*Figs. 2* and *3*). These novel *Cinchona*-alkaloid analogs were quaternized to give (+)-(a*S*,3*R*,4*S*,8*R*,9*S*)-**4**, (+)-(a*S*,3*R*,4*S*,8*S*,9*S*)-**5**, (+)-(a*S*,3*R*,4*S*,8*R*,9*R*)-**6**, and (−)-(a*S*,3*R*,4*S*,8*S*,9*R*)-**7** (*Scheme 7*) which were tested as phase-transfer agents in the asymmetric allylation of phenylindanone **1**. Without any optimization work, (+)-(a*S*,3*R*,4*S*,8*R*,9*S*)-**4** was found to catalyze the allylation of **1** yielding the predicted enantiomer (+)-(*S*)-**3b** in 32% ee. The three diastereoisomeric catalysts (+)-**5**, (+)-**6**, and (−)-**7** gave access to lower enantioselectivities (6 to 22% ee's), which could be rationalized by computer modeling (*Fig. 4*).

1. Introduction. – Chiral catalysts for asymmetric synthesis are in increasing demand [1–4]. In asymmetric phase-transfer catalysis (PTC), the most commonly used catalysts are either chiral quaternary ammonium salts (quats) derived from *Cinchona* and *Ephedra* alkaloids, or chiral crown ethers [5–9]. A particularly successful example for the use of quats derived from *Cinchona* alkaloids in asymmetric PTC was described by *Dolling* and co-workers [10]. The methylation of phenylindanone **1** with MeCl, catalyzed by the *cinchonine*-derived quaternary benzyl ammonium salt (+)-(3*R*,4*S*,8*R*,9*S*)-**2**, was reported to provide methylated indanone (+)-(*S*)-**3a** with an ee (enantiomeric excess) up to 92% (*Scheme 1*). Based on molecular-model examinations and an X-ray crystal structure of the quat, the authors proposed a tight ion-pair model for the interaction between the cationic catalyst and the enolate form of substrate **1** in the transition state of the alkylation step. In this model, the enolate binds to the

catalyst by a combination of ion-pairing, H-bonding, and π-π stacking interactions. The alkylating agent subsequently approaches the less hindered face of the enolate, opposite to the catalyst, which accounts for the observed asymmetric induction.

Scheme 1. *Phase-Transfer-Catalyzed Alkylation of Phenylindanone* **1** [10].



Other examples of asymmetric PTC by quats derived from *Cinchona* alkaloids and modified derivatives are the stereoselective syntheses of α-amino acids by alkylation of *Schiff*-base derivatives of glycine esters [11–13]. In addition to enantioselective alkylation reactions, *Cinchona* alkaloid quats have been used in asymmetric aldol reactions [14], *Michael* additions [15], epoxidations [16], α-hydroxylations [17], and reductions [18].

Recently, we became interested in substituting the quinoline part in *Cinchona* alkaloids by chiral cleft-type aromatic moieties such as 2,2′-disubstituted 9,9′-spirobi[9*H*-fluorenes] [19] or 2,2′-disubstituted 1,1′-binaphthalenes, hoping to generate hybrid materials with enhanced molecular-recognition and catalytic properties. Here, we present the computer-assisted design, synthesis, and catalytic properties of the first such hybrid systems composed of the quinuclidine moiety of *Cinchona* alkaloids and a 1,1′-binaphthalene derivative. In addition to their application as ligands in asymmetric catalysis [16d][20], *Cinchona* alkaloids are the most widely used components in chiral auxiliaries for enantiomer separations [21][22]. Similarly, substituted 1,1′-binaphthalenes are popular chiral ligands in asymmetric transition-metal catalysis [23], and represent versatile chiral scaffolds in molecular recognition [24–26].

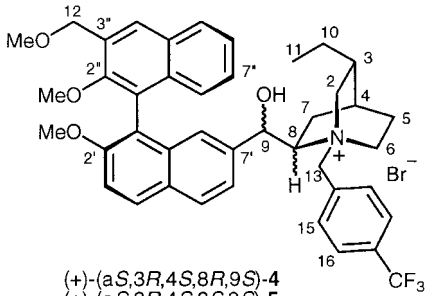
The hybrid system (+)-(a*S*,3*R*,4*S*,8*R*,9*S*)-**4**[1])[2]) was designed with the aid of computer modeling as a new phase-transfer catalyst for the enantioselective allylation of phenylindanone **1**. The stereoselective formation of quaternary C-atom stereocenters as in the alkylation of **1** (*Scheme 1*) remains a challenging task in synthetic organic chemistry [28]. Three diastereoisomeric catalysts, (+)-(a*S*,3*R*,4*S*,8*S*,9*S*)-**5**, (+)-(a*S*,3*R*,4*S*,8*R*,9*R*)-**6**, and (−)-(a*S*,3*R*,4*S*,8*S*,9*R*)-**7** were also obtained and tested as

---

[1]) The descriptors (a*R*) and (a*S*) are used for assignments of the sense of axial chirality; for recent examples, see [27].

[2]) The arbitrary numbering corresponds to that in use for the natural *Cinchona* alkaloids quinine and quinidine.

phase-transfer catalysts. The observed trends in enantioselectivities could be, in all cases, rationalized by the molecular modeling, and the preferentially formed enantiomers predicted.



(+)-(a*S*,3*R*,4*S*,8*R*,9*S*)-**4**
(+)-(a*S*,3*R*,4*S*,8*S*,9*S*)-**5**
(+)-(a*S*,3*R*,4*S*,8*R*,9*R*)-**6**
(–)-(a*S*,3*R*,4*S*,8*S*,9*R*)-**7**

2. Results and Discussion. – 2.1. *Computer-Assisted Design of Phase-Transfer Catalyst (+)-(a*S,*3*R,*4S,8*R,*9S*)-**4**. It is notable that only 1,1′-binaphthalenes bearing ligating functionalities at the 2,2′-positions in the minor groove have so far been successfully used in catalysis. A 1,1′-binaphthalene ligand with phosphine substituents at the 7,7′-positions in the major groove has been described [29]; however, no application in asymmetric catalysis has been reported to date. Molecular-recognition studies had previously demonstrated a high potential of the major groove, with its large polarizable aromatic surfaces, for selective substrate recognition [22][26], and, therefore, it seemed worthwhile to explore the attachment of the quinuclidinemethanol moiety to C(7′) of the 1,1′-binaphthalene fragment. This attachment was also suggested by a computer-assisted screening of potential catalyst geometries.

A series of binaphthalene derivatives with the quaternized quinuclidinemethanol moiety attached to either the minor or the major groove and having various configurations at C(8) and C(9) of the *Chinchona*-alkaloid fragment (for the numbering, see *Formulae* **4**–**7**), as well as opposite axial chirality ((a*S*) or (a*R*)) with respect to the binaphthalene moiety were, therefore, examined as potential phase-transfer catalysts. Pseudo-Monte-Carlo Multiple Minimum (MCMM) conformational searches (5000 steps) in $CHCl_3$, with the MM2* force field[3]) and the GB/SA solvation model [31] implemented in MacroModel V. 6.0 [32], were performed to estimate the most stable ion-pairing complex with one clear conformational preference formed between the various potential catalysts and the enolate of phenylindanone **1**. These modeling studies predicted that compound (+)-(a*S*,3*R*,4*S*,8*R*,9*S*)-**4**, with the quinuclidine moiety attached to the major groove, would have the highest stereoelectronic complementarity for the enolate substrate (*Fig. 1*). The two MeO groups in the minor groove of the binaphthalene moiety in (+)-**4** would result from the synthesis of the chiral cleft (*vide infra*) whereas the $MeOCH_2$ substituent at C(3″) would be introduced as a site for potential further functionalization targeting the immobilization of the catalyst in aerogel materials [33][34].

---

[3]) MM2* is a modification of the MM2 force field [30].

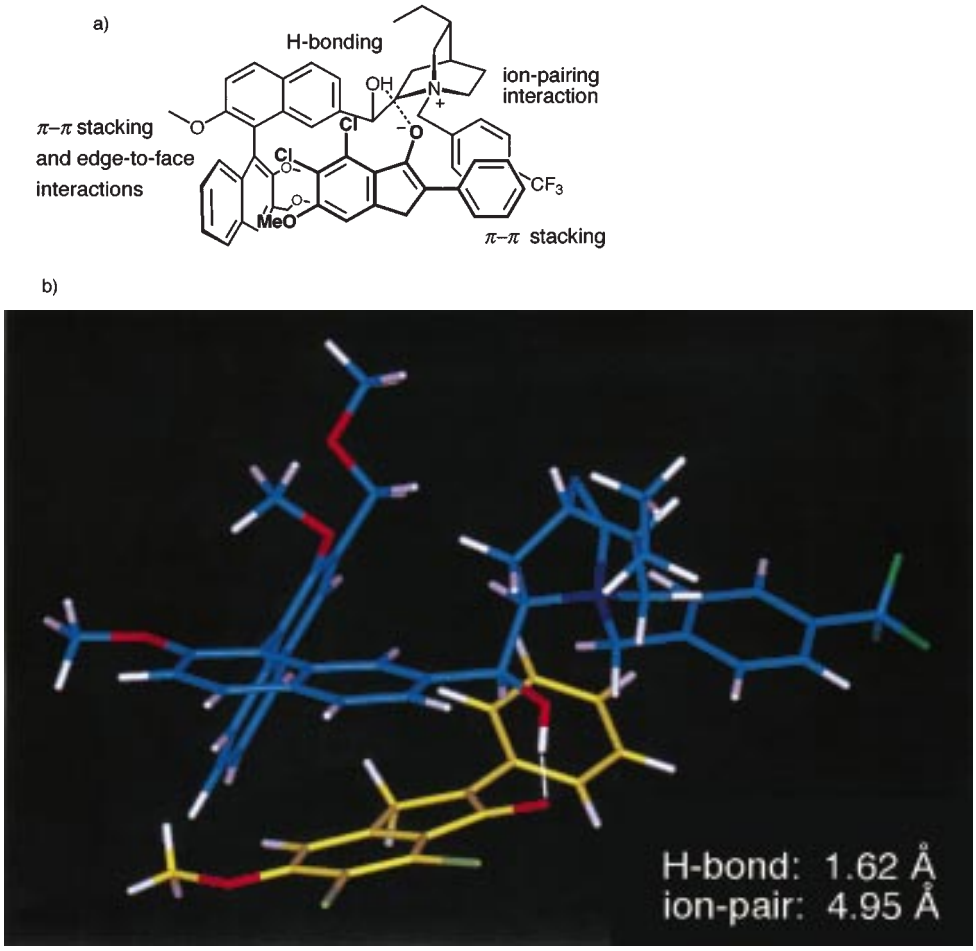


Fig. 1. *Schematic* (a) *and computer-calculated* (b) *representations of the complex between the designed catalyst (+)-(*a*S,*3*R,*4*S,*8*R,*9*S)-***4*** *and the enolate of phenylindanone* **1**

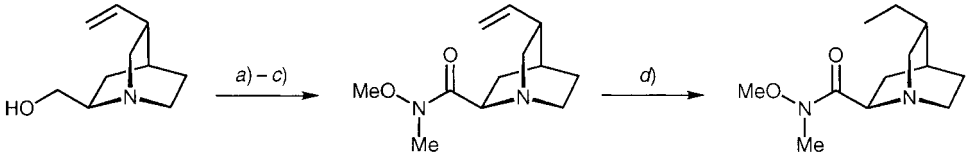
The calculated most favorable conformation of the ion-pairing complex between (+)-**4** and the enolate of **1** (*Fig. 1*) resembles the one postulated by *Dolling* and co-workers for the corresponding complex of (+)-**2** [10]. The absolute configurations at C(8) and C(9) in both catalysts are the same. The enolate O-atom forms a strong H-bond to the OH group at C(9) (H···O distance: 1.62 Å) and is located at a distance of 4.95 Å from the quaternary N-atom in (+)-**4**. The Ph ring of **1** undergoes π-π stacking interactions with the electron-deficient 4-(trifluoromethyl)benzyl residue. The indanone moiety in **1** is buried within the major groove of the binaphthalene, resulting in multiple hydrophobic contacts. On one hand, it undergoes π-π stacking interactions with one naphthalene ring, similar to those observed between the indanone fragment and the quinoline ring in the complex of (+)-**2**. On the other hand, the complex formed by (+)-**4** features additional edge-to-face (C–H···π) interactions between the

indanone fragment and the second naphthalene ring of the chiral cleft. As a result, the computed ion-pairing complex of (+)-**4** features a total of 54 *van der Waals* contacts under 4 Å, whereas only 30 such contacts are calculated for the complex of (+)-**2**. Thus, the enolate should be tightly oriented in the complex formed by (+)-**4**, leading to a strong preference for attack by the alkylation agent from the side not shielded by the catalyst.

2.2. *Synthesis of the New Phase-Transfer Catalyst.* Among the various protocols for the synthesis of *Cinchona* alkaloids published by *Uskokovic* and co-workers [35], the reaction of a quinuclidine-8-carboxylic acid with a metallated arene to give the corresponding ketone, and subsequent diastereoselective reduction [35f] appeared to be the most convenient preparation of (+)-**4** [35j]. This method had already been applied to the synthesis of analogs of *Cinchona* alkaloids incorporating a 9,9′-spirobifluorene moiety [19].

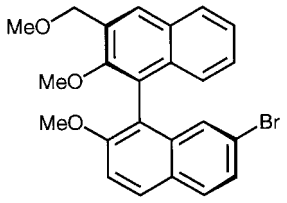
As the activated quinuclidine-8-carboxylic-acid derivative, we chose the *Weinreb* amide (+)-(3*R*,4*S*,8*R*)-**8** (*Scheme 2*) [36]. Oxidation of the commercially available 5-vinylquinuclidine-2-methanol ((+)-(3*R*,4*S*,8*R*)-**9**) to the corresponding carboxylic acid, followed by *in situ* formation of the acyl chloride and subsequent reaction with *N*,*O*-dimethylhydroxylamine hydrochloride under basic conditions afforded (+)-(3*R*,4*S*,8*R*)-**10** in 44% yield. Subsequent hydrogenation gave the desired *Weinreb* amide (+)-(3*R*,4*S*,8*R*)-**8** in quantitative yield.

Scheme 2. *Synthesis of* Weinreb *Amide (+)-(3*R,*4*S,*8*R*)-**8**



(+)-(3*R*,4*S*,8*R*)-**9** (+)-(3*R*,4*S*,8*R*)-**10** (+)-(3*R*,4*S*,8*R*)-**8**

a) CrO_3, H_2SO_4, acetone, 0° to r.t., 5 h. *b*) PCl_5, CH_2Cl_2, reflux 4 h. *c*) MeHNOMe · HCl, Et_3N, 0° to r.t., 3 h; 44% (starting from (+)-**9**). *d*) H_2, Pd/C, EtOH, 2 bar, 3 h, quant.

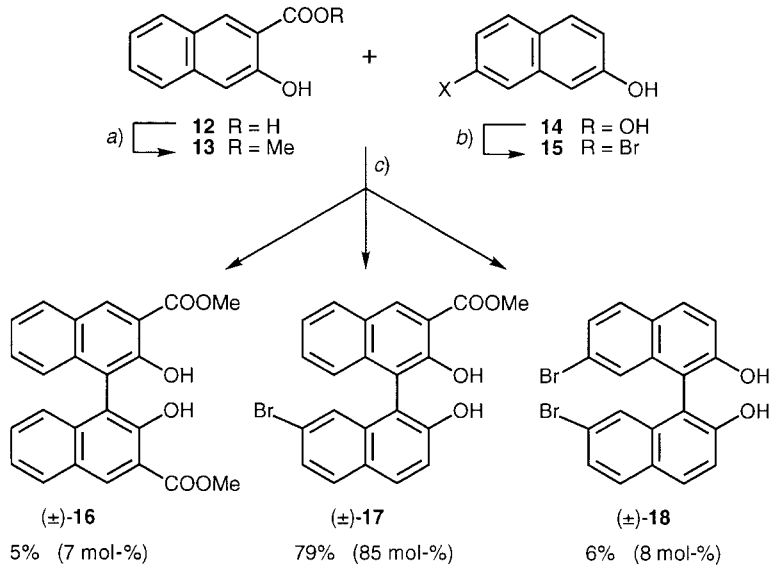


(–)-(a*S*)-**11**

The preparation of the 7′-bromo-1,1′-binaphthalene building block (–)-(a*S*)-**11** on the way to (+)-**4** proved quite challenging owing to its unsymmetrical structure. Whereas protocols for the synthesis of symmetric 1,1′-binaphthalene derivatives by oxidative homo-coupling of naphthalene-2-ols are well-established [37], cross-coupling methods leading to unsymmetrical 1,1′-binaphthalene-2,2′-diols remain relatively

unexplored [37–39]. *Hovorka et al.* reported that the efficiency of Cu^{II}-mediated cross-coupling reactions between two differently substituted naphthalene-2-ols depends on the nature of the substituents in both partners [37] [38]. A synthetically useful degree of cross-coupling was obtained only when the difference in electron density in the naphthalene rings of both reacting partners was large, a finding which became the subject of further mechanistic studies [40] and *ab initio* calculations [41]. Therefore, we prepared two naphthalene-2-ols with different electron densities in the aromatic rings, in order to favor cross-coupling over undesirable homo-coupling. Methyl 3-hydroxynaphthalene-2-carboxylate (**13**) was synthesized from the corresponding carboxylic acid **12** (*Scheme 3*). Monobromination of diol **14** by the method published for the preparation of 2-bromonaphthalene from naphthalen-2-ol [42] afforded 7-bromonaphthalen-2-ol (**15**). As expected from the work by *Hovorka et al.*, the subsequent Cu^{II}-mediated cross-coupling between **13** and **15** indeed provided the desired unsymmetrical 1,1′-binaphthalene (+)-**17** in very good yield (79%) and with high selectivity (85 mol-%) over the two homo-coupled products (+)-**16** (7 mol-%) and (+)-**18** (8 mol-%).

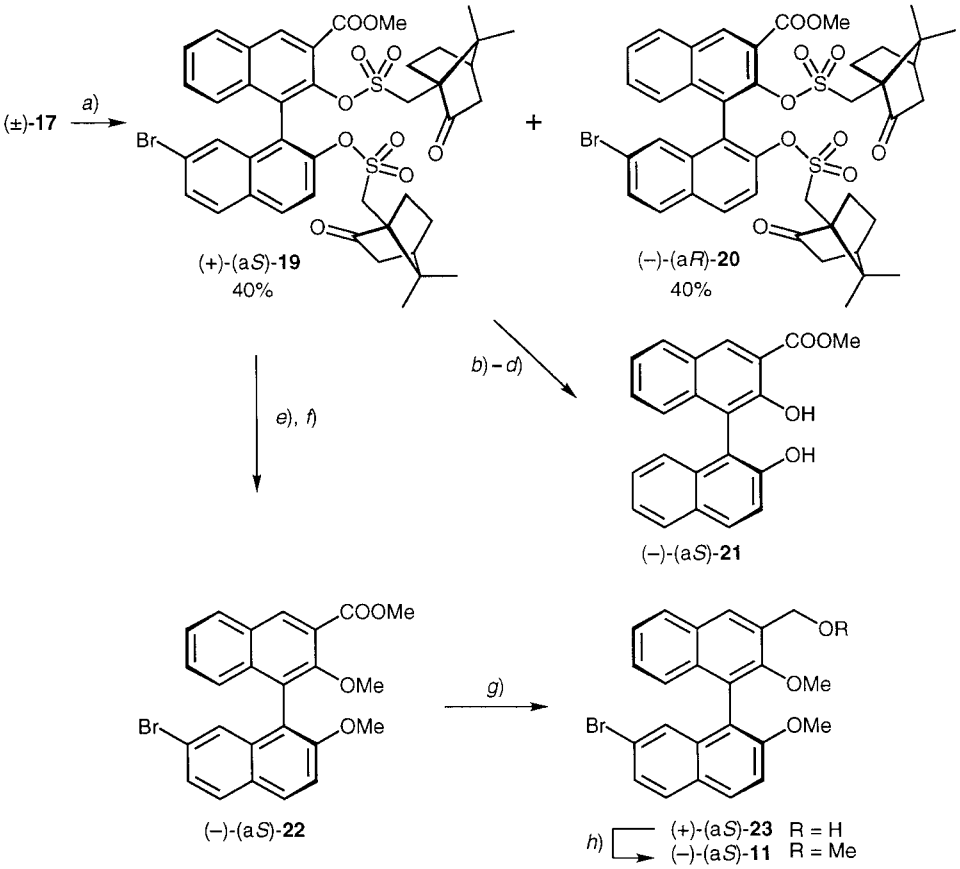
Scheme 3. *Synthesis of 1,1′-Binaphthalene (±)-***17** *by* Cu^{II}*-Mediated Cross-Coupling*



a) HCl (g), MeOH, r.t., 12 h; quant. *b*) Br_2, PPh_3, MeCN, 250°, 1 h; 64%. *c*) $CuCl_2$, *t*-$BuNH_2$, MeOH, 50°, 2 h; 79%.

The optical resolution of (±)-**17** was achieved by a procedure recently published [43] for the resolution of substituted 1,1′-binaphthalene-2,2′-diols. Diol (±)-**17** was reacted with (+)-(1*S*)-camphor-10-sulfonyl chloride, and the resulting two diastereoisomers (+)-(a*S*)-**19** (40%) and (−)-(a*R*)-**20** (40%) were separated by column chromatography (SiO_2; CH_2Cl_2/AcOEt 99 : 1; *Scheme 4*). Analytical HPLC analysis (SiO_2; CH_2Cl_2/AcOEt 100 : 0 → 80 : 20) showed that the purity of each diastereoisomer was above 99%.

Scheme 4. *Optical Resolution of Diol (±)-***17** *and Synthesis of (−)-(aS)-***11**, *the Precursor to the New* Cinchona-*Alkaloid Analogs*



a) (+)-(1*S*)-Camphor-10-sulfonyl chloride, Et_3N, CH_2Cl_2, 0° to r.t., 5 h. *b*) BuLi, THF, − 78°, 2 h, then 1M HCl, MeOH. *c*) NaOH, H_2O, MeOH, reflux, 12 h. *d*) HCl (g), MeOH, r.t., 12 h; 60% (starting from (+)-**19**). *e*) NaOH, MeOH, H_2O, reflux, 20 h. *f*) $(MeO)_2SO_2$, KOH, reflux, 3 h; 97% (starting from (+)-**19**). *g*) DIBAL-H, CH_2Cl_2, − 78° to r.t., 2.5 h; 72%. *h*) $(MeO)_2SO_2$, NaH, acetone, r.t., 1 h; 97%.

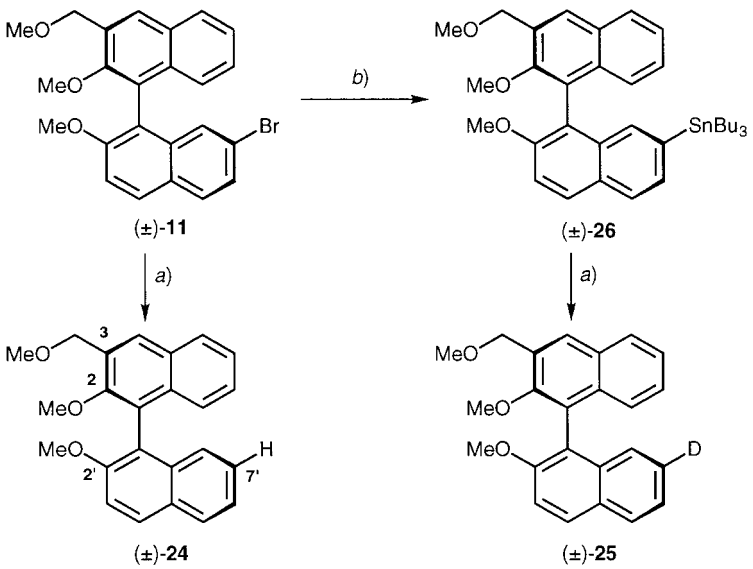
The absolute configuration of (+)-(a*S*)-**19** was determined through derivatization to a product of known configuration. The Br substituent was reductively removed by treatment of (+)-(a*S*)-**19** with BuLi, followed by quenching with MeOH and 1M HCl (*Scheme 4*). Subsequent cleavage of the camphorsulfonyl auxiliaries and reesterification of the resulting carboxylic acid afforded (−)-**21** (60%), which had been reported to have the (a*S*)-configuration [39c]. In a separate study, the (a*R*)-configuration was assigned to (+)-**21** by comparing its circular-dichroism (CD) spectrum to that of (+)-(a*R*)-dimethyl 2,2′-dihydroxy-1,1′-binaphthalene-3,3′-dicarboxylate [38b].

After chromatographic separation of the diastereoisomers, the camphorsulfonyl auxiliary in (+)-(a*S*)-**19** was removed by hydrolysis (*Scheme 4*). Subsequent methylation of the two resulting OH groups and the carboxylic acid yielded (−)-(a*S*)-**22**

(97%), reduction with DIBAL-H afforded alcohol (+)-(a*S*)-**23** (72%), and methylation with $(MeO)_2SO_2$ eventually provided (−)-(a*S*)-**11** (97%).

The coupling to *Weinreb* amide (+)-**8** was first investigated with racemic 1,1′-binaphthalene (±)-**11**. However, sequential addition of BuLi and (+)-**8** to bromide (±)-**11** under various conditions repeatedly failed to furnish the desired ketone. A more detailed investigation of the lithiation step unexpectedly showed that the starting material was completely recovered when one equivalent of BuLi or *t*-BuLi was added (with or without TMEDA (*N*,*N*,*N*′,*N*′-tetramethylethylenediamine) as co-solvent). The first equivalent of base is presumably complexed by the three MeO groups, thereby preventing the halogen-lithium exchange. Lithiation was achieved with an excess of BuLi (2 or more equiv.). However, the lithiated intermediate proved to be very labile in Et_2O and THF. This was shown by deuteration experiments in which the mixture was quenched with CD_3OD directly after the addition of BuLi. Bromide (±)-**11** was completely reduced to (±)-**24**, demonstrating complete lithiation, but a proton and not a deuterium was present at C(7′) as indicated by the ^{1}H- and ^{2}D-NMR spectra (*Scheme 5*). The same experiment carried out in (D_8)THF afforded the deuterated product (±)-**25**, which established that the proton or deuterium comes from the solvent. A very different result was obtained when bromide (±)-**11** was first converted to the corresponding tin derivative (±)-**26** by treatment with Bu_3SnLi [44]. In that case, the lithiated derivative obtained by transmetallation of (±)-**26** with BuLi was found to be stable at −78° for prolonged periods of time and could be trapped by CD_3OD to afford (±)-**25**. Apparently, the other products of the two lithiation reactions, starting from either (±)-**11** or (±)-**26**, differentially affect the reactivity of the aggregates of the lithiated 1,1′-binaphthalene in THF [45].

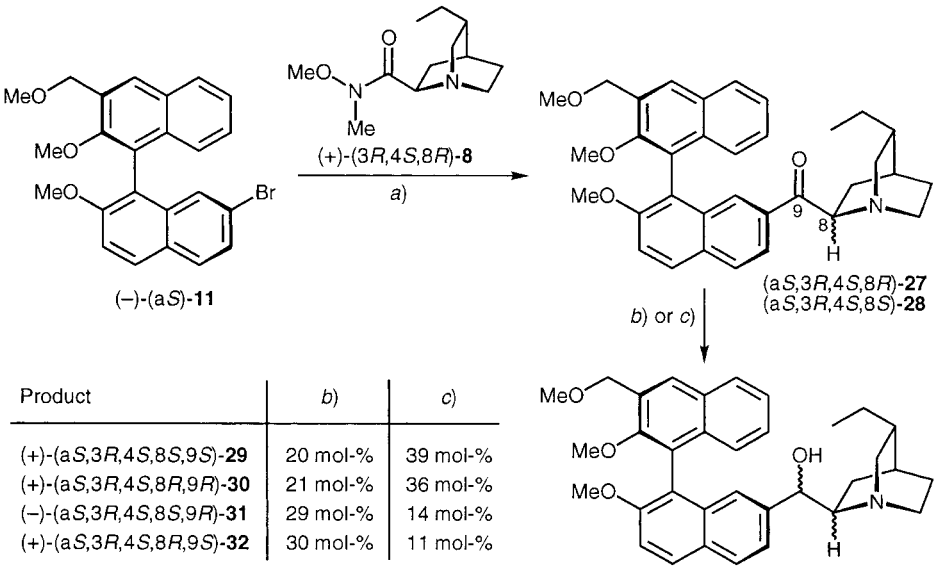
Scheme 5. *Deuteration Experiments*



a) BuLi, THF, −78°, then CD_3OD. *b*) Bu_3SnLi, THF, 0°, 30 min; 51%.

Based on these results, the addition of the lithiated 1,1′-binaphthalene to the *Weinreb* amide was re-investigated (*Scheme 6*). In a first approach, BuLi was added to a pre-formed mixture of (−)-(a*S*)-**11** and (+)-(3*R*,4*S*,8*R*)-**8**, giving, in 46% yield, (a*S*,3*R*,4*S*,8*R*)-**27** and (a*S*,3*R*,4*S*,8*S*)-**28** as an inseparable mixture of diastereoisomers (*ca.* 1:1), owing to rapid epimerization at C(8). A second approach was to first transmetallate stannane (±)-**26** with BuLi and then add a solution of (+)-(3*R*,4*S*,8*R*)-**8** in THF, which afforded the same product mixture in 42% yield. Epimerization at C(8) could again not be prevented, even by using less than 1 equiv. of BuLi; therefore, the direct route *via* lithiation of (−)-(a*S*)-**11** was preferred.

Scheme 6. *Synthesis of the* Cinchona-*Alkaloid Analogs (+)-***29**, *(+)-***30**, *(−)-***31**, *and (+)-***32**



Product	*b)*	*c)*
(+)-(a*S*,3*R*,4*S*,8*S*,9*S*)-**29**	20 mol-%	39 mol-%
(+)-(a*S*,3*R*,4*S*,8*R*,9*R*)-**30**	21 mol-%	36 mol-%
(−)-(a*S*,3*R*,4*S*,8*S*,9*R*)-**31**	29 mol-%	14 mol-%
(+)-(a*S*,3*R*,4*S*,8*R*,9*S*)-**32**	30 mol-%	11 mol-%

a) BuLi, THF, −78°, 15 min; 46%. *b*) DIBAL-H, benzene, 0°, 4 h. *c*) $NaBH_4$, EtOH, 0°, 15 min. The diastereoisomeric ratios were determined by analytical HPLC in the case of the DIBAL-H reduction and by integration of the ^{1}H-NMR signals in case of the reduction with $NaBH_4$.

In the subsequent reduction of the diastereoisomer mixture with DIBAL-H in benzene, we hoped to selectively obtain the C(8)–C(9) *erythro*-diastereoisomers as was observed in the reduction of quininone and quinidinone to give quinine and quinidine, respectively [35f], or in the reduction of a related ketone in which the quinoline moiety was replaced by a 9,9′-spirobifluorene moiety [19]. The diastereoselectivity of the reduction step is presumably a result of initial chelation of the *Lewis*-acidic Al-atom of the reducing agent to the quinuclidine N-atom, followed by intramolecular delivery of hydride to the ketone. The reduction of the mixture of (a*S*,3*R*,4*S*,8*R*)-**27** and (a*S*,3*R*,4*S*,8*S*)-**28** under the reported conditions [35f] afforded the diastereoisomeric alcohols (+)-(a*S*,3*R*,4*S*,8*S*,9*S*)-**29**, (+)-(a*S*,3*R*,4*S*,8*R*,9*R*)-**30**, (−)-(a*S*,3*R*,4*S*,8*S*,9*R*)-**31**, and (+)-(a*S*,3*R*,4*S*,8*R*,9*S*)-**32**, which were separated and configurationally assigned (see below). Thus, the selectivity of the reduction was incomplete and the expected diastereoisomers with the *erythro*-configuration at C(8)–C(9) (−)-

(a*S*,3*R*,4*S*,8*S*,9*R*)-**31** and (+)-(a*S*,3*R*,4*S*,8*R*,9*S*)-**32** were obtained with only 18% de (diastereoisomeric excess). Steric hindrance might account for this reduced selectivity since the 1,1′-binaphthalene moiety is much larger than the quinoline ring present in the naturally occurring *Cinchona* alkaloids. $NaBH_4$ reduction of quininone and quinidinone in EtOH has also been reported to proceed stereoselectively, affording the C(8)–C(9) *threo*-pair of diastereoisomers presumably by attack from the less hindered face of the C=O group [35f]. Again, with the diastereoisomer mixture of binaphthalene-substituted ketones, reduced stereocontrol was observed and the C(8)–C(9) *threo*-pair of diastereoisomers, (+)-(a*S*,3*R*,4*S*,8*S*,9*S*)-**29** and (+)-(a*S*,3*R*,4*S*,8*R*,9*R*)-**30** was obtained with 50% de (*Scheme 6*). Nevertheless, the stereoselectivity of the reductions with DIBAL-H and $NaBH_4$ is similar to that reported by *Gutzwiller* and *Uskokovic* [35f], and the relative configurations at C(8) and C(9) can hence be attributed on this basis.

Separation of the four enantiomerically pure *Cinchona*-alkaloid analogs was achieved by column chromatography on SiO_2 with CH_2Cl_2/MeOH/conc. aq. NH_4OH 90:9:1 as the eluent, and the elucidation of their absolute configurations was subsequently addressed by ^{1}H-NMR methods. In each case, all H-atoms of the binaphthalene moiety could be assigned on the basis of their chemical shifts and coupling patterns. The protons in the quinuclidine ring were assigned on the basis of {^{1}H,^{1}H}-COSY experiments, and ^{1}H{^{1}H}-NOE (nuclear *Overhauser* effect) measurements were then performed to determine the absolute configuration of the diastereoisomers. The (8*S*)-configuration was assigned to compounds (+)-(a*S*,3*R*,4*S*,8*S*,9*S*)-**29** and (−)-(a*S*,3*R*,4*S*,8*S*,9*R*)-**31** on the basis of a strong NOE between H_A–C(2) and H–C(8) (*Fig. 2*). For diastereoisomer (+)-(a*S*,3*R*,4*S*,8*R*,9*R*)-**30**, irradiation of H–C(9) yielded a strong NOE of the resonance around $\delta = 2.40$ ppm which corresponds to H_A–C(2). Correspondingly, irradiation of H_A–C(2) gave an NOE of the resonance at $\delta = 4.15$–4.30 ppm corresponding to H–C(9). Consequently, proton H–C(8) must be in an axial position, and the (8*R*)-configuration was attributed to (+)-(a*S*,3*R*,4*S*,8*R*,9*R*)-**30**. In the case of (+)-(a*S*,3*R*,4*S*,8*R*,9*S*)-**32**, no NOE was detected between H_A–C(2) and H–C(8), but signal overlap interfered with the assignment of the absolute configuration. Having established the C(8) configuration for the three other diastereoisomers, however, the configuration of the last diastereoisomer could be unambiguously deduced. Owing to the rotational freedom around the C(8)–C(9) and C(9)–C(7′) bonds, the absolute configuration at C(9) could, unfortunately, not be directly established by the NOE experiments. The absolute configuration at C(9) could nonetheless be deduced on the assumption that the reduction steps described above proceeded with stereoselectivity similar to that of the reported examples.

The CD spectra of the four diastereoisomeric *Cinchona*-alkaloid analogs are very similar, since they are dominated by the chiroptical contributions from the 1,1′-binaphthalene chromophore. Thus, they were not very useful in providing further support for the configurational assignments made.

The synthesis of the target phase-transfer catalysts was completed by quaternization of the four diastereoisomeric *Cinchona*-alkaloid analogs (+)-**29**, (+)-**30**, (−)-**31**, and (+)-**32** with 4-(trifluoromethyl)benzyl bromide (*Scheme 7*). Three of the resulting diastereoisomeric quats, (+)-(a*S*,3*R*,4*S*,8*R*,9*S*)-**4**, (+)-(a*S*,3*R*,4*S*,8*S*,9*S*)-**5**, and (−)-(a*S*,3*R*,4*S*,8*S*,9*R*)-**7**, were obtained in good yields between 50 and 57%, whereas (+)-

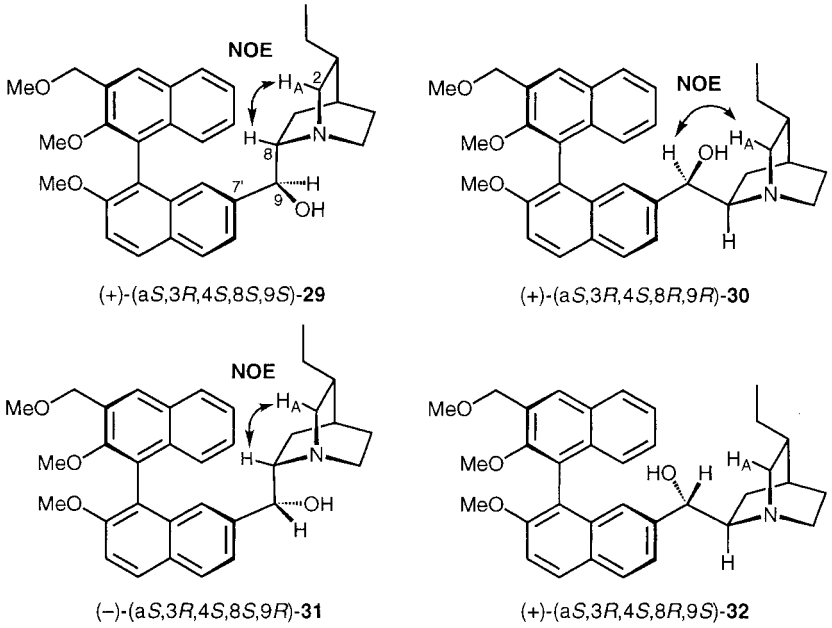
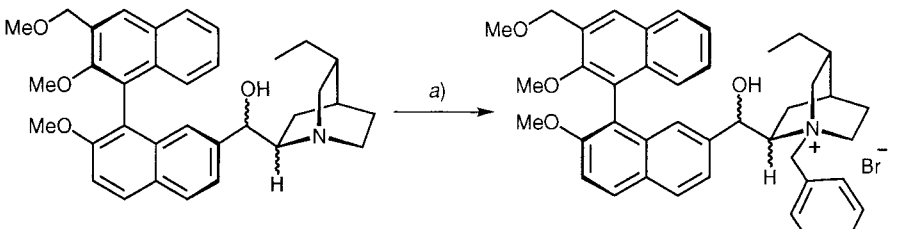


Fig. 2. *Assignment of the absolute configuration at C(8) in the novel* Cinchona-*alkaloid analogs based on NOEs*

(a*S*,3*R*,4*S*,8*R*,9*R*)-**6** was only obtained in very low yield (up to 12%). The presence of a particularly sterically shielded and, therefore, poorly nucleophilic quinuclidine N-atom in precursor (+)-**30** could explain this result. To support this hypothesis, a conformational analysis was undertaken.

Scheme 7. *Formation of the Novel Phase-Transfer Catalysts by Quaternization*



(+)-(a*S*,3*R*,4*S*,8*S*,9*S*)-**29**
(+)-(a*S*,3*R*,4*S*,8*R*,9*R*)-**30**
(–)-(a*S*,3*R*,4*S*,8*S*,9*R*)-**31**
(+)-(a*S*,3*R*,4*S*,8*R*,9*S*)-**32**

(+)-(a*S*,3*R*,4*S*,8*S*,9*S*)-**5** 56%
(+)-(a*S*,3*R*,4*S*,8*R*,9*R*)-**6** 12%
(–)-(a*S*,3*R*,4*S*,8*S*,9*R*)-**7** 54%
(+)-(a*S*,3*R*,4*S*,8*R*,9*S*)-**4** 50%

a) 4-$F_3CC_6H_4CH_2Br$, THF, reflux, 3 d.

2.3. *Conformational Analysis of the Novel* Cinchona-*Alkaloid Analogs.* The four tertiary amines (+)-**29**, (+)-**30**, (–)-**31**, and (+)-**32** were each subjected to a 1000-step pseudo-MCMM conformational search in $CHCl_3$ using the MM2* force field and the GB/SA solvation model implemented in MacroModel V. 6.0.

Similarly to quinine and quinidine derivatives [19][46], the overall conformation of the four new *Cinchona*-alkaloid analogs is largely determined by the freedom of rotation around the C(8)–C(9) and C(9)–C(7′) bonds (for the numbering, see *Fig. 3*) which link the rigid quinuclidine and 1,1′-binaphthalene ring systems together. Four preferred conformations, named 'closed 1', 'closed 2', 'open 1', and 'open 2', defined after the orientation of the quinuclidine N-atom with respect to the binaphthalene moiety [19][46], were obtained from the pseudo-MCMM calculations for each one of the four diastereoisomers. They are shown in *Fig. 3* for the particular case of (+)-(a*S*,3*R*,4*S*,8*R*,9*R*)-**30**, which proved so difficult to be quaternized. Two 'closed' conformations, with a H–C(8)–C(9)–H dihedral angle of *ca.* 60° (*gauche*-conformers), have the quinuclidine N-atom pointing towards the adjacent naphthalene ring, while the two 'open' conformations have the quinuclidine N-atom pointing away from the adjacent naphthalene ring, with H–C(8) and H–C(9) antiperiplanar (dihedral angle of 180°). These conformations can be further distinguished according to the rotation about the C(9)–C(7′) bond. Conformation 'closed 1', with proton H–C(9) close to H–C(8′), has the quinuclidine N-atom pointing inside the 1,1′-binaphthalene major groove. When H–C(9) is near H–C(6′) ('closed 2'), the quinuclidine N-atom is directed towards the face of the adjacent naphthalene ring outside the major groove. The 'open' conformations can be similarly distinguished: the quinuclidine N-atom is located either on one side of the adjacent naphthalene ring (H–C(9) near H–C(6′)) for 'open 1' or on the opposite side (H–C(9) near H–C(8′)) for 'open 2'. By further rotation around the C(8)–C(9) bond, two additional *gauche*-conformations are theoretically possible. They are, however, presumably not found among the calculated low-energy conformations because of unfavorable steric repulsions between the 1,1′-binaphthalene and quinuclidine moieties.

In the two open and two closed conformations of the three other diastereoisomers, the orientation of the quinuclidine N-atom with respect to the binaphthalene moiety is similar to that shown in *Fig. 3* for (+)-**30**. However, due to differences in the configuration at C(8) and C(9), the orientation of H–C(9) with respect to H–C(8) and the naphthalene protons H–C(6′) and H–C(8′) varies among the diastereoisomers. As an example, in the 'closed 1' conformation, both 'pseudo-enantiomers' (+)-**29** and (+)-**30** feature H–C(9) and H–C(8) in a *gauche*-relationship; however, in the former, H–C(9) is located near H–C(6′), whereas, in the latter, H–C(9) is near H–C(8′). Also, H–C(8) and H–C(9) in (+)-**29** and (+)-**30** adopt an *anti*-orientation in the 'open 1' and 'open 2' conformations, whereas, in (–)-**31** and (+)-**32**, they feature the *anti*-orientation in the 'closed 1' and 'closed 2' conformations.

We did not find the computational searches, which also included calculations *in vacuo* and the use of the two other force fields AMBER* [47] and OPLS* [48] implemented in MacroModel, of sufficient accuracy to predict conformational preferences that matched the experimental ^{1}H-NMR spectroscopic data. They were, however, quite helpful for the interpretation of these data. Among the different calculated conformations, we searched for those matching the ^{1}H-NMR coupling constants and NOEs. On this basis, we deduced that diastereoisomer (+)-**30** adopts a 'closed 1' conformation, as indicated by the NOE between H–C(9) and H–C(8′), and the ^3J(8,9) coupling constant of 9.6 Hz (compatible with a dihedral angle of 60°). In the case of compound (+)-**29**, a similar vicinal coupling constant and the NOE between

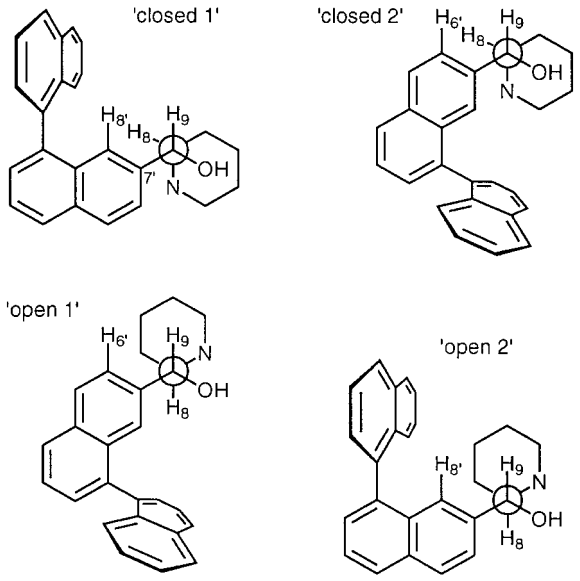


Fig. 3. Newman *projections of the C(8)–C(9) bond for the four possible conformations of diastereoisomer (+)-***30**. The MeO and $MeOCH_2$ substituents on the 1,1′-binaphthalene were omitted for clarity. The three other diastereoisomers (+)-**29**, (−)-**31**, and (+)-**32** also adopt these four conformations; however, due to differences in the configuration at C(8) and C(9), the orientation of H–C(9) with respect to H–C(8) and with respect to the naphthalene protons H–C(6′) and H–C(8′) may vary.

H–C(9) and H–C(8′) suggest a preference for the 'closed 2' conformation, although some 'closed 1' conformation is also present in the equilibrium, as indicated by a weaker NOE between H–C(9) and H–C(6′). For compound (−)-**31**, the 'open 1' conformation, with a 90° H–C(8)–C(9)–H dihedral angle, matched the ^{1}H-NMR coupling constant ($^3J = 6.7$ Hz) and the NOE signal between H–C(9) and H–C(8′). A weak NOE between H–C(9) and H–C(6′) indicated that 'open 2' is also present as a minor conformer. Finally, compound (+)-**32** prefers the 'closed 1' and 'closed 2' conformations. Thus, the spectra of (+)-**32** show a large coupling constant ($^3J(8,9) = 13.4$ Hz) in agreement with an antiperiplanar orientation of H–C(8) and H–C(9) as well as NOEs on H–C(6′) and H–C(8′) upon irradiation of H–C(9).

The conformational analysis by ^{1}H-NMR spectroscopy, aided by the computer modeling, clearly revealed that diastereoisomer (+)-**30** is the only one adopting exclusively 'closed 1' as a preferred conformation. Since this conformation is the one in which the quinuclidine N-atom is the most hindered, it possibly accounts for the low yield obtained in the quaternization reaction. It should, however, be noted that the quaternization was carried out in THF at reflux, whereas the Monte-Carlo minimization and the NMR experiments were performed in chloroform.

2.4. *Catalysis Experiments.* The conditions reported to give the highest enantioselectivity in the asymmetric methylation of phenylindanone **1** in the presence of (+)-(3*R*,4*S*,8*R*,9*S*)-**2** as the chiral phase-transfer agent [10] were used for the catalysis experiments with the novel 1,1′-binaphthalene-derived quats (+)-(a*S*,3*R*,4*S*,8*R*,9*S*)-**4**, (+)-(a*S*,3*R*,4*S*,8*S*,9*S*)-**5**, (+)-(a*S*,3*R*,4*S*,8*R*,9*R*)-**6**, and (−)-(a*S*,3*R*,4*S*,8*S*,9*R*)-**7**. The high

toxicity of gaseous MeCl, however, prompted us to change the alkylating agent to allyl chloride. The phase-transfer catalyzed allylation was first carried out with the achiral catalyst Bu_4NBr, affording racemic indanone (±)-**3b** in 43% yield (*Table*). Catalysis by the cinchonine quat (+)-(3*R*,4*S*,8*R*,9*S*)-**2** afforded indanone (+)-(*S*)-**3b** in 59% yield and 74% ee. Both the chemical and optical yields were lower than those reported for the methylation reaction (95% yield, 92% ee) [10a]. The lower yield, together with the recovery of some starting material, indicated that the allylation is slower than the methylation.

Table. *Enantiomeric Excess* (ee [%]) *Obtained in the Phase-Transfer-Catalyzed Allylation of Phenylindanone* **1**

Catalyst	Yield [%]	(+)-(*S*)-**3b** [%]	(−)-(*R*)-**3b** [%]	ee[a]) [%]
Bu_4NBr	43	50	50	0
(+)-(3*R*,4*S*,8*R*,9*S*)-**2**	59	87	13	74 (*S*)
(+)-(a*S*,3*R*,4*S*,8*R*,9*S*)-**4**	57	66	34	32 (*S*)
(+)-(a*S*,3*R*,4*S*,8*S*,9*S*)-**5**	13	53	47	6 (*S*)
(+)-(a*S*,3*R*,4*S*,8*R*,9*R*)-**6**	45	39	61	22 (*R*)
(−)-(a*S*,3*R*,4*S*,8*S*,9*R*)-**7**	38	42	58	16 (*R*)

[a]) The ee values were determined by analytical HPLC on a '*Pirkle Covalent* D-*Phenylglycine*' chiral stationary phase with 0.1% EtOH in hexane as the mobile phase and a flow rate of 3 ml min^{-1}.

The allylation of phenylindanone **1** was then carried out with the four new quats (+)-**4**, (+)-**5**, (+)-**6**, and (−)-**7** as catalysts. Diastereoisomer (+)-**5** afforded indanone (+)-(*S*)-**3b** in 13% yield in a slow reaction and with a poor ee of 6% (*Table*). Catalysts (+)-**6** and (−)-**7** were more efficient and yielded indanone (−)-(*R*)-**3b** in 22% and 16% ee, and 45% and 38% yield, respectively. The best result was obtained with the designed catalyst (+)-(a*S*,3*R*,4*S*,8*R*,9*S*)-**4**, which afforded (+)-(*S*)-**3b** in 57% yield and 32% ee. The predominant formation of this enantiomer is in accordance with the ion-pair model on which the catalyst design was based (*Fig. 1*). It should be noted that, at this stage, no optimization of the reaction conditions was attempted, which is usually necessary to achieve high ee and yield. We consider the 32% ee obtained in a first, reproducible attempt a very encouraging result, and the accurate prediction of which enantiomer is preferentially formed underlines the potential of molecular modeling as a tool in the development of enantioselective catalysts.

The structures of the ion-pair complexes formed by the three other 1,1′-binaphthalene quats were now calculated with the computational protocol described in *Section 2.1* in order to rationalize the obtained enantioselectivities. To reject structures lacking the H-bond between the OH group of the catalyst and the enolate O-atom, a maximal O−H···O distance of 2.0 Å was defined as a constraint. This H-bond is largely responsible for stereoselective ion-pair formation, and the constraint therefore allows selection only for structures which might explain the enantioselectivity.

The calculated, most stable ion-pair complex formed by (−)-(a*S*,3*R*,4*S*,8*S*,9*R*)-**7** (*Fig. 4*, *A*) displays a set of intermolecular interactions (*i.e.*, a reasonably short O−H···O H-bond, π-π stacking interactions in the 1,1′-binaphthalene major groove, and edge-to-face interactions between the 4-(trifluoromethyl)benzyl ring and the Ph ring of the

enolate) similar to those seen in the complex formed by (+)-(a*S*,3*R*,4*S*,8*R*,9*S*)-**4** (*Fig. 1*). Due to the change in configuration at C(8) and C(9), however, the enolate approaches the catalyst (−)-**7** with its opposite face (as compared to the ion-pair complex of (+)-**4**) in order to undergo these three major interactions. Hence, allylation from the open side of the enolate generates the enantiomeric indanone (−)-(*R*)-**3b**.

In the calculated most stable complex of (+)-(a*S*,3*R*,4*S*,8*R*,9*R*)-**6**, the required H-bond and the π-π stacking interactions between the two Ph rings are effective, whereas the indanone moiety hardly interacts at all with the 1,1′-binaphthalene moiety (*Fig. 4*, *B*). The calculated ion-pair structure, however, correctly predicts the preferential formation of indanone (−)-(*R*)-**3b**.

In the case of catalyst (+)-**5**, no ion-pair complex with the required H-bond was obtained, and all generated structures were rejected by the constraint. Although one should be careful when interpreting negative results, it is perhaps noteworthy that this modeling result matches the low ee (6%) experimentally obtained.

3. Conclusion. – Covalent attachment of quinuclidinemethanol moieties to C(7′) in the major groove of a 1,1′-binaphthalene derivative afforded the novel unnatural *Cinchona*-alkaloid analogs (+)-(a*S*,3*R*,4*S*,8*S*,9*S*)-**29**, (+)-(a*S*,3*R*,4*S*,8*R*,9*R*)-**30**, (−)-(a*S*,3*R*,4*S*,8*S*,9*R*)-**31**, and (+)-(a*S*,3*R*,4*S*,8*R*,9*S*)-**32**. A detailed conformational analysis, combining ^{1}H-NMR spectroscopy and molecular-mechanics computations, revealed that the four diastereoisomers displayed different conformational preferences. Compound (+)-**30** exclusively adopts the 'closed 1' conformation in which the quinuclidine N-atom points into the major groove of the 1,1′-binaphthalene moiety. As a result of this steric hindrance, *N*-alkylation of this diastereoisomer proved to be very difficult. Diastereoisomers (+)-**29** and (+)-**32** exist at room temperature in both the 'closed 1' and the less sterically hindered 'closed 2' conformation, in which the quinuclidine N-atom points towards the adjacent naphthalene ring, whereas (−)-**31** prefers the 'open 1' conformation with the N-atom turned away from the binaphthalene moiety. These unnatural *Cinchona*-alkaloid analogs are now being tested as catalysts in various asymmetric syntheses, such as the *Sharpless* dihydroxylation reaction [20]. Furthermore, a new series of hybrid compounds, in which quinuclidinemethanol moieties are attached to C-atoms in the minor groove of 1,1′-binaphthalene derivatives, are currently under construction.

The four diastereoisomeric *Cinchona*-alkaloid analogs were quaternized with 4-(trifluoromethyl)benzyl bromide and the resulting phase-transfer agents used for the enantioselective allylation of phenylindanone **1**. ee Values ranging from 6 to 32% (13 to 57% yield) were obtained without optimization of the reaction conditions. Although the yields and enantioselectivities remain to be improved, this research demonstrates the potential of incorporating 1,1′-binaphthalene moieties into *Cinchona*-alkaloid analogs for obtaining stereoselective catalysts. A remarkable performance of computer modeling both in the catalyst design and the rationalization of the PTC results was obtained. The designed catalyst (+)-**4** showed the best performance, as predicted, and the computer calculations could rationalize the enantioselectivity observed with two of the other catalysts and predict which enantiomer would be preferentially formed. We, therefore, believe that this study demonstrates the potential of molecular modeling in asymmetric catalysis, and expect that modeling strategies will be generalized over the

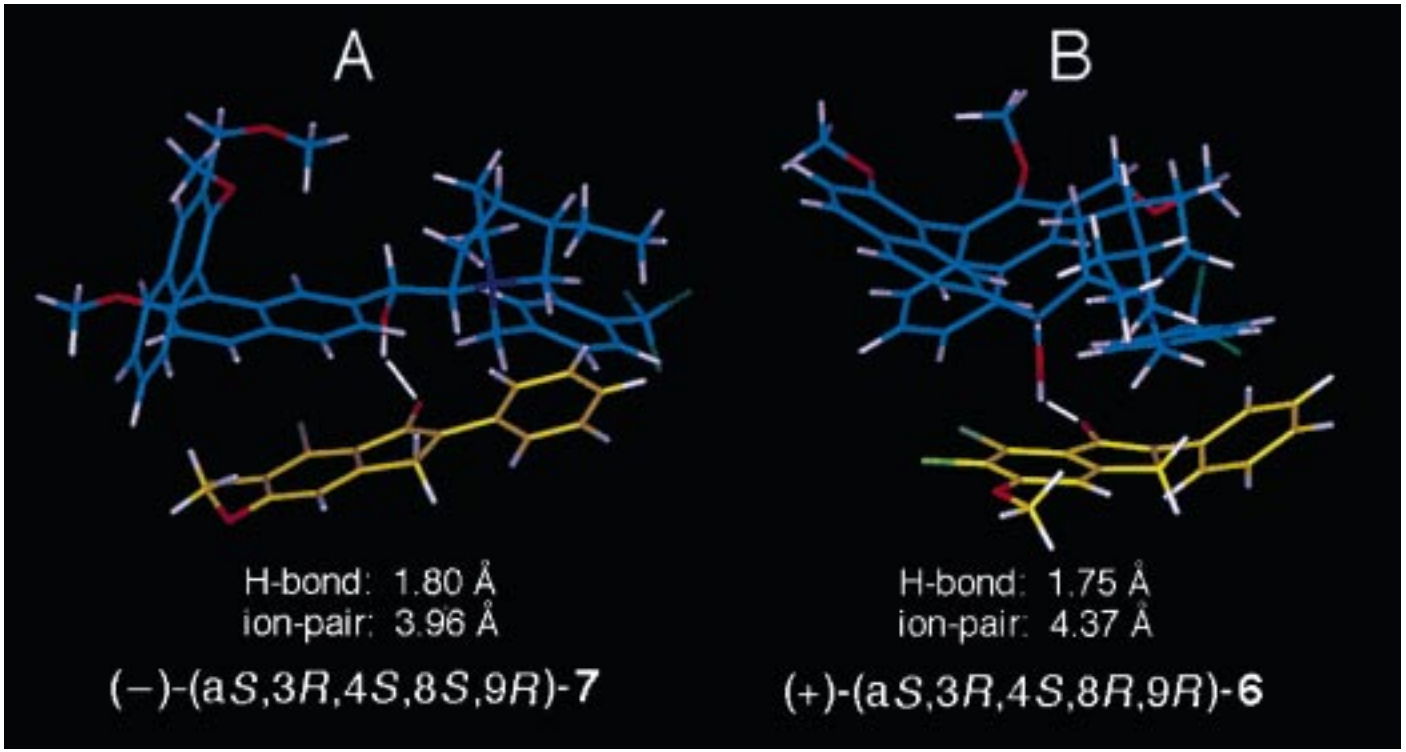


Fig. 4. *Structures of the ion-pairing complexes formed by the 1,1′-binaphthalene quats (−)-***7** (A) *and (+)-***6** (B) *with the enolate of* **1**, *as calculated in 5000-step pseudo-MCMM searches*

next few years to allow for a more systematic, less empirical approach to the design of new catalysts.

Experimental Part

General. Solvents and reagents were of reagent-grade, purchased from commercial suppliers, and used without further purification unless otherwise stated. Quinuclidine derivative (+)-**9** was purchased from *Buchler GmbH*, Braunschweig. THF and Et_2O were freshly distilled from sodium benzophenone ketyl. Evaporation *in vacuo* was conducted at H_2O aspirator pressure. Column chromatography (CC): SiO_2 *60* (230–400 mesh, 0.040–0.063 mm) from *Fluka*. M.p.: *Büchi SMP-20*; uncorrected. IR Spectra [cm^{-1}]: *Perkin-Elmer 1600-FT IR*. NMR Spectra: *Bruker AMX 500* and *Varian Gemini 300* or *200* at 296 K, with solvent peak as reference. MS (*m*/*z* (%)): EI and DEI: *VG TRIBRID* spectrometer at 70 eV; FAB: *VG ZAB2-SEQ* spectrometer with 3-nitrobenzyl alcohol as matrix. Elemental analyses were performed by the Mikrolabor at the Laboratorium für Organische Chemie, ETH-Zürich.

*(3*R*,4*S*,8*R*)*-N-*Methoxy*-N-*methyl-3-vinyl-1-azabicyclo[2.2.2]octane-8-carboxamide* ((+)-**10**). To a soln. of (+)-**9** (130 mg, 0.78 mmol) in acetone (10 ml) cooled to 0°, CrO_3 (94 mg, 0.94 mmol) and conc. H_2SO_4 (0.42 ml, 7.78 mmol), were added and the soln. was stirred at r.t. for 5 h. The mixture was neutralized with 1M aq. NaOH (*ca*. 8 ml), washed with CH_2Cl_2 (50 ml), filtered, and purified by ion-exchange chromatography (H_2O, then 1M aq. NH_4OH) on *Dowex* ion-exchange resin *50WX4* (H^+ form). To the residue, CH_2Cl_2 (100 ml) and PCl_5 (145 mg, 0.72 mmol) were added, and the soln. was heated at reflux for 4 h. The soln. was then cooled to 0°, MeHNOMe · HCl (68 mg, 0.72 mmol) was added, followed by Et_3N (dropwise up to pH 9), and the soln. was stirred at r.t. for 3 h. The mixture was quenched with a sat. aq. $NaHCO_3$ soln. (100 ml), the org. phase separated, and the aq. phase extracted with CH_2Cl_2 (2 × 100 ml). The combined org. extracts were dried (Na_2SO_4), evaporated *in vacuo*, and purified by CC (SiO_2; CH_2Cl_2/MeOH/NH_4OH 90 : 9 : 1) to give (+)-**10** (76 mg, 44%). Yellow oil. $[\alpha]_D^{r.t.} = +121.1$ (*c* = 1.00, $CHCl_3$). IR ($CHCl_3$): 2939*m*, 1658*s*, 1456*w*, 1178*w*, 1136*w*, 909*m*. ^{1}H-NMR (200 MHz, $CDCl_3$): 6.11–5.94 (*m*, 1 H); 5.10–5.04 (*m*, 1 H); 5.00 (*d*, *J* = 0.8, 1 H); 3.83–3.71 (*m*, 1 H); 3.75 (*s*, 3 H); 3.22 (*s*, 3 H); 3.02–2.77 (*m*, 4 H); 2.32–2.16 (*m*, 2 H); 1.84–1.77 (*m*, 1 H); 1.68–1.58 (*m*, 2 H); 1.53–1.38 (*m*, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 140.7; 114.9; 61.4; 55.3; 49.0; 48.7; 40.2; 27.7; 26.5; 22.6. EI-MS: 224 (10, M^+), 193 (34, [*M* − OMe]$^+$), 164 (21, [*M* − N(Me)OMe]$^+$), 136 (100, [*M* − CON(Me)OMe]$^+$). EI-HR-MS: 224.1531 (M^+, $C_{12}H_{20}N_2O_2$; calc. 224.1525).

*(3*R*,4*S*,8*R*)*-N-*Methoxy*-N-*methyl-3-ethyl-1-azabicyclo[2.2.2]octane-8-carboxamide* ((+)-**8**). A soln. of (+)-**10** (90 mg, 0.40 mmol) in EtOH (10 ml) was treated with 10% Pd/C (10 mg) under H_2 (2 bar) for 3 h. The mixture was filtered through *Celite* and evaporated *in vacuo* to give (+)-**8** (90 mg, 99%). Colorless oil. $[\alpha]_D^{r.t.} = +111.5$ (*c* = 1.00, $CHCl_3$). IR ($CHCl_3$): 2937*s*, 2873*m*, 1657*s*, 1456*m*, 983*m*. ^{1}H-NMR (200 MHz, $CDCl_3$): 3.75 (*s*, 3 H); 3.75–3.65 (*m*, 1 H); 3.22 (*s*, 3 H); 2.98–2.40 (*m*, 4 H); 2.28–2.10 (*m*, 1 H); 1.74–1.26 (*m*, 7 H); 0.86 (*t*, *J* = 7.1, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 61.4; 55.3; 50.7; 48.9; 37.5; 27.5; 25.8; 25.3; 22.4; 12.0. EI-MS: 226 (2, M^+), 195 (41, [*M* − OMe]$^+$), 166 (51, [*M* − N(Me)OMe]$^+$), 138 (100, [*M* − CON(Me)OMe]$^+$). EI-HR-MS: 226.1681 (M^+, $C_{12}H_{22}N_2O_2$; calc. 226.1682).

Methyl 3-Hydroxynaphthalene-2-carboxylate (**13**). To a stirred soln. of **12** (20.00 g, 106.28 mmol) in MeOH (100 ml) cooled to 0°, dry HCl gas was added until no more absorption could be observed. The soln. was then heated to reflux for 2 h, left to stand at r.t. for 12 h, and evaporated *in vacuo* to give **13** (21.27 g, 99%). Light-brown solid. M.p. 74–75° ([49]: 72°). ^{1}H-NMR (200 MHz, $CDCl_3$): 10.43 (*s*, 1 H); 8.50 (*s*, 1 H); 7.83–7.79 (*m*, 1 H); 7.72–7.67 (*m*, 1 H); 7.55–7.47 (*m*, 1 H); 7.37–7.29 (*m*, 1 H); 7.32 (*s*, 1 H); 4.04 (*s*, 3 H).

7-Bromonaphthalen-2-ol (**15**). To a mechanically stirred soln. of Ph_3P (14.41 g, 54.94 mmol) in MeCN (12.5 ml), Br_2 (2.82 ml, 54.94 mmol) was added dropwise at 0°. The soln. was allowed to reach r.t., and **14** (8.00 g, 45.95 mmol) in MeCN (10 ml) was added in one portion. The mixture was heated to 60–70° for 30 min, then the solvent was distilled under reduced pressure. The mixture was heated to 250° for 1 h, cooled down to r.t., and dissolved in CH_2Cl_2 (200 ml). The soln. was washed with 1M aq. NaOH (200 ml), acidified with 1M aq. HCl (250 ml), and extracted with CH_2Cl_2 (3 × 200 ml). The combined org. extracts were dried ($MgSO_4$), evaporated *in vacuo*, and purified by CC (SiO_2; CH_2Cl_2) to give **15** (7.11 g; 64%). Colorless solid. M.p. 130–132° ([50]: 132–133°). ^{1}H-NMR (200 MHz, $CDCl_3$): 7.84 (*d*, *J* = 1.9, 1 H); 7.72 (*d*, *J* = 8.7, 1 H); 7.63 (*d*, *J* = 8.7, 1 H); 7.40 (*dd*, *J* = 8.7, 1.9, 1 H); 7.11 (*dd*, *J* = 8.7, 2.3, 1 H); 7.06 (*d*, *J* = 2.3, 1 H); 5.14 (br. *s*, 1 H).

(±)-Methyl 7′-Bromo-2,2′-dihydroxy-1,1′-binaphthalene-3-carboxylate ((±)-**17**). To a degassed soln. of **13** (4.53 g, 22.41 mmol), **15** (5.00 g, 22.41 mmol), and $CuCl_2$ (12.05 g, 89.64 mmol) in MeOH (800 ml), *t*-$BuNH_2$ (37.84 ml, 358.56 mmol) was slowly added, and the soln. was heated to 50° for 2 h. The mixture was then allowed to cool to r.t., 1M aq. HCl (400 ml) was added, and MeOH was evaporated *in vacuo*. H_2O (100 ml) was added

and the soln. extracted with CH_2Cl_2 (500 ml). The org. phase was washed with H_2O (300 ml) and sat. aq. $NaHCO_3$ soln. (300 ml), dried ($MgSO_4$), evaporated *in vacuo*, and purified by CC (SiO_2; CH_2Cl_2) to give (±)-**17** (7.46 g, 79%). Light-yellow solid. M.p. 229–232°. IR ($CHCl_3$): 1684*m*, 1616*w*, 1503*m*, 1445*w*, 1433*w*, 1340*m*, 1322*m*, 1279*w*, 1183*m*, 1156*s*, 1136*s*. ^{1}H-NMR (200 MHz, $CDCl_3$): 10.88 (*s*, 1 H); 8.76 (*s*, 1 H); 7.99–7.94 (*m*, 1 H); 7.89 (*d*, *J* = 8.7, 1 H); 7.74 (*d*, *J* = 8.7, 1 H); 7.44–7.35 (*m*, 4 H); 7.22–7.13 (*m*, 2 H); 4.98 (*s*, 1 H); 4.10 (*s*, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 170.6; 155.4; 152.5; 137.5; 135.1; 134.5; 130.7; 130.4; 130.3; 130.2; 128.0; 127.7; 127.1; 126.9; 124.9; 124.6; 121.5; 118.4; 114.7; 113.7; 111.2; 53.0. DEI-MS: 424/422 (100/96, M^+), 348/346 (48/50, $[M - COOMe - OH]^+$), 239(49), 226(88). Anal. calc. for $C_{22}H_{15}BrO_4$ (423.3): C 62.43, H 3.57, Br 18.88; found: C 62.31, H 3.34, Br 18.96.

Methyl 7′-Bromo-2,2′-bis[(1S)-camphor-10-(sulfonyloxy)]-1,1′-binaphthalene-3-carboxylates ((+)-**19**) and ((−)-**20**). To a soln. of (±)-**17** (100 mg, 0.23 mmol) in CH_2Cl_2 (10 ml), Et_3N (0.08 ml, 0.58 mmol) was added at 0°, followed by (+)-(1*S*)-camphor-10-sulfonyl chloride (128 mg, 0.51 mmol). The soln. was stirred at 0° for 3 h and then at r.t. for 2 h. The reaction was quenched with H_2O (50 ml) and the mixture extracted with CH_2Cl_2 (3 × 50 ml). The combined org. extracts were dried ($MgSO_4$), evaporated *in vacuo*, and purified by CC (SiO_2; CH_2Cl_2/AcOEt 99 : 1) to yield (+)-**19** and (−)-**20**.

*Data of (+)-(a*S*)-***19***: 80 mg, 40%. Colorless solid. M.p. 105–107°. $[\alpha]_D^{r.t.} = +29.1$ (*c* = 1.00, $CHCl_3$). IR ($CHCl_3$): 2961*m*, 1746*s*, 1496*m*, 1453*m*, 1378*s*, 1365*s*, 1290*m*, 1189*m*, 1167*s*. ^{1}H-NMR (200 MHz, $CDCl_3$): 8.66 (*s*, 1 H); 8.07–8.01 (*m*, 2 H); 7.86–7.80 (*m*, 2 H); 7.65–7.46 (*m*, 3 H); 7.39–7.36 (*m*, 1 H); 7.32–7.27 (*m*, 1 H); 4.01 (*s*, 3 H); 3.05, 2.58 (*AB*, J_{AB} = 15.0, 2 H); 3.02, 2.87 (*AB*, J_{AB} = 14.7, 2 H); 2.31–1.72 (*m*, 10 H); 1.53–1.14 (*m*, 4 H); 0.88 (*s*, 3 H); 0.77 (*s*, 3 H); 0.66 (*s*, 3 H); 0.59 (*s*, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 213.8; 213.7; 166.1; 147.2; 143.0; 134.9; 134.6; 131.2; 131.0; 130.3; 130.1 (2×); 129.9; 129.5; 128.5; 127.8; 126.9; 126.2; 125.2; 122.6; 122.2; 121.5; 58.0; 57.8; 52.8; 49.3; 49.2; 47.8; 47.7; 42.8; 42.8; 42.3; 42.3; 26.8; 26.7; 24.9; 24.8; 19.6; 19.4; 19.3 (2×). DEI-MS: 852/850 (1/1, M^+), 821/819 (1/1, $[M - OMe]^+$), 638/636 (80/75), 424/422 (100/99). Anal. calc. for $C_{42}H_{43}BrO_{10}S_2$ (851.8): C 59.22, H 5.09, S 7.53, Br 9.38; found: C 59.08, H 5.11, S 7.28, Br 9.10.

*Data of (−)-(a*R*)-***20***: 80 mg, 40%. Colorless solid. M.p. 101–104°. $[\alpha]_D^{r.t.} = -36.6$ (*c* = 1.00, $CHCl_3$). IR ($CHCl_3$): 2962*w*, 1747*s*, 1496*w*, 1454*w*, 1376*m*, 1367*m*, 1290*w*, 1189*m*, 1167*s*. ^{1}H-NMR (200 MHz, $CDCl_3$): 8.66 (*s*, 1 H); 8.08–8.03 (*m*, 2 H); 7.89–7.81 (*m*, 2 H); 7.63–7.42 (*m*, 3 H); 7.34–7.33 (*m*, 1 H); 7.22–7.18 (*m*, 1 H); 4.02 (*s*, 3 H); 3.32, 2.46 (*AB*, J_{AB} = 14.9, 2 H); 3.19, 2.36 (*AB*, J_{AB} = 14.5, 2 H); 2.28–1.73 (*m*, 10 H); 1.42–1.19 (*m*, 4 H); 0.80 (*s*, 3 H); 0.74 (*s*, 3 H); 0.54 (*s*, 3 H); 0.48 (*s*, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 213.8; 213.6; 166.2; 147.0; 143.1; 134.9; 134.5; 131.2 (2×); 130.4; 130.3; 130.2; 129.8; 129.5; 128.5; 127.7; 126.9; 126.0; 125.5; 122.6; 122.5; 121.7; 58.0; 57.8; 52.8; 49.5; 49.3; 47.7; 47.5; 42.8 (2×); 42.3 (2×); 26.7 (2×); 24.8; 24.6; 19.5; 19.4; 19.2; 19.2. DEI-MS: 852/850 (1/1, M^+), 821/819 (1/1, $[M - OMe]^+$), 638/636 (97/87), 424/422 (96/100). Anal. calc. for $C_{42}H_{43}BrO_{10}S_2$ (851.8): C 59.22, H 5.09, S 7.53, Br 9.38; found: C 58.94, H 5.27, S 7.28, Br 9.11.

*(a*S*)-Methyl 2,2′-Dihydroxy-1,1′-binaphthalene-3-carboxylate* ((−)-**21**) [39c]. To (+)-**19** (165 mg, 0.19 mmol) in dry THF (10 ml) at −78° under Ar, BuLi (1.6M soln. in hexanes, 0.36 ml, 0.58 mmol) was added, and the soln. was stirred at r.t. for 2 h. The reaction was quenched with MeOH (0.5 ml) and 1M aq. HCl (50 ml), and the mixture was extracted with CH_2Cl_2 (3 × 50 ml). The combined org. extracts were dried (Na_2SO_4) and evaporated *in vacuo*. The residue was dissolved in MeOH (25 ml) and 1M aq. NaOH (25 ml), and the soln. was heated at reflux for 12 h. MeOH was evaporated *in vacuo*, 1M aq. HCl (50 ml) added, and the soln. extracted with CH_2Cl_2 (3 × 50 ml). The combined org. extracts were dried (Na_2SO_4) and evaporated *in vacuo*. The residue was diluted with MeOH (50 ml), treated with dry HCl gas at 0° for 15 min, and left to stand at r.t. for 12 h. MeOH was evaporated *in vacuo* and the product purified by CC (SiO_2; CH_2Cl_2) to give (−)-**21** (40 mg, 60%). Yellow, amorphous solid. $[\alpha]_D^{r.t.} = -48.0$ (*c* = 1.00, $CHCl_3$), −126.0 (*c* = 1.00, THF). ^{1}H-NMR (200 MHz, $CDCl_3$): 10.88 (*s*, 1 H); 8.76 (*s*, 1 H); 7.99–7.87 (*m*, 2 H); 7.74 (*d*, *J* = 8.7, 1 H); 7.44–7.13 (*m*, 7 H); 4.99 (*s*, 1 H); 4.10 (*s*, 3 H).

*(a*S*)-Methyl 7′-Bromo-2,2′-dimethoxy-1,1′-binaphthalene-3-carboxylate* ((−)-**22**). A soln. of (+)-**19** (760 mg, 0.89 mmol) in MeOH (50 ml) and 1M aq. NaOH (25 ml) was heated to reflux for 20 h. MeOH was evaporated *in vacuo*, 1M aq. HCl (60 ml) added, and the soln. extracted with CH_2Cl_2 (3 × 60 ml). The combined org. extracts were dried ($MgSO_4$) and evaporated *in vacuo*. The residue was dissolved in acetone (100 ml), and KOH (400 mg, 7.12 mmol) was added. After stirring for 30 min, $(MeO)_2SO_2$ (0.51 ml, 5.34 mmol) was added and the soln. heated to reflux for 3 h. The reaction was quenched with 1M aq. HCl (50 ml), the acetone was evaporated *in vacuo*, and the soln. was extracted with CH_2Cl_2 (3 × 50 ml). The combined org. extracts were dried (Na_2SO_4), evaporated *in vacuo*, and purified by CC (SiO_2; hexane/AcOEt 8 : 2) to afford (−)-**22** (389 mg, 97%). Colorless, amorphous solid. $[\alpha]_D^{r.t.} = -43.5$ (*c* = 1.00, $CHCl_3$). IR ($CHCl_3$): 1705*s*, 1257*m*, 1175*m*, 1150*m*,

1139*m*. ^{1}H-NMR (200 MHz, $CDCl_3$): 8.55 (*s*, 1 H); 8.00–7.96 (*m*, 2 H); 7.74 (*d*, *J* = 8.7, 1 H); 7.50–7.30 (*m*, 4 H); 7.23 (*d*, *J* = 1.7, 1 H); 7.12–7.07 (*m*, 1 H); 4.01 (*s*, 3 H); 3.79 (*s*, 3 H); 3.49 (*s*, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 167.3; 155.9; 154.7; 135.9; 135.5; 133.6; 130.2; 130.0; 129.9; 129.4; 128.7; 127.6; 127.4; 127.2; 126.6; 125.8; 125.5; 125.0; 121.7; 118.1; 113.8; 61.9; 56.5; 52.5. DEI-MS: 452/450 (100/100, M^+). Anal. calc. for $C_{24}H_{19}BrO_4$ (451.3): C 63.87, H 4.24, Br 17.70; found: C 63.93, H 4.22, Br 17.59.

*(a*S*)-7′-Bromo-2,2′-dimethoxy-1,1′-binaphthalene-3-methanol* ((+)-**23**). To (−)-**22** (360 mg, 0.80 mmol) in CH_2Cl_2 (30 ml) at −78° under Ar, DIBAL-H (1M soln. in hexane, 3.19 ml, 3.19 mmol) was added, and the soln. was stirred at r.t. for 2.5 h. The reaction was quenched with a sat. aq. NaCl soln. (50 ml), the org. phase separated, and the aq. phase extracted with CH_2Cl_2 (2 × 50 ml). The combined org. extracts were dried ($MgSO_4$), evaporated *in vacuo*, and purified by CC (SiO_2; CH_2Cl_2/MeOH 99 : 1) to give (+)-**23** (243 mg, 72%). Colorless, amorphous solid $[\alpha]_D^{r.t.} = +63.2$ (*c* = 1.00, $CHCl_3$). IR ($CHCl_3$): 3422*m*, 1611*m*, 1500*m*, 1255*s*. ^{1}H-NMR (200 MHz, $CDCl_3$): 8.76–7.88 (*m*, 3 H); 7.75 (*d*, *J* = 8.7, 1 H); 7.51–7.37 (*m*, 3 H); 7.30–7.21 (*m*, 2 H); 7.11–7.07 (*m*, 1 H); 5.04–4.88 (*m*, 2 H); 3.80 (*s*, 3 H); 3.41 (*s*, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 156.0; 155.0; 135.5; 134.0; 133.8; 131.0; 130.2; 129.9; 128.5; 128.3; 127.7; 127.5; 127.4; 126.5; 125.3; 125.3; 124.0; 121.7; 118.6; 113.9; 62.5; 60.8; 56.6. DEI-MS: 424/422 (97/100, M^+). DEI-HR-MS: 422.0516 (M^+, $C_{23}H_{19}BrO_3$; calc. 422.0518).

*(a*S*)-7′-Bromo-2,2′-dimethoxy-3-(methoxymethyl)-1,1′-binaphthalene* ((−)-**11**). To (+)-**23** (180 mg, 0.43 mmol) in acetone (20 ml), $(MeO)_2SO_2$ (0.12 ml, 1.29 mmol) was added, followed by NaH (41 mg, 1.72 mmol), and the soln. was stirred at r.t. for 1 h. The reaction was quenched with 1M aq. HCl (50 ml) and the mixture extracted with CH_2Cl_2 (3 × 50 ml). The combined org. extracts were dried (Na_2SO_4), evaporated *in vacuo*, and purified by CC (SiO_2; hexane/AcOEt 90 : 10) to give (−)-**11** (180 mg, 97%). Colorless, amorphous solid. $[\alpha]_D^{r.t.} = -14.6$ (*c* = 1.00, $CHCl_3$). IR ($CHCl_3$): 1499*m*, 1257*s*, 1150*s*, 1136*s*, 1111*s*. ^{1}H-NMR (200 MHz, $CDCl_3$): 8.05 (*s*, 1 H); 7.99 (*d*, *J* = 8.7, 1 H); 7.93 (*d*, *J* = 8.3, 1 H); 7.76 (*d*, *J* = 8.7, 1 H); 7.51–7.39 (*m*, 3 H); 7.29–7.23 (*m*, 2 H); 7.12–7.07 (*m*, 1 H); 4.78 (*s*, 2 H); 3.80 (*s*, 3 H); 3.59 (*s*, 3 H); 3.41 (*s*, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 156.0; 155.0; 135.7; 133.8; 131.7; 131.0; 130.1; 129.9; 129.1; 128.4; 127.7; 127.4 (2×); 126.4; 125.3; 125.1; 124.2; 121.6; 118.9; 114.0; 70.6; 61.1; 58.7; 56.6. DEI-MS: 438/436 (100/100, M^+), 407/405 (16/16, $[M - OMe]^+$). Anal. calc. for $C_{24}H_{21}BrO_3$ (437.3): C 65.91, H 4.84, Br 18.27; found: C 65.97, H 4.87, Br 18.35.

*(a*RS*)-2,2′-Dimethoxy-3-(methoxymethyl)-1,1′-binaphthalene* ((±)-**24**). Colorless solid, M.p. 132–134° (AcOEt). IR ($CHCl_3$): 3007*m*, 1359*m*, 1266*s*, 1248*s*, 1148*m*, 1112*s*, 1089*m*. ^{1}H-NMR (200 MHz, $CDCl_3$): 8.04–8.00 (*m*, 2 H); 7.92–7.86 (*m*, 2 H); 7.47 (*d*, *J* = 9.1, 1 H); 7.43–7.10 (*m*, 6 H); 4.77 (*s*, 2 H); 3.80 (*s*, 3 H); 3.57 (*s*, 3 H); 3.38 (*s*, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 155.3; 154.9; 134.3; 134.0; 131.7; 130.9; 130.0; 129.3; 128.6; 128.2; 128.1; 126.9; 126.2; 125.6; 125.5; 125.0; 123.9; 119.4; 113.8; 70.6; 61.0; 58.7; 56.7. DEI-MS: 358 (100, M^+). Anal. calc. for $C_{24}H_{22}O_3$ (358.4): C 80.42, H 6.19; found: C 80.40, H 6.30.

*(a*RS*)-Tributyl[2,2′-dimethoxy-3′-(methoxymethyl)-1,1′-binaphthalen-7-yl]stannane* ((±)-**26**). To hexabutyldistannane (1.35 ml, 2.70 mmol) in dry THF (10 ml) at 0° under Ar, BuLi (1.6M soln. in hexanes, 1.56 ml, 2.50 mmol) was added, and the soln. was stirred at 0° for 15 min to afford a 0.17M soln. of Bu_3SnLi [44]. A portion of this soln. (5.56 ml, 0.95 mmol) was added at 0° under Ar to (±)-**11** (277 mg, 0.63 mmol) in dry THF (20 ml), and the soln. was stirred at 0° for 30 min. The reaction was quenched with a sat. aq. NH_4Cl soln. (50 ml), and the mixture was extracted with AcOEt (2 × 50 ml). The combined org. extracts were dried (Na_2SO_4), evaporated *in vacuo*, and purified by CC (SiO_2; hexane/AcOEt 90 : 10) to give (±)-**26** (209 mg, 51%). Colorless oil. IR ($CHCl_3$): 2973*s*, 2928*s*, 1247*s*, 1139*m*, 1111*m*, 1047*s*. ^{1}H-NMR (200 MHz, $CDCl_3$): 8.00 (*s*, 1 H); 7.97 (*d*, *J* = 9.1, 1 H); 7.88 (*d*, *J* = 8.3, 1 H); 7.81 (*d*, *J* = 7.9, 1 H); 7.46–7.32 (*m*, 3 H); 7.23–7.09 (*m*, 3 H); 4.77 (*s*, 2 H); 3.79 (*s*, 3 H); 3.55 (*s*, 3 H); 3.35 (*s*, 3 H); 1.37–1.01 (*m*, 12 H); 0.84–0.69 (*m*, 15 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 155.2; 154.9; 140.7; 134.4; 134.0; 133.8; 131.4; 131.1; 130.9; 129.8; 129.2; 128.4; 128.2; 126.9; 126.1; 125.7; 124.8; 119.1; 114.0; 70.6; 60.9; 58.5; 56.9; 28.9; 27.2; 13.6; 9.5. DEI-MS: 648/646 (4/3, M^+ (^{120}Sn/^{118}Sn)), 561/559 (100/73, $[M - OMe - Bu + H]^+$), 447/445 (49/39, $[M - OMe - 3\,Bu + H^+$), 282 (36). Anal. calc. for $C_{36}H_{48}O_3Sn$ (647.5): C 66.78, H 7.47; found: C 66.51, H 7.47.

*(a*S*,3*R*,4*S*,8*R*)- and (a*S*,3*R*,4*S*,8*S*)-[2,2′-Dimethoxy-3′-(methoxymethyl)-1,1′-binaphthalen-7-yl](3-ethyl-1-azabicyclo[2.2.2]oct-8-yl)methanone* (**27**/**28**). To (−)-**11** (250 mg, 0.57 mmol) and (+)-**8** (258 mg, 1.14 mmol) in dry THF (25 ml) at −78° under Ar, BuLi (1.6M soln. in hexanes, 0.71 ml, 1.14 mmol) was added dropwise, and the soln. was stirred at this temp. for 10 min. The reaction was quenched with sat. aq. $NaHCO_3$ soln. (50 ml) and the mixture extracted with CH_2Cl_2 (3 × 50 ml). The combined org. extracts were dried (Na_2SO_4), evaporated *in vacuo*, and purified by CC (SiO_2; AcOEt) to afford **27**/**28** (137 mg, 46%) as an inseparable 1 : 1 mixture. Colorless oil. IR ($CHCl_3$): 2956*s*, 2935*s*, 1683*w*, 1459*m*, 1136v*s*. ^{1}H-NMR (200 MHz, $CDCl_3$): 8.05–7.85 (*m*, 6 H); 7.56 (*dd*, *J* = 9.1, 1.7, 1 H); 7.43–7.36 (*m*, 1 H); 7.23–7.04 (*m*, 2 H); 4.78–4.77 (*m*, 2 H); 3.83 (*s*, 1.5 H); 3.82 (*s*, 1.5 H); 3.82–3.69 (*m*, 1 H); 3.58 (*s*, 1.5 H); 3.57 (*s*, 1.5 H); 3.38 (*s*, 1.5 H); 3.35 (*s*, 1.5 H);

2.95–2.04 (*m*, 4 H); 1.68–0.91 (*m*, 8 H); 0.82 (*t*, *J* = 6.9, 1.5 H); 0.76 (*t*, *J* = 6.9, 1.5 H). ^{13}C-NMR (75 MHz, $CDCl_3$): [199.4; 199.3]; [155.8; 155.7]; [155.1; 155.0]; 134.3; 134.1; 133.9; 133.9; 133.6; 133.5; 131.8; 131.5; 131.3; 131.2; 130.9; 129.8; 129.7; 128.9; 128.9; 128.8; 128.8; 128.4 (2×); 128.2; [126.4; 126.3]; 125.7; 125.5; [125.1; 125.0]; [124.3; 124.3]; 122.6; 122.5; 121.2; 116.1; 116.0; [70.7; 70.6]; [61.2; 61.1]; 60.5; [58.7; 58.7]; [56.8; 56.7]; 50.8; 48.2; 42.8; [37.5; 37.5]; 28.1; 27.7; 27.5; 25.9; 25.4; 25.3; 22.6; 22.5; 21.8. DEI-MS: 523 (14, M^+), 508 (20, $[M - Me]^+$), 357 (13, $[M - COC_9H_{16}N]^+$), 138 (100, $[C_9H_{16}N]^+$). DEI-HR-MS: 523.2713 (M^+, $C_{34}H_{37}NO_4$; calc. 523.2722).

Four Diastereoisomers of [2,2′-Dimethoxy-3′-(methoxymethyl)-1,1′-binaphthalen-7-yl](3-ethyl-1-azabicyclo[2.2.2]oct-8-yl)methanol ((+)-**29**, (+)-**30**, (−)-**31**, and (+)-**32**). To the 1:1 mixture **27**/**28** (120 mg, 0.23 mmol) in benzene (50 ml) at 0°, DIBAL-H (1M soln. in hexane, 0.69 ml, 0.69 mmol) was added, and the soln. was stirred at r.t. for 4 h. The reaction was quenched with a sat. aq. $NaHCO_3$ soln. (50 ml) and the mixture extracted with CH_2Cl_2 (3 × 50 ml). The combined org. extracts were dried (Na_2SO_4), evaporated *in vacuo*, and purified by CC (SiO_2; CH_2Cl_2/MeOH/NH_4OH 90:9:1) to give the pure four diastereoisomers.

*Data of (+)-(a*S,*3*R,*4*S,*8*S,*9*S*)-***29***: 12 mg, 10%. Yellow, highly viscous oil. $[\alpha]_D^{r.t.} = +36.7$ ($c = 0.50$, $CHCl_3$). IR ($CHCl_3$): 2925*w*, 1133*vs*. ^{1}H-NMR (300 MHz, $CDCl_3$)^2): 8.02 (*s*, H−C(4″)); 7.98 (*d*, *J* = 9.0, H−C(4′)); 7.90 (*d*, *J* = 7.4, H−C(5″)); 7.88 (*d*, *J* = 8.7, H−C(5′)); 7.47–7.45 (*m*, H−C(6′)); 7.44 (*d*, *J* = 9.0, H−C(3′)); 7.40–7.35 (*m*, H−C(6″)); 7.22–7.17 (*m*, H−C(7″)); 7.08 (*d*, *J* = 8.4, H−C(8″)); 7.04 (*s*, H−C(8′)); 4.79 (*d*, *J* = 12.5, 1 H−C(12)); 4.73 (*d*, *J* = 12.5, 1 H−C(12)); 4.13 (*d*, *J* = 9.7, H−C(9)); 3.77 (*s*, MeO); 3.55 (*s*, MeO); 3.33 (*s*, MeO); 3.08 (*dd*, *J* = 13.5, 10.1, 1 H−C(2)); 2.96–2.84 (*m*, 1 H−C(6)); 2.64–2.52 (*m*, 2 H, H−C(8), H−C(6)); 2.38–2.31 (*m*, 1 H−C(2)); 1.57–1.53 (*m*, H−C(4)); 1.48–1.30 (*m*, H−C(3), CH_2(5)); 1.21–1.10 (*m*, 1 H−C(7), CH_2(10)); 0.78 (*t*, *J* = 7.3, CH_3(11)); 0.73–0.66 (*m*, 1 H−C(7)). ^{13}C-NMR (75 MHz, $CDCl_3$): 155.5; 155.1; 139.3; 134.1; 134.0; 131.5; 130.9; 129.8; 129.1; 128.7; 128.6; 128.2; 126.3; 125.7; 125.0; 124.7; 124.6; 123.1; 119.6; 113.9; 74.9; 70.6; 61.8; 61.0; 58.6; 57.2; 56.8; 40.7; 37.7; 28.3; 27.6; 25.0; 24.2; 12.1. DEI-MS: 525 (39, M^+), 510 (30, $[M - Me]^+$), 495 (31, $[M - 2\,Me]^+$), 386 (49, $[M - C_9H_{16}N - H]^+$), 356 (38, $[M - CH(OH)C_9H_{16}N - H]^+$), 302(76), 139 (100, $[C_9H_{16}N + H]^+$). DEI-HR-MS: 525.2875 (M^+, $C_{34}H_{39}NO_4$; calc. 525.2879).

*Data of (+)-(a*S,*3*R,*4*S,*8*R,*9*R*)-***30***: 12 mg, 10%. Yellow, highly viscous oil. $[\alpha]_D^{r.t.} = +33.2$ ($c = 0.50$, $CHCl_3$). IR ($CHCl_3$): 2935*w*, 1261*w*, 1136*vs*, 1111*s*. ^{1}H-NMR (300 MHz, $CDCl_3$)^2): 8.03 (*s*, H−C(4″)); 7.98 (*d*, *J* = 9.2, H−C(4′)); 7.90 (*d*, *J* = 8.4, H−C(5′)); 7.87 (*d*, *J* = 9.3, H−C(5″)); 7.50 (*dd*, *J* = 8.4, 1.6, H−C(6′)); 7.46 (*d*, *J* = 9.2, H−C(3′)); 7.33–7.28 (*m*, H−C(6″)); 7.12–7.07 (*m*, H−C(7″)); 7.01 (*d*, *J* = 8.4, H−C(8″)); 6.88 (*s*, H−C(8′)); 4.80 (*d*, *J* = 12.5, 1 H−C(12)); 4.75 (*d*, *J* = 12.5, 1 H−C(12)); 4.28 (*d*, *J* = 9.6, H−C(9)); 3.80 (*s*, MeO); 3.72 (*s*, MeO); 3.59 (*s*, MeO); 3.10–2.89 (*m*, 1 H−C(2), CH_2(6), H−C(8)); 2.51–2.44 (*m*, 1 H−C(2)); 1.64–1.56 (*m*, 1 H−C(5)); 1.54–1.50 (*m*, 1 H−C(4)); 1.47–1.37 (*m*, 1 H−C(3)); 0.90–0.68 (*m*, 1 H−C(5), CH_2(7), CH_2(10)); 0.71 (*t*, *J* = 7.1, CH_3(11)). ^{13}C-NMR (75 MHz, $CDCl_3$): 155.8; 155.2; 138.1; 133.8; 133.8; 132.0; 131.0; 129.8; 129.2; 129.1; 128.6; 128.3; 125.8; 125.7; 124.9; 124.6; 124.5; 121.8; 119.4; 114.4; 73.2; 70.6; 63.8; 61.1; 58.9; 57.0; 48.4; 48.0; 36.1; 25.5; 25.2; 24.7; 23.2; 11.7. DEI-MS: 525 (5, M^+), 510 (5, $[M - Me]^+$), 495 (5, $[M - 2\,Me]^+$), 386 (9, $[M - C_9H_{16}N - H]^+$), 139 (100, $[C_9H_{16}N + H]^+$). DEI-HR-MS: 525.2881 (M^+, $C_{34}H_{39}NO_4$; calc. 525.2879).

*Data of (−)-(a*S,*3*R,*4*S,*8*S,*9*R*)-***31***: 12 mg, 10%. Yellow, highly viscous oil. $[\alpha]_D^{r.t.} = -3.2$ ($c = 0.50$, $CHCl_3$). IR ($CHCl_3$): 2964*w*, 1265*s*, 1136*vs*. ^{1}H-NMR (300 MHz, $CDCl_3$)^2): 8.01 (*s*, H−C(4″)); 7.96 (*d*, *J* = 9.0, H−C(4′)); 7.87 (*d*, *J* = 9.0, H−C(5″)); 7.84 (*d*, *J* = 8.7, H−C(5′)); 7.41 (*d*, *J* = 9.0, H−C(3′)); 7.40–7.36 (*m*, H−C(6′)); 7.37–7.32 (*m*, H−C(6″)); 7.19–7.14 (*m*, H−C(7″)); 7.09 (*d*, *J* = 8.4, H−C(8″)); 6.99 (*s*, H−C(8′)); 4.77 (*d*, *J* = 12.5, 1 H−C(12)); 4.72 (*d*, *J* = 12.5, 1 H−C(12)); 4.57 (*d*, *J* = 6.7, H−C(9)); 3.76 (*s*, MeO); 3.56 (*s*, MeO); 3.34 (*s*, MeO); 2.93–2.72 (*m*, 1 H−C(2), 1 H−C(6), H−C(8)); 2.31–2.17 (*m*, 1 H−C(2), 1 H−C(6)); 1.66–1.55 (*m*, H−C(4), 1 H−C(7)); 1.47–1.16 (*m*, H−C(3), CH_2(5), 1 H−C(7), CH_2(10)); 0.80 (*t*, *J* = 7.2, CH_3(11)). ^{13}C-NMR (75 MHz, $CDCl_3$): 155.5; 154.9; 141.7; 134.1; 134.0; 131.5; 130.9; 129.8; 129.0; 129.0; 128.8; 128.7; 128.2; 126.2; 125.7; 124.9; 123.3; 122.3; 119.5; 113.8; 111.2; 70.7; 61.0 (2×); 58.7; 58.0; 56.7; 42.3; 37.4; 28.1; 27.5; 25.5; 23.8; 12.1. DEI-MS: 525 (20, M^+), 510 (33, $[M - Me]^+$), 495 (35, $[M - 2\,Me]^+$), 138 (100, $[C_9H_{16}N]^+$). DEI-HR-MS: 525.2874 (M^+, $C_{34}H_{39}NO_4$; calc. 525.2879).

*Data of (+)-(a*S,*3*R,*4*S,*8*R,*9*S*)-***32***: 15 mg, 12%. Yellow, highly viscous oil. $[\alpha]_D^{r.t.} = +38.0$ ($c = 0.50$, $CHCl_3$). IR ($CHCl_3$): 2922*w*, 1139*vs*. ^{1}H-NMR (300 MHz, $CDCl_3$)^2): 8.01 (*s*, H−C(4″)); 7.97 (*d*, *J* = 9.0, H−C(4′)); 7.89 (*d*, *J* = 8.1, H−C(5″)); 7.84 (*d*, *J* = 8.4, H−C(5′)); 7.42 (*d*, *J* = 9.0, H−C(3′)); 7.39–7.32 (*m*, H−C(6′), H−C(6″)); 7.20–7.15 (*m*, H−C(7″)); 7.08 (*d*, *J* = 9.0, H−C(8″)); 7.04 (*s*, H−C(8′)); 5.28 (*s*, CH_2(12)); 4.72 (*d*, *J* = 13.4, H−C(9)); 3.77 (*s*, MeO); 3.55 (*s*, MeO); 3.35 (*s*, MeO); 2.84–2.76 (*m*, H−C(8)); 2.69–2.26 (*m*, CH_2(2), CH_2(6)); 1.63–1.06 (*m*, H−C(3), H−C(4), CH_2(5), CH_2(7), CH_2(10)); 0.74 (*t*, *J* = 7.3, CH_3(11)). ^{13}C-NMR (75 MHz, $CDCl_3$): 155.5; 155.0; 141.1; 134.1; 134.0; 131.6;

131.0; 129.8; 128.9; 128.7; 128.3; 128.2; 126.1; 125.7; 124.8; 123.2; 122.7; 119.5; 113.8; 75.2; 70.6; 61.3; 61.0; 58.6; 56.7; 50.4; 49.6; 37.1; 26.7; 26.0; 24.9; 22.7; 11.8. DEI-MS: 525 (12, M^+), 510 (17, $[M - Me]^+$), 495 (17, $[M - 2\,Me]^+$), 168 (25, $[CH(OH)C_9H_{16}N]^+$), 138 (100, $[C_9H_{16}N]^+$). DEI-HR-MS: 525.2875 (M^+, $C_{34}H_{39}NO_4$; calc. 525.2879).

General Procedure (*GP*) *for the Quaternization*. A soln. of (+)-**29**, (+)-**30**, (−)-**31**, or (+)-**32** (0.50 mmol) and 4-(trifluoromethyl)benzyl bromide (0.50 mmol) in THF (10 ml) was heated to reflux for 72 h. The mixture was then evaporated *in vacuo* and purified by CC (SiO_2; CH_2Cl_2/MeOH 95:5).

*(a*S,2S,*4*S,5R*)-1-[4-(Trifluoromethyl)benzyl]-2-[(*S*)-2,2′-dimethoxy-3′-(methoxymethyl)-1,1′-binaphthalen-7-yl)hydroxymethyl]-5-ethylazoniabicyclo[2.2.2]octane Bromide* ((+)-**5**). Conversion of (+)-**29** (11 mg, 0.02 mmol) afforded (+)-**5** (9 mg, 56%). Colorless solid. $[\alpha]_D^{r.t.} = +4.1$ ($c = 0.25$, $CHCl_3$). IR ($CHCl_3$): 3456*s*, 1461*w*, 1322*s*, 1250*w*, 1167*w*, 1122*m*, 1067*m*. ^{1}H-NMR (500 MHz, $CDCl_3$)^2): 8.03 (*s*, H−C(4″)); 7.99 (*d*, *J* = 9.0, H−C(4′)); 7.87 (*d*, *J* = 8.4, 1 arom. H); 7.84 (*d*, *J* = 8.0, 1 arom. H); 7.78, 7.51 (*AA′BB′*, *J* = 7.9, H−C(15), H−C(16), H−C(18), H−C(19)); 7.48 (*d*, *J* = 9.0, H−C(3′)); 7.47–7.45 (*m*, H−C(6′)); 7.34–7.29 (*m*, H−C(6″)); 7.17–7.13 (*m*, H−C(7″)); 7.08–7.05 (*m*, H−C(8′), H−C(8″)); 5.52 (*d*, *J* = 12.8, 1 H−C(13)); 5.28 (*d*, *J* = 10.0, 1 H); 5.09 (*d*, *J* = 12.8, 1 H−C(13)); 4.75 (*d*, *J* = 12.3, 1 H−C(12)); 4.69 (*d*, *J* = 12.3, 1 H−C(12)); 4.45–4.39 (*m*, 1 H); 3.95–3.89 (*m*, 1 H); 3.80 (*s*, MeO); 3.56–3.51 (*m*, 1 H); 3.53 (*s*, MeO); 3.33 (*s*, MeO); 2.32–2.26 (*m*, 1 H); 2.02–1.95 (*m*, 1 H); 1.92–1.80 (*m*, 2 H); 1.80–1.75 (*m*, H−C(4)); 1.32–0.80 (*m*, 5 H); 0.76 (*t*, *J* = 7.4, CH_3(11)). ^{13}C-NMR (125 MHz, $CDCl_3$): 155.5; 154.8; 138.1; 134.0; 133.7; 133.6; 132.1 ([*q*, *J* = 31.5], C(17)); 131.9; 131.5; 130.7; 129.8; 129.1; 128.9; 128.2; 125.9; 125.8; 125.8; 125.3; 124.6; 124.0; 124.0; 123.9; 123.7 ([*q*, *J* = 273.0], CF_3); 119.1; 114.2; 70.6; 66.6; 65.3; 63.2; 61.0; 58.7; 56.5; 51.2; 35.3; 29.7; 25.6; 24.7; 24.6; 24.3; 11.1. FAB-MS: 684 (100, $(M - Br]^+$). FAB-HR-MS: 684.3304 ($[M - Br]^+$, $C_{42}H_{45}F_3NO_4$, calc. 684.3300).

*(a*S,2R,*4*S,5R*)-1-[4-(Trifluoromethyl)benzyl]-2-[(*R*)-(2,2′-dimethoxy-3′-(methoxymethyl)-1,1′-binaphthalen-7-yl)hydroxymethyl]-5-ethylazoniabicyclo[2.2.2]octane Bromide* ((+)-**6**). Conversion of (+)-**30** (11 mg, 0.02 mmol) afforded (+)-**6** (2 mg, 12%). Colorless solid. $[\alpha]_D^{r.t.} = +3.9$ ($c = 0.25$, $CHCl_3$). IR ($CHCl_3$): 3422*s*, 1461*w*, 1322*s*, 1250*w*, 1167*w*, 1122*m*, 1067*m*. ^{1}H-NMR (300 MHz, $CDCl_3$)^2): 8.03 (*s*, H−C(4″)); 7.92 (*d*, *J* = 8.9, H−C(4′)); 7.90 (*d*, *J* = 6.5, H−C(5″)); 7.76 (*d*, *J* = 8.1, H−C(5′)); 7.74, 7.56 (*AA′BB′*, *J* = 7.9, H−C(15), H−C(16), H−C(18), H−C(19)); 7.67–7.63 (*m*, H−C(6′)); 7.44 (*d*, *J* = 8.9, H−C(3′)); 7.39–7.26 (*m*, H−C(6″), H−C(7″)); 7.10 (*d*, *J* = 8.4, H−C(8″)); 6.99 (*s*, H−C(8′)); 6.00–5.96 (*m*, 1 H); 5.72 (*d*, *J* = 12.1, 1 H−C(13)); 4.80–4.65 (*m*, CH_2(12), 1 H−C(13)); 4.28–4.16 (*m*, 1 H); 3.80 (*s*, MeO); 3.62–3.57 (*m*, 1 H); 3.55 (*s*, MeO); 3.31 (*s*, MeO); 3.24–3.14 (*m*, 1 H); 3.06–2.94 (*m*, 1 H); 2.74–2.66 (*m*, 1 H); 2.18–0.83 (*m*, 8 H); 0.77 (*t*, *J* = 7.3, CH_3(11)). FAB-MS: 684 (100), $[M - Br]^+$). FAB-HR-MS: 684.3302 ($[M - Br]^+$, $C_{42}H_{45}F_3NO_4$; calc. 684.3300).

*(a*S,2S,*4*S,5R*)-1-[4-(Trifluoromethyl)benzyl]-2-[(*R*)-(2,2′-dimethoxy-3′-(methoxymethyl)-1,1′-binaphthalen-7-yl)hydroxymethyl]-5-ethylazoniabicyclo[2.2.2]octane Bromide* ((−)-**7**). Conversion of (−)-**31** (14 mg, 0.03 mmol) afforded (−)-**7** (11 mg, 54%). Colorless solid. $[\alpha]_D^{r.t.} = -1.4$ ($c = 0.25$, $CHCl_3$). IR ($CHCl_3$): 3444*s*, 1461*w*, 1328*s*, 1250*w*, 1172*w*, 1117*m*, 1067*m*. ^{1}H-NMR (300 MHz, $CDCl_3$)^2): 8.02 (*s*, H−C(4″)); 7.88 (*d*, *J* = 7.8, H−C(5″)); 7.86 (*d*, *J* = 8.9, H−C(4′)); 7.66, 7.46 (*AA′BB′*, *J* = 7.9, H−C(15), H−C(16), H−C(18), H−C(19)); 7.64 (*d*, *J* = 6.7, H−C(5′)); 7.56–7.52 (*m*, H−C(6′)); 7.42 (*d*, *J* = 8.9, H−C(3′)); 7.39–7.34 (*m*, H−C(6″)); 7.24–7.19 (*m*, H−C(7″)); 7.11 (*d*, *J* = 8.4, H−C(8″)); 7.03 (*s*, H−C(8′)); 5.95–5.92 (*m*, 1 H); 5.56 (*d*, *J* = 12.9, 1 H−C(13)); 4.99 (*d*, *J* = 12.9, 1 H−C(13)); 4.76 (*d*, *J* = 12.5, 1 H−C(12)); 4.70 (*d*, *J* = 12.5, 1 H−C(12)); 4.63–4.52 (*m*, 1 H); 3.79 (*s*, MeO); 3.52 (*s*, MeO); 3.29 (*s*, MeO); 3.22–2.96 (*m*, 3 H); 2.82–2.74 (*m*, 1 H); 1.88–0.80 (*m*, 8 H); 0.75 (*t*, *J* = 7.3, CH_3(11)). ^{13}C-NMR (75 MHz, $CDCl_3$): 155.5; 155.2; 138.1; 134.2; 133.9; 133.7; 132.4 ([*q*, *J* = 33.0], C(17)); 131.9; 131.5; 130.9; 129.9; 128.9; 128.7; 128.7; 128.4; 126.0; 125.9; 125.6; 124.8; 124.5; 123.8 ([*q*, *J* = 272.0], CF_3); 122.4; 122.1; 119.2; 114.0; 70.7; 69.9; 67.2; 63.0; 62.2; 61.0; 58.7; 56.8; 36.3; 29.7; 26.3; 25.5; 24.1; 20.7; 11.4. FAB-MS: 684 (100, $[M - Br]^+$). FAB-HR-MS: 684.3300 ($[M - Br]^+$, $C_{42}H_{45}F_3NO_4$; calc. 684.3300).

*(a*S,2R,*4*S,5R*)-1-[4-(Trifluoromethyl)benzyl]-2-[(*S*)-(2,2′-dimethoxy-3′-(methoxymethyl)-1,1′-binaphthalen-7-yl)hydroxymethyl]-5-ethylazoniabicyclo[2.2.2]octane Bromide* ((+)-**4**). Conversion of (+)-**32** (11 mg, 0.02 mmol) afforded (+)-**4** (8 mg, 50%). Colorless solid. $[\alpha]_D^{r.t.} = +15.2$ ($c = 0.25$, $CHCl_3$). IR ($CHCl_3$): 3433*s*, 1461*w*, 1322*s*, 1250*w*, 1167*w*, 1117*m*, 1067*m*. ^{1}H-NMR (300 MHz, $CDCl_3$)^2): 8.06 (*s*, H−C(4″)); 7.88 (*d*, *J* = 7.8, H−C(5″)); 7.60, 7.35 (*AA′BB′*, *J* = 8.3, H−C(15), H−C(16), H−C(18), H−C(19)); 7.49 (*d*, *J* = 9.0, H−C(4′)); 7.38 (*d*, *J* = 9.0, H−C(3′)); 7.29–7.24 (*m*, H−C(5′), H−C(6′)); 7.20–7.16 (*m*, H−C(6″)); 7.04–6.99 (*m*, H−C(7″)); 6.91–6.87 (*m*, H−C(8′), H−C(8″)); 5.97 (*d*, *J* = 11.7, 1 H−C(13)); 5.87–5.83 (*m*, 1 H); 5.03 (*d*, *J* = 11.7, 1 H−C(13)); 4.87 (*s*, CH_2(12)); 4.26–4.17 (*m*, 1 H); 4.13–4.01 (*m*, 1 H); 3.83–3.73 (*m*, 1 H); 3.81 (*s*, MeO); 3.63 (*s*, MeO); 3.62 (*s*, MeO); 3.01–2.94 (*m*, 1 H); 2.48–2.36 (*m*, 1 H); 1.80–1.22

(*m*, 5 H); 0.98–0.83 (*m*, 3 H); 0.65 (*t*, *J* = 7.2, CH_3(11)). ^{13}C-NMR (75 MHz, $CDCl_3$): 155.5; 155.3; 137.4; 134.2; 134.0; 132.2 ([*q*, *J* = 33.0], C(17)); 132.0; 132.0; 131.1; 129.7; 128.7; 128.3; 128.1; 125.9; 125.6; 125.6; 125.3; 124.8; 124.4; 123.6 ([*q*, *J* = 271.5], CF_3); 123.0; 121.9; 119.5; 114.1; 70.7; 68.4; 68.2; 61.5; 60.2; 58.8; 57.1; 55.8; 36.0; 29.7; 24.5; 24.5; 23.6; 20.8; 11.4. FAB-MS: 684 (100, $[M - Br]^+$). FAB-HR-MS: 684.3324 ($[M - Br]^+$, $C_{42}H_{45}F_3NO_4$; calc. 684.3300).

6,7-Dichloro-5-methoxy-2-phenyl-2-(prop-2-enyl)-indan-1-one (**3b**). A suspension of **1** (50 mg, 0.16 mmol), phase-transfer catalyst (0.02 mmol, 10 mol-%), and allyl chloride (0.07 ml, 0.80 mmol) in PhMe (2.5 ml), and 50% aq. NaOH soln. (0.5 ml) was shaken at r.t. for 20 h. After addition of H_2O (10 ml) and AcOEt (10 ml), the org. phase was separated, washed with 1M aq. HCl soln. (2 × 10 ml) and H_2O (10 ml), dried (Na_2SO_4), evaporated *in vacuo*, and purified by CC (SiO_2; hexane/Et_2O 8 : 2) to give **3b** (for yields, see the *Table*). Colorless solid. M.p. 118–121°. IR (KBr): 1700*s*, 1578*s*, 1300*m*, 1267*w*, 1156*m*, 1067*m*. ^{1}H-NMR (200 MHz, $CDCl_3$): 7.42–7.18 (*m*, 5 H); 6.91 (*s*, 1 H); 5.70–5.50 (*m*, 1 H); 5.18–5.08 (*m*, 1 H); 5.07–5.01 (*m*, 1 H); 4.01 (*s*, 3 H); 3.49 (*dd*, *J* = 17.7, 0.8, 1 H); 3.36 (*dd*, *J* = 17.7, 1.0, 1 H); 2.86–2.82 (*m*, 2 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 202.6; 161.4; 154.7; 142.0; 133.8; 132.4; 128.9; 127.2; 126.7; 126.1; 123.3; 119.3; 106.7; 57.7; 57.0; 42.7; 39.2. EI-MS: 348/346 (21/32, M^+), 307/305 (66/100, $[M - C_3H_5]^+$). Anal. calc. for $C_{19}H_{16}Cl_2O_2$ (347.2): C 65.72, H 4.64, Cl 20.42; found: C 65.65, H 4.87, Cl 20.33.

This work was supported by the *TEMA* grant from the ETH research council. The authors are indebted to Dr. *U.-H. Dolling*, *Merck*, Rahway, New Jersey, for providing generous amounts of phenylindanone **1** and to Dr. *Monica Sebova* for NMR measurements.

REFERENCES

[1] G. R. Stephenson, 'Advanced Asymmetric Synthesis', Chapman & Hall, London, 1996.
[2] D. J. Ager, M. B. East, 'Asymmetric Synthetic Methodology', CRC Press, Boca Raton, 1995.
[3] R. E. Gawley, J. Aubé, 'Principles of Asymmetric Synthesis', Eds. J. E. Baldwin, P. D. Magnus, Pergamon, Oxford, 1996.
[4] R. S. Atkinson, 'Stereoselective Synthesis', Wiley, Chichester, 1995.
[5] M. J. O'Donnell in 'Catalytic Asymmetric Synthesis', Ed. I. Ojima, VCH, New York, 1993, pp. 389–411.
[6] T. Shioiri in ' Handbook of Phase Transfer Catalysis', Ed. Y. Sasson and R. Neumann, Blackie Academic & Professional, London, 1997, pp. 462–479.
[7] R. Noyori in 'Asymmetric Catalysis in Organic Chemistry', Wiley, New York, 1994, pp. 333–341.
[8] T. Shioiri, A. Ando, M. Masui, T. Miura, T. Tatematsu, A. Bohsako, M. Higashiyama, C. Asakura in 'Phase-Transfer Catalysis Mechanism and Synthesis', Ed. M. E. Halpern, ACS Symposium Series 659, Washington, D.C., 1997, pp. 136–147.
[9] C. M. Starks, C. L. Liotta, M. Halpern in 'Phase-Transfer Catalysis Fundamentals, Applications, and Industrial Perspectives,' Chapman & Hall, New York, 1994, pp. 576–593.
[10] a) U.-H. Dolling, P. Davis, E. J. J. Grabowski, *J. Am. Chem. Soc.* **1984**, *106*, 446; b) A. Bhattacharya, U.-H. Dolling, E. J. J. Grabowski, S. Karady, K. M. Ryan, L. M. Weinstock, *Angew. Chem.* **1986**, *98*, 442; *ibid., Int. Ed.* **1986**, *25*, 476; c) D. L. Hughes, U.-H. Dolling, K. M. Ryan, E. F. Schoenewaldt, E. J. J. Grabowski, *J. Org. Chem.* **1987**, *52*, 4745; d) U.-H. Dolling, D. L. Hughes, A. Bhattacharya, K. M. Ryan, S. Karady, L. M. Weinstock, E. J. J. Grabowski in 'Phase-Transfer Catalysis', Ed. C. M. Starks, ACS Symposium Series 326, Washington D.C., 1987, pp. 67–81.
[11] M. J. O'Donnell, *J. Am. Chem. Soc.* **1989**, *111*, 2353; K. B. Lipkowitz, M. W. Cavanaugh, B. Baker, M. J. O'Donnell, *J. Org. Chem.* **1991**, *56*, 5181; M. J. O'Donnell, S. Wu, *Tetrahedron: Asymmetry* **1992**, *3*, 591; M. J. O'Donnell, S. Wu, J. C. Huffman, *Tetrahedron* **1994**, *50*, 4507; M. J. O'Donnell, F. Delgado, C. Hostettler, R. Schwesinger, *Tetrahedron Lett.* **1998**, *39*, 8775.
[12] E. J. Corey, F. Xu, M. C. Noe, *J. Am. Chem. Soc.* **1997**, *119*, 12414; E. J. Corey, M. C. Noe, F. Xu, *Tetrahedron Lett.* **1998**, *39*, 5347; see also: E. J. Corey, Y. Bo, J. Busch-Petersen, *J. Am. Chem. Soc.* **1998**, *120*, 13000.
[13] B. Lygo, J. Crosby, J. A. Peterson, *Tetrahedron Lett.* **1999**, *40*, 1385; B. Lygo, *ibid.* **1999**, *40*, 1389.
[14] A. Ando, T. Miura, T. Tatematsu, T. Shioiri, *Tetrahedron Lett.* **1993**, *34*, 1507; C. M. Gasparski, M. J. Miller, *Tetrahedron* **1991**, *47*, 5367.
[15] R. S. E. Conn, A. V. Lovell, S. Karady, L. M. Weinstock, *J. Org. Chem.* **1986**, *51*, 4710; A. Loupy, J. Sansoulet, A. Zaparucha, C. Merienne, *Tetrahedron Lett.* **1989**, *30*, 333; S. Colonna, H. Hiemstra, H. Wynberg, *J. Chem. Soc., Chem. Commun.* **1978**, 238.

[16] a) Y. Harigaya, H. Yamaguchi, M. Onda, *Chem. Pharm. Bull*. **1981**, *29*, 1321; b) H. Takahashi, Y. Kobuta, H. Miyazaki, M. Onda, *Chem. Pharm. Bull*. **1984**, *32*, 4852; c) R. Helder, J. C. Hummelen, R. W. P. M. Laane, J. S. Wiering, H. Wynberg, *Tetrahedron Lett*. **1976**, 1831; d) H. Wynberg in 'Topics in Stereochemistry', Vol. 16, Eds. E. L. Eliel, S. H. Wilen, N. L. Allinger, Wiley, New York, 1986, pp. 87–129.
[17] M. Masui, A. Ando, T. Shioiri, *Tetrahedron Lett*. **1988**, *29*, 2835.
[18] S. Colonna, R. Fornasier, *Synthesis* **1975**, 531; S. Juliá, A. Ginebreda, J. Guixer, J. Masana, A. Tomás, S. Colonna, *J. Chem. Soc., Perkin Trans. 1* **1981**, 574.
[19] B. Winter-Werner, F. Diederich, V. Gramlich, *Helv. Chim. Acta* **1996**, *79*, 1338.
[20] R. A. Johnson, K. B. Sharpless in 'Catalytic Asymmetric Synthesis', Ed. I. Ojima, VCH, New York, 1993, pp. 227–272; H. C. Kolb, M. S. VanNieuwenhze, K. B. Sharpless, *Chem. Rev*. **1994**, *94*, 2483.
[21] S. H. Wilen, 'Tables of Resolving Agents and Optical Resolutions', Ed. E. L. Eliel, University of Notre Dame Press, Notre Dame, 1972; J. Jacques, A. Collet, S. H. Wilen in 'Enantiomers, Racemates and Resolution', Wiley, New York, 1981.
[22] J. Reeder, P. P. Castro, C. B. Knobler, E. Martinborough, L. Owens, F. Diederich, *J. Org. Chem*. **1994**, *59*, 3151.
[23] C. Rosini, L. Franzini, A. Raffaelli, P. Salvadori, *Synthesis* **1992**, 503; L. Pu, *Chem. Rev*. **1998**, 2405; H. Brunner and W. Zettlmeier, ' Handbook of Enantioselective Catalysis with Transition Metal Compounds', VCH, Weinheim, 1993, Vols. 1 and 2; R. Noyori, 'Asymmetric Catalysis' Wiley, New York, 1994.
[24] G. W. Gokel, 'Crown Ethers and Cryptands, Monographs in Supramolecular Chemistry', Ed. J. F. Stoddart, The Royal Society of Chemistry, Cambridge, 1991; D. J. Cram, J. M. Cram, *Acc. Chem. Res*. **1978**, *11*, 8.
[25] S. Anderson, U. Neidlein, V. Gramlich, F. Diederich, *Angew. Chem*. **1995**, *107*, 1722; *ibid., Int. Ed* **1995**, *34*, 1596; U. Neidlein, F. Diederich, *J. Chem. Soc., Chem. Commun*. **1996**, 1493; A. Bähr, A. S. Droz, M. Püntener, U. Neidlein, S. Anderson, P. Seiler, F. Diederich, *Helv. Chim. Acta* **1998**, *81*, 1931.
[26] E. Martinborough, T. Mordasini Denti, P. P. Castro, T. B. Wyman, C. B. Knobler, F. Diederich, *Helv. Chim. Acta* **1995**, *78*, 1037; P. Lustenberger, E. Martinborough, T. Mordasini Denti, F. Diederich, *J. Chem. Soc., Perkin Trans. 2* **1998**, 747; P. P. Castro, T. M. Georgiadis, F. Diederich, *J. Org. Chem*. **1989**, *54*, 5835.
[27] H.-Y. Li, T. Nehira, M. Hagiwara, N. Harada, *J. Org. Chem*. **1997**, *62*, 7222; T. Hattori, K. Sakurai, N. Koike, S. Miyano, H. Goto, F. Ishiya, N. Harada, *J. Am. Chem. Soc*. **1998**, *120*, 9086.
[28] E. J. Corey, A. Guzman-Perez, *Angew. Chem*. **1998**, *110*, 402; *ibid., Int. Ed*. **1998**, *37*, 388.
[29] T. Horiuchi, T. Ohta, M. Stephan, H. Takaya, *Tetrahedron: Asymmetry* **1994**, *5*, 325.
[30] N. L. Allinger, *J. Am. Chem. Soc*. **1977**, *99*, 8127.
[31] W. C. Still, A. Tempczyk, R. C. Hawley, T. Hendrickson, *J. Am. Chem. Soc*. **1990**, *112*, 6127.
[32] F. Mohamadi, N. G. J. Richards, W. C. Guida, R. Liskamp, M. Lipton, C. Caufield, G. Chang, T. Hendrickson, W. C. Still, *J. Comput. Chem*. **1990**, *11*, 440.
[33] A. Baiker, C. A. Müller, F. Diederich, L. Ducry, unpublished results.
[34] M. Schneider, A. Baiker, *Cat. Rev.-Sci. Eng*. **1995**, *37*, 515; N. Hüsing, U. Schubert, *Angew. Chem*. **1998**, *110*, 22; *ibid., Int. Ed*. **1998**, *37*, 22; R. J. P. Corriu, D. Leclercq, *Angew. Chem*. **1996**, *108*, 1524; *ibid., Int. Ed*. **1996**, *35*, 1420.
[35] a) M. Uskokovic, J. Gutzwiller, T. Henderson, *J. Am. Chem. Soc*. **1970**, *92*, 203; b) J. Gutzwiller, M. Uskokovic, *J. Am. Chem. Soc*. **1970**, *92*, 204; c) M. Uskokovic, C. Reese, H. L. Lee, G. Grethe, J. Gutzwiller, *J. Am. Chem. Soc*. **1971**, *93*, 5902; d) G. Grethe, H. L. Lee, T. Mitt, M. R. Uskokovic, *J. Am. Chem. Soc*. **1971**, *93*, 5904; e) G. Grethe, H. L. Lee, T. Mitt, M. R. Uskokovic, *Helv. Chim. Acta* **1973**, *56*, 1485; f) J. Gutzwiller, M. R. Uskokovic, *Helv. Chim. Acta* **1973**, *56*, 1494; g) M. R. Uskokovic, T. Henderson, C. Reese, H. L. Lee, G. Grethe, J. Gutzwiller, *J. Am. Chem. Soc*. **1978**, *100*, 571; h) J. Gutzwiller, M. R. Uskokovic, *J. Am. Chem. Soc*. **1978**, *100*, 576; i) G. Grethe, H. L. Lee, T. Mitt, M. R. Uskokovic, *J. Am. Chem. Soc*. **1978**, *100*, 581; j) G. Grethe, H. L. Lee, T. Mitt, M. R. Uskokovic, *J. Am. Chem. Soc*. **1978**, *100*, 589.
[36] S. Nahm, S. M. Weinreb, *Tetrahedron Lett*. **1981**, *22*, 3815; J.-A. Fehrentz, B. Castro, *Synthesis* **1983**, 676.
[37] M. Hovorka, J. Günterová, J. Závada, *Tetrahedron Lett*. **1990**, *31*, 413.
[38] a) M. Hovorka, J. Závada, *Org. Prep. Proc. Int*. **1991**, *23*, 200; b) M. Hovorka, R. Scigel, J. Gunterová, M. Tichy, J. Závada, *Tetrahedron* **1992**, *48*, 9503.
[39] a) M. Smrcina, M. Lorenc, V. Hanus, P. Kocovsky, *Synlett* **1991**, 231; b) M. Smrcina, M. Lorenc, V. Hanus, P. Sedmera, P. Kocovsky, *J. Org. Chem*. **1992**, *57*, 1917; c) M. Smrcina, J. Poláková, S. Vyskocil, P. Kocovsky, *J. Org. Chem*. **1993**, *58*, 4534.
[40] M. Hovorka, J. Závada, *Tetrahedron* **1992**, *48*, 9517.

[41] M. Smrcina, S. Vyskocil, B. Máca, M. Polásek, T. A. Claxton, A. P. Abbott, P. Kocovsky, *J. Org. Chem.* **1994**, *59*, 2156.
[42] J. P. Schaefer, J. Higgins, P. K. Shenoy, *Org. Synth.* **1969**, *49*, 6.
[43] H.-F. Chow, C.-W. Wan, M.-K. Ng, *J. Org. Chem.* **1996**, *61*, 8712.
[44] W. C. Still, *J. Am. Chem. Soc.* **1978**, *100*, 148.
[45] A. Loupy, B. Tchoubar 'Salt Effects in Organic and Organometallic Chemistry', VCH, Weinheim, 1992, Chapt. 7, pp. 241 – 288.
[46] G. D. H. Dijkstra, R. M. Kellogg, H. Wynberg, J. S. Svendsen, I. Marko, K. B. Sharpless, *J. Am. Chem. Soc.* **1989**, *111*, 8069; G. D. H. Dijkstra, R. M. Kellogg, H. Wynberg, *J. Org. Chem.* **1990**, *55*, 6121; F. I. Carroll, P. Abraham, K. Gaetano, S. W. Mascarella, R. A. Wohl, J. Lind, K. Petzoldt, *J. Chem. Soc., Perkin Trans. 1* **1991**, 3017; U. Berg, M. Aune, O. Matsson, *Tetrahedron Lett.* **1995**, *36*, 2137.
[47] S. J. Weiner, P. A. Kollman, D. A. Case, U. C. Singh, C. Ghio, G. Alagona, S. Profeta, Jr., P. Weiner, *J. Am. Chem. Soc.* **1984**, *106*, 765; D. Q. McDonald, W. C. Still, *Tetrahedron Lett.* **1992**, *33*, 7743.
[48] W. L. Jorgensen, J. Tirado-Rives, *J. Am. Chem. Soc.* **1988**, *110*, 1657.
[49] H. Meyer, *Monatsh. Chem.* **1901**, *22*, 777.
[50] M. Jakes, *Collect. Czech. Chem. Commun.* **1929**, *100*, 573.

Received March 19, 1999