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Asymmetric synthesis of *N*-aryl aziridines

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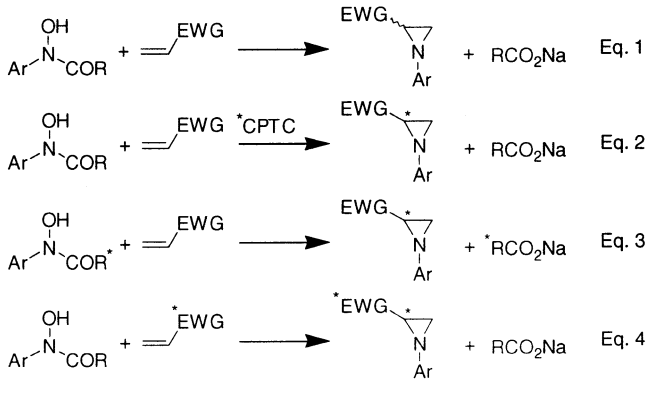
Abstract—The reactions of a variety of *N*-arylhydroxamates as nitrogen transfer reagents to acryloyl derivatives of (–)-8-phenylmenthol, (–)-quinine and (–)-Oppolzer's sultam acting as Michael acceptors was studied. Poor to modest diastereoselection was observed in the formation of aziridines. The absolute structure of one of the pure diastereomers secured from Oppolzer's auxiliary was established by X-ray crystallography and hence the absolute configuration of the derived methyl-*N*-phenylaziridine-2-carboxylate could be assigned. Whilst only poor facial selectivity was observed for chiral hydroxamic acid prepared from dehydroabietic acid, moderate to good enantioselection of aziridines could be achieved with the chiral quaternary salts based on cinchona alkaloids, especially with that of cinchonine. A model is presented to explain the origin of enantioselection and a mechanism is proposed for the aziridination reaction.

1. Introduction

Aziridines are valuable compounds in organic synthesis due to the regio- and stereoselective ring opening reactions that they undergo.[1] Chiral aziridines are of greater interest because they often serve as important synthetic precursors for many biologically useful substances.[2]

We have previously described the aziridination of a variety of electron-deficient olefins with aryl hydroxamic acids (Eq. (1), Scheme 1) and showed that the process is stereoselective.[3] Subsequently, the method was applied to a number of Michael acceptors in the presence of quaternary salts of cinchona alkaloids under phase transfer conditions (CPTC)[4] to provide chiral aziridines with varying degrees of asymmetric induction.

We report herein full details pertaining to the above work and also describe various experiments made to improve the enantioselectivity of the process. Furthermore, other methods consisting of addition of chiral hydroxamic acids to prochiral olefins (Eq. (3)) and vice versa (Eq. (4)) were examined and the results compared with those obtained using CPTC (Eq. (2)).



Scheme 1.

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2. Results and discussion

2.1. Chiral hydroxamic acid (Eq. (3))

N-Hydroxy-*N*-phenyl-dehydroabietamide **1** (Table 1), prepared from dehydroabietic acid, was selected as the recyclable chiral auxiliary for the study. Whilst its reaction with ethyl acrylate **2a** furnished the aziridine **3a** in low yield (37%, entry 1), reaction of **1** with the corresponding *tert*-butyl ester **2b** occurred with greater efficiency to form **3b**. However, since in both cases the asymmetric induction was low, the study was not pursued further.

2.2. Chiral olefins and *N*-aryl hydroxamic acids (Eq. (4))

The following chiral auxiliaries were selected for the aziridination reaction: (a) the acrylate of (−)-8-phenylmenthol; (b) *O*-acryloyl quinine, and (c) (−)-*N*-propenoyl bornane-2,10-sultam.

In anticipation of the blocking of one face of the acrylate **4** by the aromatic ring due to π–π attraction,[5] its reaction with phenylhydroxamic acid **5a**, under standard experimental conditions (NaH/THF/rt), was investigated. Although a diastereoisomeric mixture of aziridines **6**, separable by pTLC, was obtained in reasonable chemical yield (65%), the d.e. of the process was too low (28%) to render the process useful.

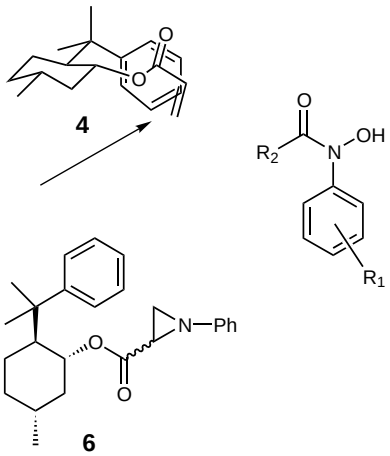
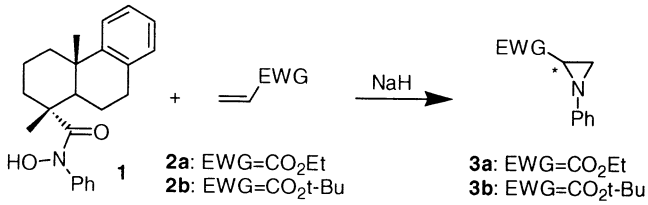


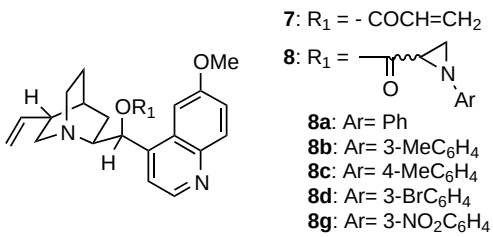
Table 1. Enantioselective aziridination with chiral hydroxamic acid **1**



Entry	EWG	$[\alpha]_D^{20}$ (CH_2Cl_2)	E.e.[a] (%)	Yield (%)	Abs. config.
1	CO_2Et	−27 ($c=1.50$)	17	37	(*S*)-(−)[b]
2	CO_2 *t*-Bu	−26 ($c=0.87$)	18	58	(*S*)-(−)[b]

[a] Determined by ^1H NMR with $Eu(tfc)_3$.
[b] For the attribution of configuration on the basis of the sign of rotation, see Section 2.3.

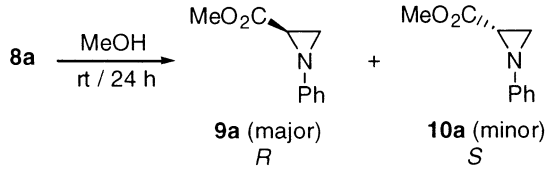
Table 2. Diastereoselective aziridination of chiral olefin **7**



Entry	Hydroxamic acid	Aziridine **8**	Yield (%)	Temp. (°C)	D.e. (%)
1	**5a**	**8a**	78	Rt	24
2	**5a**	**8a**	78	−4	34
3	**5a**	**8a**	47	−80	16
4	**5b**	**8b**	80	Rt	16
5	**5c**	**8c**	77	Rt	28
6	**5d**	**8d**	77	Rt	34
7	**5g**	**8g**	74	Rt	38

Free cinchona bases have been successfully employed as catalysts to induce chirality in addition reactions involving prochiral substances.[6] However, there have been no reports, to our knowledge, of their use as chiral auxiliaries. Therefore, it was thought worthwhile to examine *O*-acryloyl derivatives of cinchona bases as the chiral Michael acceptors for the reaction with hydroxamic acids (Scheme 1, Eq. (4)). It was found that whilst cinchonidine and cinchonine esters underwent aziridination with little or no diastereoselection (0 and 6% d.e., respectively), better results were obtained with *O*-acryloyl quinine **7**.[7] These aziridines **8**, formed in consistently good yields, were secured once again with poor diastereoselection (16–38%) (Table 2).

Due to separation difficulties, the relative proportions of the isomers in the mixture (entries 1–7) were determined in each case by integrating the two methoxy signals (for **8**) from the respective ^{1}H NMR spectrum. The mixture of methyl esters **9a** and **10a**, readily secured by simple dissolution of the diastereomers **8a** in dry methanol (Scheme 2), was found to contain an excess of the (*R*)-isomer, by comparison of its ^{1}H NMR spectrum taken in the presence of Eu(tfc)$_3$ with that of the pure enantiomer (obtained by an alternative method).

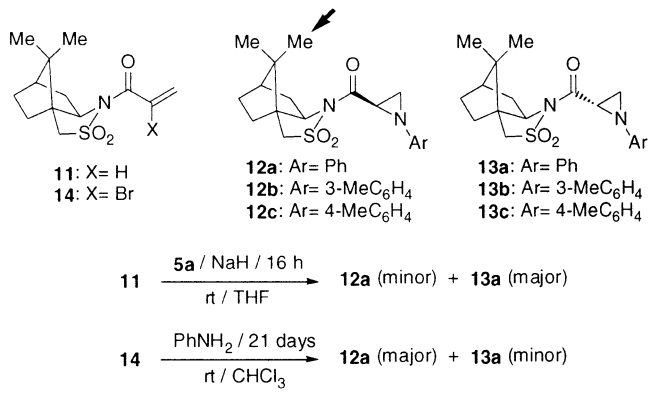


Scheme 2.

2.3. Chiral olefin 11/phenylhydroxamic acid 5a/X-ray/absolute configuration/sign of optical rotation

Aziridination of *N*-acryloyl derivative **11**,[8] derived from (*S*)-(−)-2,10-camphor sultam (Scheme 3), a valuable chiral auxiliary[9] introduced by Oppolzer,[10] with **5a** occurred in poor yield (30%) and low diastereoselection (32% de) to afford the isomeric **12a** and **13a**. On the other hand, the method of Garner[11a] applied to the reaction of **14** and aniline[11b] provided an improved chemical yield of a mixture, wherein **12a** was the major product (44% d.e.). The isomers obtained from the two reactions had identical NMR, IR, and R_f.

It was possible from the X-ray analysis of **12a** (Figs. 1 and 2) to deduce that the asymmetric carbon of the aziridine ring possesses (*R*)-absolute configuration.



Scheme 3.

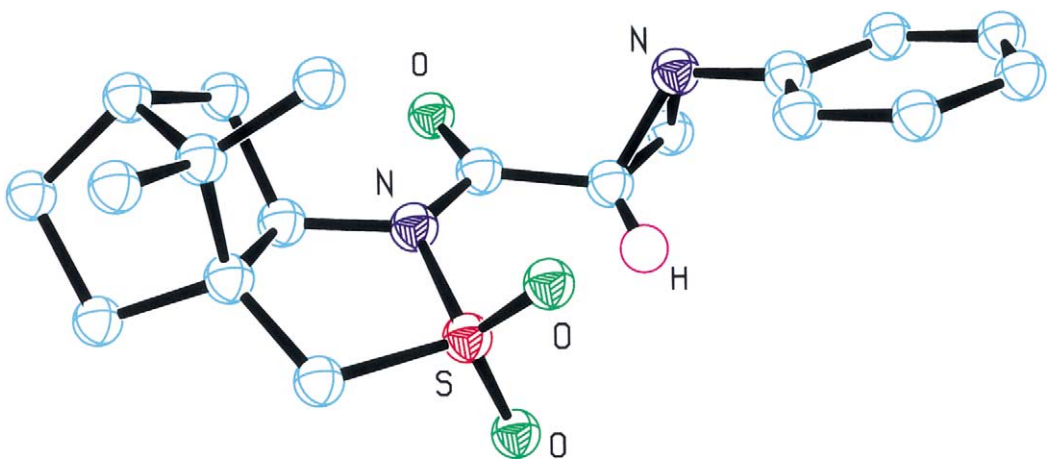


Figure 1. The molecular structure of **12a** showing the (*R*)-configuration at the aziridine center.

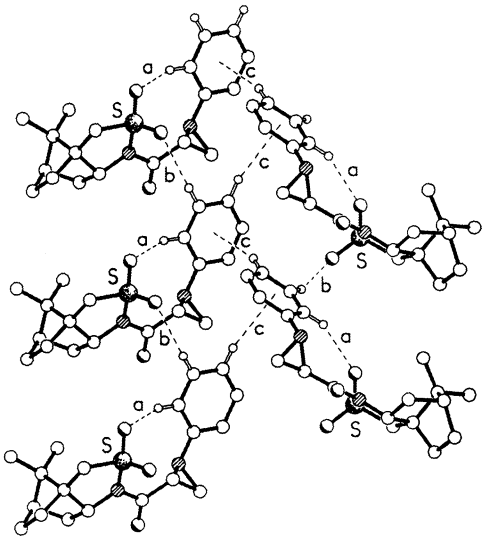
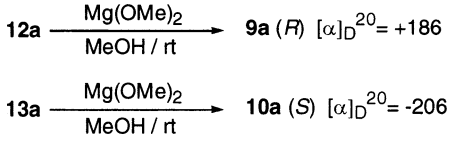


Figure 2. Part of one of the helically linked chains of molecules (along the crystallographic *a* direction) present in the crystals of **12a**. Hydrogen bonding geometries: [C···O], [H···O] distances (Å) and [C–H···O] angles (°); (**a**) 3.31, 2.42, 155; (**b**) 3.38, 2.49, 154; [H···π] distance (Å) and [C–H···π] angle (°); (**c**) 2.82, 162.

Methyl-1-phenyl-2-carboxylate **9a**, secured from **12a** by treatment with $Mg(OMe)_2$ in dry methanol and possessing $[\alpha]_D^{20}$ +186, therefore has the absolute configuration *R*. This substance was found to be virtually enantiomerically pure by ^1H NMR. This information, i.e. the sign of rotation and its relation to the absolute stereochemistry, coupled with the knowledge of the chemical shift of either the methoxy group or the aromatic hydrogen *ortho* to the nitrogen of the homochiral esters, enabled the attribution of the absolute configuration to all those enantiomers generated in excess in all reactions leading to *N*-phenylaziridine carboxylic esters (Scheme 4).



Scheme 4.

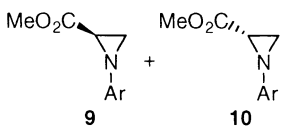
Similarly other sultam-aziridines isolated as diastereomeric mixtures by pTLC, were converted into the corresponding enantiomeric mixtures of aziridine esters. Application of the above criteria for absolute configuration assignment (Tables 3 and 4) is, strictly speaking, not entirely valid. But the fact that these substances were all accessed by the same method that originated **9a**+**10a**, with their signs of rotation measured at the same wavelength and temperature, and δ values on shift reagent addition being very similar, provide fairly strong circumstantial evidence in favor of such an attribution.

In a separate experiment, a 1.9:1 mixture (as determined from the ^1H NMR signals of one of the *gem*-dimethyl groups of the bornane half, **12a** arrow) of the diastereomers **12a** and **13a** was converted into the corresponding methyl esters. The proportion of the enantiomers thus obtained was found to be the same as the starting mixture, thereby showing that $Mg(OMe)_2$ does not alter the stereochemical integrity of the stereogenic centers of either **12a**+**13a** or **9a**+**10a**.

2.4. Studies with chiral phase transfer catalysts based on the cinchona alkaloids

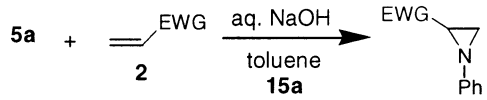
The induction of chirality in prochiral substances by chiral phase transfer (CPT) catalysts is an attractive process because of its simplicity and economy. However, its success, as measured by the chemical yield and the degree of enantioselection, depends on a variety of factors. Amongst these, of relevance to the present study involving quaternary ammonium salts of cinchona bases, are: (a) the nature of the electrophiles

Table 3. Enantiomeric aziridines from diastereomeric sultam-aziridines by methanolysis

	Yield (%)	E.e.[a] (%)	$[\alpha]_D^{20}$ (CH_2Cl_2)	Abs. config. major enant.	δ (^1H NMR)	δ after addition of Eu(tfc)$_3$	
Ar = Ph **9a** + **10a**	30	32	Nd	*S*	3.81	3.90 (+)[b]	3.82 (−)[b] m[c]
Ar = 3-MeC_6H_4 **9b** + **10b**	28	20	−43 (*c* = 0.45)	*S*	3.81	3.89 (+)[b]	3.80 (−)[b] m[c]
Ar = 4-MeC_6H_4 **9c** + **10c**	8	49	−71 (*c* = 0.04)	*S*	3.81	3.98 (+)[b]	3.81 (−)[b] m[c]
Ar = 3-BrC_6H_4 **9d** + **10d**	41	0	–	–	3.81	3.90	3.81
Ar = 4-$NO_2C_6H_4$ **9f** + **10f**	15	17	−51 (*c* = 0.20)	*S*	3.83	3.88 (+)[b]	3.83 (−)[b] m[c]

[a] Determined by ^1H NMR with Eu(tfc)$_3$.
[b] + or − refers to the sign of optical rotation.
[c] m = major enantiomer.

Table 4. Effect of steric factors (EWG) on asymmetric induction and chemical yield

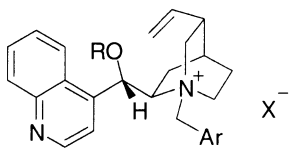


Entry	EWG	Aziridine	Yield (%)	E.e.[a] (%)	Abs. config.
1	CO_2Et	**3a**	27	+55	*R*
2	CO_2t-Bu	**3b**	79	+45	*R*
3	CO_2Me	**9a**+**10a**	11	+62	*R*

[a] Determined by ^1H NMR with $Eu(tfc)_3$.

(steric and electronic); (b) the structure of the nucleophile; (c) the structure of the CPT catalyst; (d) the nature of the counter ion associated with the latter; (e) the polarity of the solvent; and (f) the inorganic base, its associated metal cation and the concentration used to generate, in situ, the chiral quaternary ammonium hydroxide. We examined these factors in some depth, with a view to achieve an efficient aziridination reaction expressed in Eq. (2), Scheme 1.

Thus, methyl acrylate **2c** was aziridinated most rapidly in the presence of **15a** in aq. sodium hydroxide and also with the highest optical induction, the latter decreasing with increasing bulk of the ester group, i.e. Me>Et>*t*-Bu. However, in view of the low chemical yield obtained with **2c** (Table 4, entry 3) all further studies were conducted with the compromise candidate, the *tert*-butyl ester as it provided the highest yield of the product. It is important to note that the *enantiomeric excess of the mixture, once isolated, remained unaltered when resubmitted to conditions that generated it, as did the optical rotation of the racemic mixture.*



15a: Ar = 4-$CF_3C_6H_4$; R = H; X = Br

2.5. Nature of the nucleophile

N-Benzoyl-*N*-phenylhydroxylamine **16** was next examined as the aziridinating agent to determine if the presence of an additional aromatic ring vis a vis **5a** would enhance the facial selectivity by a favorable interaction with the CPT catalyst. Although the yields were vastly different, the e.e. of the aziridine ester **3b** remained in the same order of magnitude (45 versus 53%) (Scheme 5).

2.6. Variation in CPTCs

A total of 13 related CPT catalysts derived from cinchonine **15** and cinchonidine **17**, differing in the nature of the benzyl group attached to the aliphatic nitrogen and the counter ion, were examined from the standpoint of chemical yield and asymmetric induction (Tables 5 and 6).

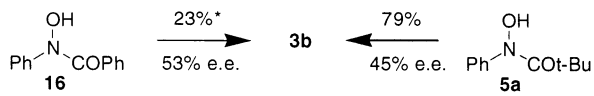
Examination of the results (Table 5) shows that the best result (entry 1) was obtained for the catalyst with a CF_3 group. A similar beneficial effect of the same functionality had been previously observed and was ascribed[12] to tighter contact-ion formation. Although the change of counter ion from Br to Cl caused a decrease in yield (entries 2 and 8, respectively) the enantiomeric excess was practically unchanged and the (*R*)-isomer was always predominant. The last entry involving the catalyst derived from 10,11-dihydrocinchonine reveals that the double bond of the vinyl group was not responsible for the observed optical induction.

Cinchonine and cinchonidine salts usually behave as pseudoenantiomeric catalysts for a selected reaction in which a new asymmetric center is created. Surprisingly the same derivatives of both these catalysts, i.e. the pairs **15a**/**17a**, **15b**/**17b**, **15h**/**17c**, and **15g**/**17d** generated an excess of the (*R*)-enantiomer in their reactions with **5a** and **2b**.

2.7. Solvent effect

The results obtained (Table 7) with various solvents differing in their dielectric constants, for the aziridination of *tert*-butyl ester (**5a**+**2b**+**15a**), clearly show that the solvent of choice is toluene.

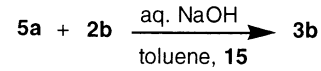
Our results are concordant with previous studies[12] which had also revealed that solvents of relatively high polarity tend to diminish the e.e. This effect has been attributed to the disruption of the favorable coulombic attraction in the molecular assembly prior to chiral induction.



* The poor yield is due to rapid decomposition of **16** under the reaction conditions

Scheme 5.

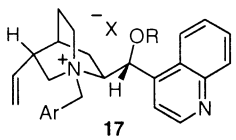
Table 5. Dependence of enantioselection (%) on cinchoninium quaternary salt structure in the aziridination reaction



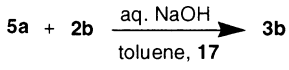
Entry	Compound no.	R	Ar	X	Yield (%)	E.e.[a] (%)	Abs. config. of **3b**
1	**15a**	H	4-$CF_3C_6H_4$	Br	79	45	*R*
2	**15b**	H	Ph	Br	43	17	*R*
3	**15c**	H	2-Naphthhyl	Br	62	40	*R*
4	**15d**	H	3-$NO_2C_6H_4$	Br	19	12	*R*
5	**15e**	H	4-$NO_2C_6H_4$	Cl	37	8	*R*
6	**15f**	H	3,4-diClC_6H_3	Cl	14	32	*R*
7	**15g**	H	9-Anthracenyl	Cl	16	5	*R*
8	**15h**	H	Ph	Cl	18	18	*R*
9	**15i**	H	10,11-Dihydro deriv. of **15a**	Br	53	50	*R*

[a] Determined by ^{1}H NMR with Eu(tfc)$_3$.

Table 6. Dependence of enantioselection (%) on cinchonidinium quaternary salt structure in the aziridination reaction



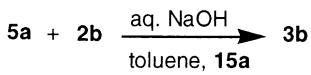
17



Entry	Compound no.	R	Ar	X	Yield[a] (%)	E.e.[a,b] (%)	Abs. config. of **3b**
1	**17a**	H	4-$CF_3C_6H_4$	Br	50 (79)	28 (45)	*R*
2	**17b**	H	Ph	Br	40 (43)	14 (17)	*R*
3	**17c**	H	Ph	Cl	18 (18)	16 (18)	*R*
4	**17d**	H	9-Anthracenyl	Cl	20 (16)	5 (5)	*R*

[a] Values in parenthesis refer to yield and e.e. obtained for the corresponding cinchoninium salt.
[b] Determined by ^{1}H NMR with Eu(tfc)$_3$.

Table 7. Influence of solvent polarity in enantioselection (%) in aziridination reaction



Entry	Solvent	ε	Yield (%)	E.e.[a] (%)	Abs. config. of **3b**
1	Cyclohexane	2.01	61	50	*R*
2	Benzene	2.27	59	43	*R*
3	Toluene	2.4	79	45	*R*
4	Toluene))))[b]	2.4	43	43	*R*
5	Ethyl ether	4.2	66	4	*R*
6	CH_2Cl_2	9.1	29	34	*R*

[a] Determined by ^{1}H NMR with Eu(tfc)$_3$.
[b] Under ultrasound irradiation.

Table 8. Influence of base concentration on the aziridination of **2b** by **5a** with **15a**

Entry	Aq. NaOH	Yield (%)	$[\alpha]_D^{20}$ (CH_2Cl_2)	E.e.[a] (%)	Abs. config. of **3b**
1	9% 24 equiv.	12	+95	61	*R*
2	20% 24 equiv.	18	+82	58	*R*
3	33% 24 equiv.	79	+66	45	*R*

[a] Determined by ^{1}H NMR with Eu(tfc)$_3$.

2.8. Base and its concentration

After some preliminary experiments involving LiOH, NaOH, KOH, and $Ca(OH)_2$ it was found that NaOH afforded better results than the others. The results obtained with this base under different concentrations are collected (Table 8). Although the highest e.e. was seen when a 9% aq. solution was used (entry 1), the chemical yield was too low to be of practical value. Therefore, the conditions of entry 3 were chosen as the general procedure for all the aziridination reactions, the results of which are presented in Table 9.

This study shows that (1) a variety of electrophiles undergo the reaction; (2) the yields are in general moderate; (3) the e.e. is found to depend not only on the EWG but also on the position of the substituent in the aniline ring of **5**; (4) both electronic and steric factors seem to have an influence on the e.e. and the chemical yield; (5) the predominant isomers formed (entries 1–5) possess (*R*)-configuration. Of particular interest are entries 6 and 8. The initial e.e. of the aziridine sulfones could be raised above 80% by crystallizing them only once from dichloromethane and *n*-hexane.

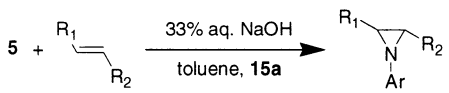
It is known that quaternary salts derived from cinchona bases suffer base-induced alterations under phase transfer conditions.[13] In order to maintain their structural integrity, *O*-alkylated derivatives have been prepared and they have often provided high enantioselectivity as, for example, in the epoxidation of chalcones.[14] Accordingly, aziridinations were performed in the presence of the *O*-allyl derivatives of both cinchonine and cinchonidine salts. Although the aziridines (Table 10) were obtained in acceptable yields, these catalysts only elicited poor enantioselection. Significantly, the absolute configuration of the enantiomer formed in excess with these catalysts, low as it may be, was *R* and *S*, respectively. It could therefore be concluded that for the aziridination to occur with acceptable enantioselectivity, the presence of a free hydroxyl group in the CPT catalyst is important.

Table 10. Effect of *O*-allylation of quaternary salts of cinchona bases in optical induction

Entry	CPT catalyst	Yield (%)	E.e.[a,b] (%)	Abs. config.
1	**15a**′ R = allyl Ar = 4-$CF_3C_6H_4$ X = Br	85	22 (45*R*)	*R*
2	**15g**′ R = allyl Ar = 9-anthracenyl X = Br	60	32	*R*
3	**17a**′ R = allyl Ar = 4-$CF_3C_6H_4$ X = Br	60	6 (28*R*)	*S*
4	**17d**′ R = allyl Ar = 9-anthracenyl X = Br	55	21	*S*

[a] Determined by ^{1}H NMR with $Eu(tfc)_3$.
[b] The values in parentheses refer to e.e. obtained with the OH group free.

Table 9. Michael acceptors and enantio- and diastereoselection

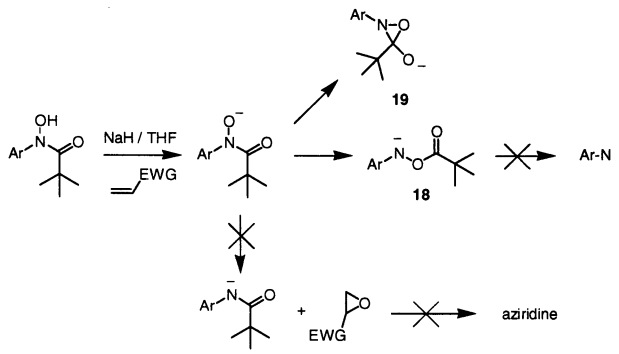


Entry	Hydroxamic acid **5**	R_1	R_2	Aziridine	Yield (%)	E.e. (%)	$[\alpha]_D^{20}$ (CH_2Cl_2)	Abs. config.
1	**5a**	CO_2t-Bu	H	**3b**	79	45[a]	+66 (c=1.1)	*R*
2	**5b**	CO_2t-Bu	H	**3b-1**	40	43[b]	+69 (c=0.60)	*R*
3	**5c**	CO_2t-Bu	H	**3b-2**	50	51[b]	+84 (c=0.64)	*R*
4	**5d**	CO_2t-Bu	H	**3b-3**	28	16[b]	+20 (c=0.84)	*R*
5	**5e**	CO_2t-Bu	H	**3b-4**	50	36[b]	+46 (c=0.56)	*R*
6	**5a**	$PhSO_2$	H	**3b-5**	43	44[c]	+104 (c=0.7)	Nd[d]
	On crystallization				20	84[b]		Nd
7	**5c**	$PhSO_2$	H	**3b-6**	39	20[c]	+39 (c=0.17)	Nd
8	**5e**	$PhSO_2$	H	**3b-7**	34	60[b]		Nd
	On crystallization				15	82[c]	+172 (c=0.33)	Nd
9	**5a**	PhSO	H	**3b-8**	45	16:1[e]	Nd	Nd
10	**5a**	COPh	Ph	**3b-9**	15	0[b]	Nd	Nd

[a] Determined by ^{1}H NMR with $Eu(tfc)_3$.
[b] Determined by chiral HPLC.
[c] Determined by ^{1}H NMR with $Yb(hfc)_3$.
[d] Nd: not determined.
[e] Diastereomeric mixture.

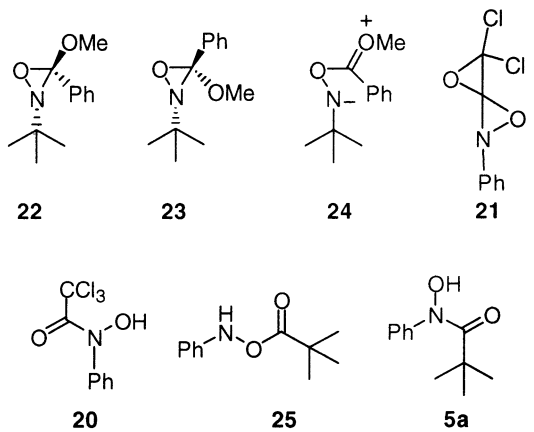
2.9. The structure of the aziridinating agent

We had previously produced evidence that the aziridination occurs neither via the prior formation of the epoxide and the amide anion nor the nitrene intermediate in Scheme 6.[3]



Scheme 6.

Boche et al.[15] have demonstrated that *N*-(3-bromophenyl)-*N*-pivaloyl hydroxylamine **5d** is isomerized to the *O*-acyl derivative **18** in 95% yield on heating with triethylamine. It is reasonable to assume that this transformation, which is thermodynamically driven, involves the oxaziridine **19** as a transient intermediate. **19** and similar species derived from other hydroxamic acids used in the present study could, in principle, act as the nucleophilic nitrogen transfer agent depending on its $t_{1/2}$. Germane, in this context, is the report that configurationally pure (*E*)-methoxyoxaziridine **22**,[16] structurally similar to **19**, rapidly generates, at rt, an equilibrium mixture (3:7) of **22** and the (*Z*)-isomer **23** via the zwitterion **24**. It is, therefore, very likely that **19**, possessing as it does a full negative charge on the oxygen, would isomerize to **18** at an even faster rate. Our inability[17] to capture or detect spectroscopically an intermediate such as **21**, from the hydroxamic acid **20**, indicates that the N→O acyl transfer is indeed, in the NMR time scale, an extremely rapid process.



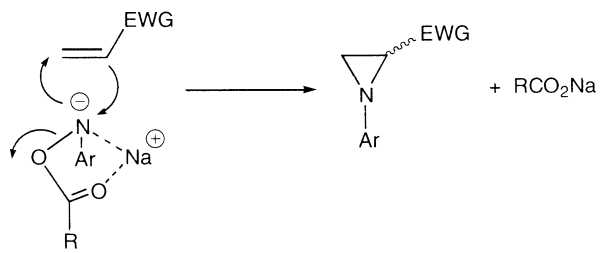
However, strong evidence in favor of an anion such as **18** as being the true aziridinating agent was forthcoming from the observation that PhNH-O-C(=O)-*t*-Bu,[3] prepared independently, provided under our CPT conditions the aziridine **3b** with an e.e. (52%) very similar to that obtained from the corresponding isomeric hydroxamic acid **5a** (e.e. = 45%).

These observations coupled with the finding that the reaction is stereoselective[3] suggest that the most probable mechanism[18] of this aziridination process is as shown in Scheme 7.

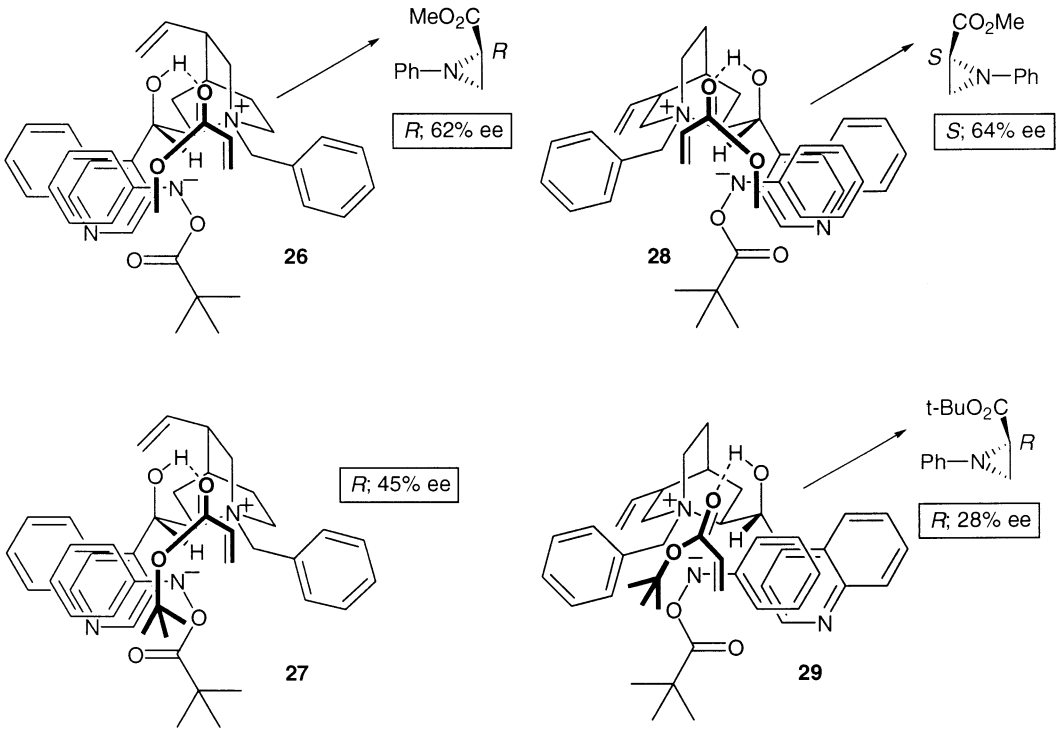
2.10. The molecular assembly leading to enantioselection

Before a coherent model[19] could be presented to explain our results, the one discordant feature of our CPT reactions, namely the fact that the sense of enantioselection remained the same, with the (*R*)-enantiomer predominating (entry 1 in Tables 5 and 6, respectively) irrespective of the pseudoenantiomeric nature of the two catalysts **15a** and **17a** used, had to be satisfactorily explained. It was suspected that this anomaly could have its origin in the steric bulk of the *tert*-butyl ester. Therefore, the reaction was conducted with the less sterically encumbered methyl acrylate and the cinchonidinium salt **17a**. It was gratifying to observe that the aziridine thus obtained possessed $[\alpha]_D^{20} = -98$, indicating that the isomer formed in excess has the opposite (*S*)-configuration (11% η, 64% e.e.).

Thus, for the cinchoninium salt the molecular assembly during chiral transmission would consist of a contact ion-pair formed between the positive quaternary nitrogen and the *N*-acyloxy anion with the quinoline part of the former serving as the platform[20] for the aromatic ring of the latter (Scheme 8). The hydrogen bonded ester is oriented from above in such a manner as to place its electrophilic β-carbon within or about the bonding distance of the anionic species. Thus, two such arrangements **26** and **27**, wherein the olefinic bond is directed towards the positive nitrogen (R_4N^+-π attraction?) could be designed for the methyl and the *tert*-butyl esters, respectively. Both of them would originate the (*R*)-isomers, as is found to be the case experimentally.[21] For the cinchonidinium salt and the sterically less demanding methyl ester, the situation as represented in **28** prevails and as a consequence leads to the (*S*)-isomer. A similar orientation perhaps becomes disfavored for the bulkier *tert*-butyl ester so that the expression **29** becomes more important.[22] Therefore, the product formed is enriched in the (*R*)-isomer.



Scheme 7.



Scheme 8.

3. Conclusions

Details of an enantioselective aziridination of deactivated olefins with chiral phase-transfer catalysis utilizing inexpensive reagents and simple reaction conditions are disclosed. Some of the several factors influencing the course of the reaction were investigated. Reactions of common β-unsubstituted Michael acceptors with chiral hydroxamic acids or those of chiral olefins with hydroxamic acids generally yield products with lower enantio- or diastereoselectivity. The latter method involving the Oppolzer chiral auxiliary of defined stereochemistry, however, provided two diastereomeric aziridines. The structure of one of them, determined by X-ray crystallography, permitted definitive attribution of absolute configuration to the stereogenic center of the derived *N*-phenylaziridine methyl ester, and to other alkyl esters (on the basis of their signs of rotation) and presumably to all *N*-aryl aziridines except the sulfones and the sulfoxide obtained in enantiomeric excess in the CPT-catalyzed reactions detailed in the paper.

4. Experimental

Melting points were determined using a Köfler hot plate apparatus and are uncorrected. IR spectra were recorded on a Buck Scientific 500 or ATI Mattson Genesis Series FTIR™ spectrophotometer and are reported in wave numbers (cm^{-1}). ^1H and ^{13}C NMR spectra were obtained on a Bruker ARX 400 or Bruker CXP 300 spectrometer. Unless otherwise stated ^1H NMR spectra were taken in $CDCl_3$ at 400 MHz and ^{13}C NMR spectra at 100 MHz in $CDCl_3$. Chemical shifts are given in parts per million (ppm) relative to TMS. Coupling constants, *J*, are given in hertz. Mass spectra were recorded on a GC–MS Shimadzu QP 1000 EX spectrometer at 70 eV in the EI mode. High resolution mass spectra were obtained by the Mass Spectrometry Laboratory of the Imperial College of Science Technology and Medicine, London. Optical rotations were measured on a Perkin–Elmer 241 MC polarimeter using a 1 cm^3 capacity, 1 dm path length, quartz cell. HPLC analyses were performed on a combination of Merck/Hitachi L-600A, L-4250, T-6300 and D-6000 components and a Chiralcel® OD column (Daicel Chem. Ind. Ltd, 4.6 mm×250 mm). The HPLC column was thermostatized at 25°C, the UV detector was set at 236 nm and a mixture of *n*-hexane/*i*-propanol (9:1) was used as solvent with flow rate 1.0 mL/min. Elemental analyses were performed by the Microanalytical Laboratory of the Imperial College of Science Technology and Medicine, London. Thin layer chromatography (TLC) was used routinely to monitor the progress of the reactions and was performed on Merck Kieselgel GF sheets (0.2 mm thick) containing fluorescent indicator. TLC plates were visualized when possible with 254 nm ultraviolet light and by treatment with either a solution of 5% aq. $FeCl_3$ (for aziridines and *N*-acylhydroxylamines) or 10% phosphomolybdic acid in ethanol (for aziridines) followed by warming at ca. 100°C.

Cinchonine, cinchonidine, *N*-[4-(trifluoro-methyl)-benzyl]cinchoninium bromide, *N*-(benzyl)cinchoninium chloride and *N*-(benzyl)cinchonidinium chloride were purchased from Aldrich. (–)-8-Phenylmenthol and

dihydrocinchonine was acquired from Fluka. Dehydroabietic acid was a gift from INETI (Instituto Nacional de Engenharia e Tecnologia Industrial, Lisbon). Acrylate of (–)-8-phenylmenthol,5a (–)-*N*-propenoylbornane-2,10-sultam,[8b] and *N*-arylhydroxylamines[23–25] were prepared according to literature procedures. THF was freshly distilled from $LiAlH_4$. KH (35%) and NaH (60%) used are dispersions in mineral oil.

4.1. *N*-Aryl-*N*-hydroxyamide: general procedure

A stirred mixture of $NaHCO_3$ (1.2 mmol) and *N*-aryl hydroxylamine (1 mmol) in dry ether (15 mL) cooled in an ice bath, was treated under nitrogen with a solution of the appropriate acyl chloride (1 mmol) in the same solvent (5 mL) over a period of 30 min. On completion of the reaction (TLC control; silica, CH_2Cl_2/MeOH, 98:2) the mixture was filtered, the filtrate washed with brine and dried (Na_2SO_4). The residue obtained on evaporation of the solvent was crystallized from CH_2Cl_2/*n*-hexane to furnish the title compound.

The following hydroxamic acids were prepared by the above method.

4.1.1. *N*-Hydroxy-*N*-phenyldehydroabietamide 1. A mixture of freshly distilled $SOCl_2$ (0.93 mL) and dehydroabietic acid (638 mg) was heated under reflux (3 h) and the unreacted $SOCl_2$ removed by evaporation in vacuo. The crude acid chloride thus secured was converted into the title compound **1** (254 mg, 31%), mp 160–162°C; $[\alpha]_D^{20}$ +36 ($c=0.99$, CH_2Cl_2); IR (KBr): ν 3220, 1614; ^{1}H NMR (300 MHz): δ 0.96 (s, 3H), 1.16 (s, 3H), 1.22 (d, $J=7.4$ Hz, 6H), 2.54 (dd, $J=2.2$, 12.1 Hz, 1H), 2.80–2.99 (m, 3H), 6.88 (s, 1H), 6.97 (d, $J=8.1$ Hz, 1H), 7.11 (d, $J=8.1$ Hz, 1H), 7.37–7.43 (m, 5H), 9.2 (1H, s); anal. calcd for $C_{26}H_{33}NO_2$: C, 79.76; H, 8.50; N, 3.58. Found: C, 79.51; H, 8.53; N, 3.36%.

4.1.2. *N*-Hydroxy-2,2-dimethyl-*N*-(3-methylphenyl)propanamide 5b. Obtained from *N*-(3-methylphenyl)-hydroxylamine and 2,2-dimethylpropanoyl chloride in 94% yield; mp 104–105°C; IR (KBr): ν 3180, 1620; ^{1}H NMR (300 MHz): δ 1.13 (s, 9H), 2.39 (s, 3H), 7.28 (m, 4H), 9.00 (s, 1H); anal. calcd for $C_{12}H_{17}NO_2$: C, 69.54; H, 8.27; N, 6.76. Found: C, 69.42; H, 8.32; N, 6.71%.

4.1.3. *N*-(4-Bromophenyl)-*N*-hydroxy-2,2-dimethylpropanamide 5e. Obtained from *N*-(4-bromophenyl)-hydroxylamine and 2,2-dimethylpropanoyl chloride in 82% yield: white needles, mp 158–159°C; IR (KBr): ν 3250, 1605; ^{1}H NMR (300 MHz): δ 1.15 (s, 9H), 7.40 (m, 4H), 8.26 (s, 1H); anal. calcd for $C_{11}H_{14}NO_2Br$: C, 48.55; H, 5.19; N, 5.15. Found: C, 48.50; H, 5.18; N, 5.09%.

4.1.4. *N*-(4-Nitrophenyl)-*N*-hydroxy-2,2-dimethylpropanamide 5f. Obtained from *N*-(4-nitrophenyl)hydroxylamine and 2,2-dimethylpropanoyl chloride in 77%; mp 118–120°C; IR (KBr): ν 3250, 1625; ^{1}H NMR (300 MHz): δ 1.35 (s, 9H), 7.70 (d, $J=6.0$ Hz, 2H), 8.15 (d, $J=6.0$ Hz, 2H); anal. calcd for $C_{11}H_{14}N_2O_4$: C, 55.46; H, 5.92; N, 11.78. Found: C, 55.33; H, 5.92; N, 11.78%.

Similarly *N*-phenyl-*N*-hydroxy-2,2-dimethylpropanamide[26] **5a**, *N*-hydroxy-2,2-dimethyl-*N*-(4-methylphenyl)propanamide[27] **5c**, *N*-(3-bromophenyl)-*N*-hydroxy-2,2-dimethylpropanamide **5d**[15] and *N*-phenyl-*N*-hydroxybenzamide[28] **16** were prepared from the respective *N*-arylhydroxylamines and acyl chloride.

4.2. Aziridination of olefins in THF: general procedure

N-Aryl-*N*-hydroxyamide (1 equiv.) and olefin (0.5–3 equiv.) in THF under argon were cooled in an ice bath and NaH (1 equiv.) was added. The cooling bath was removed, the mixture was stirred overnight and then evaporated to dryness in vacuo. The residue was leached with *n*-pentane and the solution was concentrated. Chromatography on silica (eluent: CH_2Cl_2 or *n*-hexane/ethyl acetate, 8:2) yielded pure aziridines.

The following compounds were thus prepared.

4.2.1. (1′*R*,2′*S*,5′*R*)-5′-Methyl-2′-(1-methyl-1-phenylethyl)-cyclohexyl *N*-phenylaziridine-2-carboxylates 6a and 6b. Obtained from *N*-hydroxy-2,2-dimethyl-*N*-phenylpropanamide (54 mg, 0.28 mmol), 8-phenylmenthol acrylate (53 mg, 0.19 mmol), THF (10 mL) and NaH (11 mg, 0.28 mmol). Work-up followed by chromatographic purification afforded the two diastereoisomers **6a** and **6b**, respectively, of undefined stereochemistry.

Diastereoisomer 6a: 29 mg (42% yield), oil, $[\alpha]_D^{20}$ –33 ($c=1.03$, CH_2Cl_2); IR (film): ν 1740; ^{1}H NMR: δ 0.7–2.18 (m, 8H), 0.86 (d, $J=6.4$ Hz, 3H), 1.26 (s, 3H), 1.40 (s, 3H), 2.05 (dd, $J=1.6$, 6.3 Hz, 1H), 2.21 (dd, $J=1.6$, 3.0 Hz, 1H), 2.32 (dd, $J=3.1$, 6.3 Hz, 1H), 4.95 (td, $J=4.4$, 11 Hz, 1H), 6.93 (d, $J=8.6$ Hz, 2H), 7.00 (t, $J=7.4$ Hz, 1H), 7.13 (t, $J=7.0$ Hz, 1H), 7.21–7.36 (m, 6H); MS: m/z (%) 377 (M, 30), 163 (85), 119 (100), 91 (68), 77 (18); HRMS calcd for $C_{25}H_{31}NO_2$: 377.2355. Found: 377.2353.

Diastereoisomer 6b: 16 mg (23% yield), oil, $[\alpha]_D^{20}$ +113 ($c=0.46$, CH_2Cl_2); IR (film): ν 1738; ^{1}H NMR: δ 0.7–2.18 (m, 10H), 0.89 (d, $J=6.7$ Hz, 3H), 1.24 (s, 3H), 1.32 (s, 3H), 2.51 (m, 1H), 4.91 (m, 1H), 6.87 (d, $J=8.0$ Hz, 2H), 6.97 (t, $J=7.9$ Hz, 1H), 7.07 (t, $J=7.8$ Hz, 1H), 7.18–7.31 (m, 6H); MS: m/z (%) 377 (M, 32), 163 (98), 119 (100), 91 (79), 77 (22); HRMS calcd for $C_{25}H_{31}NO_2$: 377.2355. Found: 377.2350.

4.2.2. Quininyl *N*-phenylaziridine-2-carboxylate 8a. Obtained from *N*-hydroxy-2,2-dimethyl-*N*-phenylpropanamide (115 mg), *O*-acryloyl quinine (150 mg), THF (10 mL), and NaH (24 mg). Work-up followed by chromatographic purification afforded an inseparable mixture of diastereoisomers **8a** (145 mg, 78% yield), oil; IR (film): ν 1738; ^{1}H NMR: δ 1.58 (m, 2H), 1.78–1.90 (m, 3H), 2.31–2.37 (m, 2H), 2.62–2.67 (m, 3H), 2.79–2.83 (m, 1H), 3.04–3.15 (m, 2H), 3.43–3.47 (m, 1H), 3.95 and 3.97 (2s, 3H, two diastereoisomers), 4.99–5.06 (m, 2H), 5.79–5.90 (m, 1H), 6.58–6.64 (m, 1H), 6.91–7.09 (m, 4H), 7.23–7.25 (m, 1H), 7.37–7.40 (m, 2H),

7.48 (s, 1H), 8.01–8.05 (m, 1H), 8.68–8.78 (m, 1H); HRMS calcd for $C_{29}H_{31}N_3O_3$: 469.2365. Found: 469.2371.

Methyl-*N*-phenylaziridine-2-carboxylates **9a**+**10a** were readily obtained from the above diastereomers **8a** by simply dissolving it (ca. 20 mg) in MeOH (1 mL) and allowing the reaction mixture to stand at rt (24 h). Evaporation of the solvent under reduced pressure followed by purification of the resulting mixture (pTLC; silica; EtOAc/MeOH, 8:2) furnished the title compounds in virtually quantitative yield as an oil. Addition of $Eu(tfc)_3$ resulted in the splitting of the OMe signal (^{1}H NMR, 400 MHz, $CDCl_3$) into two, one at δ 3.86 and the other at 3.81 for the (*R*)- and (*S*)-isomers, respectively, with a relative ratio of ca. 3:1.

4.2.3. Quininyl *N*-(*m*-methylphenyl)aziridine-2-carboxylate 8b. Obtained from *N*-hydroxy-2,2-dimethyl-*N*-(3-methylphenyl)propanamide (123 mg), *O*-acryloyl quinine (150 mg) in THF (10 mL) and NaH (24 mg, 0.59 mmol). Work-up followed by chromatographic purification afforded **8b** as a mixture of diastereoisomers: 152 mg (80% yield), oil; IR (film): ν 1740; ^{1}H NMR: δ 1.64–1.67 (m, 2H), 1.82–1.90 (m, 2H), 2.28–2.30 (m, 3H), 2.36 (t, $J=5.9$ Hz, 1H), 2.65–2.81 (m, 6H), 3.08–3.23 (m, 2H), 3.42–3.46 (m, 1H), 3.96 and 3.99 (2s, 3H, two diastereoisomers), 4.93–5.06 (m, 2H), 5.75–5.87 (m, 1H), 6.63–6.78 (m, 2H), 6.84 (t, $J=7.4$ Hz, 1H), 7.09–7.16 (m, 1H), 7.35–7.43 (m, 2H), 7.46–7.49 (m, 1H), 8.01–8.05 (m, 1H), 8.73–8.77 (m, 1H); HRMS calcd for $C_{30}H_{33}N_3O_3$: 483.2522. Found: 483.2520.

4.2.4. Quininyl *N*-(*p*-methylphenyl)aziridine-2-carboxylate 8c. Obtained from *N*-hydroxy-2,2-dimethyl-*N*-(4-methylphenyl)propanamide (103 mg), *O*-acryloyl quinine (125 mg), in THF (10 mL) and NaH (20 mg). Work-up followed by chromatographic purification afforded a mixture of diastereoisomers: **8c**: 122 mg (77% yield), oil; IR (KBr): ν 1743; ^{1}H NMR: δ 1.62–1.71 (m, 2H), 1.77–1.92 (m, 3H), 2.28 and 2.29 (2s, 3H, two diastereoisomers), 2.33–2.38 (m, 2H), 2.64–2.80 (m, 4H), 3.07–3.45 (m, 3H), 3.97 and 3.99 (2s, 3H, two diastereoisomers), 5.00–5.06 (m, 2H), 5.72–5.83 (m, 1H), 6.73 (dd, $J=5.2$, 1H), 6.84–6.88 (m, 2H), 7.03–7.08 (m, 2H), 7.34–7.49 (m, 2H), 8.02–8.06 (m, 1H), 8.73–8.77 (m, 1H); HRMS calcd for $C_{30}H_{33}N_3O_3$: 483.2522. Found: 483.2515.

4.2.5. Quininyl *N*-(*m*-bromophenyl)aziridine-2-carboxylate 8d. Obtained from *N*-hydroxy-2,2-dimethyl-*N*-(3-bromophenyl)propanamide (159 mg), *O*-acryloyl quinine (150 mg) in THF (10 mL) and 24 mg (0.59 mmol) of NaH. Work-up followed by chromatographic purification afforded a mixture of diastereoisomers: **8d**: 166 mg (77% yield), oil; IR (film): ν 1741; ^{1}H NMR: δ 1.64 (m, 2H), 1.84–1.92 (m, 3H), 2.38 (m, 1H), 2.66–2.76 (m, 3H), 2.86 (m, 1H), 3.08–3.25 (m, 2H), 3.46 (q, $J=7.6$ Hz, 1H), 3.97 and 3.99 (2s, 3H, two diastereoisomers), 5.00–5.06 (m, 2H), 5.75–5.88 (m, 1H), 6.64–6.73 (m, 1H), 6.88 (t, $J=10.1$ Hz, 1H), 7.08–7.15 (m, 3H), 7.34–7.42 (m, 2H), 7.48 (m, 1H), 8.03 (m, 1H), 8.75 (m, 1H); HRMS calcd for $C_{29}H_{30}N_3O_3Br$: 549.1450. Found: 549.1475.

4.2.6. Quininyl *N*-(*m*-nitrophenyl)aziridine-2-carboxylate 8g. Obtained as a foam (152 mg; 75% yield) from *N*-hydroxy-2,2-dimethyl-*N*-(3-nitrophenyl)propanamide (159 mg), *O*-acryloyl quinine (150 mg) in THF (10 mL) and NaH (24 mg). Work-up followed by chromatographic purification afforded a mixture of diastereoisomers: **8g**: IR (film): ν 1744; ^{1}H NMR: δ 1.65 (m, 2H), 1.84–1.96 (m, 3H), 2.37 (s, 1H), 2.48 (m, 1H), 2.67–2.80 (m, 3H), 2.97 (m, 1H), 3.08–3.24 (m, 2H), 3.44 (m, 1H), 3.97 and 3.98 (2s, 3H, two diastereoisomers), 5.06 (m, 2H), 5.74–5.89 (m, 1H), 6.65–6.73 (m, 1H), 7.21 (m, 1H), 7.47–7.33 (m, 3H), 7.79 (m, 1H), 7.88 (t, $J=5.2$ Hz, 1H), 8.04 (m, 1H), 8.75 (m, 1H); HRMS calcd for $C_{29}H_{30}N_4O_5$: 514.2216. Found: 514.2221.

4.3. Aziridination of (−)-*N*-propenoylbornane-2,10-sultam (11) by *N*-hydroxy-2,2-dimethyl-*N*-arylpropanamide: general procedure

N-Hydroxy-2,2-dimethyl-*N*-arylpropanamide (0.25 mmol), (−)-*N*-propenoylbornane-2,10-sultam (200 mg, 0.74 mmol) in THF (3 mL) under argon was cooled in an ice bath and NaH (0.25 mmol; 10 mg) was added. The cooling bath was removed and the solution was stirred overnight. On completion of the reaction (TLC control), the mixture containing the diastereomeric sultam-aziridines was treated with $Mg(OMe)_2$ in methanol (0.41 M; 1 mL). The solution was vigorously stirred for 1 h until the methanolysis was complete and the solvent evaporated in vacuo. The resulting residue was triturated with *n*-pentane, the extract concentrated and purified by chromatography on silica gel (eluent: *n*-hexane/Et_2O, 2:1) to give the following products.

4.3.1. Methyl *N*-phenylaziridine-2-carboxylates (9a+10a) (*R+S*). Obtained from *N*-hydroxy-2,2-dimethyl-*N*-phenylpropanamide in 30% yield (32% e.e. ^{1}H NMR with $Eu(tfc)_3$, major enantiomer: levorotatory). IR (film): ν 1750; ^{1}H NMR: δ 2.32 (dd, $J=1.6$, 6.0 Hz, 1H), 2.67 (dd, $J=1.8$, 3.0 Hz, 1H), 2.80 (dd, $J=3.0$, 6.2 Hz, 1H), 3.81 (s, 3H), 7.00–7.04 (m, 3H), 7.23–7.27 (m, 2H); MS: *m*/*z* (%) 177 (M, 32), 162 (25), 118 (18), 104 (100), 91 (55), 77 (45); HRMS calcd for $C_{10}H_{11}NO_2$: 177.0789. Found: 177.0786.

4.3.2. Methyl *N*-(*m*-methylphenyl)aziridine-2-carboxylates (9b+10b) (*R+S*). Obtained from *N*-hydroxy-2,2-dimethyl-*N*-(3-methylphenyl)propanamide in 28% yield (20% e.e. ^{1}H NMR with $Eu(tfc)_3$): $[\alpha]_D^{20}$ −43 ($c=0.45$, CH_2Cl_2); IR (film): ν 1754; ^{1}H NMR: δ 2.29–2.31 (m, 4H), 2.65 (dd, $J=1.8$, 3.0 Hz, 1H), 2.78 (dd, $J=3.1$, 6.3 Hz, 1H), 3.81 (s, 3H), 6.80–6.84 (m, 3H), 7.11–7.15 (m, 1H); MS: *m*/*z* (%) 191 (M, 79), 176 (47), 132 (36), 118 (100), 105 (60), 91 (45); HRMS calcd for $C_{11}H_{13}NO_2$: 191.0946. Found: 191.0945.

4.3.3. Methyl *N*-(*p*-methylphenyl)aziridine-2-carboxylates (9c+10c) (*R+S*). Obtained from *N*-hydroxy-2,2-dimethyl-*N*-(4-methylphenyl)propanamide in 8% yield

(49% e.e. ^{1}H NMR with Eu(tfc)$_3$): $[\alpha]_D^{20}$ −71 (c=0.04, CH_2Cl_2); IR (film): ν 1754; ^{1}H NMR: δ 2.27–2.29 (m, 4H), 2.64 (dd, J=1.8, 3.0 Hz, 1H), 2.75 (dd, J=3.1, 6.3 Hz, 1H), 3.81 (s, 3H), 6.90 (d, J=8.3 Hz, 2H), 7.05 (d, J=8.0 Hz, 2H); MS: m/z (%) 191 (M, 76), 176 (43), 132 (38), 118 (100), 105 (64), 91 (59); HRMS calcd for $C_{11}H_{13}NO_2$: 191.0946. Found: 191.0940.

4.3.4. Methyl *N*-(*m*-bromophenyl)aziridine-2-carboxylates (9d+10d) (*R+S*). Obtained from *N*-(3-bromophenyl)-*N*-hydroxy-2,2-dimethylpropanamide in 41% yield (0% e.e. ^{1}H NMR with Eu(tfc)$_3$); IR (film): ν 1750; ^{1}H NMR: δ 2.32 (dd, J=1.5, 6.4 Hz, 1H), 2.68 (dd, J=1.6, 3.1 Hz, 1H), 2.81 (dd, J=3.1, 6.4 Hz, 1H), 3.81 (s, 3H), 6.94 (td, J=1.7, 7.6 Hz, 1H), 7.09–7.16 (m, 3H); MS: m/z (%) 255 (M, 78), 240 (74), 196 (28), 182 (100), 169 (49), 155 (35); HRMS calcd for $C_{10}H_{10}NO_2Br$: 254.9895. Found: 254.9856.

4.3.5. Methyl *N*-(*p*-nitrophenyl)aziridine-2-carboxylates (9f+10f) (*R+S*). Obtained from *N*-hydroxy-2,2-dimethyl-*N*-(4-nitrophenyl)propanamide in 15% yield (17% e.e. ^{1}H NMR with Eu(tfc)$_3$): mp 51–53°C; $[\alpha]_D^{20}$ −51 (c=0.20, CH_2Cl_2); IR (KBr): ν 1756; ^{1}H NMR: δ 2.45 (d, J=6.2 Hz, 1H), 2.79 (s, 1H), 2.96 (dd, J=3.0, 6.1 Hz, 1H), 3.83 (s, 3H), 7.08 (d, J=9.0 Hz, 2H), 8.15 (d, J=9.0 Hz, 2H); anal. calcd for $C_{10}H_{10}N_2O_4$: C, 54.05; H, 4.54; N, 12.61. Found: C, 54.11; H, 4.53; N, 12.53.

4.4. Preparation, separation and characterization of aziridines 12a and 13a by Garner's method

Br_2 (0.032 mL, 0.61 mmol) was added to **11** (150 mg, 0.56 mmol) in chloroform (3 mL). The solution was stirred under nitrogen (1 h) and then treated with NEt_3 (0.31 mL, 2.23 mmol). After 24 h at rt, the mixture was diluted with chloroform (25 mL), washed successively with aq. HCl (20 mL, 0.1N), aq. saturated $NaHCO_3$ (20 mL), brine, and dried over anhydrous sodium sulfate. Purification by chromatography (silica gel, eluent: *n*-hexane/ethyl acetate, 7:3) followed by crystallization of the product (CH_2Cl_2/*n*-hexane) afforded the bromoolefin **14**, 124 mg (64% yield), mp 139–141°C; ^{1}H NMR: δ 1.00 (s, 3H), 1.21 (s, 3H), 1.31–1.47 (m, 2H), 1.90–2.13 (m, 5H), 3.44 (d, J=13.6 Hz, 1H), 3.54 (d, J=13.6 Hz, 1H), 4.04 (dd, J=4.6, 7.8 Hz, 1H), 6.53 (d, J=3.2 Hz, 1H), 6.30 (d, J=3.2 Hz, 1H); MS: m/z (%) 349 (M, $C_{13}H_{18}NO_3S^{81}Br^+$, 2), 347 (M′, $C_{13}H_{18}NO_3S^{79}Br^+$, 2), 285 (6), 283 (6), 268 (26), 204 (60), 135 (100), 133 (49); HRMS calcd for $C_{13}H_{18}NO_3S^{81}Br$: 349.0170. Found: 349.0162. Calcd for $C_{13}H_{18}NO_3S^{79}Br$: 347.0191. Found: 347.0191.

Aziridine sultams 13a and 12a by addition of aniline to 14. Compound **14** (100 mg, 0.29 mmol), NEt_3 (0.06 mL, 0.43 mmol) and aniline (0.04 mL, 0.43 mmol) in chloroform (3 mL) were magnetically stirred (21 days) at room temperature under nitrogen until all the electrophile had reacted (absence of olefinic protons at δ 6.53 (1H, d, J=3.2 Hz, HC=C–C=O) and 6.30 (1H, d, J=3.2 Hz, HC=C–C=O). The solution was diluted with chloroform (25 mL), washed in succession with aq. HCl (0.1N), aq. saturated $NaHCO_3$, brine and dried over anhydrous Na_2SO_4. Preparative TLC (silica, eluent: *n*-hexane/Et_2O, 1:1) afforded aziridines **12a** and **13a**, which were crystallized from chloroform/*n*-hexane.

12a: 49 mg (47%), needles, mp 164.5–166°C; $[\alpha]_D^{20}$ +27 (c=0.23, CH_2Cl_2); IR (KBr): ν 1704, 1332, 1141; ^{1}H NMR: δ 1.01 (s, 3H), 1.27 (s, 3H), 1.34–1.48 (m, 2H), 1.90–2.26 (m, 5H), 2.41 (dd, J=1.8, 6.2 Hz, 1H), 2.74 (dd, J=1.9, 2.9 Hz, 1H), 3.47–3.51 (m, 2H), 3.58 (d, J=13.8 Hz, 1H), 3.95 (dd, J=4.9, 7.8 Hz, 1H), 6.98–7.04 (m, 3H), 7.22–7.26 (m, 2H).

Crystal data for **12a**:[29] $C_{19}H_{24}N_2O_3S$, M=360.5, orthorhombic, $P2_12_12_1$ (no. 19), a=7.575(1), b=11.224(1), c=21.098(1) Å, V=1793.7(1) Å^3, Z=4, D_{calcd}=1.335 g cm^{-3}, μ(Cu-Kα)=17.7 cm^{-1}, $F(000)$=768, T=223 K; clear blocks, 0.60×0.27×0.23 mm, Siemens P4 rotating anode diffractometer, ω-scans, 2010 independent reflections. The structure was solved by direct methods and the non-hydrogen atoms were refined anisotropically using full-matrix least-squares based on F^2 to give R_1=0.028, wR_2=0.073 for 1990 independent observed reflections [$|F_o|>4\sigma(|F_o|)$, $2\theta\leq$ 126°] and 239 parameters. The absolute structure of **12a** was unambiguously determined by a combination of an *R*-factor test [R_1^+=0.0279, R_1^-=0.0428] and by use of the Flack parameter [x^+=0.02(2), x^-=0.98(2)]. As can be seen in Figs. 1 and 2, the conformation of the molecule is in part controlled by an intramolecular C–H–O hydrogen bond between one of the *o*-phenelene (hydrogens *ortho* to the nitrogen of the aniline ring) and one of the sulfone oxygen atoms. A study of the packing of the crystal reveals the linking of helically related molecules via a combination of C–H–O and C–H···π interactions (b and c, respectively, in Fig. 2).

13a: 19 mg (18%), needles, mp 187.5–189°C; $[\alpha]_D^{20}$ −456 (c=0.01, CH_2Cl_2); IR (KBr): ν 1698, 1330, 1135; ^{1}H NMR: δ 1.00 (s, 3H), 1.20 (s, 3H), 1.25–1.50 (m, 2H), 1.90–2.13 (m, 5H), 2.38 (dd, J=2.1, 6.0 Hz, 1H), 2.75 (t, J=2.5 Hz, 1H), 3.52–3.56 (m, 2H), 3.59 (d, J=13.8 Hz, 1H), 4.01 (t, J=6.4 Hz, 1H), 7.00 (t, J=7.3 Hz, 1H), 7.13 (d, J=7.6 Hz, 2H), 7.23 (d, J=7.5 Hz, 2H); anal. calcd for $C_{19}H_{24}N_2SO_3$: C, 63.31; H, 6.71; N, 7.77. Found: C, 63.38; H, 6.34; N, 7.66%.

4.4.1. 1-(*m*-Methylphenyl)aziridine-2-carboxylic acid, bornane-10′,2′-sultam amide (12b+13b). Obtained from Br_2 (0.02 mL), **11** (100 mg) and *m*-toluidine (0.06 mL) by the method described in Section 4.4 in 84% yield: white powder; mp 193–201°C; IR (KBr): ν 1700, 1332, 1138; ^{1}H NMR: δ 1.00 and 1.19 (s, 3H, two diastereoisomers), 1.28 (s, 3H), 1.90–1.95 (m, 4H), 2.11–2.14 (m, 2H), 2.30 (m, 4H), 2.36 and 2.40 (dd, J=1.8, 6.2 Hz, 1H, two diastereoisomers), 2.70–2.72 (m, 1H), 3.42–3.48 (m, 2H), 3.91 and 4.01 (dd, J=4.9, 7.8 Hz, 1H, two diastereoisomers), 6.80–6.83 and 6.95 (m, 3H, two diastereoisomers), 7.09–7.13 and 7.24 (m, 1H, two diastereoisomers). Anal. calcd for $C_{20}H_{26}N_2SO_3$: C, 64.14; H, 7.00; N, 7.48. Found: C, 64.03; H, 6.86; N, 7.43%.

4.4.2. 1-(*p*-Methylphenyl)aziridine-2-carboxylic acid, bornane-10′,2′-sultam amide (12c+13c). Obtained from Br_2 (0.02 mL), **11** (100 mg) and *p*-toluidine (0.06 mL) by the method described in Section 4.4 in 90% yield: mp 170–180°C; IR (KBr): ν 1700, 1332, 1134; ^{1}H NMR: δ 0.99 and 1.01 (s, 3H, two diastereoisomers), 1.19 and 1.27 (s, 3H), 1.90–1.98 (m, 3H), 2.09–2.17 (m, 1H), 2.22–2.27 (m, 4H), 2.33 and 2.37 (dd, $J=1.7$, 6.2 Hz, 1H, two diastereoisomers), 2.69–2.72 (m, 1H), 3.94 and 4.00 (dd, $J=4.9$, 7.8 Hz, 1H, two diastereoisomers), 6.92 (d, $J=8.0$, 2H), 7.04 (d, $J=8.3$, 2H). Anal. calcd for $C_{20}H_{26}N_2SO_3$: C, 64.14; H, 7.00; N, 7.48. Found: C, 64.17; H, 6.99; N, 7.45%.

4.5. Preparation of quaternary salts of cinchonine and cinchonidine: general procedure

A mixture of cinchonine or cinchonidine (1 equiv.) and the appropriate benzyl halide (1 equiv.) in acetonitrile or *i*-propanol was magnetically stirred while being heated under reflux (4 h). On completion of the reaction (TLC control: silica gel, CH_2Cl_2/MeOH, 9:1) the solid was collected and recrystallized (CH_2Cl_2/Et_2O) yielding pure quaternary salts of cinchona bases.

4.5.1. *N*-(2-Naphthylmethyl)-cinchoninium bromide 15c. Obtained from (+)-cinchonine (500 mg, 1.7 mmol) and 2-(bromomethyl)naphthalene (376 mg, 1.7 mmol) in 65% yield: white powder; mp 192°C (dec.); $[\alpha]_D^{20}$ +148 ($c=0.075$, $CHCl_3$); IR (KBr): ν 1120; ^{1}H NMR: δ 0.69–0.78 (m, 1H), 1.62–1.73 (m), 2.04–2.17 (m, 2H), 2.68 (q, $J=11.0$ Hz, 1H), 3.25 (t, $J=11.5$ Hz, 1H), 4.19–4.28 (m, 2H), 4.48 (t, $J=10.4$ Hz, 1H), 5.12 (d, $J=17.2$ Hz, 1H), 5.19 (d, $J=10.4$ Hz, 1H), 5.58 (d, $J=11.9$ Hz, 1H), 5.80 (m, 1H), 6.35 (d, $J=11.8$ Hz, 1H), 6.58–6.60 (m, 1H), 6.68 (s, 1H), 6.98–7.00 (m, 2H), 7.12 (d, $J=7.8$ Hz, 1H), 7.28–7.29 (m, 2H), 7.50–7.59 (m, 3H), 7.89 (d, $J=4.4$ Hz, 1H), 7.94 (s, 1H), 8.32–8.36 (m, 1H), 8.83 (d, $J=4.4$ Hz, 1H); ^{13}C NMR: δ 149.3, 146.8, 144.3, 135.1, 134.1, 132.8, 132.0, 129.6, 129.3, 128.1, 127.9, 127.8, 127.2, 127.0, 127.0, 126.1, 124.0, 123.3, 123.2, 119.6, 117.9, 66.4, 65.7, 61.4, 56.2, 53.5, 37.9, 27.1, 23.6, 21.8. Anal. calcd for $C_{30}H_{31}N_2OBr$: C, 69.90; H, 6.06; N, 5.43. Found: C, 70.14; H, 5.96; N, 5.58%.

4.5.2. *N*-(3-Nitrobenzyl)-cinchoninium bromide 15d. Prepared from (+)-cinchonine (1.3 g, 4.4 mmol) and 3-nitrobenzyl bromide (0.95 g, 4.4 mmol) in 77% yield: white powder; mp 248–250°C (dec.); $[\alpha]_D^{20}$ +156 ($c=0.11$, $CHCl_3$); IR (KBr): ν 1124; ^{1}H NMR: δ 0.74–0.85 (m), 1.74–1.87 (m), 2.12 (t, $J=12.3$ Hz, 1H), 2.32 (q, $J=8.5$ Hz, 1H), 2.68 (q, $J=10.3$ Hz, 1H), 3.14 (t, $J=11.2$ Hz, 1H), 4.13–4.24 (m, 2H), 4.57 (t, $J=10.2$ Hz, 1H), 5.21 (d, $J=17.2$ Hz, 1H), 5.27 (d, $J=10.4$ Hz, 1H), 5.62 (d, $J=12.0$ Hz, 1H), 5.84 (m, 1H), 6.41–6.54 (m, 3H), 6.93–7.01 (m, 2H), 7.40 (t, $J=7.9$ Hz, 1H), 7.54 (d, $J=8.0$ Hz, 1H), 7.83 (d, $J=4.3$ Hz, 1H), 7.97 (d, $J=8.0$ Hz, 1H), 8.17 (s, 1H), 8.29 (d, $J=8.0$ Hz, 1H), 8.42 (d, $J=7.1$ Hz, 1H), 8.83 (d, $J=4.3$ Hz, 1H); ^{13}C NMR: δ 149.4, 147.9, 146.9, 143.8, 140.3, 134.7, 129.7, 129.6, 129.4, 128.3, 128.1, 127.1, 124.7, 123.3, 123.1, 119.5, 118.5, 67.3, 65.4, 59.9, 56.4, 54.2, 37.9, 27.1, 23.6, 21.7. Anal. calcd for $C_{26}H_{28}N_3O_3Br$: N, 8.23. Found: N, 8.03%.

4.5.3. *N*-[4-(Trifluoromethyl)benzyl]dihydrocinchoninium bromide 15i. Prepared from dihydrocinchonine (50 mg, 0.17 mmol) and 4-(trifluoromethyl)benzyl bromide (68 mg, 0.28 mmol) in 67% yield: white powder; mp 264–265°C (dec.); $[\alpha]_D^{20}$ +114 ($c=0.08$, $CHCl_3$); ^{1}H NMR: δ 0.69–0.82 (m), 1.46–1.75 (m), 2.02 (t, $J=11.0$ Hz, 1H), 2.60 (m, 1H), 3.16 (m, 1H), 4.08–4.17 (m, 3H), 5.35 (d, $J=11.6$ Hz, 1H), 6.35–6.53 (m, 3H), 6.93–6.99 (m, 2H), 7.38 (d, $J=6.6$ Hz, 2H), 7.51 (d, $J=7.6$ Hz, 1H), 7.83 (m, 3H), 8.23 (d, $J=7.2$ Hz, 1H), 8.82 (s, 1H); ^{13}C NMR: δ 149.4, 146.9, 144.0, 134.4, 131.2, 129.6, 128.2, 127.1, 125.3, 123.3, 123.0, 119.6, 67.3, 65.5, 60.1, 56.6, 56.0, 35.9, 24.6, 24.2, 24.0, 21.6, 11.3. HRMS (FAB) calcd for $C_{27}H_{30}F_3N_2O$: 455.2310. Found: 455.2317.

N-(Benzyl)cinchoninium bromide **15b**,[12] *N*-(4-nitrobenzyl)cinchoninium chloride **15e**,[12] *N*-(3,4-dichlorobenzyl)cinchoninium chloride **15f**,[12] *N*-[4-(trifluoromethyl)-benzyl]cinchonidinium bromide **17a**,[30] *N*-(benzyl)cinchonidinium bromide **17b**,[13] *N*-(9-anthracenylmethyl)cinchonidinium chloride **17d**[31] and *N*-(9-anthracenylmethyl)cinchoninium chloride **15g**[14] were prepared according to literature procedures.

4.6. *O*-Allylation of quaternary salts of cinchonine and cinchonidine: general procedure[31]

To a suspension of the quaternary salt of cinchonine or cinchonidine (1 equiv.) in CH_2Cl_2 (10 mL) was added allyl bromide (3 equiv.) followed by 50% aqueous KOH (5 equiv.). The resulting mixture was stirred vigorously at 20°C (4 h) after which time it was diluted with water (20 mL) and extracted with CH_2Cl_2. The combined organic extracts were dried (Na_2SO_4), filtered and evaporated in vacuo. The product was obtained pure on crystallization from methanol–diethyl ether.

4.6.1. *O*-Allyl-*N*-(9-anthracenylmethyl)cinchoninium bromide 15g′. Prepared from *N*-(9-anthracenylmethyl)-cinchoninium chloride (0.5 g, 0.96 mmol) and allyl bromide (0.25 mL, 2.9 mmol) in 75% yield: mp 133–135°C; $[\alpha]_D^{20}$ +270 ($c=0.16$, $CHCl_3$); ^{1}H NMR (400 MHz, CD_3OD): δ 1.25 (s, 1H), 1.61 (m, 1H), 1.83 (m, 3H), 2.08 (m, 2H), 2.31 (m, 1H), 2.64 (m, 1H), 3.03 (t, $J=11.2$ Hz, 1H), 4.38 (m, 3H), 5.02 (d, $J=17.2$ Hz, 1H), 5.22 (d, $J=10.3$ Hz, 1H), 5.61 (m, 3H), 5.77 (ddd, $J=17.0$, 10.5, 6.4 Hz, 1H), 5.88 (m, 1H), 6.29 (m, 1H), 6.61 (s, 1H), 7.46–7.63 (m, 4H), 7.84 (1H), 7.91 (1H), 8.03–8.27 (m, 5H), 8.67 (s, 1H), 9.03 (m, 1H), 9.28 (m, 1H), 9.86 (m, 1H); ^{13}C NMR (400 MHz, CD_3OD): δ 149.9, 139.8, 135.7, 134.1, 133.6, 132.7, 132.5, 131.7, 131.5, 131.1, 130.3, 129.8, 129.0, 127.9, 127.2, 126.5, 126.2, 125.0, 123.5, 119.8, 118.2, 117.7, 69.9, 61.2, 57.1, 54.4, 38.0, 37.7, 26.1, 24.3, 23.7, 22.7; HRMS calcd for $C_{37}H_{37}N_2O$: 525.2906. Found: 525.2908.

4.6.2. *O*-Allyl-*N*-[4-(trifluoromethyl)benzyl]cinchoninium bromide 15a′. Obtained from *N*-[4-(trifluoro-methyl)-benzyl]cinchoninium bromide (0.8 g, 1.5 mmol) and allyl bromide (0.4 mL, 4.6 mmol) in 61% yield: mp

137–138°C; $[\alpha]_D^{20}$ +134 ($c=0.18$, $CHCl_3$); IR (KBr): ν 1153, 1020; ^{1}H NMR (400 MHz, CD_3OD): δ 1.10 (m, 1H), 1.80 (m, 1H), 1.92–2.02 (m, 3H), 2.33 (m, 1H), 2.49 (m, 1H), 2.78 (m, 1H), 3.47 (t, $J=11.2$ Hz, 1H), 3.97 (dd, $J=12.4$, 6.7 Hz, 1H), 4.20–4.31 (m, 2H), 4.49 (d, $J=11.4$ Hz, 1H), 4.76 (s, 1H), 5.22 (d, $J=17.2$ Hz, 1H), 5.32 (d, $J=10.4$ Hz, 1H), 5.39–5.44 (m, 2H), 5.89 (ddd, $J=17.2$, 10.4, 7.0 Hz, 1H), 6.09 (m, 1H), 6.19 (s, 1H), 6.74 (d, $J=11.7$ Hz, 1H), 7.55 (m, 1H), 7.73–7.81 (m, 3H), 7.95 (s, 1H), 8.09–8.14 (m, 3H), 8.96 (m, 2H); ^{13}C NMR (400 MHz, CD_3OD): δ 149.5, 148.7, 139.4, 135.1, 134.7, 132.9, 132.4, 131.2, 130.5, 130.0, 129.3, 126.2, 125.1, 120.1, 119.5, 118.5, 74.3, 70.4, 65.9, 60.3, 55.7, 54.7, 37.6, 26.9, 23.2, 22.0; HRMS calcd for $C_{30}H_{32}N_2OF_3$: 493.2466. Found: 493.2455.

4.6.3. *O*-Allyl-*N*-[4-(trifluoromethyl)benzyl]cinchonidinium bromide 17a′. Prepared from *N*-[4-(trifluoromethyl)benzyl]cinchonidinium bromide (1 g, 2.2 mmol) and allyl bromide (0.6 mL, 6.6 mmol) in 95% yield: mp 149–151°C; $[\alpha]_D^{20}$ −149 ($c=0.12$, $CHCl_3$); IR (KBr): ν 1167, 1020; ^{1}H NMR (400 MHz, CD_3OD): δ 1.42 (m, 1H), 1.81 (m, 1H), 1.07–2.21 (m, 3H), 2.61 (m, 1H), 3.15 (t, $J=11.6$ Hz, 1H), 3.32 (m, 1H), 4.07 (dd, $J=6.6$, 12.2 Hz, 1H), 4.27 (dd, $J=12.3$, 4.7 Hz, 1H), 4.39 (m, 1H), 4.70 (m, 2H), 5.02 (m, 2H), 5.40 (m, 3H), 5.32 (d, $J=10.4$ Hz, 1H), 5.39–5.44 (m, 2H), 5.89 (ddd, $J=17.2$, 10.4, 7.0 Hz, 1H), 6.09 (m, 1H), 6.19 (s, 1H), 6.74 (d, $J=11.7$ Hz, 1H), 7.55 (m, 1H), 7.73–7.81 (m, 3H), 7.95 (s, 1H), 8.09–8.14 (m, 3H), 8.96 (m, 2H); ^{13}C NMR (400 MHz, CD_3OD): δ 149.6, 148.7, 139.7, 135.9, 134.8, 132.8, 132.6, 131.4, 130.4, 130.1, 129.2, 126.1, 125.3, 124.9, 124.7, 120.1, 118.7, 70.3, 66.3, 65.7, 61.1, 59.6, 51.5, 37.6, 26.6, 25.1, 22.6; HRMS calcd for $C_{30}H_{32}N_2OF_3$: 493.2466. Found: 493.2460.

O-Allyl-*N*-(9-anthracenylmethyl)cinchonidinium bromide **17d′** was prepared according to literature procedures.[31]

4.7. Aziridination of olefins with phase-transfer catalysis: general procedure

NaOH (1 mL, aq. 33%) was added to a solution of *N*-arylhydroxamic acid (1 equiv.) in toluene. The mixture was vigorously stirred (2 min) during which time formation of a flocculent precipitate was observed. The electrophile (10 equiv.) and the catalyst (0.1 equiv.) were added and stirring was continued for ca. 1 h. An additional quantity of catalyst was added if necessary, and the mixture stirred until reaction was adjudged complete (TLC control on silica, CH_2Cl_2 or *n*-hexane/ethyl acetate, 8:2). The residue obtained on evaporation was taken up in Et_2O, washed several times with brine until pH ca. 7, dried (Na_2SO_4), filtered and the solvent removed in vacuo. The aziridines were purified by chromatography on silica (pTLC, eluent: CH_2Cl_2 or *n*-hexane/ethyl acetate, 8:2).

4.7.1. Ethyl *N*-phenylaziridine-2-carboxylate 3a (*R+S*). Obtained from *N*-hydroxy-2,2-dimethyl-*N*-phenylpropanamide (100 mg, 0.52 mmol), NaOH (1 mL, aq. 33%), ethyl acrylate (0.56 mL, 5.52 mmol) and *N*-[4-(trifluoromethyl)benzyl]cinchoninium bromide (28 mg, 0.052 mmol) in toluene (8 mL). Work-up and chromatographic purification afforded a yellow oil of **3a** (27 mg, 27% yield, 55% e.e. ^{1}H NMR analysis with Eu(tfc)$_3$, major enantiomer: dextrorotatory). Spectroscopic properties similar to those described in the literature for the same compound.[32]

4.7.2. *tert*-Butyl *N*-phenylaziridine-2-carboxylate 3b (*R+S*). Obtained from *N*-hydroxy-2,2-dimethyl-*N*-phenylpropanamide (100 mg, 0.52 mmol), NaOH (1 mL, aq. 33%), *tert*-butyl acrylate (0.76 mL, 5.2 mmol), *N*-[4-(trifluoromethyl)benzyl]cinchoninium bromide (28 mg, 0.052 mmol) and toluene (8 mL). Work-up and chromatographic purification furnished a yellow oil of **3b** (89 mg, 79% yield, 45% e.e. chiral HPLC): $[\alpha]_D^{20}$ +66 ($c=1.06$, CH_2Cl_2); IR (film): ν 1742; ^{1}H NMR: δ 1.50 (s, 9H), 2.25 (dd, $J=1.8$, 6.2 Hz, 1H), 2.59 (dd, $J=1.8$, 3.0 Hz, 1H), 2.69 (dd, $J=3.0$, 6.2 Hz, 1H), 6.97–7.02 (m, 3H), 7.21–7.26 (m, 2H); MS: m/z (%) 219 (M, 32), 163 (79), 118 (100), 104 (30), 91 (65), 77 (21), 57 (23); HRMS calcd for $C_{13}H_{17}NO_2$: 219.1259. Found: 219.1265.

4.7.3. *tert*-Butyl *N*-phenylaziridine-2-carboxylate 3b (*R+S*) from *O*-pivaloyl-*N*-phenylhydroxylamine. A vigorously stirred mixture of NaOH (2 mL aq. 33%), *tert*-butyl acrylate (1.7 mL; 12 mmol) and *N*-[(4-trifluoromethyl)benzyl]cinchoninium bromide (64 mg; 0.12 mmol) in toluene (5 mL) was treated, during 40 min, with *N*-phenyl-*O*-pivaloylhydroxylamine[15] (230 mg; 1–2 mmol) in toluene (15 mL). Work-up as above, gave **3b** (31 mg, 12% yield, 52% e.e. by ^{1}H NMR with Eu(tfc)$_3$; major isomer *R*).

4.7.4. *tert*-Butyl *N*-(*m*-methylphenyl)aziridine-2-carboxylate 3b-1. Obtained from *N*-hydroxy-2,2-dimethyl-*N*-(3-methylphenyl)propanamide (108 mg, 0.52 mmol), NaOH (1 mL, aq. 33%), *tert*-butyl acrylate (0.76 mL, 5.2 mmol), *N*-[4-(trifluoromethyl)benzyl]cinchoninium bromide (28 mg, 0.052 mmol) in toluene (8 mL). Work-up and chromatographic purification gave a yellow oil of **3b-1** (48 mg, 40% yield, 43% e.e. chiral HPLC): $[\alpha]_D^{20}$ +69 ($c=0.60$, CH_2Cl_2); IR (film): ν 1744; ^{1}H NMR (300 MHz): δ 1.50 (s, 9H), 2.23 (dd, $J=1.8$, 6.0 Hz, 1H), 2.30 (s, 3H), 2.57 (dd, $J=1.8$, 3.0 Hz, 1H), 2.67 (dd, $J=3.0$, 6.0 Hz, 1H), 6.77–6.85 (m, 3H), 7.12 (t, $J=7.8$ Hz, 1H); MS: m/z (%) 233 (M, 32), 177 (97), 132 (100), 118 (44), 105 (60), 91 (20), 57 (28); HRMS calcd for $C_{14}H_{19}NO_2$: 233.1416. Found: 233.1391.

4.7.5. *tert*-Butyl *N*-(*p*-methylphenyl)aziridine-2-carboxylate 3b-2. Obtained from *N*-hydroxy-2,2-dimethyl-*N*-(4-methylphenyl)propanamide (108 mg, 0.52 mmol), NaOH (1 mL aq. 33%), *tert*-butyl acrylate (0.76 mL, 5.2 mmol) and *N*-[4-(trifluoro-methyl)benzyl]-cinchoninium bromide (28 mg, 0.052 mmol) in toluene (8 mL). Work-up followed by chromatographic purification gave a yellow oil of **3b-2** (61 mg, 50% yield, 51% e.e. chiral HPLC): $[\alpha]_D^{20}$ +84 ($c=0.64$, CH_2Cl_2); IR (film): ν 1749; ^{1}H NMR: δ 1.50 (s, 9H), 2.20 (dd, $J=1.8$, 6.2 Hz, 1H), 2.27 (s, 3H), 2.56 (dd, $J=1.8$, 3.0

Hz, 1H), 2.64 (dd, $J=3.0$, 6.2 Hz, 1H), 6.89 (d, $J=8.4$ Hz, 2H), 7.03 (d, $J=8.0$ Hz, 2H); MS: m/z (%) 233 (M, 21), 177 (90), 132 (97), 118 (63), 105 (100), 91 (40), 57 (43); HRMS calcd for $C_{14}H_{19}NO_2$: 233.1416. Found: 233.1419.

4.7.6. *tert*-Butyl *N*-(*m*-bromophenyl)aziridine-2-carboxylate 3b-3. Obtained from *N*-(3-bromophenyl)-*N*-hydroxy-2,2-dimethylpropanamide (142 mg, 0.52 mmol), NaOH (1 mL aq. 33%), *tert*-butyl acrylate (0.76 mL, 5.2 mmol) and *N*-[4-(trifluoromethyl)benzyl]cinchoninium bromide (28 mg, 0.052 mmol) in toluene (8 mL). Chromatographic purification yielded a yellow oil of **3b-3** (43 mg, 28% yield, 16% e.e. chiral HPLC): $[\alpha]_D^{20}$ +20 ($c=0.84$, CH_2Cl_2); IR (film): ν 1745; ^{1}H NMR (300 MHz): δ 1.50 (s, 9H), 2.26 (dd, $J=2.0$, 6.3 Hz, 1H), 2.60 (dd, $J=1.8$, 3.3 Hz, 1H), 2.72 (dd, $J=3.3$, 6.5 Hz, 1H), 6.93 (td, $J=2.9$, 9.2 Hz, 1H), 7.09–7.15 (m, 3H); MS: m/z (%) 299 (M, $C_{13}H_{16}NO_2{}^{81}Br^+$, 34), 297 (M′, $C_{13}H_{16}NO_2{}^{79}Br^+$, 37), 243 (93), 241 (90), 198 (81), 196 (83), 171 (52), 169 (55), 117 (100), 57 (88); HRMS calcd for $C_{13}H_{16}NO_2{}^{81}Br$: 299.0344. Found: 299.0373. Calcd for $C_{13}H_{16}NO_2{}^{79}Br$: 297.0364. Found: 297.0379.

4.7.7. *tert*-Butyl *N*-(*p*-bromophenyl)aziridine-2-carboxylate 3b-4. Obtained from *N*-(4-bromophenyl)-*N*-hydroxy-2,2-dimethylpropanamide (55 mg, 0.20 mmol), NaOH (0.4 mL, aq. 33%), *tert*-butyl acrylate (0.29 mL, 2.0 mmol) and *N*-[4-(trifluoromethyl)benzyl]-cinchoninium bromide (11 mg, 0.02 mmol) in toluene (3 mL). Chromatographic purification furnished a yellow oil of **3b-4** (30 mg, 50% yield, 36% e.e. chiral HPLC): $[\alpha]_D^{20}$ +46 ($c=0.56$, CH_2Cl_2); IR (film): ν 1754; ^{1}H NMR: δ 1.49 (s, 9H), 2.22 (dd, $J=1.2$, 6.0 Hz, 1H), 2.59 (d, $J=1.2$ Hz, 1H), 2.67 (dd, $J=3.0$, 5.8 Hz, 1H), 6.87 (d, $J=8.4$ Hz, 2H), 7.34 (d, $J=8.4$ Hz, 2H); MS: m/z (%) 299 (M, $C_{13}H_{16}NO_2{}^{81}Br^+$, 24), 297 (M′, $C_{13}H_{16}NO_2{}^{79}Br$, 22), 243 (75), 241 (82), 198 (63), 196 (67), 171 (42), 169 (41), 117 (100), 57 (75); HRMS calcd for $C_{13}H_{16}NO_2{}^{81}Br$: 299.0344. Found: 299.0354; calcd for $C_{13}H_{16}NO_2{}^{79}Br$: 297.0364. Found: 297.0377.

4.7.8. *N*-Phenyl-2-(phenylsulfonyl)aziridine 3b-5. Obtained from *N*-hydroxy-2,2-dimethyl-*N*-phenylpropanamide (100 mg, 0.52 mmol), NaOH (1 mL, aq. 33%), phenyl vinyl sulfone (88 mg, 0.5 mmol), *N*-[4-(trifluoromethyl)benzyl]cinchoninium bromide (28 mg, 0.052 mmol) in toluene (8 mL) as a colorless solid (43% yield, 44% e.e. ^{1}H NMR with Yb(hfc)$_3$): $[\alpha]_D^{20}$ +104 ($c=0.7$, CH_2Cl_2). Recrystallization with CH_2Cl_2/*n*-hexane yielded **3b-5** (27 mg, 20%, 84% e.e. chiral HPLC): mp 93–94°C; IR (KBr): ν 1320, 1150; ^{1}H NMR: δ 2.49 (d, $J=5.7$ Hz, 1H), 3.05 (d, $J=1.4$ Hz, 1H), 3.48 (dd, $J=1.9$, 5.5 Hz, 1H), 6.51 (d, $J=7.8$ Hz, 2H), 6.97 (t, $J=7.3$ Hz, 1H), 7.12 (t, $J=7.5$ Hz, 2H), 7.64 (t, $J=7.5$ Hz, 2H), 7.75 (t, $J=7.3$ Hz, 1H), 8.06 (d, $J=7.7$ Hz, 2H). Anal. calcd for $C_{14}H_{13}NSO_2$: C, 64.84; H, 5.05; N, 5.40. Found: C, 64.55; H, 5.18; N, 5.21%.

4.7.9. *N*-(*p*-Methylphenyl)-2-(phenylsulfonyl)aziridine 3b-6. Obtained from *N*-hydroxy-2,2-dimethyl-*N*-(4-methylphenyl)propanamide (283 mg, 0.15 mmol), NaOH (0.29 mL, aq. 33%), phenyl vinyl sulfone (25 mg, 0.15 mmol), *N*-(4-trifluoromethyl)benzyl cinchoninium bromide (8 mg, 0.015 mmol) in toluene (2.3 mL). Chromatographic purification gave a white solid of **3b-6** (16 mg, 39% yield, 20% e.e. ^{1}H NMR with Yb(hfc)$_3$): mp 78–79.5°C; $[\alpha]_D^{20}$ +39 ($c=0.17$, CH_2Cl_2); IR (KBr): ν 1324, 1150; ^{1}H NMR: δ 2.21 (s, 3H), 2.46 (d, $J=5.7$ Hz, 1H), 3.03 (d, $J=1.6$ Hz, 1H), 3.42 (dd, $J=2.4$, 5.6 Hz, 1H), 6.40 (d, $J=8.1$ Hz, 2H), 6.92 (d, $J=8.0$ Hz, 2H), 7.63 (t, $J=7.6$ Hz, 2H), 7.74 (t, $J=7.3$ Hz, 1H), 8.06 (d, $J=7.6$ Hz, 2H); MS: m/z (%) 273 (M, 14), 132 (100), 117 (71), 105 (9), 91 (13), 77 (15); HRMS calcd for $C_{15}H_{15}NO_2S$: 273.0824. Found: 273.0822.

4.7.10. *N*-(*p*-Bromophenyl)-2-(phenylsulfonyl)aziridine 3b-7. Obtained from *N*-(4-bromophenyl)-*N*-hydroxy-2,2-dimethylpropanamide (283 mg, 0.15 mmol), NaOH (2 mL, aq. 33%), phenyl sulfone (175 mg, 1.04 mmol), *N*-[4-(trifluoromethyl)benzyl]cinchoninium bromide (56 mg, 0.104 mmol) in toluene (16 mL) as a colorless solid (34%, 60% e.e. ^{1}H NMR with Yb(hfc)$_3$ and chiral HPLC, major enantiomer. Recrystallization from CH_2Cl_2/*n*-hexane gave **3b-7** (53 mg, 15%, 82% e.e. ^{1}H NMR with Yb(hfc)$_3$): mp 127–129°C; $[\alpha]_D^{20}$ +172 ($c=0.33$, CH_2Cl_2); IR (KBr): ν 1310, 1152; ^{1}H NMR: δ 2.46 (d, $J=5.7$ Hz, 1H), 3.04 (s, 1H), 3.44 (d, $J=3.2$ Hz, 1H), 6.38 (d, $J=8.4$ Hz, 2H), 7.21–7.25 (m, 2H), 7.64 (t, $J=7.5$ Hz, 2H), 7.75 (t, $J=7.2$ Hz, 1H), 8.04 (d, $J=7.6$ Hz, 2H); MS: m/z (%) 339 (M, $C_{14}H_{12}NO_2S^{81}Br^+$, 6), 337 (M′, $C_{14}H_{12}NO_2S^{79}Br^+$, 6), 198 (18), 196 (18), 157 (6), 155 (6), 117 (100), 77 (10); HRMS calcd for $C_{14}H_{12}NO_2S^{81}Br$: 338.9752. Found: 338.9742. Calcd for $C_{14}H_{12}NO_2S^{79}Br$: 336.9772. Found: 336.9773.

4.7.11. *N*-Phenyl-2-(phenylsulfinyl)aziridine 3b-8. Obtained from *N*-hydroxy-2,2-dimethyl-*N*-phenylpropanamide (100 mg, 0.52 mmol), NaOH (1 mL, aq. 33%), phenyl vinyl sulfoxide (0.21 mL, 1.55 mmol), *N*-[4-(trifluoromethyl)benzyl]cinchoninium bromide (56 mg, 0.104 mmol) in toluene (8 mL), as a viscous oil after the excess phenyl vinyl sulfoxide had been removed at 50°C under vacuum (ca. 0.1 mbar). Crystallization from CH_2Cl_2/Et_2O gave **3b-8** (57 mg, 45%) mp 71–101°C; IR (KBr): ν 1055; ^{1}H NMR: δ 2.41 (d, $J=6.0$ Hz) and 2.44 (d, $J=5.5$ Hz) (1H, two diastereomers), 2.79 (d, $J=2.8$ Hz) and 3.00 (d, $J=2.6$ Hz) (1H, two diastereomers)), 3.31 (dd, $J=2.9$ Hz and $J=6.0$ Hz, 1H), 6.58 (d, $J=7.5$ Hz, 2H), 6.95 (t, $J=7.4$ Hz, 1H), 7.13 (t, $J=7.9$ Hz, 2H), 7.58–7.61 (m, 3H), 7.74–7.76 (m, 2H). Anal. calcd for $C_{14}H_{13}NSO$: C, 69.14; H, 5.35; N, 5.76. Found: C, 69.16; H, 5.32; N, 5.59%.

4.7.12. 2-Benzoyl-1,3-diphenylaziridine 3b-9. Obtained from *N*-hydroxy-*N*-phenyl-2,2-dimethylpropanamide (300 mg, 1.55 mmol), NaOH (3 mL, aq. 33%), *trans*-chalcone (108 mg, 0.52 mmol), *N*-[4-(trifluoromethyl)benzyl]cinchoninium bromide (56 mg, 0.104 mmol) in toluene (18 mL) as white needles after recrystallization from THF/Et_2O (15% yield, 0% e.e. determined by chiral HPLC): mp 109–110°C; IR (KBr): ν 1674; ^{1}H NMR δ 3.99 (d, $J=2.0$ Hz, 1H), 4.17 (d,

$J=2.0$ Hz, 1H), 6.82 (d, $J=8.0$ Hz, 2H), 6.96 (t, $J=7.2$ Hz, 1H), 7.19 (t, $J=8.0$ Hz, 1H), 7.30–7.43 (m, 6H), 7.51 (t, $J=7.6$ Hz, 2H), 7.62 (t, $J=7.6$ Hz, 1H), 8.05 (d, $J=8.0$ Hz, 2H). Anal. calcd for $C_{21}H_{17}NO$: C, 84.15; H, 5.29; N, 4.43. Found: C, 84.25; H, 5.72; N, 4.68%; MS: m/z (%) 299 (M, 100), 222 (41), 207 (58), 194 (74), 105 (58), 77 (60); HRMS calcd for $C_{21}H_{17}NO$: 299.1310. Found: 299.1307.

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