Preparation of Axially Chiral *N*,*N*′-Diarylimidazolium and *N*-Arylthiazolium Salts and Evaluation of Their Catalytic Potential in the Benzoin and in the Intramolecular Stetter Reactions

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Keywords: Asymmetric catalysis / Atropisomerism / Carbenes / Heterocycles / Umpolung

N-Aryl-substituted imidazoles **14b**, **15b** and thiazoles **17**–**22**, **25** were prepared which contain a stereogenic axis and which can occur as atropisomers. The imidazolium salts **15b** could be obtained from 2-isopropylaniline (**12b**) and diacetyl (**11**) in three steps (19% yield) whereas the synthesis of their *tert*-butyl analogues failed. The *meso*-isomer *meso*-**15b** prevailed (*dr* = 90/10). The chiral thiazolium salts *rac*-**17** (53% yield) and *rac*-**22** (49% yield) were prepared in two steps from 2-*tert*-butylaniline (**12a**). The enantiomerically pure thiazolium salt **19** was obtained from α-bromomenthone (**23**) and the aniline **12a** (27% overall yield). In contrast to the imidazolium salts **15b**, the thiazolium salts proved to be suitable catalysts in the benzoin condensation of benzaldehyde (**1** → **2**) and in the intramolecular Stetter reaction of the α,β-unsaturated ester **9a**. The best results obtained with catalyst **19** (20 mol %) were 85% yield of product **2** (40% *ee*) and 75% yield of product **10a** (50% *ee*). The stereogenic axis of catalyst **19** is not configurationally stable in the catalytically active carbene intermediate **28**. The catalyst is recovered as a mixture of diastereomeric atropisomers **19** and **26** in a ratio of 70:30 to 75:25.

Introduction

The study presented in this report is concerned with the preparation of axially chiral azolium salts of the general structure **A** (Figure 1). These compounds are accessible from the thiones **B**[1] and can be converted into the carbenes **C** by deprotonation at carbon atom C-2. As a major application for these compounds we envisaged their use as catalysts for enantioselective C−C bond-forming reactions such as the benzoin condensation[2,3] or the Stetter reaction.[4,5] The fact that the nitrogen atom does not carry a stereogenic center but is part of the stereogenic element appeared to be an attractive new concept not yet pursued in this area.

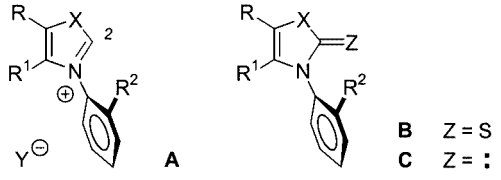

Figure 1. General structure of the axially chiral azolium salts **A**, their precursor **B** and the intermediate carbenes **C**

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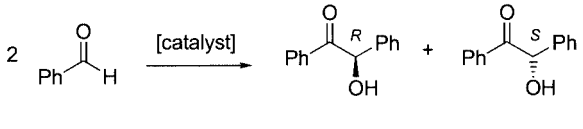
Before discussing our results in detail an overview is given which describes briefly the development of organocatalysts for nucleophilic aldehyde activation. Outstanding results that have recently been achieved[6,7] prompted us to disclose our own results.

N-Heterocyclic carbenes (NHC)[8] add to aldehydes and allow for a polarity reversal (Umpolung) at the carbonyl carbon atom via the corresponding electron-rich enols. The most prominent C−C bond-forming reactions characterized by this mechanistic feature are the previously mentioned benzoin and Stetter reactions.[9] The thiazolium salt-catalyzed benzoin condensation has been investigated intensively by Breslow.[10] The mode of action of the thiazolium salt is fully analogous to the role that natural thiamine (vitamin B_1) pyrophosphate plays in many biochemical reactions.[11] It was this analogy which led Stetter et al.[4b,5] to devise 3-benzyl-5-hydroxyethyl-3-methyl-substituted thiazolium salts as catalysts for the addition of aliphatic aldehydes to electrophiles.



Scheme 1. The benzoin reaction of benzaldehyde (**1**) generating the two enantiomeric products **2** and *ent*-**2**

As apparent from the benzoin condensation of benzaldehyde (**1**) depicted in Scheme 1, the addition of the aldehyde to a prostereogenic center leads to the formation of enantiomers. In this simple case, (*R*)-benzoin (**2**) and its enantiomer *ent*-**2** are obtained.

In early attempts to conduct the benzoin condensation enantioselectively, Sheehan et al. employed thiazolium salts derived from simple α-chiral primary amines.[12] The best result was obtained with catalyst **3** (Figure 2) which delivered the dextrorotatory benzoin *ent*-**2** in 38.5% optical purity (21% yield). In another experiment, benzoin **2** was obtained from *ent*-**3** in 51.5% optical purity (6% yield) after a shorter reaction time. The stereochemical result was explained by invoking (*E*)-enol **4** as an intermediate. Free rotation around the N−C bond is restricted due to 1,3-allylic strain. As a consequence the electrophilic aldehyde attacks from the top face via transition state $\mathbf{5}^{\neq}$ in which the steric interactions between the substituents at the two prostereogenic carbon atoms are minimized. Despite several attempts to achieve higher enantiomeric excesses in the benzoin condensation the improvements remained insignificant for some time.[13] Even the appealing idea to embed the stereogenic center into a cyclic array as realized by Leeper et al.[13d,13e] and by Rawal et al.[13f] did not lead to higher enantioselectivities.

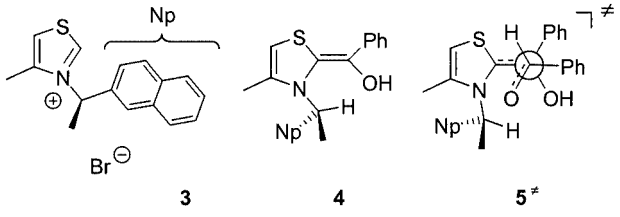


Figure 2. The Sheehan catalyst **3**,[12] its enol intermediate **4** and the potential transition $\mathbf{5}^{\neq}$ state of its enantioselective benzoin condensation

The observation by Teles, Enders et al.[14] that triazolium salts exhibit higher catalytic activity than thiazolium salts in the benzoin condensation turned out to be the key discovery for the development of highly enantioselective catalysts. Initial studies were conducted with a triazolium salt in which the chiral substituent was attached to the nitrogen atom by an exocyclic single bond (up to 86% *ee*).[15] The same catalyst delivered up to 71% *ee* in intramolecular Stetter reactions (vide infra).[16] Leeper et al. studied the enantioselective benzoin condensation (up to 82.5% *ee*) employing the bicyclic triazolium chloride **6** (Figure 3).[17] The catalyst was designed by applying the previously used concept of a conformationally locked endocyclic stereogenic center to triazolium salts. Excellent results in the benzoin condensation (up to 95% *ee*) were eventually achieved by Enders et al. who used triazolium salt **7**.[6] A related catalyst **8** was designed by Rovis et al.[7] who aimed at enantioselective intramolecular Stetter reactions.

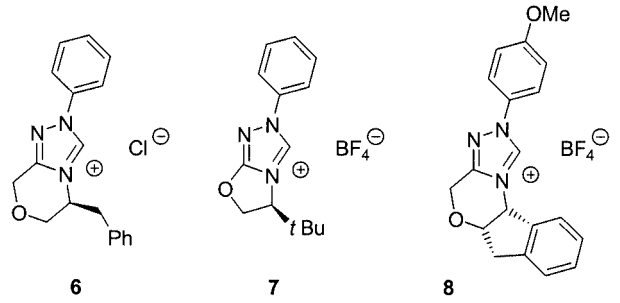
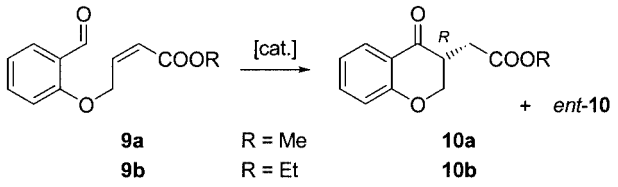


Figure 3. The chiral triazolium catalysts **6**,[17] **7**,[6] and **8**[7]

The more complex architecture of the Stetter reaction products obtained by Enders et al.[16] and Rovis et al.[7] holds promise for further applications in synthesis. A typical example of the reaction studied is provided in Scheme 2. The easily available salicylaldehyde-derived substrate **9** underwent cyclization to the 4-chromanones **10** and *ent*-**10**. If the reaction was conducted in the presence of catalyst **8** (20 mol %) the (*R*)-product **10b** was the major enantiomer obtained from **9b** in 94% yield with 94% *ee*.[7]



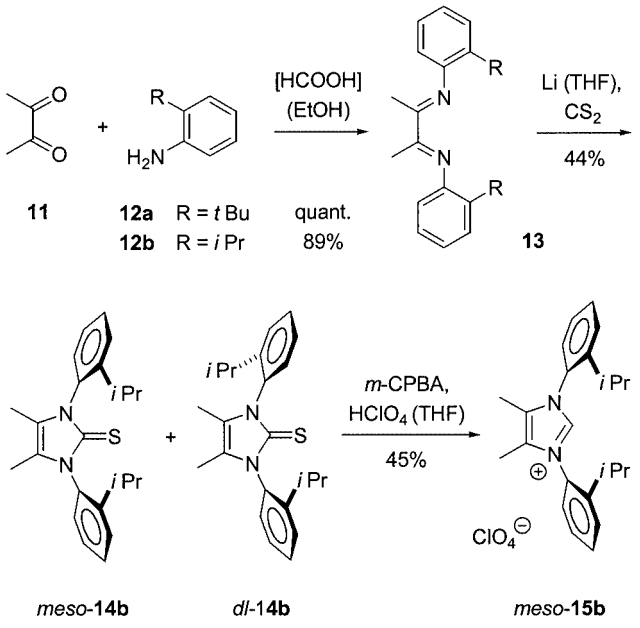
Scheme 2. The intramolecular Stetter reaction of ester **9** generating the two enantiomeric products **10** and *ent*-**10**

Results and Discussion

Our research was initiated in 1999[18] and was triggered by earlier studies we had conducted using axially chiral enamides in the Paternò−Büchi reaction.[19] There was no information on the rotational barrier around the C_{aryl}−N bond in axially chiral carbenes of type **C**. Based on known data for biphenyls[20] and *N*-aryl-2*H*-1,3-thiazole-2-thiones[21] it was expected that azolium salts **A** and 2*H*-1,3-azole-2-thiones **B** with a large *ortho*-alkyl substituent R^2, ideally *tert*-butyl, and a substituent R^1 that was not H would be configurationally stable.

N,*N*′-Diarylimidazolium Salts

The possibility to obtain C_2-symmetric chiral azolium salts was so attractive that we turned our first synthetic study towards *N*,*N*′-diarylimidazolium salts (Scheme 3). Condensation of diacetyl (**11**) with *ortho*-substituted anilines **12** yielded the diimines **13**.[22] Whereas the isopropyl-substituted product **13b** could be further converted into the corresponding thione **14b** the *tert*-butyl-substituted product **13a**[22] failed to react under the same reaction conditions. Other attempts to convert diimine **13a** or aniline **12a** into the desired thione **14a**, to another cyclic imidazole derivative, or directly to the imidazolium salt **15a** also failed.



Scheme 3. Synthesis of the imidazolium salt *meso*-**15b**

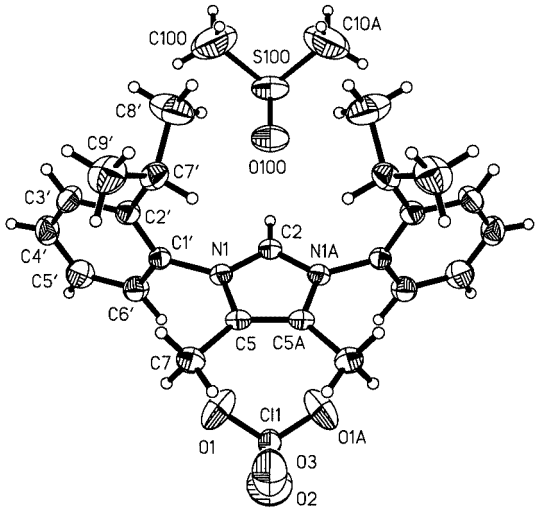


Figure 4. A molecule of compound *meso*-**15b**·DMSO in the crystal[24]

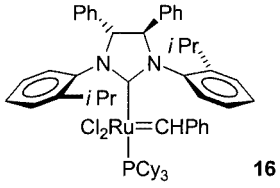


Figure 5. Configuration of the N-heterocyclic carbene used as ligand in the chiral Ru complex **16**[25]

Upon treatment with lithium in THF, the diimine **13b** was converted into its dianion, which was subsequently quenched with carbon disulfide. Two diastereoisomers were formed and could be separated by chromatography. There was no interconversion between the two diastereoisomers. The racemic *dl*-product *dl*-**14b** was identified by single-crystal X-ray crystallography.[23] The structure of *meso*-product *meso*-**14b** was consequently assigned to the other diastereoisomer. The subsequent oxidation to the imidazolium salt was conducted with *meta*-chloroperbenzoic acid (*m*CPBA) and perchloric acid in THF at −78 °C. Irrespective of which diastereoisomer was taken as starting material for the oxidation, the imidazolium ion **15b** was always obtained as a mixture of diastereoisomers in which the *meso*-product *meso*-**15b** prevailed (*dr* = 90:10). Other oxidation methods[1] delivered similar results and yielded the *meso*-product predominantly. The imidazolium salt *meso*-**15b** was obtained as the perchlorate and gave crystals suitable for single-crystal X-ray crystallography. The structure of the imidazolium ion is shown in Figure 4.[24]

Upon dissolving the diastereomerically pure imidazolium perchlorate *meso*-**15b** there was no equilibration to the diastereomeric mixture. Based on this result and on the previously mentioned observation that the thiones **14b** do not equilibrate, the interconversion of the *dl*-diastereoisomer to the *meso*-diastereoisomer must have occurred in some intermediate involved in imidazolium salt formation. We assume that the free carbene is responsible for the equilibration and that the preference for the *meso*-diastereoisomer is due to attractive van der Waals interactions of the lipophilic substituents. Recent results by Grubbs et al.,[25] who employed a C_2-symmetric chiral 1,3-bis(2-isopropylphenyl)-4,5-dihydro-4,5-diphenylimidazole-2-ylidene as ligand in a ruthenium complex (**16**, Figure 5) support the notion that the rotation around the C_{aryl}−N bond in the N-heterocyclic carbene is not restricted.

Work in the area of imidazolium salts was discontinued as the preparation of *N*,*N′*-bis(2-*tert*-butylphenyl)imidazolium salts was not feasible (vide supra). Furthermore, we observed, in line with previous results by Teles, Enders et al.,[14a] that the reactivity of *N*,*N′*-diarylimidazolium salts in benzoin and Stetter reactions is inferior to the reactivity of thiazolium salts.

N-Arylthiazolium Salts

Work in this area centered around three major topics which are best illustrated by the target compounds that we attempted to prepare and that are depicted in Figure 6. The simple *N*-(2-*tert*-butylphenyl)thiazolium salt **17** was to be separated by conventional resolution via the corresponding diastereomeric salts using a chiral counterion Y^-. A 2*H*-1,3-thiazole-2-thione of type **18** with a 5-hydroxyethyl (R = H) side chain can be esterified and possibly separated via the corresponding diastereoisomers. Oxidation of compounds **18** (R = acyl, alkylsulfonyl) and cleavage of the ester should lead to enantiomerically pure thiazolium salts. Finally, the chiral thiazolium salt **19** was to be obtained as a single enantiomerically pure diastereoisomer due to the chiral menthol-derived backbone. The three topics will be

individually discussed in the sequence in which the compounds **17**−**19** are shown in Figure 6.

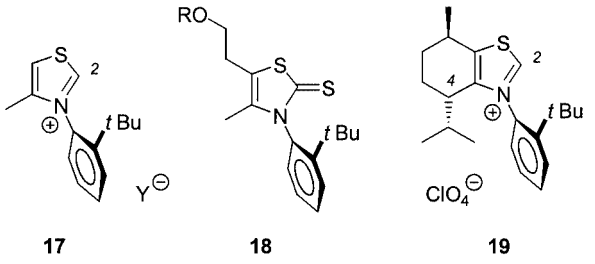
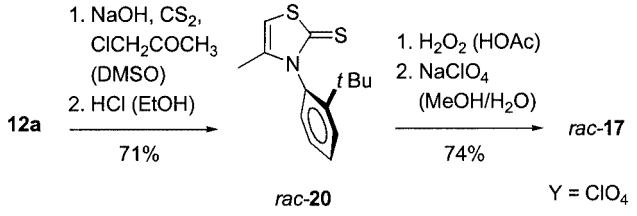


Figure 6. Structure of three chiral thiazole derivatives **17**, **18**, and **19** which are potential precursors for axially chiral N-heterocyclic carbenes

In an approach to thiazole *rac*-**17**, the racemic thione *rac*-**20** was easily obtained by treating aniline **12a** under basic conditions with carbon disulfide and chloroacetone in DMSO (Scheme 4). Subsequent condensation under acidic conditions in ethanol yielded the desired intermediate *rac*-**20** which was further oxidized to the thiazolium salt. Ion exchange with perchlorate gave compound *rac*-**17** ($Y^- = ClO_4^-$) in good yield.



Scheme 4. Synthesis of the thiazolium salt *rac*-**17**

All attempts to achieve a fractional crystallization upon ion exchange with a chiral counterion remained unsuccessful. However, despite this unsatisfactory result there was also some good news: the crystal structure of compound *rac*-**17** ($Y = ClO_4$)[26] revealed that the *tert*-butyl group provides an extremely efficient shielding of one diastereotopic face at carbon atom C-2 (Figure 7). In addition, we could show that the catalytic activity of the thiazolium salt *rac*-**17** is similar to the typical Stetter catalyst 3-benzyl-5-hydroxyethyl-3-methylthiazolium bromide.[5] A conceivable decrease in reactivity due to the sterically bulky *N*-(2-*tert*-butylphenyl) substituent was not observed. In the benzoin condensation (cf. Scheme 1), product *rac*-**2** was obtained in 74% yield at 80 °C after 1.5 h employing the Stetter catalyst (5 mol % catalyst, 30 mol % NEt_3 in EtOH). With catalyst *rac*-**17** under otherwise identical conditions, the yield was 75%. After 19 h at room temperature, the Stetter catalyst allowed for a yield of 96% whereas *rac*-**17** gave 98%.

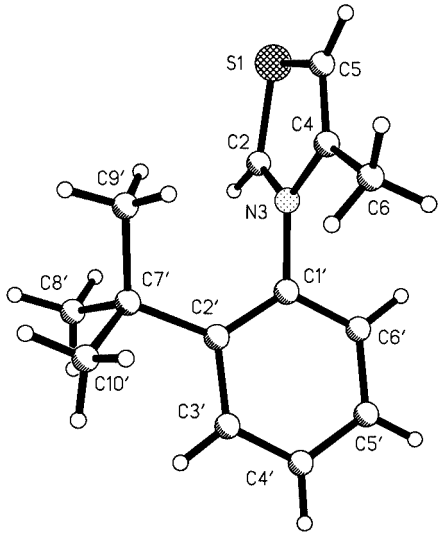
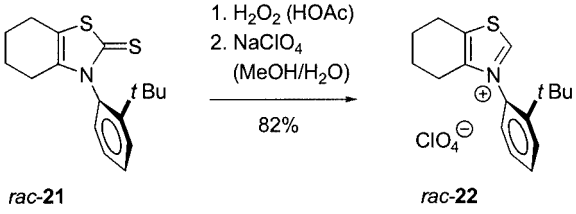


Figure 7. A molecule of compound *rac*-**17** in the crystal;[26] the counterion ($Y = ClO_4$) is not shown

The second approach towards an enantiomerically pure thiazolium salt was based on compounds **18** (Figure 6). Unfortunately, the attempted resolution of the 5-hydroxyethyl-2*H*-1,3-thiazole-2-thione *rac*-**18** (R = H) also failed. The compound was prepared in analogy to thione *rac*-**20** from aniline **12a** and 3-chloro-5-hydroxy-2-pentanone (49% yield). Upon esterification with camphorsulfonyl chloride [NEt_3 (CH_2Cl_2); 78%] and with *O*-methylmandelic acid chloride [NEt_3 (CH_2Cl_2); 99%] the diastereomeric thiones could be detected by NMR spectroscopy as separate compounds but could not be separated either chromatographically or by crystallization.

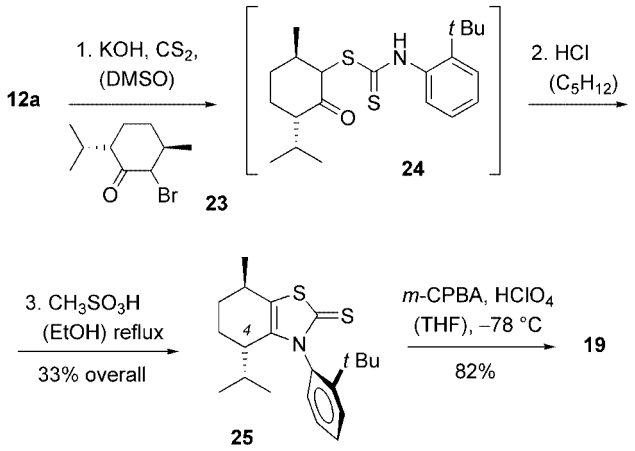
More successful was the third strategy which aimed at the preparation of compound **19** (Figure 6). In a test run with α-bromocyclohexanone[27] we checked whether the previously used thiazolethione synthesis starting from α-chloroketones was applicable to cyclic substrates. This was proved to be the case (60% yield starting from aniline **12a**). Thione *rac*-**21** was further converted into the thiazolium salt *rac*-**22** (Scheme 5).



Scheme 5. Synthesis of the thiazolium salt *rac*-**22**

For the synthesis of compound **19** the known α-bromomenthone (**23**)[28] was prepared from (−)-menthone by treatment with LDA and bromine (89% yield). It was obtained as a mixture of diastereoisomers (*dr* = 58:42). The mixture was taken directly into the thione synthesis which

was conducted stepwise (Scheme 6). In the first reaction step the dithiocarbamate **24** was generated by treating aniline **12a** with carbon disulfide and subsequently with bromide **23**. Contrary to the cyclohexanone-derived dithiocarbamate, dithiocarbamate **24** did not cyclize spontaneously to the corresponding bicyclic N,O-acetal. A solvent change to pentane was required to induce a cyclization with HCl in diethyl ether. Finally, water was eliminated under acidic conditions to yield the desired product, after crystallization, as a mixture of two atropisomers (*dr* = 97:3). The shown *anti*-isomer **25** prevailed. Its relative and absolute configuration was proven by single-crystal X-ray analysis.[29] Some experimentation was required until we found optimal conditions for the conversion of thione **25** into the desired thiazolium salt **19**. A clean conversion into the diastereomerically pure product **19** was finally achieved upon treatment with *m*CPBA at low temperature. Under these conditions no epimerization was observed. The configuration of this product was again proven by X-ray crystallography (Figure 8).[30]



Scheme 6. Synthesis of the thiazolium salt **19**

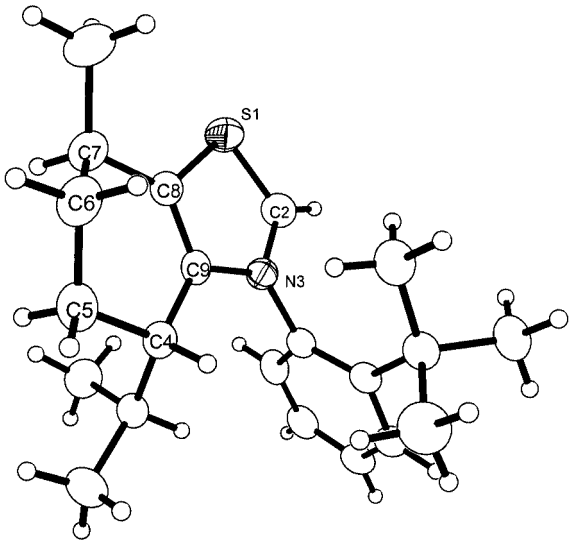


Figure 8. A molecule of compound **19** in the crystal;[30] the counterion is not shown

Conventional oxidation with H_2O_2 at room temperature surprisingly led to a mixture of *three* diastereoisomers in a ratio of 60:20:20. Based on X-ray crystallographic[30] and NMR spectroscopic evidence the two minor diastereoisomers were identified as the atropisomer **26** and its epimer at C-4 **27** (Figure 9). Apparently, the hydrogen atom at C-4 is sufficiently acidic to account for an epimerization. The fact that the other atropisomer was formed at room temperature, possibly via a carbene intermediate, was somewhat discouraging but we decided to look at some catalysis results first. For these experiments, the diastereomerically pure thiazolium salt **19** was employed. For preliminary studies, we used either the racemic compound *rac*-**22** or the more easily available diastereomeric mixture obtained by oxidation of compound **25**.

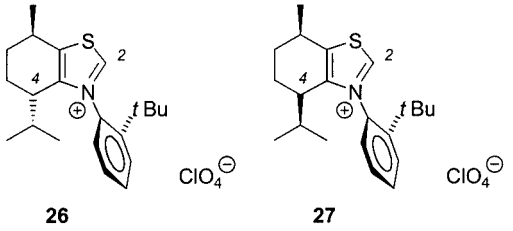


Figure 9. The diastereoisomers of compound **19**, thiazolium salts **26** and **27**

Catalysis Experiments

In our search for optimal reaction conditions, the benzoin condensation (cf. Scheme 1) was conducted first. Possible solvents were screened using 5 mol % catalyst and 5-mol % NEt_3 at ambient temperature. Best conversions were achieved in EtOH, MeCN or CH_2Cl_2 (reaction time: 15 h; quantitative yield) but the enantioselectivities were low. The best enantioselectivity was achieved in THF but in this case the conversion was not satisfactory (15% yield after 15 h). A variation of base (*t*BuOK, NaOEt, KHMDS) in THF as the solvent did not lead to an improvement. A successful remedy was to increase the amount of catalyst and the amount of base to 20 mol %. Under these conditions, benzoin **2** was isolated in 85% yield (reaction time: 18 h at ambient temperature) and with 40% *ee* (HPLC, column: Daicel ChiralPak AD). The reaction did not proceed at lower temperature (0 °C). The absolute configuration of the major enantiomer was determined from its known specific rotation.

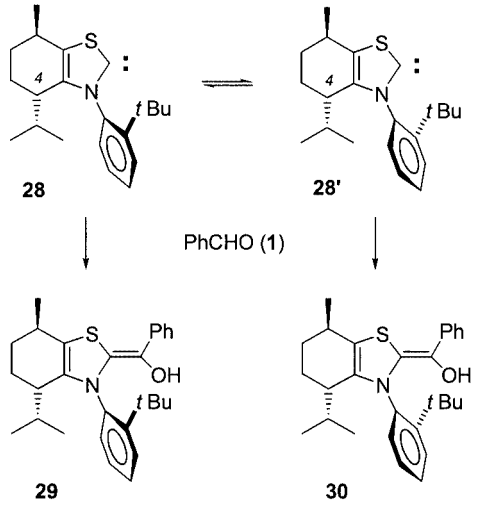
The Stetter reaction studies conducted with starting material **9a** (cf. Scheme 2) delivered results similar to the results obtained in the benzoin condensation. THF was the superior solvent and NEt_3 the base of choice. With 20 mol % of catalyst **19**, product **10a** was obtained in 75% yield (reaction time: 16 h) and with 50% *ee* (HPLC, column: Daicel ChiralPak AD). The absolute configuration of the product was determined by comparison of the HPLC retention times for either enantiomer with known data,[7,16] and is in agreement with the specific rotation. The enantioselectivity was monitored relative to the reaction time. It was

essentially constant during the first 10−15 h but deteriorated significantly after an extended period of time (14% *ee* after 48 h).

The experiments which were conducted with 20 mol % catalyst and which aimed at the highest possible enantioselectivity were all performed with the enantio- and diastereomerically pure catalyst **19** obtained from low temperature oxidation of thione **25**. Despite the perfect stereochemical purity of the thiazolium salt the recovered catalyst was *always* recovered as a mixture of atropisomers **19** and **26**. The ratio varied between 75:25 and 70:30. The phenomenon was studied more closely by treating the pure thiazolium salt **19** with NEt_3 in THF. An isomerization (reaction time: 48 h at ambient temperature) occurred and a mixture of atropisomers was detected in a ratio of 75:25 by ^1H NMR spectroscopy. With $NaHCO_3$ an additional epimerization at C-4 occurred and four products were identified. The ratio of products was 60:20:15:5 as determined by integration of the ^1H NMR signal of the hydrogen atom at C-2. The three major isomers were identified as compounds **19**, **26** and **27**. The minor isomer is assumed to be the atropisomer of compound **27**.

Discussion

The result described at the end of the preceding section left little doubt about the fact that the intermediate N-heterocyclic carbene **28** formed by deprotonation of thiazolium salt **19** is *not* configurationally stable at room temperature. The rotational barrier around the $C_{aryl}-N$ bond is too low and allows for an equilibration between the two conformations **28** and **28′** (Scheme 7). It is reasonable to assume that the ratio **28/28′** is equal to the ratio of atropisomers **19/26** present in the equilibrated mixture obtained after the catalysis experiments or after simple base treatment. It is the very same steric interaction between the isopropyl group at C-4 and the 2-*tert*-butylphenyl group that is responsible for the thermodynamic preference of **28** over **28′** and of **19** over **26**.



Scheme 7. Equilibration of the two atropisomeric carbenes **28** and **28′** and their reaction with benzaldehyde (**1**)

The transition states for the formation of enols **29** and **30** should differ energetically to the same extent as the conformations **28** and **28′**. In the benzoin condensation we therefore expected 70−75% of the product to be formed via intermediate **29** and 25−30% of the product to be formed via intermediate **30**. The face differentiation observed in the benzoin condensation is in agreement with intermediate **29** being responsible for the formation of the major enantiomer. Assuming a transition state **31**$^{\neq}$ similar to **5**$^{\neq}$ the nucleophilic benzaldehyde carbonyl carbon atom is attacked from its *Si*-face leading to the (*R*)-configured product **2** (Figure 10). In full analogy, the prostereogenic β-carbon atom of the α,β-unsaturated ester of substrate **9a** is intramolecularly attacked by the enol carbon atom via transition state **32**$^{\neq}$. Both prostereogenic carbon atoms react at their *Si*-face and the (*R*)-configured product **10a** is formed. The mode of face differentiation is in line with previous results obtained for the first generation chiral triazolium salt developed by Enders et al.[15,16] This catalyst was also used for both benzoin and Stetter reactions and it was also assumed to shield the *Re*-face of the nucleophilic enol carbon atom.[31]

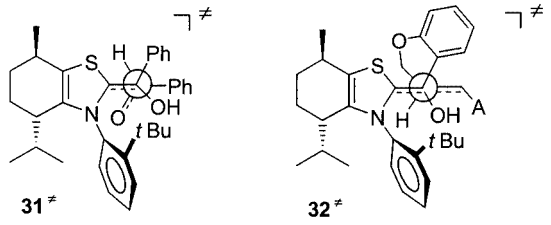


Figure 10. Possible transition states **31**$^{\neq}$ and **32**$^{\neq}$ for the enantioselective benzoin and Stetter reaction catalyzed by thiazolium salt **19**

In the diastereoisomer **30** of compound **29** the *Si*-face is shielded and the *Re*-face is accessible. This intermediate consequently accounts for the formation of the other enantiomer. In other words, the stereochemical outcome (40% *ee* in favor of **2**, 50% *ee* in favor of **10a**) of the catalysis experiments can be semi-quantitatively understood based on the assumed intermediacy of compounds **28** and **28′** in a ratio of 75:25. A further improvement cannot be achieved unless the ratio of the two atropisomers is significantly shifted in favor of a single isomer. This could be possibly achieved by a substituent in the cyclohexane ring which is bulkier than isopropyl. In line with our expectations the face differentiation exerted by the *tert*-butyl substituent on the phenyl group is excellent.

Conclusion

In summary, axially chiral *N*-arylthiazolium have been shown to be catalysts for nucleophilic aldehyde activation. In the carbene intermediate, the rotation around the stereogenic axis is not sufficiently restricted to suppress a racemization or epimerization. The diastereomerically pure thiazolium salt **19** which bears a 2-*tert*-butylphenyl substituent at the nitrogen atom was converted into a mixture of **19**

and its atropisomer **26** (*dr* = 75:25) upon treatment with base. The stereogenic center in the intermediate carbene favors one rotamer **28**, which, in turn, is responsible for the formation of the major diastereoisomer **19** upon reprotonation. Upon reaction with benzaldehyde it accounts in a similar fashion for the formation of the major enol diastereoisomer **29**, which, in turn, leads to the major enantiomer **2** observed in the benzoin condensation catalyzed by **19**. Given recent work in this area[6,7] the results we obtained in the benzoin (up to 40% *ee*) and in the intramolecular Stetter reaction (up to 50% *ee*) are certainly not competitive. The concept of axial chirality, however, was proven to be viable for an efficient chirality transfer. The shielding of the diastereotopic face in transition states **31**$^{\neq}$ and **32**$^{\neq}$ is close to perfect. The obstacle to overcome is associated with the above-mentioned free rotation around the stereogenic axis. If the preference **28** vs. **28′** or **29** vs. **30** was more pronounced the enantiomeric excess is likely to increase. A straightforward idea would for example be to replace the isopropyl group at carbon atom C-4 by the bulkier 2-phenyl-2-propyl substituent using 8-phenylmenthone as the starting material.

Experimental Section

General: All reactions involving water-sensitive chemicals were carried out in flame-dried glassware with magnetic stirring under Ar. Common solvents [pentane (P), diethyl ether (Et_2O), *tert*-butyl methyl ether (TBME), tetrahydrofuran (THF), dichloromethane, ethyl acetate (EtOAc), ethanol (EtOH) and methanol (MeOH)] were distilled prior to use. Anhydrous CH_2Cl_2 was distilled from CaH_2, and anhydrous THF and Et_2O were distilled from K/Na immediately prior to use. *N*,*N*-Diisopropylethylamine was distilled from calcium hydride. All other chemicals were either commercially available or prepared according to the cited references. TLC: Merck glass sheets (0.25 mm silica gel 60, F_{254}), eluent given in brackets. Detection by UV or coloration with ceric ammonium molybdate (CAM). Optical rotation: Perkin−Elmer 241 MC. HPLC: Dionex Pump P580A LPG, UV Detector UVD 340S. Columns: Phenomenex Luna Si(2) [250 × 4.60 mm, flow = 1.00 mL·min^{-1}], Daicel ChiralCel OD [250 × 4.60 mm, flow = 1.00 mL·min^{-1}], ChiralPak AD [250 × 4.60 mm, flow = 1.00 mL·min^{-1}], Solvents: Merck LiChrosolv, detection wavelength λ = 254 nm, eluent given in brackets. Melting points (uncorrected): Reichert hot bench. NMR: Bruker spectrometers ARX-200, AC-250, AC-300 and AX-500. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ at ambient temperature unless stated otherwise. Chemical shifts are reported relative to tetramethylsilane as internal standard or residual solvent signals. Apparent multiplets which occur as a result of the accidental equality of coupling constants of magnetically nonequivalent protons are marked as virtual (virt.). If there was a missing signal due to superimposition, the spectrum is marked with an asterisk (*). IR: Bruker IFS 200 or Perkin−Elmer 1600 FT-IR. MS: Varian CH7 (EI) or Finnigan MAT 8200 (EI). HRMS: Finnigan MAT 8200 (EI). GC-MS: Agilent 6890 (GC system, flow: 1.3 mL/min, column: HP 5MS (30 m), temperature: 50 → 250 °C at 10 K·min^{-1}, 10 min at 250 °C), Agilent 5973 (mass-selective detector, EI), Column: HP 5MS (30 m). Elemental analysis: Elementar vario EL. Flash chromatography:[32] Merck silica gel 60 (230−400 mesh, ca. 50 g for 1 g of material to be separated), eluent given in brackets. Eluents [Et_2O, pentane (P)] were distilled prior to use.

General Procedure for the Synthesis of *N,N′*-Bis(*ortho*-alkylaryl)butane-2,3-diimines (GP A): Anilines **12** and a catalytic amount of formic acid were dissolved in ethanol and diacetyl (**11**) was slowly added. After stirring the mixture for 24 h at ambient temperature, the precipitate was filtered and washed with water. The crude product was dissolved in CH_2Cl_2, dried with $MgSO_4$, filtered and concentrated in vacuo.

***N,N′*-Bis(2-*tert*-butylphenyl)butane-2,3-diimine (13a):**[22] According to GP A, 2-*tert*-butylaniline (**12a**; 6.57 g, 6.87 mL, 44.0 mmol) was dissolved in ethanol (15 mL) and reacted with diacetyl (**11**; 1.89 g, 1.93 mL, 22.0 mmol). After evaporation of the solvents in vacuo, compound **13a** (7.69 g, quant.) was obtained as a yellow powder. ^{1}H NMR (250 MHz): δ = 7.42 (dd, ^3J = 7.8, ^4J = 1.4 Hz, 2 H, H_{ar}-6), 7.19 (virt. td, $^3J \approx 7.8$, $^4J \approx 1.5$ Hz, 2 H, H_{ar}-5), 7.08 (virt. td, $^3J \approx 7.6$, $^4J \approx 1.4$ Hz, 2 H, H_{ar}-4), 6.51 (dd, ^3J = 7.6, ^4J = 1.5 Hz, 2 H, H_{ar}-3), 2.21 (s, 6 H, CH_3), 1.36 [s, 18 H, $C(CH_3)_3$] ppm. ^{13}C NMR (62.9 MHz): δ = 166.8 (CN), 149.3 (C_{ar}-1), 139.3 (C_{ar}-2), 126.4 (C_{ar}H), 126.3 (C_{ar}H), 124.0 (C_{ar}H-3), 119.2 (C_{ar}H-6), 35.1 [*C*$(CH_3)_3$], 29.5 [C(*C*$H_3)_3$] ppm. MS (EI, 70 eV): *m*/*z* (%) = 348 (15) [M^+], 291 (19) [$M^+ - C_4H_9$], 174 (100) [$C_4H_9C_6H_4NCCH_3^+$], 91 (42) [$C_7H_7^+$], 55 (8) [$C_4H_7^+$].

***N,N′*-Bis(2-isopropylphenyl)butane-2,3-diimine (13b):** According to GP A, 2-isopropylaniline (**12b**; 27.0 g, 28.3 mL, 200 mmol) was dissolved in ethanol (100 mL) and reacted with diacetyl (**11**; 8.61 g, 8.70 mL, 100 mmol). After evaporation of the solvents in vacuo, compound **13b** (28.7 g, 89%) was obtained as a bright-yellow powder. M.p. 83 °C. ^{1}H NMR (360 MHz): δ = 7.31 (dd, ^3J = 7.6, ^4J = 1.5 Hz, 2 H, H_{ar}-6), 7.17 (virt. td, $^3J \approx 7.6$, $^4J \approx 1.5$ Hz, 2 H, H_{ar}-5), 7.10 (virt. td, $^3J \approx 7.6$, $^4J \approx 1.5$ Hz, 2 H, H_{ar}-4), 6.60 (dd, ^3J = 7.6, ^4J = 1.5 Hz, 2 H, H_{ar}-3), 2.97 [sept, ^3J = 7.0 Hz, 2 H, C*H*$(CH_3)_2$], 2.16 (s, 6 H, CH_3), 1.20 [d, ^3J = 7.0 Hz, 12 H, CH(C*H*$_3)_2$] ppm. ^{13}C NMR (90 MHz): δ = 167.6 (CN), 148.3 (C_{ar}-1), 137.8 (C_{ar}-2), 126.1 (C_{ar}H-6), 125.7 (C_{ar}H-5), 124.3 (C_{ar}H-3), 117.9 (C_{ar}H-4), 28.5 [*C*H$(CH_3)_2$], 22.7 (CH_3), 15.6 [CH(*C*H$_3)_2$] ppm. IR (KBr): $\tilde{\nu}$ = 3045 (w, C_{ar}H), 2990 (s, C_{al}H), 1632 (s, C=N), 1481 (m, C_{ar}=C_{ar}), 1459 (m, C_{ar}=C_{ar}), 1356 (s), 1279 (w), 1115 (m), 1031 (m), 752 (s), 724 cm^{-1} (s). GC-MS (EI, 70 eV, t_R = 21.3 min): *m*/*z* (%) = 320 (2) [M^+], 277 (55) [$M^+ - C_3H_7$], 160 (100) [$C_3H_7C_6H_4NCCH_3^+$], 144 (54), 130 (30), 118 (20), 103 (19), 91 (40), 77 (20). $C_{22}H_{28}N_2$ (320.47): calcd. C 82.45, H 8.81, N 8.74; found C 82.51, H 8.79, N 8.67.

1,3-Dihydro-1,3-bis(2-isopropylphenyl)-4,5-dimethyl-2*H*-imidazole-2-thione (14b): Diimine **13b** (2.79 g, 8.70 mmol) was dissolved in dry THF (20 mL). Lithium (130 mg, 18.0 mmol) was added in small pieces and the mixture was placed in an ultrasonic bath until the lithium metal had been fully consumed. The resulting dark red solution was cooled to 0 °C and dry CS_2 (2.53 g, 2.00 mL, 33.0 mmol) was added dropwise. After stirring for 20 h at ambient temperature, the reaction was stopped by addition of water (200 mL). The resulting solution was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were washed with water (75 mL) and brine (75 mL), dried with $MgSO_4$, and filtered. The solvent was removed in vacuo. After chromatographic purification (P/Et_2O, 90:10 → 50:50), compounds **14b** (1.40 g, 44%) were obtained as dark brown solids.

***dl*-1,3-Dihydro-1,3-bis(2-isopropylphenyl)-4,5-dimethyl-2*H*-imidazole-2-thiones (*dl*-14b):** Yield 770 mg (22%); R_f = 0.33 (P/Et_2O, 60:40); m.p. 110 °C (dec.). ^{1}H NMR (250 MHz): δ = 7.49−7.41 (m, 4 H, H_{ar}-3/4), 7.28−7.35 (m, 2 H, H_{ar}-5), 7.18 (br. d, $^3J \approx$ 7.6 Hz, 2 H, H_{ar}-6), 2.80 [sept, ^3J = 6.7 Hz, 2 H, C*H*$(CH_3)_2$], 1.89 (s, 6 H, CH_3), 1.33 [d, ^3J = 6.7 Hz, 6 H, CH(C*H*$_3)_2$], 1.20 [d, ^3J =

6.7 Hz, 6 H, CH(CH_3)$_2$] ppm. ^{13}C NMR (62.9 MHz): δ = 164.6 (CS), 146.8 (C_{ar}-2), 134.5 (C_{ar}-1), 129.6 (C_{ar}H-3), 128.9 (C_{ar}H-6), 126.8 (2 × C_{ar}H), 121.8 (C-4/C-5), 28.3 [*C*H(CH$_3$)$_2$], 23.9 [CH(*C*H$_3$)$_2$], 23.4 [CH(*C*H$_3$)$_2$], 9.9 (CH$_3$) ppm. IR (KBr): ṽ = 3031 (w, C_{ar}H), 2957 (s, C_{al}H), 2864 (s, C_{al}H), 1491 (m, C_{ar}=C_{ar}), 1451 (m, C_{ar}=C_{ar}), 1385 (s), 1353 (s), 1277 (m, C=S), 1083 (w), 768 (s), 752 cm^{-1} (s). GC-MS (EI, 70 eV, t_R = 27.4 min): *m*/*z* (%) = 364 (19) [M$^+$], 349 (3) [M$^+$ − CH$_3$], 331 (100) [M$^+$ − SH], 321 (25) [M$^+$ − C$_3$H$_7$], 301 (11), 285 (3), 271 (3). HRMS (EI, 70 eV): calcd. for $C_{23}H_{28}N_2S$: 364.1973; found 364.1972.

***meso*-1,3-Dihydro-1,3-Bis(2-isopropylphenyl)-4,5-dimethyl-2*H*-imidazole-2-thiones (*meso*-14b):** Yield 770 mg (22%); R_f = 0.11 (P/Et$_2$O, 60:40); m.p. 112 °C (dec.). ^{1}H NMR (360 MHz): δ = 7.46−7.48 (m, 4 H, H_{ar}-3/H_{ar}-4), 7.31−7.36 (m, 2 H, H_{ar}-5), 7.24 (br. d, ^3J = 7.5 Hz, 2 H, H_{ar}-6), 2.72 [sept, ^3J = 7.1 Hz, 2 H, C*H*(CH$_3$)$_2$], 1.89 (s, 6 H, CH$_3$), 1.30 [d, ^3J = 7.1 Hz, 6 H, CH(C*H*$_3$)$_2$], 1.20 [d, ^3J = 7.1 Hz, 6 H, CH(C*H*$_3$)$_2$] ppm. ^{13}C NMR (90.5 MHz): δ = 164.5 (CS), 146.7 (C_{ar}-2), 134.5 (C_{ar}-1), 129.8 (C_{ar}H-3), 128.8 (C_{ar}H-6), 126.9 (2 × C_{ar}H), 121.9 (C-4/C-5), 28.4 [*C*H(CH$_3$)$_2$], 23.6 [CH(*C*H$_3$)$_2$], 23.4 [CH(*C*H$_3$)$_2$], 9.9 (CH$_3$) ppm. IR (KBr): ṽ = 3032 (w, C_{ar}H), 2956 (s, C_{al}H), 2863 (s, C_{al}H), 1491 (m, C_{ar}=C_{ar}), 1451 (m, C_{ar}=C_{ar}), 1382 (s), 1349 (s), 1278 (w, C=S), 1080 (w), 1031(w), 767 (s), 751 cm^{-1} (s). GC-MS (EI, 70 eV, t_R = 28.2 min): *m*/*z* (%) = 364 (19) [M$^+$], 349 (3) [M$^+$ − CH$_3$], 331 (100) [M$^+$ − SH], 321 (25) [M$^+$ − C$_3$H$_7$], 301 (11), 285 (3), 271 (3). HRMS (EI, 70 eV): calcd. for $C_{23}H_{28}N_2S$: 374.1973; found 374.1971.

1,3-Bis(2-isopropylphenyl)-4,5-dimethylimidazolium Perchlorate (15b): A solution of thione **14b** (91.0 mg, 0.25 mmol) in THF (2.00 mL) was cooled to −78 °C. Perchloric acid (75%, 125 mg, 100 μL, 1.25 mmol) and 75% *meta*-chloroperbenzoic acid (216 mg, 0.87 mmol) were added and the mixture was stirred for 6 h at −78 °C. After removal of the solvent in vacuo, the residue was suspended in Et$_2$O and stirred for 2 h. The crude product was filtered and washed with Et$_2$O (3 × 10 mL). After drying in vacuo, compound **15b** (49.0 mg, 45%) was obtained as a pale-yellow powder. *dr* (*meso*/*dl*) = 9:1. M.p. 205 °C. ^{1}H NMR (250 MHz): δ = 8.48 (s, 1 H, *dl*-CH$^+$), 8.31 (s, 1 H, *meso*-CH$^+$), 7.78−7.80 (m, 2 H, H_{ar}), 7.56−7.63 (m, 2 H, H_{ar}), 7.49−7.52 (m, 2 H, H_{ar}), 7.38−7.45 (m, 2 H, H_{ar}), 2.68 [sept, ^3J = 6.9 Hz, 2 H, *dl*-C*H*(CH$_3$)$_2$], 2.47 [sept, ^3J = 6.9 Hz, 2 H, *meso*-C*H*(CH$_3$)$_2$], 2.16 (s, 6 H, *meso*-CH$_3$), 2.14 (s, 6 H, *dl*-CH$_3$), 1.30 [d, ^3J = 6.9 Hz, 6 H, *meso*-CH(C*H*$_3$)$_2$], 1.27 [d, ^3J = 6.9 Hz, 6 H, *dl*-CH(C*H*$_3$)$_2$], 1.22 [d, ^3J = 6.9 Hz, 6 H, *dl*-CH(C*H*$_3$)$_2$], 1.16 [d, ^3J = 6.9 Hz, 6 H, *meso*-CH(C*H*$_3$)$_2$] ppm. ^{13}C NMR (62.9 MHz)*: δ = 145.6 (*dl*-C_{ar}-2), 144.5 (*meso*-C_{ar}-2), 133.7 (C-4/C-5), 132.0 (*dl*-CH$^+$), 131.9 (*meso*-CH$^+$), 130.4 (*meso*-C_{ar}-1), 130.2 (*dl*-C_{ar}-1), 129.5 (*dl*-C_{ar}H), 129.2 (*meso*-C_{ar}H), 128.5 (*meso*-C_{ar}H), 128.0 (*meso*-C_{ar}H), 127.8 (*dl*-C_{ar}H), 127.7 (*dl*-C_{ar}H), 127.5 (*dl*-C_{ar}H), 126.8 (*meso*-C_{ar}H), 28.3 [*meso*-*C*H(CH$_3$)$_2$], 28.0 [*dl*-*C*H(CH$_3$)$_2$], 24.7 [*meso*-CH(*C*H$_3$)$_2$], 24.6 [*dl*-CH(*C*H$_3$)$_2$], 23.1 [*dl*-CH(*C*H$_3$)$_2$], 22.8 [*meso*-CH(*C*H$_3$)$_2$], 9.0 (*dl*-CH$_3$), 8.9 (*meso*-CH$_3$) ppm. IR (KBr): ṽ = 3425 (br), 3106 (m, C_{ar}H), 2986 (s, C_{al}H), 1545 (s, C_{ar}=C_{ar}), 1478 (m, C_{ar}=C_{ar}), 1453 (m, C_{ar}=C_{ar}), 1232 (w), 1083 (br. s, C=N), 782 cm^{-1} (s). $C_{23}H_{29}N_2ClO_4$ (432.94): calcd. C 63.81, H 6.75, N 6.47; found C 63.49, H 6.81, N 6.52.

3-(2-*tert*-Butylphenyl)-4-methylthiazolium Perchlorate (*rac*-17): Thione *rac*-**20** (vide infra)[21f] (7.66 g, 29.1 mmol) was dissolved in acetic acid (120 mL) and treated with 30% aqueous H_2O_2 (8.30 mL, 96.0 mmol). Upon stirring for 30 min at ambient temperature the color of the solution turned from pale yellow to orange. The solvent was removed in vacuo. The residue was dissolved in methanol (20 mL) and treated with a solution of $NaClO_4$ (16.9 g, 120 mmol) dissolved in a 2:1 (v/v) mixture of methanol/water (100 mL). Upon stirring at 0 °C, a white solid precipitated, which was filtered and washed subsequently with water (100 mL) and Et$_2$O (100 mL). After recrystallisation from methanol, compound *rac*-**17** (7.12 g, 74%) was obtained as a colorless crystalline solid. M.p. 213 °C. ^{1}H NMR (250 MHz, [D$_6$]DMSO): δ = 10.39 (d, *J* = 2.2 Hz, 1 H, $^+$CH), 8.34 (s, 1 H, SCHC), 7.97 (d, ^3J = 8.2 Hz, 1 H, H_{ar}-6), 7.85 (virt. t, ^3J ≈ 8.2 Hz, 1 H, H_{ar}-5), 7.66 (virt. t, ^3J ≈ 7.9 Hz, 1 H, H_{ar}-4), 7.43 (d, ^3J = 7.9 Hz, 1 H, H_{ar}-3), 2.55 (s, 3 H, CH$_3$), 1.37 [s, 9 H, C(CH$_3$)$_3$] ppm. ^{13}C NMR (62.9 MHz, [D$_6$]DMSO): δ = 160.3 ($^+$CH), 147.5 (N*C*CH$_3$), 144.8 (C_{ar}-2), 132.9 (C_{ar}-1), 131.7 (C_{ar}H-5), 129.9 (C_{ar}H-6), 128.2 (C_{ar}H-3), 127.7 (C_{ar}H-4), 121.7 (SCHC), 35.6 [*C*(CH$_3$)$_3$], 31.1 [C(*C*H$_3$)$_3$], 13.8 (CH$_3$) ppm. IR (KBr): ṽ = 3113 (s, C_{ar}H), 2957 (s, C_{al}H), 2881 (w, C_{al}H), 2017 (w), 1830 (w), 1570 (m, C_{ar}=C_{ar}), 1487 (s, C_{ar}=C_{ar}), 1441 (s, C_{ar}=C_{ar}), 1083 (vs, C=N), 764 (s), 620 cm^{-1} (s, ClO). $C_{14}H_{18}ClNO_4S$ (331.82): calcd. C 50.68, H 5.47, N 4.22; found C 50.47, H 5.53, N 4.25.

3-(2-*tert*-Butylphenyl)-1,3-dihydro-5-(2-hydroxyethyl)-4-methyl-2*H*-thiazole-2-thione (*rac*-18): A solution of aniline **12a** (1.49 g, 1.56 mL, 10.0 mmol) in DMSO (5.00 mL) was treated with 20 N aqueous NaOH (0.50 mL, 10.0 mmol) at ambient temperature. The mixture was cooled to 0 °C and CS$_2$ (838 mg, 0.66 mL, 11.0 mmol) was added. Upon stirring for 1 h at ambient temperature, a change of colour occurred from dark-red to orange. The mixture was cooled to 0 °C and a freshly prepared solution of 3-chloro-5-hydroxy-2-pentanone[34] (2.11 g, 10.0 mmol) in 5 mL of 1,4-dioxane was added. After stirring for an additional 1 h at ambient temperature, water (10 mL) was added and an orange viscous oil separated. The solvent was decanted and the oily residue was dissolved in ethanol (5.0 mL). 36% Hydrochloric acid (1.0 mL) was added and the mixture was stirred at ambient temperature for 2.5 h. After washing the mixture with aqueous $NaHCO_3$ solution to pH 7.0, the solvent was removed in vacuo and the aqueous residue was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried with $MgSO_4$, filtered and the solvent was removed in vacuo. After purification by flash chromatography (Et$_2$O), compound *rac*-**18** (1.50 g, 49%) was obtained as a pale-yellow oil. R_f = 0.33 (Et$_2$O). ^{1}H NMR (250 MHz): δ = 7.64 (dd, ^3J = 8.2, ^4J = 1.4 Hz, 1 H, H_{ar}-6), 7.44 (virt. td, ^3J ≈ 7.8, ^4J ≈ 1.4 Hz, 1 H, H_{ar}-4), 7.30 (virt. td, ^3J ≈ 8.2, ^4J ≈ 1.5 Hz, 1 H, H_{ar}-5), 6.90 (dd, ^3J = 7.8, ^4J = 1.5 Hz, 1 H, H_{ar}-3), 3.76 (t, ^3J = 6.1 Hz, 2 H, CH$_2$C*H*$_2$OH), 3.13 (br. s, 1 H, CH$_2$CH$_2$O*H*), 2.82 (dt, ^3J = 6.1, ^3J = 3.1 Hz, 2 H, C*H*$_2$CH$_2$OH), 1.86 (s, 3 H, CH$_3$), 1.28 [s, 9 H, C(CH$_3$)$_3$] ppm. ^{13}C NMR (62.9 MHz): δ = 188.1 (CS), 146.6 (C_{ar}-2), 136.7 (S*C*CH$_2$), 134.9 (C_{ar}-1), 130.5 (C_{ar}H-3), 129.8 (C_{ar}H-4), 129.4 (C_{ar}H-6), 127.2 (C_{ar}H-5), 120.5 (N*C*CH$_3$), 61.4 (CH$_2$*C*H$_2$OH), 36.0 [*C*(CH$_3$)$_3$], 31.4 [C(*C*H$_3$)$_3$], 29.7 (*C*H$_2$CH$_2$OH), 14.1 (CH$_3$) ppm. IR (KBr): ṽ = 3465 (br, OH), 2959 (m, C_{al}H), 2850 (w, C_{al}H), 1609 (s, SC−NH), 1491 (m, C_{ar}=C_{ar}), 1438 (m, C_{ar}=C_{ar}), 1358 (s), 1304 (s), 1253 (vs, C=S), 1164 (s), 1052 (s), 986 (m), 768 cm^{-1} (s). GC-MS (EI, 70 eV, t_R = 27.27 min): *m*/*z* (%) = 307 (11) [M$^+$], 274 (22) [M$^+$ − SH], 250 (100) [M$^+$ − C$_4$H$_9$], 219 (13), 57 (13) [C$_4$H$_9^+$]. $C_{16}H_{21}NOS_2$ (307.48): calcd. C 62.50, H 6.88, N 4.56; found C 62.35, H 6.95, N 4.56.

(4*S*,7*R*)-3-(2-*tert*-Butylphenyl)-4-isopropyl-7-methyl-4,5,6,7-tetrahydrobenzothiazolium Perchlorate (19): The thione **25** (vide infra) (899 mg, 2.50 mmol) was dissolved in THF (10.0 mL) and cooled to −78 °C. 70% Perchloric acid (2.74 g, 1.08 mL, 12.5 mmol) and 75% *m*CPBA (2.16 g, 8.75 mmol) were added portionwise and the resulting suspension was stirred for 4 h at −78 °C. After warming to ambient temperature, the solvent was removed in vacuo. The

residue was dissolved in CH_2Cl_2 (20 mL), washed with water (3 × 20 mL) and the solvent was removed in vacuo. The residual white solid was suspended in Et_2O (50 mL) and stirred for 2 h. The crude product was filtered and washed thoroughly with Et_2O (50 mL). After drying in vacuo, compound **19** (880 mg, 82%) was obtained as a white solid. M.p. 199 °C. ^{1}H NMR (400 MHz): δ = 10.00 (s, 1 H, HC^+), 7.71 (dd, ^3J = 8.3, ^4J = 1.4 Hz, 1 H, H_{ar}-6), 7.61 (ddd, ^3J = 8.3, ^3J = 6.8, ^4J = 1.9 Hz, 1 H, H_{ar}-5), 7.39 (ddd, ^3J = 7.9, ^3J = 6.8, ^4J = 1.4 Hz, 1 H, H_{ar}-4), 7.35 (dd, ^3J = 7.9, ^4J = 1.9 Hz, 1 H, H_{ar}-3), 3.11−3.20 (m, 1 H, 7-H), 2.81 (tdd, ^3J = 7.1, ^3J = 4.2, J = 1.6 Hz, 1 H, 4-H), 2.19 (dddd, ^2J = 13.5, ^3J = 7.0, ^3J = 3.9, ^3J = 4.9 Hz, 1 H, 6-H), 1.96 (dddd, ^2J = 14.2, ^3J = 7.1, ^3J = 7.0, ^3J = 3.8 Hz, 1 H, 5-H), 1.82 (dddd, ^2J = 14.2, ^3J = 10.6, ^3J = 7.1, ^3J = 3.7 Hz, 1 H, 5-H), 1.59 [dsept, ^3J = 4.2, ^3J = 6.9 Hz, 1 H, C*H*$(CH_3)_2$], 1.45 (d, ^3J = 6.9 Hz, 3 H, CH_3), 1.36−1.45 (m, 1 H, 6-H), 1.15 [s, 9 H, $C(CH_3)_3$], 0.73 [d, ^3J = 6.9 Hz, 3 H, $CH(CH_3)_2$], 0.67 [d, ^3J = 6.9 Hz, 3 H, $CH(CH_3)_2$] ppm. ^{13}C NMR (90 MHz): δ = 159.3 (CS), 147.5 (C-4′), 144.9 (C_{ar}-2), 144.5 (C-7′), 133.3 (C_{ar}-1), 132.0 (C_{ar}H-5), 130.8 (C_{ar}H-6), 129.2 (C_{ar}H-3), 127.5 (C_{ar}H-4), 39.8 (CH-4), 36.4 [$C(CH_3)_3$], 31.5 [$C(CH_3)_3$], 30.6 (CH-7), 30.1 (CH_2-6), 28.2 [$CH(CH_3)_2$], 22.4 (CH_3), 20.4 (CH_2-5), 19.9 [$CH(CH_3)_2$], 16.6 [$CH(CH_3)_2$] ppm. IR (KBr): $\tilde{\nu}$ = 3070 (s, C_{ar}H), 2962 (s, C_{al}H), 2873 (w, C_{al}H), 1559 (m, C_{ar}=C_{ar}), 1489 (s, C_{ar}=C_{ar}), 1440 (s, C_{ar}=C_{ar}), 1097 (vs, $^+$C=N), 759 (s), 622 cm^{-1} (s, ClO). $C_{21}H_{30}ClNO_4S$ (427.99): calcd. C 58.93, H 7.07, N 3.27; found C 58.82, H 7.06, N 3.25.

3-(2-*tert*-Butylphenyl)-1,3-dihydro-4-methyl-2*H*-1,3-thiazole-2-thione (*rac*-20):[21f] A solution of aniline **12a** (1.49 g, 1.56 mL, 10.0 mmol) in DMSO (5.00 mL) was treated with 20 N aqueous NaOH (0.50 mL, 10.0 mmol) at ambient temperature. The mixture was cooled to 0 °C and CS_2 (761 mg, 0.60 mL, 10.0 mmol) was added. Upon stirring for 1 h at ambient temperature, a change of colour from dark-red to orange occurred. The mixture was cooled to 0 °C and chloroacetone (925 mg, 0.80 mL, 10.0 mmol) was added. After 1 h of stirring at ambient temperature, water (10 mL) was added and the mixture was stirred for an additional 10 min at 0 °C upon which a yellow solid precipitated. The solid was filtered, dissolved in ethanol (10 mL) and treated with 36% hydrochloric acid (0.5 mL) for 1 h at 80 °C. Upon cooling to ambient temperature the crude product precipitated. After filtration and recrystallization from 96% ethanol, *rac*-**20** (1.62 g, 62%) was obtained as pale-orange crystals. M.p. 102 °C. ^{1}H NMR (200 MHz): δ = 7.66 (dd, ^3J = 8.1, ^4J = 1.5 Hz, 1 H, H_{ar}-6), 7.44 (virt. td, $^3J \approx$ 8.1, $^4J \approx$ 1.5 Hz, 1 H, H_{ar}-5), 7.30 (virt. td, $^3J \approx$ 7.7, $^4J \approx$ 1.5 Hz, 1 H, H_{ar}-4), 6.86 (dd, ^3J = 7.7, ^4J = 1.5 Hz, 1 H, H_{ar}-3), 6.39 (quart, ^4J = 1.1 Hz, 1 H, SCH), 1.90 (d, ^4J = 1.1 Hz, 3 H, $NCCH_3$), 1.28 [s, 9 H, $C(CH_3)_3$] ppm. ^{13}C NMR (50 MHz): δ = 189.9 (CS), 146.5 (C_{ar}-2), 140.5 (s, N*C*CH_3), 134.0 (C_{ar}-1), 130.4 (C_{ar}H-3), 129.6 (C_{ar}H-6), 129.3 (C_{ar}H-4), 127.0 (C_{ar}H-5), 106.2 (SCH), 35.9 [$C(CH_3)_3$], 31.2 [$C(CH_3)_3$], 16.0 (CH_3) ppm. IR (KBr): $\tilde{\nu}$ = 3106 (w, C_{ar}H), 2958 (m, C_{al}H), 2866 (w, C_{al}H), 1591 (s, SC−NH), 1488 (s, C_{ar}=C_{ar}), 1295 (vs, C=S), 769 (m), 733 cm^{-1} (m). MS (EI, 70 eV): *m*/*z* (%) = 263 (17) [M^+], 230 (20) [M^+ − SH], 206 (100) [M^+ − C_4H_7]. $C_{14}H_{17}NS_2$ (263.42): calcd. C 63.83, H 6.50, N 5.32; found C 63.49, H 6.46, N 5.37.

3-(2-*tert*-Butylphenyl)-4,5,6,7-2*H*-tetrahydrobenzothiazole-2-thione (*rac*-21): A solution of aniline **12a** (1.49 g, 1.56 mL, 10.0 mmol) in DMSO (50 mL) was treated with 20 N aqueous NaOH (0.50 mL, 10.0 mmol) at ambient temperature. The mixture was cooled to 0 °C and CS_2 (838 mg, 0.66 mL, 11.0 mmol) was added. Upon stirring for 1 h at ambient temperature, a change of colour from dark-red to orange occurred. Again the solution was cooled to 0 °C and 2-bromocyclohexanone[27] (1.77 g, 10.0 mmol) was added. After stirring for 3 h at ambient temperature, water (20 mL) was added and the mixture was stirred for an additional 10 min at 0 °C. The precipitate was filtered and successively washed with water (20 mL), ethanol (5 mL) and pentane (50 mL). The crude cyclisation product was suspended in 96% ethanol (30 mL), 36% hydrochloric acid (1.7 mL, 21.0 mmol) was added and the mixture was heated to reflux for 1 h. After cooling to ambient temperature, the solvent was removed in vacuo. The residue was dissolved in CH_2Cl_2 (25 mL) and washed with aqueous $NaHCO_3$ (10 mL) and brine (25 mL). The organic layer was dried with Na_2SO_4, filtered and the solvent was removed in vacuo. After flash chromatographic purification (P/Et_2O, 60:40), compound *rac*-**21** (1.82 g, 60%) was obtained as a white solid. R_f = 0.45 (P/Et_2O, 60:40); m.p. 119 °C. ^{1}H NMR (400 MHz): δ = 7.64 (dd, ^3J = 8.2, ^4J = 1.4 Hz, 1 H, H_{ar}-6), 7.43 (ddd, ^3J = 8.2, ^3J = 7.2, ^4J = 1.6 Hz, 1 H, H_{ar}-5), 7.30 (virt. td, $^3J \approx$ 7.9, ^4J = 1.4 Hz, 1 H, H_{ar}-4), 6.91 (dd, ^3J = 7.9, ^4J = 1.6 Hz, 1 H, H_{ar}-3), 2.51−2.55 (m, 2 H, 4-H), 2.02−2.08 (m, 2 H, 7-H), 1.82−1.89 (m, 2 H, 6-H), 1.73−1.80 (m, 2 H, 5-H), 1.30 [s, 9 H, $C(CH_3)_3$] ppm. ^{13}C NMR (90 MHz): δ = 188.7 (CS), 147.1 (C_{ar}-2), 138.5 (C-4′), 134.4 (C_{ar}-1), 130.7 (C_{ar}H-6), 130.1 (C_{ar}H-5), 129.6 (C_{ar}H-4), 127.4 (C_{ar}H-3), 120.9 (C-7′), 36.4 [$C(CH_3)_3$], 31.8 [$C(CH_3)_3$], 25.6 (C-7), 23.2 (C-4), 22.8 (C-6), 21.8 (C-5) ppm. IR (KBr): $\tilde{\nu}$ = 3105 (w, C_{ar}H), 2951 (vs, C_{al}H), 2868 (w, C_{al}H), 1620 (s, SC−NH), 1488 (s, C_{ar}=C_{ar}), 1437 (s, C_{ar}=C_{ar}), 1357 (s), 1312 (s), 1291 (vs, C=S), 1213 (m), 1044 (m), 776 (m), 757 cm^{-1} (s). GC-MS (EI, 70 eV, t_R = 26.00 min): *m*/*z* (%) = 303 (9) [M^+], 270 (22) [M^+ − SH], 246 (100) [M^+ − $C(CH_3)_3$], 218 (6), 91 (3) [$C_6H_5N^+$], 77 (3) [$C_6H_5^+$]. $C_{17}H_{21}NS_2$ (303.49): calcd. C 67.28, H 6.97, N 4.62; found C 67.38, H 7.00, N 4.56.

3-(2-*tert*-Butylphenyl)-4,5,6,7-tetrahydrobenzothiazolium Perchlorate (*rac*-22): Thione *rac*-**21** (287 mg, 0.95 mmol) was dissolved in acetic acid (5.00 mL) and 30% H_2O_2 (83.6 mg, 0.25 mL, 3.04 mmol) was added. After stirring the resulting yellow solution for 30 min at ambient temperature, the solvent was removed in vacuo. The residue was dissolved in methanol (2.00 mL) and treated with a solution of $NaClO_4$ (0.57 g, 4.00 mmol) in a 2:1 mixture of methanol/water. After stirring for a few minutes at 0 °C, a yellow solid precipitated. The crude product was filtered and washed with water (10 mL) and Et_2O (20 mL) and dried in vacuo. Compound *rac*-**22** (288 mg, 82%) was obtained as a pale yellow solid. M.p. 203 °C. ^{1}H NMR (250 MHz, [D_6]DMSO): δ = 10.12 (s, 1 H, $^+$CH), 7.67 (dd, ^3J = 8.0, ^4J = 1.4 Hz, 1 H, H_{ar}-6), 7.39 (virt. td, $^3J \approx$ 8.0, ^4J = 1.6 Hz, 1 H, H_{ar}-5), 7.31 (virt. td, ^3J = 7.9, ^4J = 1.4 Hz, 1 H, H_{ar}-4), 6.94 (dd, ^3J = 7.9, ^4J = 1.6 Hz, 1 H, H_{ar}-3), 2.44−2.49 (m, 2 H, C-4), 2.14−2.20 (m, 2 H, 7-H), 1.69−1.89 (m, 4 H, 5-H/6-H), 1.12 [s, 9 H, $C(CH_3)_3$] ppm. ^{13}C NMR (62.9 MHz, [D_6]DMSO): δ = 160.3 (d, CS), 145.9 (C_{ar}-2), 140.3 (C_{ar}-1), 134.9 (C-4′), 131.9 (C_{ar}H-5), 130.0 (C_{ar}H-6), 129.5 (C_{ar}H-3), 127.0 (C_{ar}H-4), 121.4 (C-7′), 36.3 [$C(CH_3)_3$], 31.7 [$C(CH_3)_3$], 25.6 (CH_2-7), 23.5(CH_2-4), 22.4 (CH_2-6), 20.9 (CH_2-5) ppm. IR (KBr): $\tilde{\nu}$ = 3104 (s, C_{ar}H), 2957 (s, C_{al}H), 1584 (m, C_{ar}=C_{ar}), 1493 (m, C_{ar}=C_{ar}), 1448 (m, C_{ar}=C_{ar}), 1092 (vs, $^+$C=N), 775 (s), 622 cm^{-1} (s, ClO). $C_{17}H_{22}ClNO_4S$ (371.88): calcd. C 54.91,H 5.96, N 3.77; found C 54.67, H 6.07, N 3.81.

(4*S*,7*R*)-3-(2-*tert*-Butylphenyl)-4-isopropyl-7-methyl-4,5,6,7-2*H*-tetrahydrobenzothiazole-2-thione (25): Aniline **12a** (14.4 g, 15.0 mL, 96.3 mmol) dissolved in DMSO (100 mL) was treated with 24 N aqueous KOH (3.00 mL, 96.3 mmol) at ambient temperature. The solution was cooled to 0 °C and CS_2 (8.00 g, 6.40 mL, 105 mmol) was added. Upon stirring for 1 h at ambient temperature, a change of colour from dark-red to orange occurred. The mixture was co-

oled to 0 °C and α-bromomenthone **23**[28] (20.4 g, 87.5 mmol) was added. After stirring for 2 h at ambient temperature, the mixture was poured into ice water (300 mL) and extracted with Et_2O (3 × 250 mL). The combined organic layers were washed with water (2 × 100 mL) and brine (2 × 100 mL), dried with Na_2SO_4, filtered and the solvent removed in vacuo. The oily residue was dissolved in pentane (100 mL). Upon treatment with a mixture of 1 N HCl in Et_2O (80 mL) and pentane (200 mL) precipitation of the cyclisation product occurred. The crude product was filtered, washed with pentane (150 mL) and dissolved in ethanol (abs., 70.0 mL). 98% Methanesulfonic acid (11.5 g, 7.80 mL, 120 mmol) was added and the solution was heated under reflux for 5 h. One half of the solvent was removed in vacuo and the mixture was cooled to 4 °C. After two days of crystallization the product was filtered, washed with ice-cold ethanol (2 × 40 mL) and pentane (200 mL). After drying in vacuo, compound **25** (10.4 g, 33%) was obtained as white crystals. M.p. 125 °C. ^{1}H NMR (400 MHz): δ = 7.62 (dd, ^3J = 8.2, ^4J = 1.4 Hz, 1 H, H_{ar}-6), 7.42 (ddd, ^3J = 8.2, ^3J = 7.1, ^4J = 1.5 Hz, 1 H, H_{ar}-5), 7.26 (ddd, ^3J = 7.9, ^3J = 7.1, ^4J = 1.4 Hz, 1 H, H_{ar}-4), 7.08 (dd, ^3J = 7.9, ^4J = 1.5 Hz, 1 H, H_{ar}-3), 2.76−2.70 (m, 1 H, 7-H), 2.36 (dddd, ^3J = 7.0, ^3J = 5.8, ^3J = 4.2, ^5J = 1.6 Hz, 1 H, 4-H), 2.03 (dddd, ^3J = 13.4, ^3J = 8.5, ^3J = 5.0, ^3J = 3.7 Hz, 1 H, 6-H), 1.80 (dddd, ^3J = 14.1, ^3J = 8.5, ^3J = 7.0, ^3J = 3.7 Hz, 1 H, 5-H), 1.66 (dd, ^3J = 14.1, ^3J = 9.1, ^3J = 5.8, ^3J = 3.7 Hz, 1 H, 5-H), 1.49 (septd, ^3J = 7.0, ^3J = 4.2 Hz, C*H*$(CH_3)_2$], 1.37 (dddd, ^3J = 13.4, ^3J = 9.1, ^3J = 7.0, ^3J = 3.7 Hz, 1 H, 6-H), 1.26 [s, 9 H, C$(CH_3)_3$], 1.22 [d, ^3J = 7.0 Hz, 3 H, CH(CH_3)$_2$], 0.68 [d, ^3J = 7.0 Hz, 3 H, CH(CH_3)$_2$], 0.62 (d, ^3J = 6.8 Hz, 3 H, CH_3) ppm. ^{13}C NMR (62.9 MHz): δ = 188.6 (CS), 146.3 (C_{ar}-2), 140.9 (C-4′), 134.5 (C_{ar}-1), 132.0 (C_{ar}H-3), 130.7 (C_{ar}H-6), 129.6 (C_{ar}H-4), 129.2 (C-7′), 126.4 (C_{ar}H-5), 39.7 (CH-4), 36.2 [*C*$(CH_3)_3$], 31.7 [C(*C*H_3)$_3$], 30.1 (CH_2-6), 29.5 (CH-7), 27.8 [*C*H$(CH_3)_2$], 22.2 (CH_3), 20.3 (CH_2-5), 20.2 [CH(*C*H_3)$_2$], 17.0 [CH(*C*H_3)$_2$] ppm. IR (KBr): ṽ = 3030 (w), 2957 (m, C_{al}H), 2861 (w, C_{al}H), 1604 (s, SC−NH), 1489 (m, C_{ar}=C_{ar}), 1438 (m, C_{ar}=C_{ar}), 1368 (s), 1312 (s), 1283 (s, C=S), 1192 (s), 1051 (s), 920 (m), 819 (w), 756 cm^{-1} (s). MS (EI, 70 eV): *m*/*z* (%) = 359 (13) [M^+], 326 (19) [M^+ − SH], 302 (100) [M^+ − C_4H_9], 259 (6), 244 (8), 91 (14) [$C_6H_5N^+$]. HRMS (EI, 70 eV): calcd. for $C_{21}H_{29}NS_2$: 359.1741; found 359.1739.

Enantioselective Benzoin Condensation with Thiazolium Salt 19 as Pre-Catalyst: Thiazolium salt **19** (42.7 mg, 0.10 mmol) and benzaldehyde (104 mg, 0.10 mL, 1.00 mmol) were suspended in THF (0.50 mL). Triethylamine (10.1 mg, 14.0 μL, 0.10 mmol) was added under vigorous stirring and the solution was stirred for 16 h at ambient temperature. The mixture was directly poured onto silica gel to stop the reaction. After flash chromatographic purification (P/Et_2O, 80:20 → 50:50), (*R*)-benzoin (**2**, 88.4 mg, 85%) was obtained as a white solid in an optical purity of 40% *ee*. R_f = 0.36 (P/Et_2O, 60:40). $[\alpha]_D^{25}$ = −65 (*c* = 1.0 in MeOH); t_R = 15.4/20.8 min [(*S*)-isomer/(*R*)-isomer, ChiralPak AD, hexane/isopropanol, 95:5]. ^{1}H NMR (360 MHz): δ = 7.93−7.90 (m, 2 H, H_{ar}), 7.55−7.26 (m, 8 H, H_{ar}), 5.95 (s, 1 H, C*H*OH), 4.55 (br. s, 1 H, OH) ppm. ^{13}C NMR (90 MHz): δ = 199.0 (C=O), 139.0 (C_{ar}-1), 133.9 (C_{ar}H-4), 133.5 (C_{ar}-1′), 129.1 (C_{ar}H-2), 129.0 (C_{ar}H-3), 128.7 (C_{ar}H-2′), 128.6 (C_{ar}H-4′), 127.8 (C_{ar}H-3′), 76.2 (CHOH) ppm.

Enantioselective Intramolecular Stetter Reaction with Thiazolium Salt 19 as Pre-Catalyst: Thiazolium salt **19** (42.7 mg, 0.10 mmol) and methyl ester **9a**[34] (110 mg, 0.50 mmol) were suspended in THF (0.50 mL). Triethylamine (10.2 mg, 14.0 μL, 0.10 mmol) was added and the solution was stirred for 21 h at ambient temperature. The mixture was directly poured onto silica gel to stop the reaction. After flash chromatographic purification (P/Et_2O, 80:20 → 50:50), chromanone **10a**[7,16] (82.0 mg, 75%) was obtained as a pale-yellow solid in an optical purity of 50% *ee*. R_f = 0.36 (P/Et_2O, 60:40); t_R = 15.9/19.4 min [(*R*)-isomer/(*S*)-isomer, ChiralPak AD, hexane/isopropanol, 95:5]. ^{1}H NMR (360 MHz): δ = 7.89 (dd, ^3J = 8.0, ^4J = 1.6 Hz, 1 H, 5-H), 7.49 (ddd, ^3J = 8.3, ^3J = 7.0, ^4J = 1.6 Hz, 1 H, 7-H), 7.03 (ddd, ^3J = 8.0, ^3J = 7.0, ^4J = 0.9 Hz, 1 H, 6-H), 6.98 (dd, ^3J = 8.3, ^4J = 0.9 Hz, 1 H, 8-H), 4.61 (dd, ^2J = 11.1, ^3J = 5.2 Hz, 1 H, 2-H), 4.30 (dd, ^3J = 12.0, ^2J = 11.1 Hz, 1 H, 2-H), 3.73 (s, 1 H, $COOCH_3$), 3.35 (virt. tdd, $^3J \approx 5.2$, ^3J = 12.0, ^3J = 8.0 Hz, 1 H, 3-H), 2.95 (dd, ^2J = 17.2, ^3J = 5.0 Hz, 1 H, *C*H_2COOCH$_3$), 2.44 (dd, ^2J = 17.2, ^3J = 8.0 Hz, 3 H, *C*H_2COOCH$_3$) ppm. ^{13}C NMR (62.9 MHz): δ = 192.6 (C-4), 171.8 (*C*OOCH$_3$), 161.6 (C-8′), 136.0 (CH-7), 127.3 (CH-5), 121.5 (CH-6), 120.3 (C-5′), 117.8 (CH-8), 70.1 (CH_2-2), 52.0 (COO*C*H$_3$), 42.4 (CH-3), 30.0 (*C*H_2COOCH$_3$) ppm.

Acknowledgments

This project was supported by the Fonds der Chemischen Industrie. We would like to thank A. Stengel, T. H. Endl, T. Bartels and A. Schmid (undergraduate research participants) for skilful technical assistance.

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[24] Crystal data of compound *meso*-**15b**: ($C_{23}H_{29}ClN_2O_4$·DMSO, M_r = 511.06), crystal size 0.24 × 0.24 × 0.09 mm, orthorhombic, space group *Pnma*, a = 1347.0(1), b = 1513.6(1), c = 1346.2(1) pm, U = 2744.6(3) Å^3, $\rho_{calcd.}$ = 1.237 g·cm^{-3} for Z = 4, F(000) = 1088, μ = 2.51 cm^{-1}, Stoe IPDS diffractometer, λ = 0.71073 Å, T = 193 K, 17814 reflections (h ±16, k ±18, l ±16), $2\Theta_{max.}$ = 25.97°, 2790 independent and 1605 observed reflections [$I > 2\sigma(I)$], 2790 reflections used for refinement, 190 parameters, $R1$ = 0.0517, $wR2$ = 0.144, residual electron density 0.77 e·Å^{-3}, direct methods, hydrogen atoms refined. CCDC-218998 contains the supplementary crystallographic data for this compound. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: (internat.) +44-1223-336033; E-mail: deposit@ccdc.cam.ac.uk).
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[30] Crystal data of compounds **19** and **27**, ($C_{21}H_{30}ClNO_4S$, M_r = 427.99): crystal size 0.42 × 0.42 × 0.33 mm, triclinic, space group $P1$, a = 781.8(1), b = 913.7(1), c = 1729.5(1) pm, α = 92.20(1), β = 101.45(1), γ = 113.94(1)°, U = 1096.91(14) Å^3, $\rho_{calcd.}$ = 1.296 g cm^{-3} for Z = 2, F(000) = 456, μ = 3.0 cm^{-1}, IPDS2 diffractometer, λ = 0.71073 Å, T = 193 K, 13116 reflections (h ±9, k ±10, l ±20), $2\Theta_{max.}$ = 25.0°, 7242 independent and 6811 observed reflections [$I > 2\sigma(I)$], 7242 reflections used for refinement, 545 parameters, $R1$ = 0.0295, $wR2$ = 0.0780, residual electron density −0.24 e·Å^{-3}, direct methods, hydrogen atoms calculated, "Flack parameter" (absolute structure) = −0.02(3). CCDC-218996 contains the supplementary crystallographic data for compounds **19** and **27** which crystallized in a single crystal. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: (internat.) +44-1223-336033; E-mail: deposit@ccdc.cam.ac.uk).
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Received May 5, 2003

