Generation of cationic 2-azabutadienes from *N*,*S*-acetals and their use for the regio- and diastereoselective synthesis of 1,2,3,4-tetrahydroquinolines by intermolecular [4π$^+$ + 2π] cycloadditions

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Dedicated to Professor Dr. L. Fisera on the occasion of his 60th birthday

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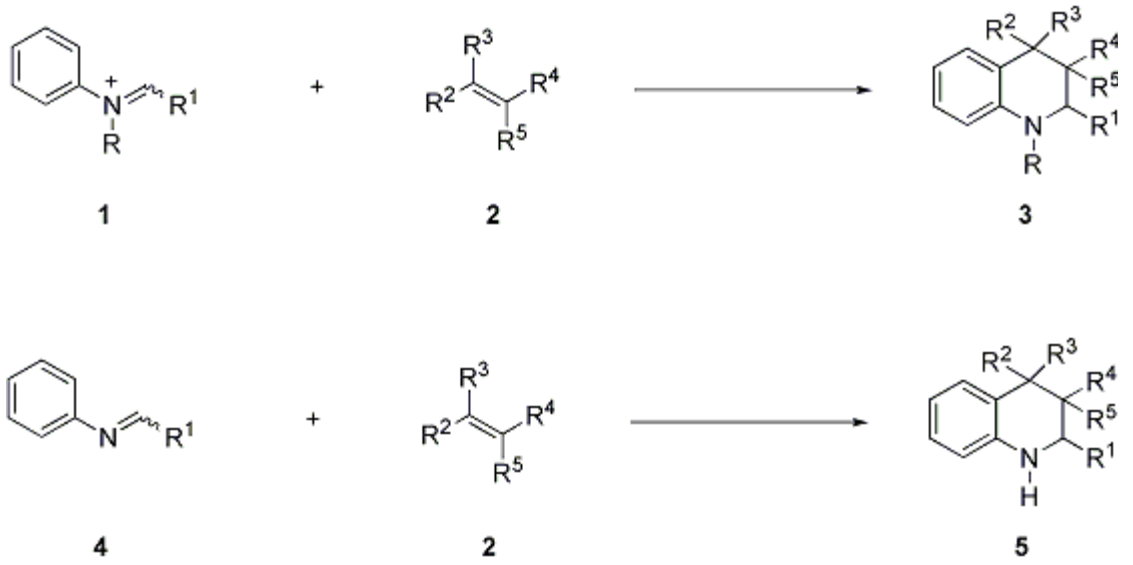
Abstract

Substituted 1,2,3,4-tetrahydroquinolines and related *N*-heterocycles are formed highly regio- and diastereoselectively with yields ranging from 57 to 100% by intermolecular polar [4π$^+$ + 2π] cycloadditions of cationic 2-azabutadienes and various dienophiles. The cationic 2-azabutadienes can be generated *in situ* by Lewis acid mediated heterolytic cleavage of *N,S*-acetals. Best results have been obtained using a new mixed Lewis acid consisting of a mixture of $TiCl_4$ and PPh_3.

Keywords: *N*,*S*-Acetals, cationic 2-azabutadienes, intermolecular [4π$^+$ + 2π] cycloadditions, 1,2,3,4-tetrahydroquinolines

Introduction

Tetrahydroquinolines and related ring systems have gained much attention in both natural product synthesis and medical research. Their efficient synthesis can be achieved, for example, by intermolecular cycloadditions of positively charged 2-azabutadienes **1** or neutral 2-azabutadienes **4** with electron-rich alkenes **2** (Scheme 1).[1]



Scheme 1

The reactions can be regarded as hetero *Diels-Alder* reactions with inverse electron demand, [2,3] with 2-azabutadiene representing the electron-poor and alkene the electron-rich component. 2-azabutadienes can be distinguished by the type of preparation. The majority of reactions so far reported have involved preformed 2-azabutadienes, [4] which are usually obtained by condensation of a primary aromatic amine with a carbonyl compound. Also, there are cycloadditions where the neutral or positively charged 2-azabutadiene is prepared *in situ*. [5-19]

Results and Discussion

AM1 calculations [20] indicate that cationic 2-azabutadienes such as **6** - due to their lower LUMO energies - exhibit much higher reactivity than the corresponding neutral 2-azabutadienes like **7** (Figure 1). In addition, the p-atomic orbital coefficients suggest that cationic 2-azabutadienes react much more selectively.

Figure 1. LUMO energies and p-atomic orbital coefficients of **6** and **7** (AM 1).[20]

Mechanistically, these reactions may either be seen to proceed in a concerted manner as polar [$4\pi^+ + 2\pi$] cycloadditions in terms of hetero *Diels Alder* reactions with inverse electron demand [2,3] (Figure 2, **A**) and subsequent aromatization, or as a multi-step process starting with the addition of an alkene **9** to an iminium ion **8** [21] (Figure 2, **B**) and formation of a carbenium ion **11** as an intermediate and finally undergoing an intramolecular *Friedel Crafts* reaction.[22]

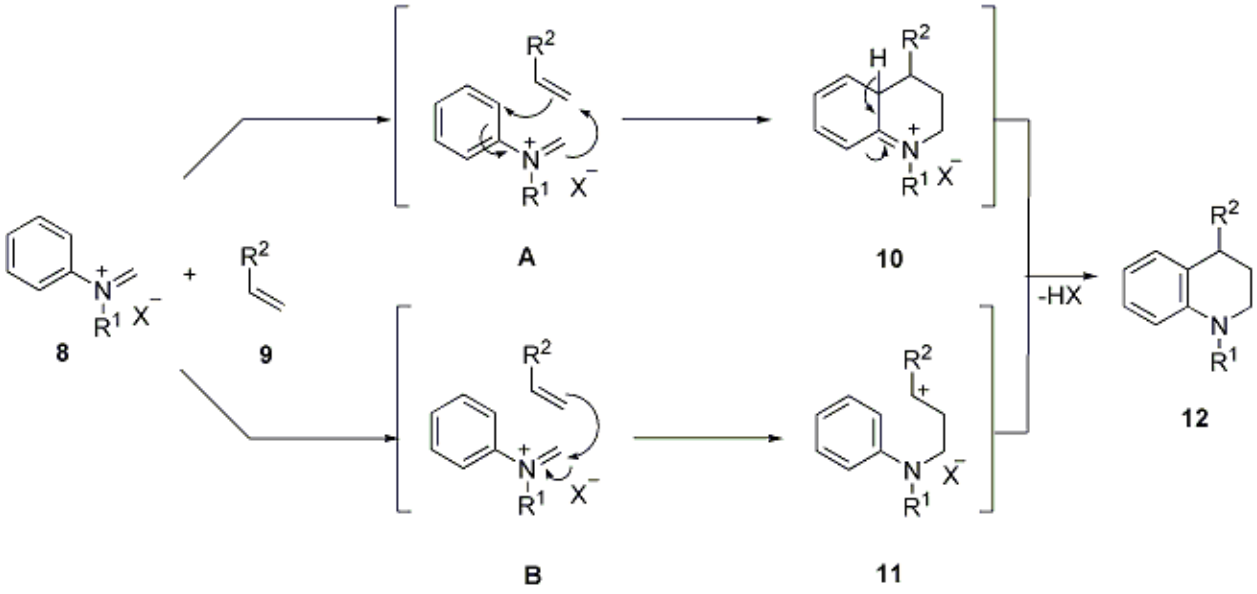
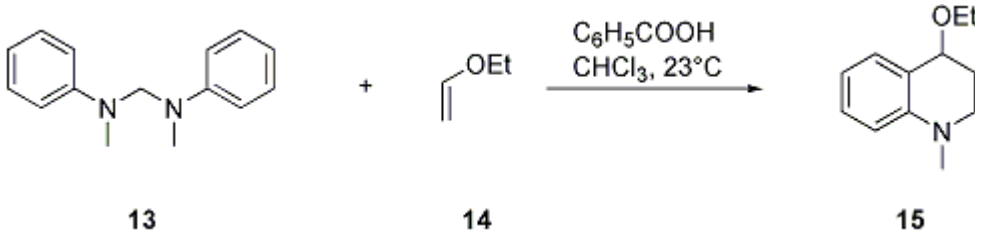


Figure 2. Alternative mechanism for the formation of tetrahydroquinolines **12** from the reaction of cationic 2-azabutadienes **8** with alkenes **9**.

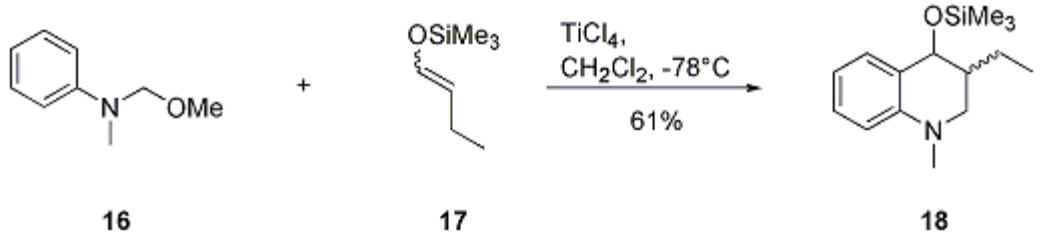
As far as we know the first example was reported by *Swan*, who reacted *N*,*N*-acetal **13** in the presence of benzoic acid with ethyl vinyl ether **14** and obtained the 4-substituted tetrahydroquinoline *rac*-**15** (Scheme 2).[5]



Scheme 2

Shono et al. demonstrated later that 2-aryl iminium ions may be generated by cleavage of *N*,*O*-acetals with Lewis acids at low temperatures. Here also, reaction with simple and electron-rich olefins leads to regioselective formation of 1,2,3,4-tetrahydroquinolines. For example,

reaction of *N*,*O*-acetal **16** with silyl enol ether **17** produces the cyclization product *rac*-**18** in 61% yield (Scheme 3).[6a]

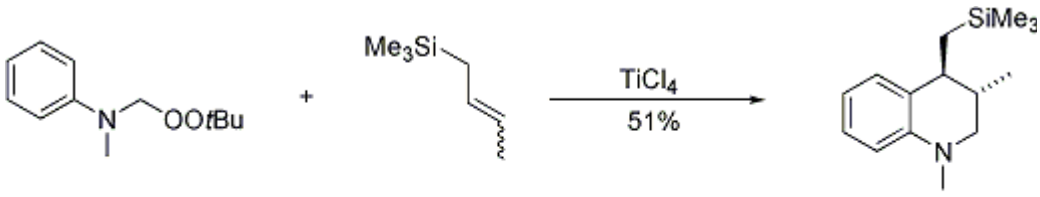


16 **17** **18**

Scheme 3

The same method has also been used recently in the synthesis of 2-difluoromethyl- and 2-trifluoromethyl-substituted quinolines.[7] Altogether, however, the role of *N*,*O*-acetals in the generation of aryl iminium ions **8** has been limited, since efficient preparation of *N*,*O*-acetals is only managed by anodic oxidation of tertiary aromatic amines such as *N*,*N*-dimethylaniline.

Another way of synthesizing tetrahydroquinolines involves the reaction of *N*-(*tert*-butyldioxymethyl)-anilines, which can be produced by ruthenium-catalyzed oxidation of tertiary *N*-methylanilines and *tert*-butyl hydroperoxide. But as the reaction of **19** with the (*E*)/(*Z*) mixture of crotyl trimethylsilane **20** shows that the transformations do not run stereospecifically, i.e. with preservation of the configuration of the dienophilic double bond, since the presumably more stable *trans* isomer *rac*-**21** is obtained in marked excess (de = 88%), which is attributed to the reaction's involving a cationic multi-step mechanism instead of a polar [$4\pi^+ + 2\pi$] cycloaddition (Scheme 4).[9]



19 **20** **21**

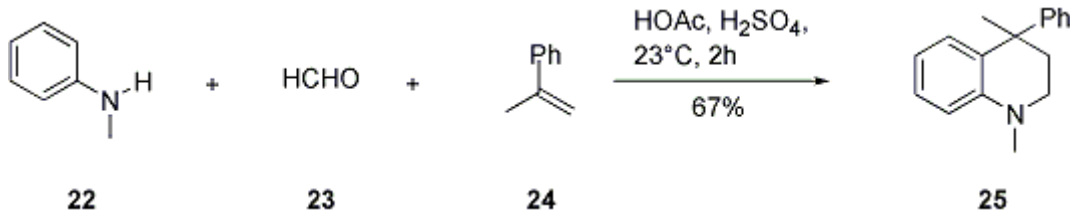
(E)/(Z) = 4:1 *trans/cis* = 94:6

Scheme 4

Katritzky et al. have reported on a highly efficient approach to tetrahydrquinolines by using *N*-[(benzotriazol-1-yl)methyl]anilines as precursors for the generation of 2-aryl iminium ions.[10]

2-Azabutadienes **8** can also be produced by reaction of aromatic anilines with carbonyl compounds.[13-19] In particular, *Hesse* regioselectively reacted primary anilines with aldehydes and alkenes in mixtures of acetic and sulfuric acid to give 1,2,3,4-tetrahydroquinolines (Scheme 5).[13]

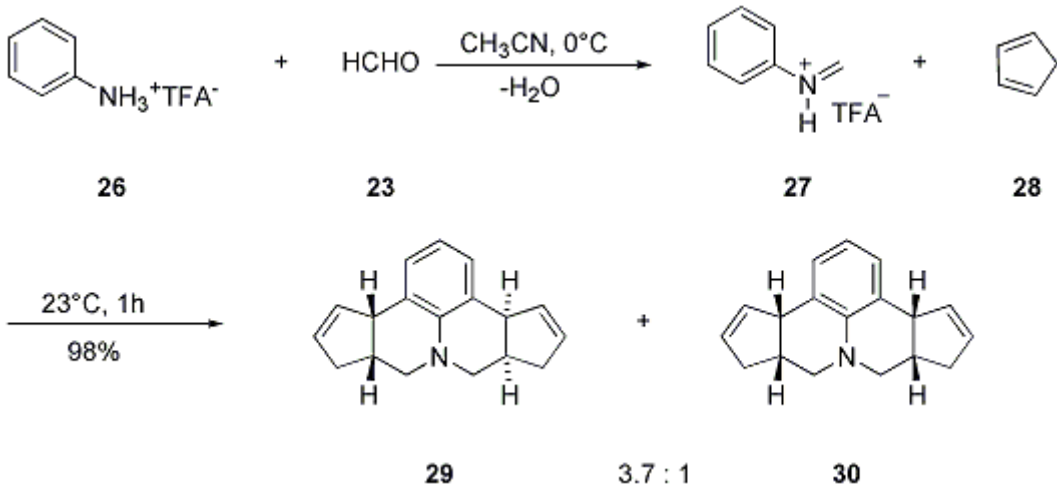
The steric course of the transformation remains unknown. If formaldehyde **23** was used as the carbonyl compound the products of the double amino alkylation were isolated, whereas reaction of secondary aromatic amines such as *N*-methylaniline **22** with formaldehyde **23** led to tetrahydroquinolines like *rac*-**25**.



22 **23** **24** **25**

Scheme 5

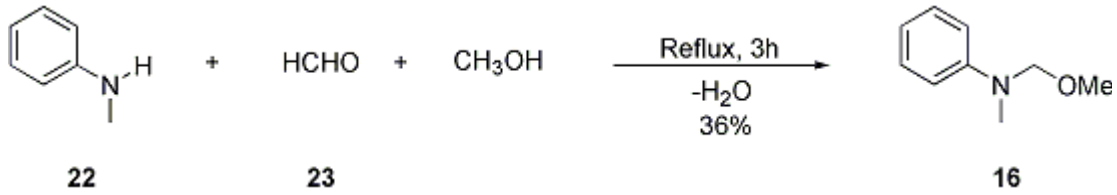
Grieco and *Bahsas* demonstrated that cationic 2-azabutadienes like **27** could be generated in considerably milder conditions from anilinium trifluoro acetate **26** and formaldehyde **23** and then reacted with dienophiles.[14] Transformation of **26** with **23** and cyclopentadiene **28** produced the diastereomeric mixture of the pentacycles *rac*-**29** and *rac*-**30** (Scheme 6). Here also only the double cyclization products are formed in transformations imvolving formaldehyde **23**. With *Grieco* and *Bahsas* the synthesis of tetrahydroquinolines can also only be managed if they evade taking formaldehyde **23** as the aldehyde component. Following this method *Mellor et al.* have gained access to a large number of polycyclic systems by transforming numerous aromatic and heteroaromatic primary amines with formaldehyde and alkenes. [15] They often selected amines that only allow a single cyclization. Even if few studies have so far been undertaken on the mechanism of the transformation of cationic 2-azabutadienes, the majority of findings indicates that the cyclizations proceed in a stepwise manner. Transformation of **19** and **20** producing *rac*-**21** favors a multi-step process since it proceeds without preserving the dienophilic double bond configuration. [9] In a number of cases *Mellor et al.* also managed to isolate follow-up products of potential intermediates which were then cyclized under reaction conditions to give the final products.[15e,f] From this they concluded that the reactions in these cases proceed stepwise. The present results, though, are insufficient to provide a satisfying answer to the question of which mechanism underlies these cyclizations.



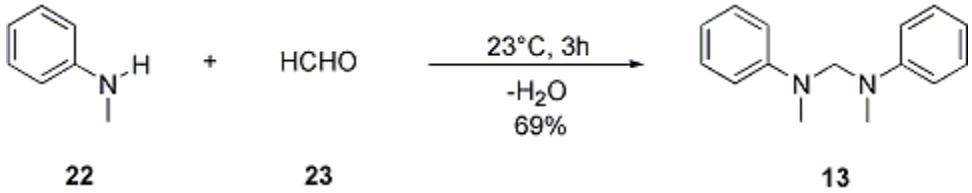
Scheme 6

Of the methods employed to generate cationic 2-azabutadienes the heterolytic cleavage of α-heterosubstituted amines is least subject to constraints on substrate selection. Further advantages are that these reactions can be run *in situ* under relatively mild conditions and that usually no side products occur with the cycloaddition products. The disadvantage though is that some of the previously employed α-heterosubstituted amines are not easily accessible. According to *Shono et al. N*,*O*-acetal **16**, for example, can only be efficiently obtained via anodic oxidation of *N*,*N*-dimethylaniline in methanol.[6a] Following previous work by *Stewart and Bradley*[23] we were – in contrast to *Shono's* report [6a] – able to show that *N*,*O*-acetal **16** may very well be produced without being contaminated with the corresponding *N*,*N*-acetal **13**, though in a yield of just 36% (Scheme 7).

Much better results (69% yield) were achieved when *N*,*N*-acetal **13** was obtained by reaction of **22** and **23** (Scheme 8).[24]



Scheme 7



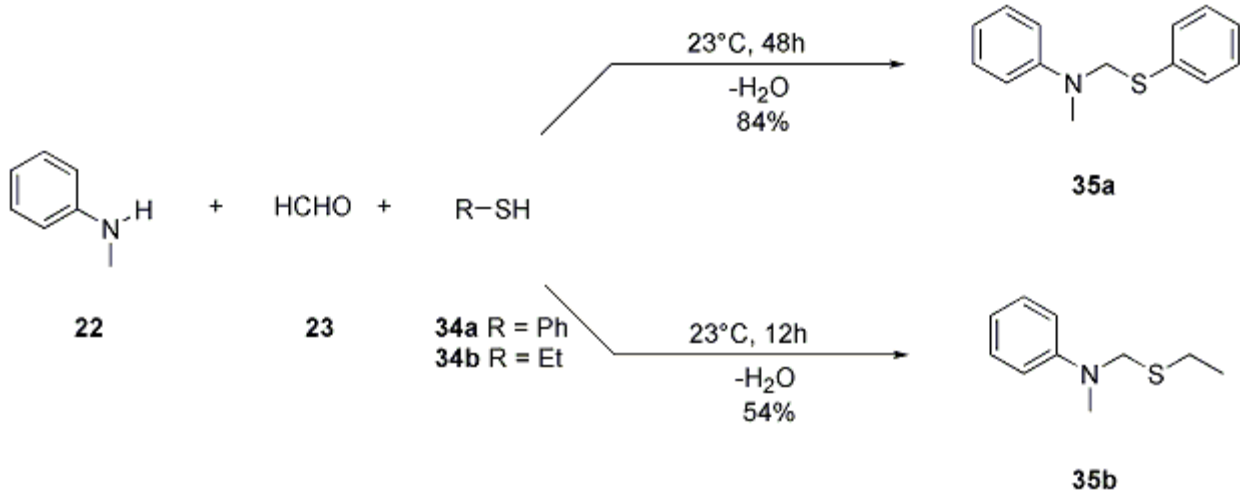
Scheme 8

Using *N*,*S*-acetals **31**,[25,26] α-aminosulfones **32** [27,28] and α-aminonitriles **33** [29,30] as substrates for cationic 2-azabutadienes **8** (Figure 3) turned out to be particularly successful.[31,32] Here we present a detailed report on the preparation of *N*,*S*-acetals, their transformation into the corresponding cationic 2-azabutadienes and their reaction with alkenes to give 1,2,3,4-tetrahydroquinolines.

31 **32** **33**

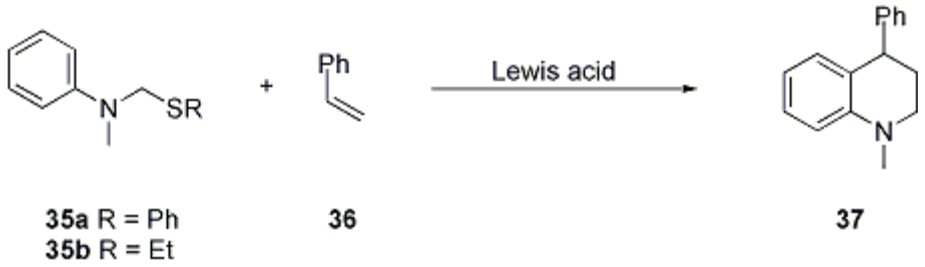
Figure 3

Synthesis of *N*,*S*-acetal **35a** was easily performed by reacting *N*-methylaniline **22** with formaldehyde **23** and thiophenol **34a** in a yield of 84% (Scheme 9).[33] The corresponding *S*-ethyl derivative **35b** was produced in a similar way. Due to lower yields of **35b**, most studies presented in this paper were undertaken with the *S*-phenyl derivative **35a**.



Scheme 9

When *N*,*S*-acetal **35a** was reacted with styrene **36** and $TiCl_4$ as a Lewis acid the single cycloadduct produced was the tetrahydroquinoline *rac*-**37** in 61% yield (Scheme 10) (Table 1, Entry 1), which indicates that in **35a** the only cleavage taking place is in the C-S bond resulting in the formation of the iminium salt **38**; obviously, cleavage of the C-N bond to give **39** does not occur (Scheme 11).



35a R = Ph
35b R = Et

36

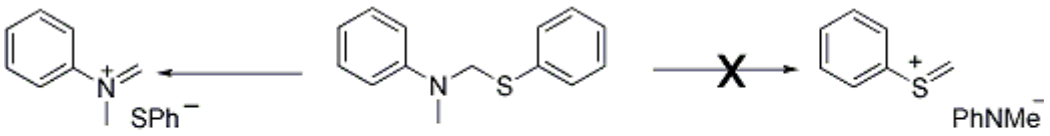
37

Scheme 10

Table 1. Reactions of the *N,S*-acetals **35a,b** with styrene **36** using different Lewis acids

Entry	*N,S*-acetal	Lewis acid (LA)	Equiv. (LA)	Equiv. **36**	T[°C]; t[h]	*rac* **37** [%][a]
1	**35a**	$TiCl_4$	1.2	1.3	-78; 1	61
2	**35a**	$SnCl_4$	1.0	1.5	-78→23; 2; then 23, 2	61
3	**35a**	$SnCl_4$	1.0	1.5	23; 1.25	81
4	**35a**	$SnCl_4$	2.0	1.5	0;0.25; then 23; 1	85
5	**35a**	$SnCl_4$	2.0	3.0	0;0.25; then 23; 1	68
6	**35a**	$BF_3{\cdot}Et_2O$	1.0	1.5	-78; 0.25; then -78→23; 2; then 23; 1	44
7	**35a**	$(CH_3)_2S(CH_3)BF_4$	2.0	1.5	23; 24	-
8	**35a**	$TiCl_4 : PPh_3$ = 1:1	2.0	1.5	0; 0.25; then 23; 96	-
9	**35a**	$TiCl_4 : PPh_3$ = 2:1	2.0	1.5	0; 0.25; then 23; 72	100
10	**35b**	$TiCl_4 : PPh_3$ = 2:1	2.0	1.5	0; 0.25; then 23; 72	80

[a] Isolated Yield.



38 **35a** **39**

Scheme 11

If $TiCl_4$ was replaced by $SnCl_4$, tetrahydroquinoline *rac*-**37** was isolated after 1 h at -78 °C, also in 61% yield (Table 1, Entry 2). Performing the reaction with 1.0 equivalents of $SnCl_4$ at higher temperatures (Table 1, Entry 3) raises the yield to 81%. A further increase may be achieved – even though more modestly – by employing 2.0 equivalents of $SnCl_4$ (Table 1, Entry 4). Since both $TiCl_4$ and $SnCl_4$ led to partial decomposition of the *N,S*-acetal weaker Lewis

acids were also included in this study. Mixtures of $TiCl_4$ and triphenylphosphine turned out to be particularly promising. In a 1 : 1 ratio they have already been successfully applied as a Lewis acid in a number of cases. [34]

If **35a** was reacted with styrene (**36**) and a 1 : 1 mixture of TiCl4 and triphenylphosphine no formation of *rac*-**37** could be observed (Table 1, Entry 8). On the other hand, *rac*-**37** was isolated in quantitative yield if the reaction was performed with a 2 : 1 mixture of $TiCl_4$ and triphenylphosphine (Table 1, Entry 9). Since the corresponding transformation with *S*-ethyl derivative **35b** produced tetrahydroquinoline in a yield of no more than 80% (Table 1, Entry 10), *S*-phenyl-derivative **35a** was employed for all transformations with other dienophiles.

Here we found that *N*,*S*-acetal **35a** may be reacted with a number of dienophiles to give the corresponding tetrahydroquinolines (Table 2). In addition to styrene (**36**), **35a** was also reacted with singly and triply substituted acyclic alkenes **40** and **42**, with the allyl ether **44** and the allylsilane **46** (Table 2, Entries 1-5). Furthermore, the cyclic alkenes cyclopentene (**48**) and cyclopentadiene (**28**) could be converted into the products **49** and **50** as expected (Table 2, Entries 6, 7). The cycloadducts were obtained in yields ranging from 57 to 100%.

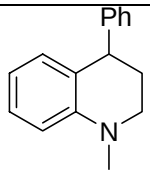
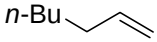
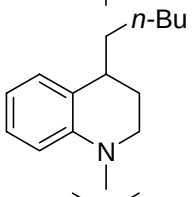
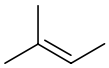
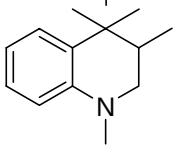
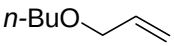
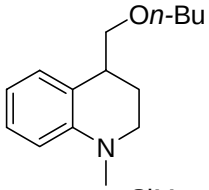
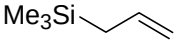
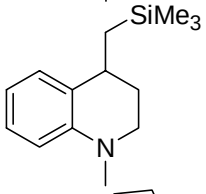
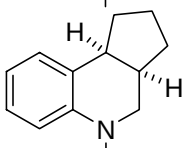
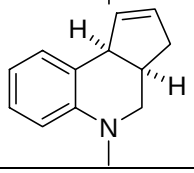
A total surprise, though, was encountered with the products isolated from the reactions of *N*,*S*-acetals with enol ethers and silyl enol ethers. While no reaction could be observed between **35a** and dihydropyran **51**, the transformation with ethyl vinyl ether **14** gave thioether *rac*-**52** as the sole cycloadduct (Scheme 12). The same product was formed by reaction with *n*-butyl vinyl ether **53**.

Transformations of **35a** with silyl enol ethers led to correspondingly substituted thioethers; for example, **35a** and **54** were converted into *rac*-**55** (Scheme 13).

Faced with these results we assumed that the transformation of the vinyl ethers **56** into the corresponding vinyl sulfides **57** proceed *in situ* under the influence of Lewis acids in a manner illustrated in Figure 4, which then react with 2-azabutadiene.

In accordance with these findings we expected the formation of the ethyl thio ether **58** when the *S*-ethyl derivative **35b** was reacted with enol ethers such as **53**; this assumption turned out to be correct (Scheme 14).

Table 2. Reactions of *N*,*S*-acetal **35a** with different dienophiles for the regio- and diastereoselective synthesis of 1,2,3,4-tetrahydroquinolines using a 2:1 mixture of $TiCl_4$ and PPh_3 as Lewis acid

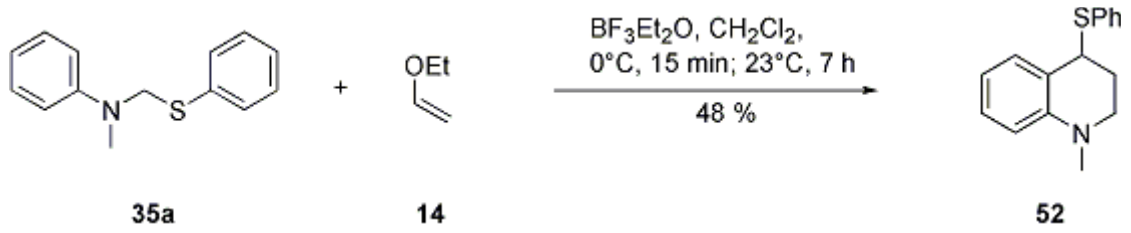
Entry	Dienophile [a]		t [h] [b]	Product		Yield [%] [c]
1		**36**	72		**37**	100
2		**40**	72		**41**	57
3		**42**	120		**43**	74
4		**44**	72		**45**	72
5		**46**	72		**47**	67
6		**14**	120		**49** [d]	87
7		**28**	48		**50** [d]	79

[a] In each case, 1.5 equiv. of the particular dienophile have been used.

[b] All the reactions were performed with 2.0 equiv. of a 2 : 1 mixture of $TiCl_4$ and triphenylphosphine at 23 °C.

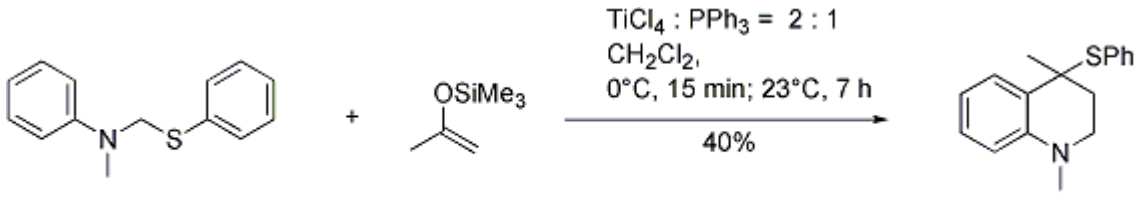
[c] Isolated yield after column chromatography.

[d] Diastereomeric purity was determined by ^1H NMR.



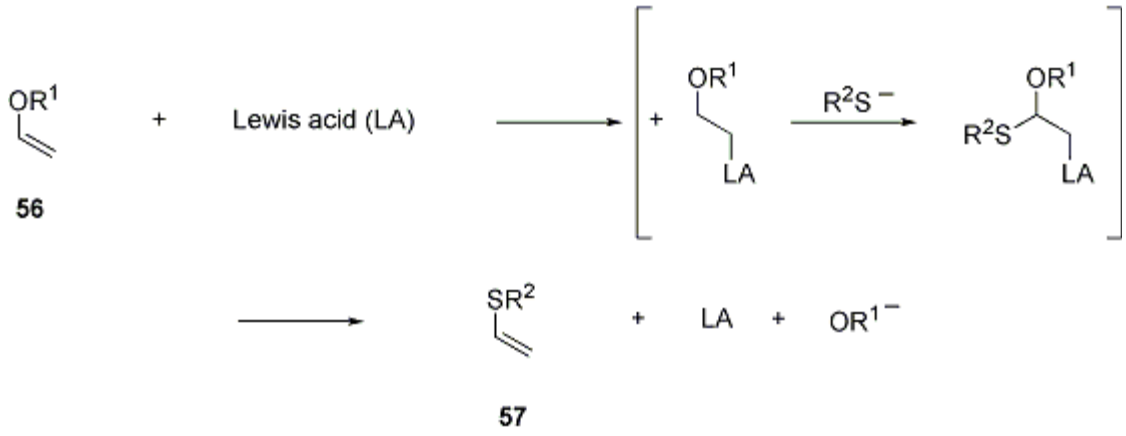
35a **14** **52**

Scheme 12



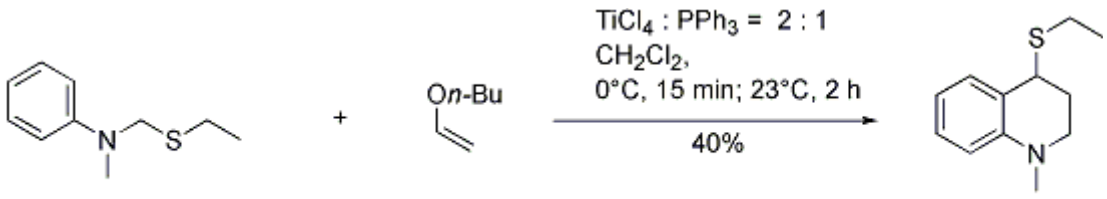
35a **54** **55**

Scheme 13



56 **57**

Figure 4. Possible mechanism for the formation of vinyl sulfides **57** by Lewis acid mediated rearrangement of vinyl ethers **56**.



35b **53** **58**

Scheme 14

According to FMO theory the regioselective formation of the cycloadducts can be interpreted as a result of the most favourable (strong/strong and weak/weak) frontier orbital interactions

between the LUMO of the diene **6** and the HOMO of the corresponding dienophile (see for example Figure 5). [35]

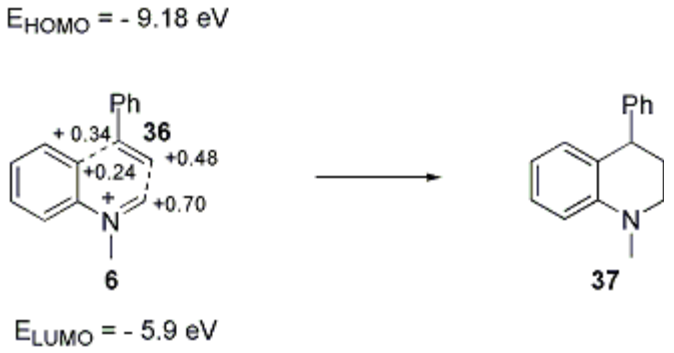
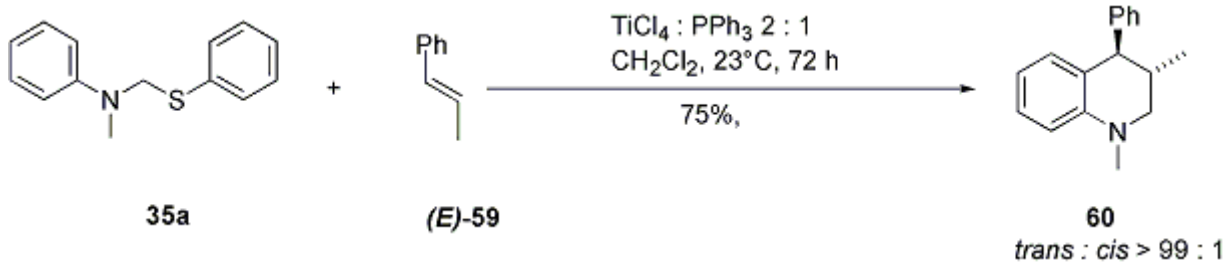


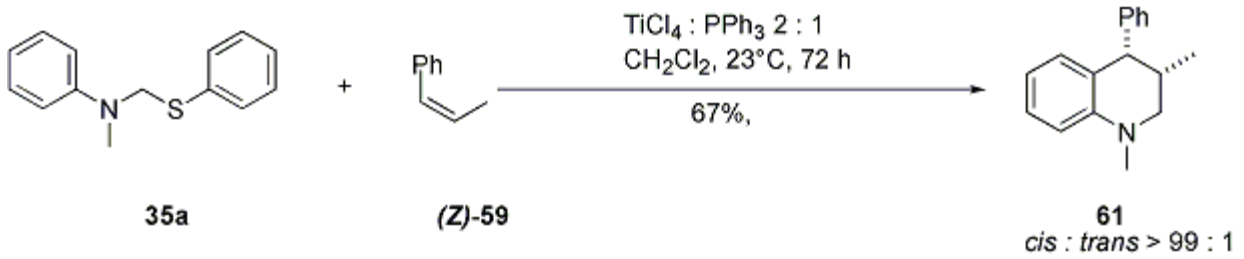
Figure 5. HOMO/LUMO energies and p-atomic orbital coefficients for **6** and **36** from AM1 and PM3 calculations. [20]

It has already been mentioned that the reactions discussed here can either proceed in a concerted manner as an intermolecular polar [$4\pi^+ + 2\pi$] cycloaddition or in a cationic multi-step process.

For elucidating this question the transformations of **35a** with (*E*)- and (*Z*)-methylstyrene [(*E*)-(**59**) and (*Z*)-(**59**) resp.] proved to be particularly revealing. GC and GC-MS as well as HPLC studies of the corresponding crude products demonstrate that the reaction of **35a** with (*E*)-methylstyrene (*E*)-(**59**) exclusively produced *trans*-derivative *rac*-**60** (Scheme 15), whereas reaction of pure (*Z*)-methylstyrene (*Z*)-(**59**) only yields the corresponding *cis*-derivative *rac*-**61** (Scheme 16). So, the transformations proceed with preservation of the dienophilic double bond configuration, indicating a concerted process.



Scheme 15



Scheme 16

AM1 and PM3 calculations [20] predict that – independent of the *equatorial* or *axial* position of the methyl group at C-3 and the *pseudoequatorial* and *pseudoaxial* position of the phenyl group at C-4, respectively - the *trans* product **60** (Table 3, Entries 1,2) is more stable than the *cis* product **61** (Table 3, Entries 3,4). In case of a thermodynamically controlled reaction we would expect - regardless of the configuration of the dienophile employed - the products to be formed in proportion to their stabilities and thus the preferred formation of the more stable *trans* product **60**.

Table 3. AM1 und PM3 calculations of **60** and **61** [20]

Entry	Compound	Geometry/ Substituents	AM1 E[kcal · mol^{-1}]	PM3 E[kcal · mol^{-1}]
1	**60**	*trans* / 3-Me$_{eq}$;4-Ph$_{eq}$	48.65	38.20
2	**60**	*trans* / 3-Me$_{ax}$; 4-Ph$_{ax}$	49.21	38.93
3	**61**	*cis* / 3-Me$_{eq}$; 4 Ph$_{ax}$	49.68	39.27
4	**61**	*cis* / 3-Me$_{ax}$; 4-Ph$_{eq}$	50.72	41.06

Isomerization experiments with *rac*-**60** and *rac*-**61** showed that their relative configuration does not alter under reaction conditions, meaning that isomerization does not take place (Table 4).

Table 4. Isomerization experiments with *rac*-**60** and *rac*-**61**

Entry	Substrate *rac*-**60** : *rac*-**61** [a]	T [°C]	t [d]	Product *rac*-**60** : *rac*-**61**[a]
1	> 99 : < 1	23	5	> 99 : < 1
2	< 1 : > 99	23	5	< 1 : > 99
3	1.6 : 98.4	23	5	1.6 : 98.4

[a] The diastereomeric ratio *rac*-**60** : *rac*-**61** was determined by HPLC.

Exclusive formation of the less stable *cis* product *rac*-**61** from **35a** and (*Z*)-methylstyrene (*Z*)-(**59**) is suggestive of a concerted process of the polar [$4\pi^+ + 2\pi$] cycloaddition with cationic 2-azabutadienes. This assumption is also supported by the absence of follow-up products of the potential intermediates of an alternative cationic multi-step process. This finding is all the more remarkable as the studies so far published indicate that reactions of this type follow a multi-step cationic mechanism.

It should be noted, though, that exclusive formation of the less stable *cis* product *rac*-**61** from **35a** and (*Z*)-methylstyrene (*Z*)-(**59**) does not offer unambiguous proof of a concerted reaction mechanism. This result could also very well be attributed to the fact that the cyclization of the benzyl cation *rac*-**62** into *rac*-**61** proceeds much quicker than the conversion into the more stable benzyl cation *rac*-**63** by rotation around the C,C single bond (Figure 6). But regardless of the reaction mechanism the method presented here guarantees the regio- and diastereoselective construction of 1,2,3,4-tetrahydroquinolines and related systems.

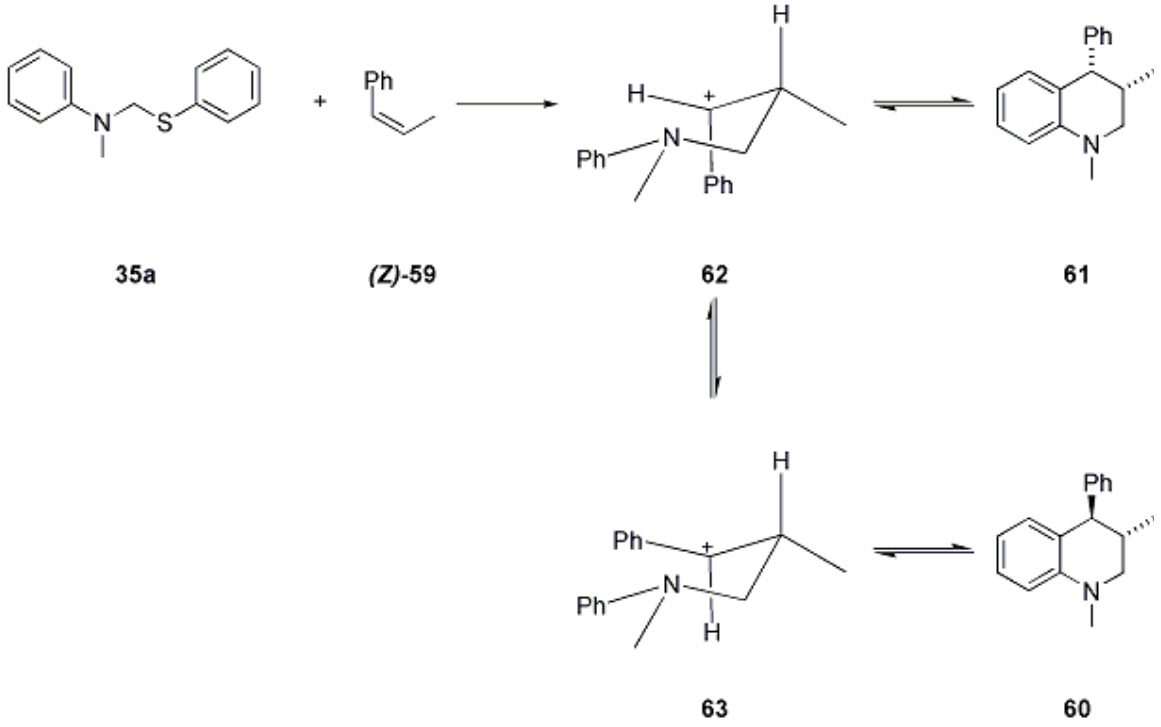


Figure 6

Assignment of the relative configuration of *rac*-**60** and *rac*-**61** was undertaken by ^{1}H NMR spectroscopy and comparison of the two spectra. The *trans* arrangement of the protons attached to C-3 and C-4 in *rac*-**60** follows from the signal for 4-H resonating at $\delta = 3.64$ ppm as a doublet with a vicinal coupling constant of $^3J_{3H,4H} = 8.5$ Hz (Figure 7). The value of the coupling constant of $J = 8.5$ Hz for the vicinal coupling between 2-H_{ax} and 3-H indicates that 3-H is

axially arranged. Altogether, these findings confirm the *pseudoequatorial* position of the phenyl group at C-4 and the *equatorial* position of the methyl group at C-3.

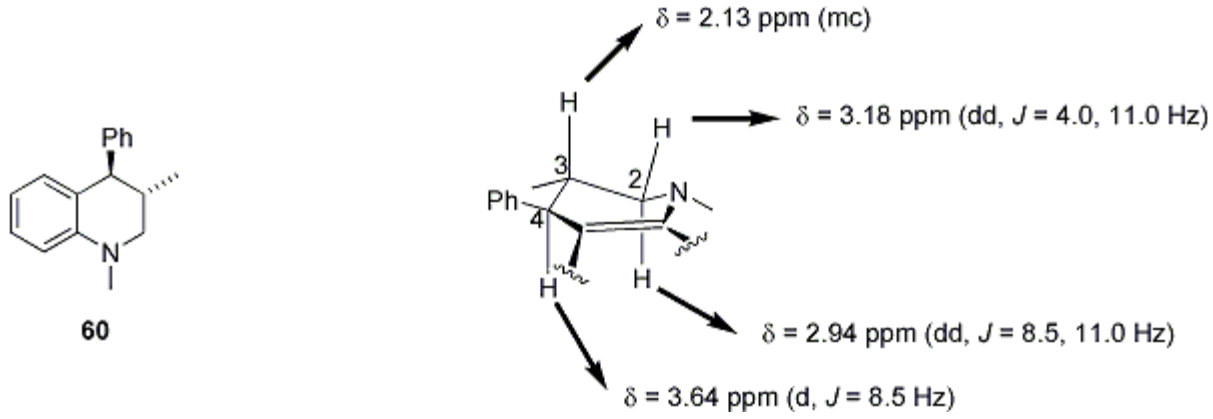


Figure 7. The relative configuration of *rac*-**60**.

In the ^{1}H NMR spectrum of *rac*-**61** the signal for 4-H at δ = 3.98 ppm appears as a doublet with a vicinal coupling constant of $^{3}J_{3H,4H}$ = 5.0 Hz (Figure 8). Comparison to the 8.0 Hz coupling constant for the corresponding coupling in *rac*-**60** provides sound evidence for the *cis* arrangement of the protons at C-3 and C-4. The *equatorial* position of 3-H can be derived from the values of the coupling constants of the vicinal couplings between 3-H and the protons at C-2. Accordingly, in *rac*-**61** an *axial* arrangement is inferred for the methyl group at C-3 and a *pseudoequatorial* arrangement of the phenyl group at C-4.

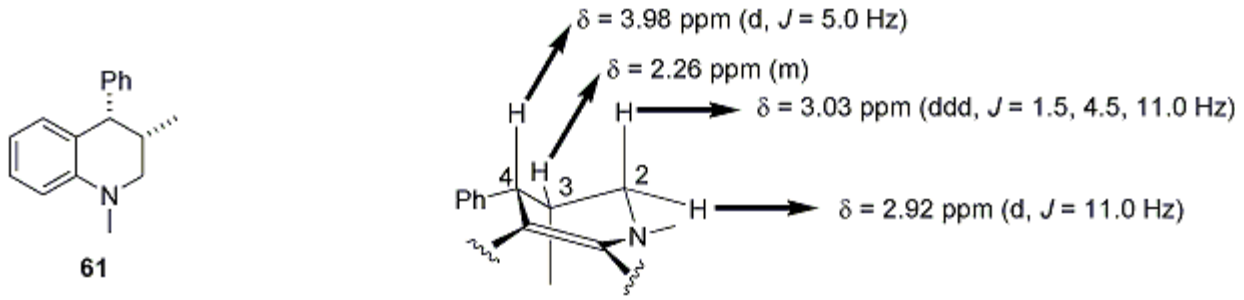


Figure 8. Relative configuration of *rac*-**61**.

Conclusions

Substituted 1,2,3,4-tetrahydroquinolines can be synthesized by polar [4π^{+} + 2π] cycloadditions of cationic 2-azabutadienes with alkenes. We found that cationic 2-azabutadienes can be generated *in situ* by Lewis acid mediated heterolytic cleavage of *N,S*-acetals. Their actions with different dienophiles have been studied and found to yield the corresponding cycloadducts as single

products with yields ranging from 57 to 100%. Best results have been obtained using a new mixed Lewis acid consisting of a mixture of $TiCl_4$ and PPh_3. Surprisingly little is known about the stereochemistry and mechanism of these [$4\pi^+ + 2\pi$] cycloadditions. Here we present stereochemical evidence to support a concerted mechanism. We have shown that the reactions of an *N,S*-acetal with either *(E)*- or *(Z)*-methylstyrene proceed with complete preservation of the stereochemistry of the dienophiles to yield the corresponding diastereomerically pure *trans*- and *cis*-cycloadducts, respectively. These results strongly point to a concerted mechanism being operative in the reactions studied.

Experimental Section

General Procedures. All moisture-sensitive reactions were performed in dried flasks (140 °C, 2 h) under argon using syringe techniques. Solvents were dried and purified by conventional methods prior to use. Dichloromethane was freshly destilled from P_4O_{10}. Petroleum ether refers to the fraction with b.p. 35-65 °C. Reagents of commercial quality were used from freshly opened containers or purified by common methods. - Melting points: Open capillaries, uncorrected values. - IR: Bruker IFS 25. - UV: Varian Cary 219, Perkin-Elmer Lambda 2, and Perkin-Elmer Lambda 9. - ^{1}H NMR: Varian FT-80 A (80 MHz), Varian XL-200 (200 MHz), Varian VXR-200 (200 MHz), Bruker AMX-300 (300 MHz). - ^{13}C NMR: Varian FT-80A (20 MHz), Varian XL-200 (50.3 MHz), Varian VXR-200 (50.3 MHz), Bruker AMX-300 (75.5 MHz); assignment in accordance with DEPT spectra. The signal of tetramethylsilane ($\delta = 0.00$) as an internal standard. - MS: Varian MAT 311A, Varian MAT 731 (EI 70 eV). - Analytical HPLC: Kontron 425 with a UV detector.- Silica gel used for column chromatography: Merck Kieselgel 60, 0.040-0.063 mm (230-400 mesh). - TLC analysis: precoated plates, Kieselgel 60 F_{254}, Merck; precoated plates, Alugram SIL G/UV_{254}, Macherey & Nagel; detection: UV absorption or potassium permanganate solution (1%).

Methoxymethyl-methyl-phenyl-amine (16). 24.0 ml (0.30 mol) of 37 % aqueous formaldehyde solution **23** were added to a solution of 21.8 g (0.20 mol) *N*-methylaniline **22** in 9.50 g (0.30 mol) methanol at room temp. with stirring. The mixture was heated under reflux until *N*-methylaniline 22 had reacted completely (TLC monitoring, diethyl ether/petroleum ether 1:6). After cooling the reaction mixture was saturated with K_2CO_3 and stirred for 30 min at room temp. The layers were separated and the aqueous layer was extracted with diethyl ether (2 × 25 ml). The combined organic extracts were dried (K_2CO_3). The solvent was removed under reduced pressure and the crude product purified by fractional destillation to yield 16 (10.75 g, 36%) as a colourless liquid, b.p. 91 °C / 7 mbar. R_f = 0.32 (diethyl ether / petroleum ether = 1 : 6). - IR (film): $\upsilon = 3094$ cm^{-1}, 3062, 3030 (C=CH), 2984, 2924, 2894 (CH), 1602 (C=C-N), 1504 (C=C), 1448 (CH_3), 1230 (C-O), 1070 (C-O-C), 752, 694 (CH). - ^{1}H NMR (80 MHz, $CDCl_3$): δ= 3.10 (s, 3H, NCH_3), 3.30 (s, 3H, OCH_3), 4.75 (s, 2H, CH_2), 6.60 - 7.45 (m,

5H, arom. H). - ^{13}C NMR (20 MHz, $CDCl_3$): δ = 38.30 (C-7), 54.25 (C-9), 85.00 (C-8), 113.00 (C-2, C-6), 177.75 (C-4), 128.50 (C-3, C-5), 148.00 (C-1). - MS (70 eV); *m/z* (%): 151 (44) [M^+], 120 (100) [$C_8H_{10}N^+$], 105 (9) [$C_8H_9^+$], 91 (3) [$C_7H_7^+$], 77 (15) [$C_6H_5^+$], 65 (2) [$C_5H_5^+$], 51 (7) [$C_4H_3^+$], 45 (9) [$C_2H_7N^+$]. - $C_9H_{13}NO$ (151.2).

***N,N'*-Dimethyl-*N,N'*-diphenyl-methandiamine (13).** A solution of 21.4 g (0.20 mol) *N*-methylaniline **22** and 8.00 ml (0.10 mol) 37 % aqueous formaldehyde solution **23** was prepared and stirred. After some minutes a slight warming occurred. The mixture was stirred overnight at room temp. until consumption of the aldehyde was completed, as monitored by TLC (diethyl ether/petroleum ether, 1:6). The reaction mixture was extracted with diethyl ether (2 × 25 ml) and the combined organic extracts dried (Na_2SO_4). The solvent was evaporated. The crude product was purified by fractional destillation to yield **13** (15.67 g, 69%) as a viscous, colorless oil, b.p. 116 -120 °C / 0.001 mbar, which solidified in the refrigerator and formed colorless crystals.

R_f = 0.26 (diethyl ether / petroleum ether = 1 : 6). - IR (KBr) υ = 3090 cm^{-1}, 3058, 3026 (C=CH), 2920, 2882, 2814 (CH), 1600 (C=C-N), 1504 (C=C), 1448 (CH_3), 750, 692 (CH). - ^{1}H NMR (80 MHz, $CDCl_3$): δ = 2.85 (s, 6H, 2 × NCH_3), 4.70 (s, 2H, CH_2), 6.60 - 7.45 (m, 10H, arom. H). - ^{13}C NMR (20 MHz, $CDCl_3$): δ = 36.06 (2 × NCH_3), 70.11 (CH_2), 113.56 (C-2, C-6), 117.68 (C-4), 129.10 (C-3, C-5), 149.11 (C-1). - MS (70 eV); *m/z* (%): 226 (9) [M^+], 120 (100) [$C_8H_{10}N^+$], 106 (20) [$C_7H_8N^+$], 91 (17) [$C_6H_5N^+$], 77 (12) [$C_6H_5^+$]. - $C_{15}H_{18}N_2$ (226.3).

Methyl-phenyl-phenylsulfanylmethyl-amine (35a). An emulsion of *N*-methylaniline **22** (32.2 g, 0.30 mol) and water (66 ml) was prepared and paraformaldehyde **23** (9.00 g, 0.30 mol) was added with stirring. Then a solution of thiophenol **34a** (32.4 g, 0.30 mol) in diethyl ether (75 ml) and K_2CO_3 (41.5 g, 0.30 mol) were added, whereby the mixture warmed. After cooling the reaction mixture was stirred for 48 h at room temp. and monitored by TLC (diethyl ether/petroleum ether, 1:6). The layers were separated and the aqueous layer was extracted with diethyl ether (2 × 75 ml). The combined organic extracts were washed with saturated Na_2CO_3 (2 × 100 ml) and NaCl (1 × 100 ml) solutions and dried (Na_2SO_4). The solvent was evaporated and the crude product destilled to yield **35a** (57.89 g, 84%) as a colorless oil, b.p. 120 °C/0.001 mbar. To obtain an analytically pure product, **35a** was purified by column chromatography (diethyl ether/petroleum ether, 1:15). In addition to **35a,** 5% of the minor product diphenyldisulfide were isolated and identified by NMR spectroscopy.- R_f = 0.47 (diethyl ether/petroleum ether, 1:6). - IR (film): ν = 3058 cm^{-1}, 3028 (C=CH), 2940, 2900, 2814 (CH), 1600 (C=C-N), 1504 (C=C), 1478, 1438 (CH^2), 746, 692 (CH). - UV (acetonitrile): λ_{max} (lg ε) = 257 nm (4.23). - ^{1}H NMR (80 MHz, $CDCl_3$): δ = 2.90 (s, 3H, NCH_3), 4.95 (s, 2H, CH_2), 6.60-7.55 (m, 10H, aromatic H). - ^{13}C NMR (20 MHz, $CDCl_3$): δ = 38.40 (NCH_3), 61.79 (CH_2), 113.89 (C-2', C-6'), 118.20 (C-4'), 127.05 (C-4), 128.81 (C-3, C-5), 128.96 (C-2, C-6), 132.99 (C-3', C-5'), 135.78 (C-1), 147.11 (C-1'). - MS (70 eV); *m/z* (%): 229 (8) [M^+], 120 (100) [$C_8H_{10}N^+$], 106 (37) [$C_7H_8N^+$], 91 (5) [$C_6H_5N^+$], 77 (20) [$C_6H_5^+$], 65 (6) [$C_5H_5^+$], 51 (6) [$C_4H_5^+$]. - $C_{14}H_{15}NS$ (229.3): calcd. C 73.32, H 6.59, N 6.11, S 13.98; found C 73.37, H 6.68, N 6.19, S 14.03.

Ethylsulfanylmethyl-methyl-phenyl-amine (35b). Paraformaldehyde **23** (9.00 g, 0.30 mol) was added to a mixture of *N*-methylaniline **22** (32.2 g, 0.30 mol) and water (66 ml) under stirring. The reaction mixture was saturated with K_2CO_3 and warmed. A solution of ethyl mercaptan **34b** (18.6 g, 0.30 mol) in diethyl ether (75 ml) was dropped slowly into the warmed mixture and stirred for 12 h at room temp. Monitoring was performed by TLC (diethyl ether/petroleum ether, 1:6). The reaction mixture was extracted with diethyl ether (2 × 75 ml). The combined organic extracts were washed with saturated Na_2CO_3 (2 × 100 ml) and NaCl (1 × 100 ml) solutions and dried (K_2CO_3). The solvent was removed under reduced pressure and the crude product purified by fractional destillation to yield **35b** (28.94 g, 54%) as a yellow liquid, b.p. 90-95 °C/0.8 mbar. - R_f = 0.30 (diethyl ether/petroleum ether, 1:6). - IR (film): ν = 3092 cm^{-1}, 3062, 3028 (C=CH), 2966, 2926, 2870 (CH), 1600 (C=C-N), 1504 (C=C), 1480, 1450 (CH_3, CH_2), 750, 692 (CH). - UV (acetonitrile): λ_{max} (lg ε) = 203 nm (4.31), 262 (4.12). - ^{1}H NMR (80 MHz, $CDCl_3$): δ = 1.20 (t, J = 8.0 Hz, 3H, CH_3), 2.50 (q, J = 8.0 Hz, 2H, CH_2), 3.00 (s, 3H, NCH_3), 4.60 (s, 2H, NCH_2S), 6.60-7.35 (m, 5H, aromatic H). - ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 15.08 (C-4), 25.45 (C-3), 37.83 (C-1), 56.48 (C-2), 113.61 (C-2', C-6'), 117.73 (C-4'), 128.84 (C-3', C-5'), 147.85 (C-1'). - MS (70 eV); *m/z* (%): 181 (6) [M^+], 120 (100) [$C_8H_{10}N^+$], 105 (9) [$C_8H_9^+$], 91 (4) [$C_6H_5N^+$], 77 (16) [$C_6H_5^+$], 65 (2) [$C_5H_5^+$], 51 (6) [$C_4H_3^+$]. - $C_{10}H_{15}NS$ (181.3): calcd. C 66.25, H 8.33; found C 66.23, H 8.28.

(4*RS*)-(±)-1-Methyl-4-phenyl-1,2,3,4-tetrahydroquinoline (37) via cyclization of 35a with 36. 1.14 g (5.00 mmol) of **35a** were dissolved in 5 ml dry dichloromethane, treated with the equiv. Lewis acid provided in Table 1 at the given temperature and stirred for 5 min at the reaction temp. Then 1.3 - 3.0 equiv. styrene **36** was added. The mixture was stirred at the temperature and for the time given in Table 1. For work-up the reaction mixture was treated with 5 ml sat. sodium hydrogen carbonate solution: The layers were separated and the aqueous layer extracted with dichloromethane (2 x 10 ml). The combined organic layers were dried (Na_2SO_4) and the solvent removed in vacuo. The crude product was purified by column chromatography on 100 g silica gel (diethyl ether / petroleum ether, 1 : 15) (Table 1, No. 1 - 9).

General procedure for the synthesis of tetrahydroquinolines

Triphenylphosphine (1.0 equiv.) in dichloromethane (1 *M*) was added to a stirred solution of $TiCl_4$ (2.0 equiv.) in dichloromethane (1 ml/1 mmol $TiCl_4$) at 0°C. The solution which turned deep red, was stirred for another 15 min at 0 °C and added dropwise to a solution of methyl-phenyl-phenylsulfanylmethylamine **35a** (1.0 equiv) in dichloromethane (5 ml dichloromethane/1 mmol **35a**) at 0°C. After 10 min at 0 °C the appropriate dienophile (1.5 equiv.) was added dropwise, the resulting solution was warmed up to room temp. and stirred until completion (TLC). The reaction was quenched by addition of saturated Na_2CO_3 solution (10 ml/2 mmol $TiCl_4$) and stirred for 20 min. After extraction with dichloromethane (3 × 15 ml/1 mmol **35a**) the combined organic layers were dried (Na_2SO_4), the solvent was removed in vacuo and the residue was purified by column chromatography on silica gel.

(4*RS*)-(±)-1-Methyl-4-phenyl-1,2,3,4-tetrahydroquinoline (37) by cyclization of **35a** and **36**: The *N,S*-acetal **35a** (1.14 g, 5.00 mmol) and styrene **36** (0.78 g, 7.5 mmol) were allowed to react in dichloromethane (5 ml) in the presence of a 2:1-mixture of $TiCl_4$ and triphenylphosphine (2.00 equiv.) as the Lewis acid according to GP for 72 h. After work-up and column chromatography (diethyl ether/petroleum ether, 1:15) **37** (1.11 g, quantitative yield) was obtained as a colourless liquid.

(4*RS*)-(±)-1-Methyl-4-phenyl-1,2,3,4-tetrahydroquinoline (37) by cyclization of **35b** and **36**: The *N,S*-acetal **35b** (186 mg, 1.00 mmol) and styrene **36** (150 mg, 1.50 mmol) were reacted in accordance with the General Procedure. The reaction mixture was stirred at room temp. for 72 h. After work-up the crude material was purified by column chromatography on silica gel (diethyl ether/petroleum ether, 1:15) to give **37** (183.5 mg, 80%) as a colorless liquid. - R_f = 0.32 (diethyl ether/petroleum ether, 1:4). - IR (film): ν = 3060 cm^{-1}, 3026 (CH, aromatic), 1602 (C=C-N), 1504 (C=C), 1432 (CH_3), 748, 702 (CH). - UV (acetonitrile): λ_{max} (lg ε) = 212 nm (4.46), 261 (3.98), 309 (3.48). - ^{1}H NMR (80 MHz, $CDCl_3$): δ = 2.00-2.45 (m, 2H, 3-H_2), 3.00 (s, 3H, NCH_3), 3.25 (t, *J* = 6.0 Hz, 2H, 2-H_2), 4.15 (t, *J* = 5.0 Hz, 1H, 4-H), 6.45-7.50 (m, 9H, aromatic H). - ^{13}C NMR (20 MHz, $CDCl_3$): δ = 31.06 (C-3), 39.15 (NCH_3), 43.36 (C-4), 48.39 (C-2), 110.96 (C-8), 116.21 (C-6), 124.69 (C-4a), 126.04 (C-5), 127.53 (C-7), 128.22 (C-2', C-6'), 128.59 (C-3', C-5'), 129.85 (C-4'), 146.53 (C-1'), 146.78 (C-8a). - MS (70 eV); *m/z* (%): 223 (100) [M^+], 208 (30) [M^+ - CH_3], 193 (8) [M^+ - CH_2NH_2], 178 (7) [M^+ - C_2H_7N], 165 (14) [M^+ - C_3H_8N], 152 (13) [M^+ - C_5H_{11}], 146 (19) [M^+ - C_6H_{11}], 144 (86) [M^+ - C_6H_7], 130 (22) [$C_9H_8N^+$], 103 (13) [$C_8H_7^+$], 91 (41) [$C_7H_7^+$], 77 (23) [$C_6H_5^+$], 65 (8) [$C_5H_5^+$], 57 (8) [$C_4H_9^+$], 51 (16) [$C_4H_3^+$], 41 (20) [$C_2H_3N^+$]. - $C_{16}H_{17}N$ (223.3): calcd. C 86.06, H 7.67, N 6.27; found C 85.97, H 7.66, N 6.32.

(4*SR*)-(±)-1-Methyl-4-pentyl-1,2,3,4-tetrahydroquinoline (41). 1-Heptene **40** (200 mg, 2.00 mmol) was added to a solution of the *N,S* acetal **35a** (228 mg, 1.00 mmol) and a 2:1-mixture of $TiCl_4$ and triphenylphosphine in dichloromethane according to the General Procedure. The reaction mixture was stirred for 72 h at room temp. After work-up and column chromatography (diethyl ether/petroleum ether, 1:30) yielded **41** (117.6 mg, 57%) as a colorless oil. - R_f = 0.25 (diethyl ether/petroleum ether, 1:30). - UV (acetonitrile): λ_{max} (lg ε) = 209 nm (4.34), 259 (4.05), 307 (3.43). - IR (film): ν = 3064 cm^{-1}, 3024 (C=C-H), 2952, 2926, 2828 (CH), 1602 (C=C-N), 1504 (C=C), 1466, 1456 (CH_2), 744 (CH). - ^{1}H NMR (300 MHz, DMSO-d_6): δ = 0.88 (t, *J* = 7.0 Hz, 3H, 4'-CH_3), 1.20-1.60 (m, 8H, 1'-H_2, 2'-H_2, 3'-H_2, 4'-H_2), 1.68-1.92 (m, 2H 3-H_2), 2.65 (m, 1H, 4-H), 2.80 (s, 3H, NCH_3), 3.06-3.26 (m, 2H, 2-H_2), 6.50 (dt, *J* = 1.0 Hz, *J* = 8.0 Hz, 1H, 6-H), 6.52 (d, *J* = 8.0 Hz, 1H, 8-H), 6.88-7.00 (m, 2H, 5-H, 7-H). - ^{13}C NMR (50.3 MHz, DMSO-d_6): δ = 13.87 (C-5'), 22.09 (C-4'), 25.97 (C-3'), 26.01 (C-2'), 31.41 (C-3), 35.49 (C-4), 36.16 (C-1'), 38.52 (NCH_3), 46.91 (C-2), 110.62 (C-8), 115.41 (C-6), 126.41 (C-4a), 126.69 (C-5), 127.98 (C-7), 145.74 (C-8a). - MS (70 eV); *m/z* (%): 217 (59) [M^+], 147 (23) [M^+ - C_5H_{10}], 146 (100) [M^+ - C_5H_{11}], 91 (4) [$C_6H_5N^+$], 82 (5) [$C_5H_8N^+$], 57 (8) [$C_4H_9^+$], 43 (5) [$C_3H_7^+$]. - $C_{15}H_{23}N$ (217.4): calcd. C 82.89, H 10.67, N 6.44; found C 82.79, H 10.69, N 6.28.

(3*RS*)-(±)-1,3,4,4-Tetramethyl-1,2,3,4-tetrahydroquinoline (43). In accordance with the General Procedure the *N,S*-acetal **35a** (237 mg, 1.03 mmol) was transformed to the tetrahydroquinoline **43** in the presence of the freshly destilled dienophile methyl-2-butene **42** (110 mg, 1.50 mmol). The reaction mixture was stirred for 120 h at room temp. After work-up the crude material was purified by column chromatography (diethyl ether/petroleum ether, 1:30) to yield the colorless oil **43** (144.4 mg, 74%). - R_f = 0.39 (diethyl ether/petroleum ether, 1:30). - IR (film): ν = 3062 cm^{-1}, 3032 (C=C-H), 2966, 2936, 2882 (CH), 1602 (C=C-N), 1504 (C=C), 1388 [$C(CH_3)_2$], 1374 (CH_3), 742 (CH). - ^{1}H NMR (300 MHz, DMSO-d_6): δ = 0.88 (d, *J* = 8.0 Hz, 3H, 3-CH_{3eq}), 1.07 (s, 3H, 4-CH_{3ax}), 1.21 (s, 3H, 4-CH_{3eq}), 1.75 (m, 1H, 3-H_{ax}), 2.82 (s, 3H, NCH_3), 2.92 (dd, *J* = 8.0 Hz, *J* = 12.0 Hz, 1H, 2-H_{ax}), 3.18 (dd, *J* = 4.0 Hz, *J* = 12.0 Hz, 1H, 2-H_{eq}), 6.52 (d, *J* = 8.0 Hz, 1H, 8-H), 6.54 (dt, *J* = 1.5 Hz, *J* = 7.5 Hz, 1H, 6-H), 6.96 (ddd, *J* = 1.5 Hz, *J* = 7.5 Hz, *J* = 8.0 Hz, 1H, 7-H), 7.12 (dd, *J* = 1.5 Hz, *J* = 7.5 Hz, 1H, 5-H). - ^{13}C NMR (50.3 MHz, DMSO-d_6): δ = 13.88 (3-CH_3), 25.34 (4-CH_{3ax}), 29.07 (4-CH_{3eq}), 34.97 (C-3), 36.70 (C-4), 38.69 (NCH_3), 53.77 (C-2), 110.37 (C-8), 115.56 (C-6), 125.57 (C-5), 126.38 (C-7), 130.91 (C-4a), 144.79 (C-8a). - MS (70 eV); *m/z* (%): 189 (96) [M^+], 174 (100) [M^+ - CH_3], 159 (22) [M^+ - C_2H_6], 144 (61) [M^+ - C_3H_9], 132 (52) [M^+ - C_4H_9], 117 (14) [M^+ - $C_4H_{10}N$], 91 (9) [$C_6H_5N^+$], 77 (9) [$C_6H_5^+$], 65 (3) [$C_5H_5^+$], 51 (3) [$C_4H_5^+$], 41 (3) [CH_3CN^+]. - $C_{13}H_{19}N$ (189.3): calcd. C 82.48, H 10.12, N 7.40; found C 82.32, H 10.06, N 7.45.

(4*SR*)-(±)-1-Methyl-4-methylbutoxy-1,2,3,4-tetrahydroquinoline (45). In accordance with the General Procedure *N,S*-acetal **35a** (233 mg, 1.02 mmol) and allyl-*n*-butyl ether **44** (170 mg, 1.50 mmol) were reacted to give tetrahydroquinoline **45**. For this purpose the reaction mixture was stirred for 72 h at room temp. After work-up the crude material was purified by column chromatography (diethyl ether/petroleum ether, 1:15) to yield **45** (169.5 mg, 72%) as a colorless oil. - R_f = 0.25 (diethyl ether/petroleum ether, 1:15). - IR (film): ν = 3066 cm^{-1}, 3026 (C=C-H), 2956, 2930, 2864 (CH), 1604 (C=C-N), 1504 (C=C), 1458, 1432 (CH_2), 1322, 1108 (C-O), 746 (CH). - UV (acetonitrile): λ_{max} (lg ε) = 209 nm (4.33), 258 (4.04), 307 (3.41). - ^{1}H NMR (300 MHz, DMSO-d_6): δ = 0.90 (t, *J* = 7.5 Hz, 3H, 4'-CH_3), 1.26-1.40 (m, 2H, 3'-H_2), 1.44-1.56 (m, 2H, 2'-H_2), 1.76-1.96 (m, 2H, 3-H_2), 2.80 (s, 3H, NCH_3), 2.93 (m, 1H, 4-H), 3.04-3.20 (m, 2H, 2-H_2), 3.32-3.48 (m, 4H, 1'-H_2, 4-CH_2), 6.52 (dt, *J* = 1.0 Hz, *J* = 7.5 Hz, 1H, 6-H), 6.56 (d, *J* = 7.5 Hz, 1H, 8-H), 6.94-7.04 (m, 2H, 5-H, 7-H). - ^{13}C NMR (50.3 MHz, DMSO-d_6): δ = 13.72 (C-4'), 18.94 (C-3'), 23.67 (C-2'), 31.39 (C-3), 35.80 (C-4), 38.69 (NCH_3), 46.73 (C-2), 69.91 (4-CH_2), 74.34 (C-1'), 110.88 (C-8), 115.63 (C-6), 122.41 (C-4a), 127.17 (C-5), 128.67 (C-7), 146.54 (C-8a). - MS (70 eV); *m/z* (%): 233 (23) [M^+], 146 (100) [M^+ - $C_5H_{11}O$], 132 (6) [M^+ - $C_6H_{14}O$], 117 (14) [M^+ - $C_4H_{10}N$], 105 (2) [$C_7H_7N^+$], 91 (4) [$C_6H_5N^+$], 77 (3) [$C_6H_5^+$], 69 (5) [$C_4H_5O^+$], 60 (2) [$C_3H_8O^+$], 55 (9) [$C_4H_7^+$], 41 (14) [CH_3CN^+]. - $C_{15}H_{23}NO$ (233.4): calcd. C 77.21, H 9.93, N 6.00; found C 77.30, H 9.95, N 6.27.

(4*SR*)-(±)-1-Methyl-4-methyltrimethylsilyl-1,2,3,4-tetrahydroquinoline (47). The *N,S*-acetal **35a** (228 mg, 1.00 mmol) and allyltrimethylsilane **46** (170 mg, 1.50 mmol) were reacted in accordance with the General Procedure. The reaction mixture was stirred for 72 h at room temp. After work-up column chromatography (diethyl ether/petroleum ether, 1:100) yielded **47**

(155.6 mg, 67%) as a colorless oil. - R_f = 0.22 (diethyl ether/petroleum ether, 1:100). - IR (film): ν = 3064 cm^{-1}, 3026 (C=C-H), 2900, 2874 (CH), 1602 (C=C-N), 1502 (C=C), 1468, 1452 (CH_2), 838 [$Si(CH_3)_3$], 742 (CH). - UV (acetonitrile): λ_{max} (lg ε) = 210 nm (4.35), 258 (4.04), 307 (3.45). - ^{1}H NMR (300 MHz, DMSO-*d*$_6$): δ = 0.02 [s, 9H, $Si(CH_3)_3$], 0.78 [dd, *J* = 9.5 Hz, *J* = 14.5 Hz, 1H, C*H*Si(CH$_3$)$_3$], 0.90 [dd, *J* = 5.0 Hz, *J* = 14.5 Hz, 1H, C*H*Si(CH$_3$)$_3$], 1.58-1.70 (m, 1H, 3-H_{ax}), 1.84-1.98 (m, 1H, 3-H_{eq}), 2.80 (s, 3H, NCH_3), 2.88 (dt, *J* = 5.0 Hz, *J* = 10.0 Hz, 1H, 2-H), 3.12 (dt, *J* = 10.0 Hz, *J* = 5.0 Hz, 1H, 2-H), 3.18-3.20 (m, 1H, 4-H), 6.50 (dt, *J* = 1.0 Hz, *J* = 7.5 Hz, 1H, 6-H), 6.52 (d, *J* = 7.5 Hz, 1H, 8-H), 6.88-6.98 (m, 2H, 5-H, 7-H). - ^{13}C NMR (50.3 MHz, DMSO-*d*$_6$): δ = 0.01 [$Si(CH_3)_3$], 25.71 (4-CH_2), 29.62 (C-3), 32.67 (C-4), 39.15 (NCH_3), 47.52 (C-2), 111.22 (C-8), 116.19 (C-6), 127.20 (C-5), 128.13 (C-7), 129.67 (C-4a), 146.10 (C-8a). - MS (70 eV); *m/z* (%): 233 (93) [M^+], 218 (11) [M^+ - CH_3], 190 (10) [M^+ - C_3H_7], 146 (100) [M^+ - $C_4H_{11}Si$], 120 (17) [$C_8H_{10}N^+$], 91 (2) [$C_6H_5N^+$], 77 (3) [$C_6H_5^+$], 73 (5) [$C_3H_9Si^+$], 45 (3) [$C_2H_7N^+$]. - $C_{14}H_{23}NSi$ (233.4): calcd. C 72.04, H 9.93, N 6.00; found C 72.15, H 9.99, N 6.01.

(3a*RS*,9b*SR*)-(±)-5-Methyl-2,3,3a,4,5,9b-hexahydro-1H-cyclopenta-[c]quinoline (49). According to the General Procedure the *N,S*-acetal **35a** (236 mg, 1.03 mmol) and freshly destilled cyclopentene **48** (100 mg, 1.50 mmol) were allowed to react in dichloromethane (5 ml) in the presence of a 2:1-mixture of $TiCl_4$ and triphenylphosphine (2.00 equiv.) as the Lewis acid for 20 h. After work-up and column chromatography (diethyl ether/petroleum ether, 1:30) **49** (168.2 mg, 87%) was obtained as a yellow oil. - R_f = 0.31 (diethyl ether/petroleum ether, 1:30). - IR (film): ν = 3066 cm^{-1} (C=C-H), 2948, 2864 (CH), 1602 (C=C-N), 1500 (C=C), 1476, 1450 (CH_2), 746 (CH). - UV (acetonitrile): λ_{max} (lg ε) = 210 nm (4.38), 255 (4.00), 303 (3.42). - ^{1}H NMR (300 MHz, DMSO-*d*$_6$): δ = 1.30-1.68 (m, 4H, 2-H_2, 3-H_2), 1.86-1.98 (m, 1H, 3a-H), 2.06-2.18 (m, 1H, 1-H), 2.28-2.40 (m, 1H, 1-H), 2.63 (dd, *J* = 10.0 Hz, *J* = 11.0 Hz, 1H, 4-H_{ax}), 2.78 (s, 3H, NCH_3), 2.86-3.02 (m, 1H, 9b-H), 2.96 (dd, *J* = 5.0 Hz, *J* = 11.0 Hz, 1H, 4-H_{eq}), 6.60 (dt, *J* = 1.0 Hz, *J* = 7.5 Hz, 1H, 8-H), 6.61 (d, *J* = 7.5 Hz, 1H, 6-H), 6.94-7.06 (m, 2H, 7-H, 9-H). - ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 23.60 (C-3), 29.86 (C-2), 35.89 (C-1), 36.26 (C-3a), 39.59 (NCH_3), 41.09 (C-9b), 54.26 (C-4), 111.45 (C-6), 117.09 (C-8), 126.41 (C-9), 127.84 (C-9a), 129.40 (C-7), 146.83 (C-5a). - MS (70 eV); *m/z* (%): 187 (100) [M^+], 172 (4) [M^+ - CH_3], 158 (12) [M^+ - C_2H_5], 144 (60) [M^+ - C_3H_7], 130 (9) [$C_9H_8N^+$], 115 (6) [$C_9H_7^+$], 91 (6) [$C_6H_5N^+$], 77 (16) [$C_6H_5^+$], 65 (28) [$C_5H_5^+$], 51 (34) [$C_4H_5^+$], 42 (49) [$C_3H_6^+$]. - $C_{13}H_{17}N$ (187.3): calcd. C 83.37, H 9.15, N 7.48; found C 83.18, H 9.15, N 7.34.

(3a*RS*,9b*SR*)-(±)-5-Methyl-3a,4,5,9b-tetrahydro-3H-cyclopenta[c]-quinoline (50). Freshly destilled cyclopentadiene **28** (100 mg, 1.50 mmol) was added to a solution of *N,S*-acetal **35a** (233 mg, 1.02 mmol) and a 2:1-mixture of $TiCl_4$ and triphenylphophine in dichloromethane (5 ml) according to the General Procedure. The reaction mixture was stirred for 48 h at room temp. After work-up column chromatography (diethyl ether/petroleum ether, 1:30) yielded **50** (148.9 mg, 79%) as a greenish oil. - R_f = 0.31 (diethyl ether/petroleum ether, 1:30). - IR (film): ν = 3054 cm^{-1} (C=C-H), 2930, 2844, 2810 (CH), 1600 (C=C-N), 1500 (C=C), 1448 (CH_2), 750, 716, 668 (CH). - UV (acetonitrile): λ_{max} (lg ε) = 210 nm (4.40), 256 (3.96), 302 (3.45). - ^{1}H

NMR (300 MHz, DMSO-d_6): δ = 2.10 (m_c, 1H, 3-H), 2.54-2.80 (m, 2H, 3-H, 3a-H), 2.60 (dd, J = 9.0 Hz, J = 11.0 Hz, 1H, 4-H_{ax}), 2.76 (s, 3H, NCH_3), 2.96 (dd, J = 4.5 Hz, J = 11.0 Hz, 1H, 4-H_{eq}), 3.81 (dq, J = 8.0 Hz, J = 2.5 Hz, 1H, 9b-H), 5.62 (dt, J = 8.0 Hz, J = 2.5 Hz, 1H, 2-H), 5.71-5.84 (m, 1H, 1-H), 6.64 (d, J = 8.0 Hz, 1H, 6-H), 6.66 (dt, J = 1.5 Hz, J = 8.0 Hz, 1H, 8-H), 7.01 (ddt, J = 1.0 Hz, J = 1.5 Hz, J = 8.0 Hz, 1H, 7-H), 7.11 (dd, J = 1.0 Hz, J = 8.0 Hz, 1H, 9-H). - ^{13}C NMR (125.7 MHz, DMSO-d_6): δ = 35.18 (C-3a), 36.99 (C-3), 39.09 (NCH_3), 45.79 (C-9b), 53.56 (C-4), 111.67 (C-6), 117.10 (C-8), 125.55 (C-9a), 126.13 (C-9), 128.18 (C-7), 128.72 (C-1), 135.84 (C-2), 147.71 (C-5a). - MS (70 eV); *m/z* (%): 185 (100) [M^+], 170 (44) [M^+ - CH_3], 144 (54) [M^+ - C_3H_7], 131 (19) [$C_9H_9N^+$], 115 (15) [$C_9H_7^+$], 91 (9) [$C_6H_5N^+$], 77 (11) [$C_6H_5^+$], 51 (6) [$C_4H_5^+$], 42 (9) [$C_3H_6^+$]. - $C_{13}H_{15}N$ (185.3): calcd. C 84.28, H 8.16, N 7.56; found C 84.10, H 8.27, N 7.50.

(4*SR*)-(±)-1-Methyl-4-phenylsulfanyl-1,2,3,4-tetrahydroquinoline (52). The *N,S*-acetal **35a** (229 mg, 1.00 mmol) was dissolved in dichloromethane (5 ml), cooled to 0°C and $BF_3{\cdot}Et_2O$ (280 mg, 2.00 mmol) was added. Freshly destilled ethyl vinyl ether **14** (290 mg, 3.00 mmol) was slowly added and the reaction mixture was stirred at room temp. for 7 h until completion (TLC). The reaction was worked up as stated in the General Procedure. The residue was purified by column chromatography (diethyl ether/petroleum ether, 1:15) to obtain **52** (123.1 mg, 48%) as a yellow oil. - R_f = 0.32 (diethyl ether/petroleum ether, 1:15). - IR (film): ν = 3052 cm^{-1} (C=C-H), 2960, 2914, 2874, 2824 (CH), 1600 (C=C-N), 1500 (C=C), 1478, 1452, 1434, 1326, 1312 (CH_2), 748, 736, 690 (CH). - UV (acetonitrile): λ_{max} (lg ε) = 210 nm (4.47), 260 (4.19), 322 (3.65). - ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.04 (dq, J = 13.5 Hz, J = 4.0 Hz, 1H, 3-H_{eq}), 2.18 (ddt, J = 12.0 Hz, J = 13.5 Hz, J = 4.0 Hz, 1H, 3-H_{ax}), 2.90 (s, 3H, NCH_3), 3.12 (ddt, J = 1.5 Hz, J = 12.0 Hz, J = 4.0 Hz, 1H, 2-H_{eq}), 3.72 (dt, J = 4.0 Hz, J = 12.0 Hz, 1H, 2-H_{ax}), 4.52 (m, 1H, 4-H), 6.56-6.70 (m, 2H, 6-H, 8-H), 7.06-7.52 (m, 7H, 5-H, 7-H, 2'-H, 3'-H, 4'-H, 5'-H, 6'-H). - ^{13}C NMR (20 MHz, $CDCl_3$): δ = 26.92 (C-3), 38.95 (NCH_3), 46.07 (C-4), 46.29 (C-2), 111.35 (C-8), 115.98 (C-6), 119.96 (C-4a), 127.06 (C-5), 128.77 (C-7), 128.96 (C-2', C-6'), 130.57 (C-4'), 132.06 (C-3', C-5'), 135.37 (C-1'), 146.47 (C-8a). - MS (70 eV); *m/z* (%): 255 (41) [M^+], 147 (69) [M^+ - C_6H_6S], 146 (100) [M^+ - C_6H_5S], 131 (73) [$C_9H_8S^+$], 130 (57) [$C_9H_8N^+$], 109 (10) [$C_6H_5S^+$], 91 (13) [$C_6H_5N^+$], 77 (17) [$C_6H_5^+$], 65 (9) [$C_5H_5^+$], 51 (6) [$C_4H_5^+$]. - $C_{16}H_{17}NS$ (255.4): calcd. C 75.25, H 6.71, N 5.48, S 12.56; found C 75.14, H 6.87, N 5.51, S 12.62.

(4*SR*)-(±)-1,4-Dimethyl-4-phenylsulfanyl-1,2,3,4-tetrahydrochinoline (55). The *N,S*-acetal **35a** (226 mg, 0.99 mmol) and **54** (195 mg, 1.5o mmol) were reacted in the presence of a 2:1-mixture of $TiCl_4$ and triphenylphosphine (2.00 equiv.) as the Lewis acid in accordance with the General Procedure. The reaction mixture was stirred for 24 h and worked up as stated in the General Procedure. After column chromatography (diethyl ether, petroleum ether, 1:30) **55** (104.9 mg, 40%) was obtained as a yellow oil. - R_f = 0.26 (diethyl ether/petroleum ether, 1:30). - IR (film): ν = 3060 cm^{-1}, 3032 (C=C-H), 2958, 2922, 2864 (CH), 1602 (C=C-N), 1502 (C=C), 1330 (CH_3), 746, 694 (CH). - UV (acetonitrile): λ_{max} (lg ε) = 221 nm (4.37), 260 (4.03), 322 (3.51). - ^{1}H NMR (200 MHz, DMSO-d_6): δ = 1.55 (s, 3H, 4-CH_3), 1.80-2.00 (m, 2H, 3-H_2), 2.84 (s, 3H, NCH_3), 2.84-3.06 (m, 1H, 2-H), 3.06-3.24 (m, 1H, 2-H), 6.46-6.62 (m, 2H, 6-H, 8-H),

6.92-7.30 (m, 2H, 5-H, 7-H), 7.30-7.44 (m, 5H, 2'-H, 3'-H, 4'-H, 5'-H, 6'-H). - ^{13}C NMR (20 MHz, DMSO-d_6): δ = 29.75 (4-CH_3), 34.47 (C-3), 38.76 (NCH_3), 46.76 (C-2), 49.33 (C-4), 111.12 (C-8), 115.29 (C-6), 124.96 (C-4a), 127.28 (C-5), 128.08 (C-4')*, 128.57 (C-2', C-6'), 128.77 (C-7)*, 132.10 (C-1'), 136.55 (C-3', C-5'), 145.66 (C-8a). - MS (70 eV); *m/z* (%): 269 (22) [M^+], 160 (100) [M^+ - C_6H_6S], 144 (41) [M^+ - C_7H_9S], 118 (15) [M^+ - $C_4H_{11}N$], 91 (6) [$C_6H_5N_+$], 77 (6) [$C_6H_5^+$], 65 (12) [$C_5H_5^+$], 51 (4) [$C_4H_5^+$]. - $C_{17}H_{19}NS$ (269.4): calcd. C 75.79, H 7.11, N 5.20, S 11.90; found C 75.69, H 7.25, N 5.17, S 11.94.

(4*SR*)-(±)-1-Methyl-4-ethylsulfanyl-1,2,3,4-tetrahydroquinoline (58). The *N,S*-acetal **35b** (185 mg, 1.00 mmol) and freshly destilled *n*-butyl vinyl ether **53** (150 mg, 1.50 mmol) were allowed to react in dichloromethane (5 ml) in the presence of a 2:1-mixture of $TiCl_4$ and triphenylphosphine (2.00 equiv.) according to the General Procedure for 2 h. Work-up was performed in accordance with the General Procedure and the crude material was purified by column chromatography on silica gel (diethyl ether/petroleum ether, 1:30) to yield **58** (84.1 mg, 40%) as a colorless oil. - R_f = 0.32 (diethyl ether/petroleum ether, 1:30). - IR (film): ν = 3060 cm^{-1}, 3024 (C=C-H), 2958, 2922, 2868, 2826 (CH), 1604 (C=C-N), 1504 (C=C), 1452, 1436 (CH_2), 746 (CH). - UV (acetonitrile): λ_{max} (lg ε) = 261 nm (3.92), 316 (3.36). - ^{1}H NMR (200 MHz, DMSO-d_6): δ = 1.22 (t, *J* = 7.0 Hz, 3H, $SCH_2C\underline{H}_3$), 1.93-2.20 (m, 2H, 3-H_2), 2.50-2.65 (m, 2H, $SC\underline{H}_2CH_3$), 2.84 (s, 3H, NCH_3), 3.16 (dt, *J* = 11.5 Hz, *J* = 4.0 Hz, 1H, 2-H_{eq}), 3.48 (dt, *J* = 4.0 Hz, *J* = 11.5 Hz, 1H, 2-H_{ax}), 4.10 (t, *J* = 4.0 Hz, 1H, 4-H), 6.46-6.61 (m, 2H, 6-H, 8-H), 6.95-7.08 (m, 2H, 5-H, 7-H). - ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 14.58 ($SCH_2\underline{C}H_3$), 24.11 ($S\underline{C}H_2CH_3$), 26.73 (C-3), 38.42 (NCH_3), 40.85 (C-4), 45.82 (C-2), 110.91 (C-8), 115.15 (C-6), 121.24 (C-4a), 127.95 (C-5), 129.77 (C-7), 146.83 (C-8a). - MS (70 eV); *m/z* (%): 207 (19) [M^+], 146 (100) [M^+ - C_2H_5S], 131 (13) [M^+ - C_3H_8S], 130 (12) [$C_9H_8S^+$], 130 (12) [$C_9H_8N^+$], 91 (4) [$C_6H_5N^+$], 77 (5) [$C_6H_5^+$], 55 (2) [$C_4H_7^+$]. - $C_{12}H_{17}NS$: calcd. 207.1081; found 207.1081 (MS).

(3*RS*,4*RS*)-(±)-*trans*-1,3-Dimethyl-4-phenyl-1,2,3,4-tetrahydroquinoline (60). (*E*)-Methylstyrene *(E)*-**59** (180 mg, 1.50 mmol) was added to a solution of *N,S*-acetal **35a** (234 mg, 1.02 mmol) and a 2:1-mixture of $TiCl_4$ and triphenylphosphine in dichloromethane according to the General Procedure. The reaction mixture was stirred for 72 h at room temp. Work-up was performed in accordance with the General Procedure and column chromatography (diethyl ether/petroleum ether, 1:30) yielded **60** (181.3 mg, 75%) as a white solid, m.p. 82°C. The diastereomeric ratio *rac*-**60**/*rac*-**61** was determined by analytical HPLC {t_R (*rac*-**60**) = 7.60 min, t_R (*rac*-**61**) = 9.74 min (*rac*-**60** / *rac*-**61** > 99 : 1) [*Merck* LiChrospher® 60 RP - select B (5µm); acetonitrile/phosphate buffer (pH 2.13), 62 : 38]} and NMR spectroscopy. - R_f = 0.32 (diethyl ether/petroleum ether, 1:30). - IR (KBr): ν = 3058 cm^{-1}, 3032 (C=C-H), 2968, 2952, 2894, 2866 (CH), 1598 (C=C-N), 1502 (C=C), 1450 (CH_3), 1428 (CH_2), 766, 744, 690 (CH). - UV (acetonitrile): λ_{max} (lg ε) = 213 nm (4.45), 261 (3.99), 309 (3.46). - ^{1}H NMR (300 MHz, DMSO-d_6): δ = 0.83 (d, *J* = 4.0 Hz, 3H, 3-CH_{3eq}), 2.13 (m, 1H, 3-H_{ax}), 2.86 (s, 3H, NCH_3), 2.94 (dd, *J* = 8.5 Hz, *J* = 11.0 Hz, 1H, 2-H_{ax}), 3.18 (dd, *J* = 4.0 Hz, *J* = 11.0 Hz, 1H, 2-H_{eq}), 3.64 (d, *J* = 8.5 Hz, 4-H_{ax}), 6.40-6.46 (m, 2H, 6-H, 7-H), 6.64 (d, *J* = 8.0 Hz, 1H, 8-H), 6.94-7.32 (m, 6H, 5-H, 2'-H, 3'-H, 4'-H, 5'-H, 6'-H). - ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 18.12 (3-CH_3), 34.95

(C-3), 39.38 (NCH_3), 51.77 (C-4), 56.69 (C-2), 110.74 (C-8), 116.37 (C-6), 125.38 (C-4a), 126.14 (C-5), 127.18 (C-4'), 128.22 (C-2', C-6'), 129.16 (C-3', C-5'), 130.26 (C-7), 145.68 (C-1'), 146.55 (C-8a). - MS (70 eV); *m/z* (%): 237 (100) [M^+], 222 (16) [M^+ - CH_3], 194 (16) [M^+ - C_2H_4], 179 (9) [M^+ - C_3H_8N], 158 (19) [M^+ - C_5H_5N], 144 (63) [M^+ - C_6H_7N], 115 (12) [$C_9H_7^+$], 91 (27) [$C_6H_5N^+$], 77 (14) [$C_6H_5^+$], 51 (7) [$C_4H_3^+$]. - $C_{17}H_{19}N$ (237.3): calcd. C 86.03, H 8.07, N 5.90; found C 85.89, H 8.06, N 5.81.

(**3*RS*,4*SR*)-(±)-*cis*-1,3-Dimethyl-4-phenyl-1,2,3,4-tetrahydroquinoline (61).** The *N,S*-acetal **35a** (492 mg, 2.15 mmol) and (*Z*)-methylstyrene *(Z)*-**59** (470 mg, 4.00 mmol) were allowed to react in dichloromethane (5 ml) in accordance with the General Procedure for 72 h at room temp. Work-up was performed in accordance with the General Procedure and the crude material was purified by column chromatography (diethyl ether/petroleum ether, 1:100) to yield **61** (341.3 mg, 67%) as a white solid, m.p. 82°C. The diastereomeric ratio *rac*-**60**/*rac*-**61** was determined by analytical HPLC {t_R (*rac*-**60**) = 7.60 min, t_R (*rac*-**61**) = 9.74 min (*rac*-**60** / *rac*-**61**< 1 : 99) [*Merck* LiChrospher® 60 RP - select B (5µm); acetonitrile/phosphate buffer (pH 2.13), 62 : 38]} and NMR spectroscopy. - R_f = 0.32 (diethyl ether/petroleum ether, 1:30). - IR (KBr): ν = 3058 cm^{-1}, 3028 (C=C-H), 2952, 2920, 2884 (CH), 1602 (C=C-N), 1506 (C=C), 1450 (CH_3), 1430 (CH_2), 748, 700 (CH). - UV (acetonitrile): λ_{max} (lg ε) = 211 nm (4.46), 260 (3.96), 311 (3.52). - ^{1}H NMR (200 MHz, DMSO-d_6): δ = 0.70 (d, *J* = 7.0 Hz, 3H, 3-CH_{3ax}), 2.26 (m, 1H, 3-H_{eq}), 2.92 (d, *J* = 11.0 Hz, 1H, 2-H_{eq}), 2.93 (s, 3H, NCH_3), 3.03 (ddd, *J* = 1.5 Hz, *J* = 4.5 Hz, *J* = 11.0 Hz, 1H, 2-H_{ax}), 3.98 (d, *J* = 5.0 Hz, 1H, 4-H_{ax}), 6.47 (dt, *J* = 1.0 Hz, *J* = 7.5 Hz, 1H, 6-H), 6.67 (dd, *J* = 1.0 Hz, *J* = 8.0 Hz, 1H, 8-H), 6.74 (dd, *J* = 2.0 Hz, *J* = 7.5 Hz, 1H, 5-H), 6.95-7.29 (m, 6H, 7-H, 2'-H, 3'-H, 4'-H, 5'-H, 6'-H). - ^{13}C NMR (50.3 MHz, DMSO-d_6): δ = 16.04 (3-CH_3), 30.41 (C-3), 38.25 (NCH_3), 47.92 (C-4), 52.49 (C-2), 110.37 (C-8), 115.36 (C-6), 124.53 (C-4a), 125.75 (C-5), 127.30 (C-4'), 127.40 (C-2', C-6'), 129.48 (C-7), 129.52 (C-3', C-5'), 142.73 (C-1'), 145.52 (C-8a). - MS (70 eV); *m/z* (%): 237 (100) [M^+], 222 (13) [M^+ - CH_3], 194 (18) [M^+ - C_2H_4], 179 (9) [M^+ - C_3H_8N], 158 (19) [M^+ - C_5H_5N], 144 (59) [M^+ - C_6H_7N], 115 (12) [$C_9H_7^+$], 91 (31) [$C_6H_5N^+$], 77 (16) [$C_6H_5^+$], 51 (9) [$C_4H_3^+$]. - $C_{17}H_{19}N$ (237.3): calcd. C 86.03, H 8.07, N 5.90; found C 85.73, H 8.14, N 5.78.

Isomerization experiments with *rac*-60 and *rac*-61. 47.4 mg (0.2 mmol) *rac*-**60**, *rac*-**61** or 1.6 : 98.4 - mixture of *rac*-**60**/*rac*-**61** were dissolved in 1 ml dry dichloromethane and cooled to 0°C. A 1 *M* solution of $TiCl_4$: triphenylphosphin = 2 : 1 (2.0 Equiv.) was added and the reaction mixture was stirred for 5 days at room temp. The reaction was quenched by addition of 5 ml saturated Na_2CO_3 solution. After extraction with dichloromethane (2 × 15 ml) the combined organic layers were dried (Na_2SO_4). The solvent was removed in vacuo and the residue was purified by column chromatography on 5 g silica gel (diethyl ether / petroleum ether, 1 : 30). The diastereomeric ratio *rac*-**60**/*rac*-**61** was determined by analytical HPLC {t_R (*rac*-**60**) = 7.60 min, t_R (*rac*-**61**) = 9.74 min [*Merck* LiChrospher® 60 RP - select B (5µm); acetonitrile/phosphate buffer (pH 2.13), 62 : 38].

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