CHEMISTRY
A EUROPEAN JOURNAL

DOI: 10.1002/chem.200900718

1-Phenyl-1,2-cyclohexadiene: Astoundingly High Enantioselectivities on Generation in a Doering–Moore–Skattebøl Reaction and Interception by Activated Olefins**

Manfred Christl,* Hartmut Fischer, Mario Arnone, and Bernd Engels*[a]

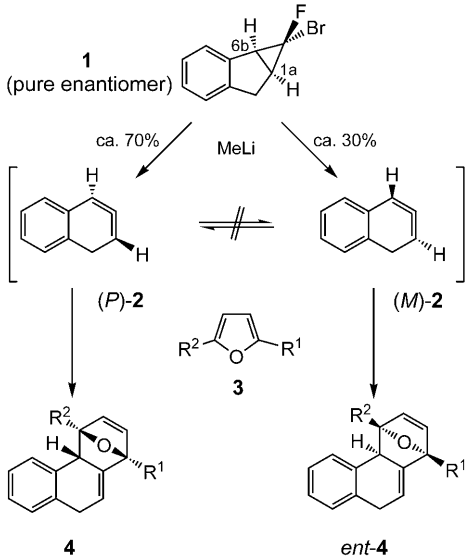
Dedicated to Professor Helmut Quast on the occasion of his 75th birthday

Abstract: The resolution of (1α,5α,6α)-6-bromo-6-fluoro-1-phenylbicyclo-[3.1.0]hexane (*rac*-**5**) provided the enantiomerically pure precursors (−)-**5** and (+)-**5** of 1-phenyl-1,2-cyclohexadiene. On treatment of (−)-**5** with methyllithium in the presence of 2,5-dimethylfuran, the pure (−)-enantiomer of the [4+2] cycloadduct of 2,5-dimethylfuran onto 1-phenyl-1,2-cyclohexadiene was obtained exclusively. From this result, it is concluded that pure (*M*)-1-phenyl-1,2-cyclohexadiene ((*M*)-**7**) emerged from (−)-**5** and was enantiospecifically intercepted to give the product. In the case of indene as trap for (*M*)-**7**, the (−)- and the (+)-enantiomer of the [2+2] cycloadduct were formed in the ratio of 95:5. Highly surprising, remarkable enantioselectivities were also observed, when (*M*)-**7** was trapped with styrene to furnish two diastereomeric [2+2] cycloadducts. Hence, the achiral conformation of the diradical conceivable as intermediate cannot play a decisive part. The enantioselective generation of (*M*)- and (*P*)-**7** by the β-elimination route was tested as well. Accordingly, 1-bromo-2-phenylcyclohexene was exposed to the potassium salt of (−)-menthol in the presence of 2,5-dimethylfuran, and the enantiomeric [4+2] cycloadducts of the latter onto (*M*)- and (*P*)-**7** were produced in the ratio of 55:45.

Keywords: asymmetric induction · cyclic allenes · cycloaddition · diradicals · enantioselectivity

Introduction

The steric course of the generation of a cyclic allene and its interception by an activated olefin raise highly interesting questions as to the mechanisms involved therein. In a first attempt to give answers, we recently generated the isonaphthalenes (*P*)-**2** and its enantiomer (*M*)-**2** from the enantiomerically pure isolatable bromofluorcarbene adducts of indene, for example, **1**, in Doering–Moore–Skattebøl reactions in the presence of 2,5-disubstituted furans (**3**) and obtained the [4+2] cycloadducts **4** and their enantiomers *ent*-**4**



Scheme 1. Generation of the isonaphthalenes (*P*)- and (*M*)-**2** from the pure precursor enantiomer **1** and interception of **2** by 2,5-disubstituted furans **3**, which gives rise to the [4+2] cycloadducts **4** and *ent*-**4** in the ratio of approximately 70:30.

[a] Prof. Dr. M. Christl, Dr. H. Fischer, Dr. M. Arnone, Prof. Dr. B. Engels
Institut für Organische Chemie
Universität Würzburg
Am Hubland, 79074 Würzburg (Germany)
Fax: (+49) 931-8884606
E-mail: christl@chemie.uni-wuerzburg.de
engels@chemie.uni-wuerzburg.de

[**] Cycloallenes, Part 22. For Part 21, see reference [5], preceding paper in this issue.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.200900718.

in a ratio of about 70:30 (Scheme 1).[1] The results of carefully designed experiments led to the conclusion that (*P*)- and (*M*)-**2** emerge from **1** in a ratio of about 70:30 and, without enantiomerisation, enantiospecifically add onto **3**. This was unexpected, since the barrier to enantiomerisation of **2** had been estimated by quantum chemical methods to be only 11 kcal mol^{-1},[2,3] which is why the reaction of **2** with **3** must be very fast.

To test the model of the stereochemical course proposed on the basis of the results with **2**, we performed a study with a 1-substituted 1,2-cyclohexadiene. For such a case, a higher retention of the stereochemical information of an enantiomerically pure precursor was anticipated than with **2**.[1] We chose 1-phenyl-1,2-cyclohexadiene ((*M*)- and (*P*)-**7**), for which the barrier to enantiomerisation is expected to be close to that of **2**, since the phenyl group should have a similar effect on the allyl-diradical structure of the transition state as the benzo group of **2**. After all, a chiral ground state of **7** is supported by the result of an AM1 calculation.[4] The racemic intermediate (*rac*-**7**) was examined by two groups in addition to the Würzburg team previously. The results are comprehensively reported in the preceding paper.[5]

Results and Discussion

Generation of the cyclic allenes (*M*)- and (*P*)-7 from the pure enantiomers 5 and *ent*-5 and trapping of the intermediates 7: As shown in the preceding paper,[5] the bromofluorocarbene adduct *rac*-**5** of 1-phenylcyclopentene is a useful precursor of *rac*-**7** with regard to the Doering–Moore–Skattebøl reaction. For the enantioselective generation of (*M*)- and (*P*)-**7**, *rac*-**5** had to be separated into the pure enantiomers **5** and *ent*-**5**. Indeed, the resolution of *rac*-**5** was achieved by HPLC using a Chiralcel OJ-H column. To determine the absolute configuration, we compared the experimental CD spectra with the calculated ones, which were obtained by the quantum chemical procedure described at the end of the Experimental Section. Such a comparison is illustrated by Figure 1, which proves that the (−)-enantiomer has the 1*R*,5*S*,6*R* configuration (**5**).

We used **5** as well as its enantiomer (*ent*-**5**) for the liberation of the cyclic allene **7**, which was trapped by 2,5-dimethylfuran, indene and styrene. The results for the case of **5** are collected in Scheme 2. The formulas represent absolute configurations. As with **5** and *ent*-**5**, those of the products (**6**, **8**–**10**) were established by resolution of the racemic products[5] by HPLC using Chiralcel columns and comparison of the experimental with the calculated CD spectra (see the end of the Experimental Section). Figures 2, 3, 4 and 5 display these comparisons. The analysis of the products as to their enantiomeric ratios was carried out by HPLC using a Chiralcel OJ-H column.

As is evident from Scheme 2, the treatment of **5** with methyllithium in the presence of 2,5-dimethylfuran furnished the pure [4+2] cycloadduct **6** of the intermediate cyclic allene in 31 % yield. Since no *ent*-**6** could be detected,

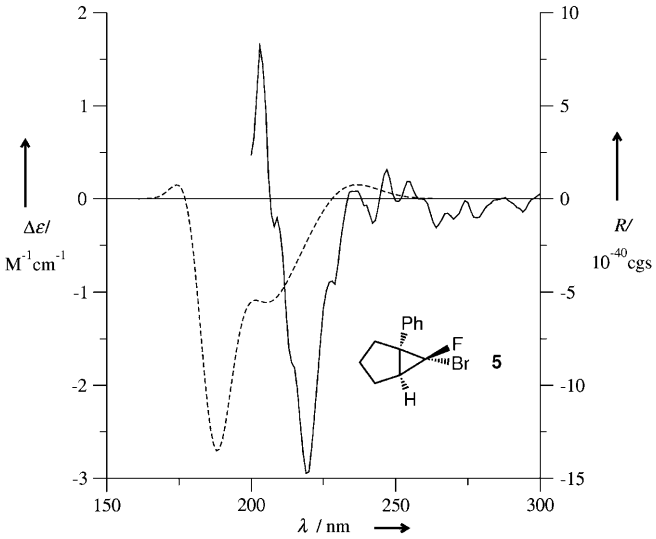
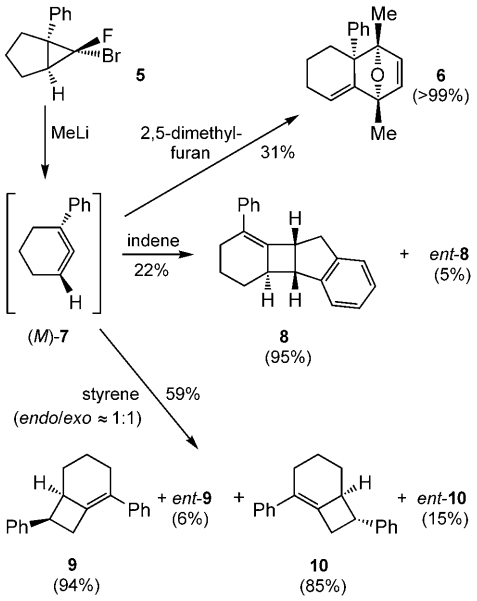


Figure 1. Comparison of the experimental (——) and calculated (B3LYP; -----) CD spectra of **5**, which is thus proved to be the (−)-enantiomer.



Scheme 2. The reaction of the pure enantiomer **5** with methyllithium most probably led to the pure *M* enantiomer of 1-phenyl-1,2-cyclohexadiene ((*M*)-**7**), which was trapped by 2,5-dimethylfuran, indene and styrene to give pure **6**, **8** and *ent*-**8** in the ratio of 95:5, **9** and *ent*-**9** in the ratio of 94:6, and **10** and *ent*-**10** in the ratio of 85:15, respectively.

the stereochemical information of **5** was completely transferred to the product, which is why the intermediate must have been also a pure enantiomer, and we propose that this was (*M*)-**7** in the next subsection. Indene as a trap afforded a 22 % yield of the [2+2] cycloadduct enantiomers **8** and *ent*-**8** in the ratio of 95:5. In the case of styrene, a mixture of the two possible diastereomeric [2+2] cycloadducts in the ratio of 53:47 was obtained in 59 % yield. The *endo* diastereomer consisted of the enantiomers **9** and *ent*-**9** in the ratio of 94:6, whereas the *exo* diastereomer comprised the enan-

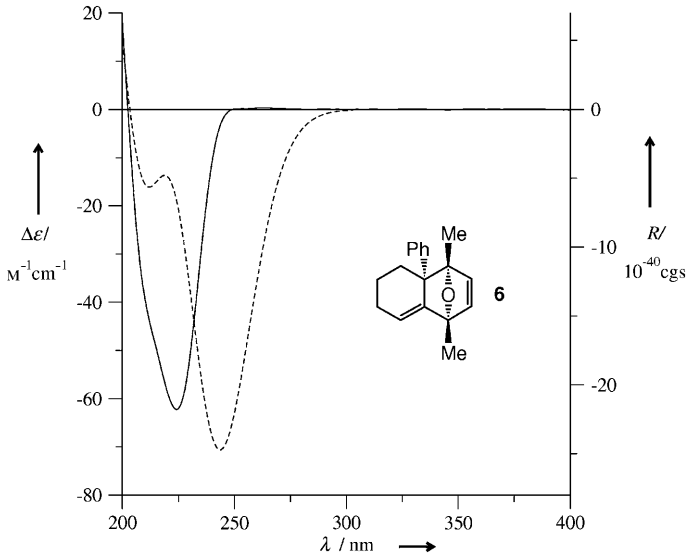


Figure 2. Comparison of the experimental (——) and calculated (B3LYP; -----) CD spectra of **6**, which is thus proved to be the (−)-enantiomer.

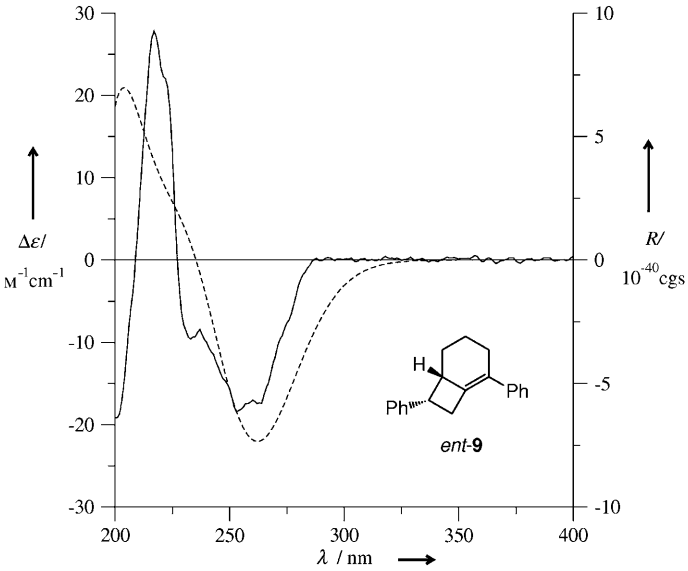


Figure 4. Comparison of the experimental (——) and calculated (B3LYP; -----) CD spectra of *ent*-**9**, which is thus proved to be the (−)-enantiomer.

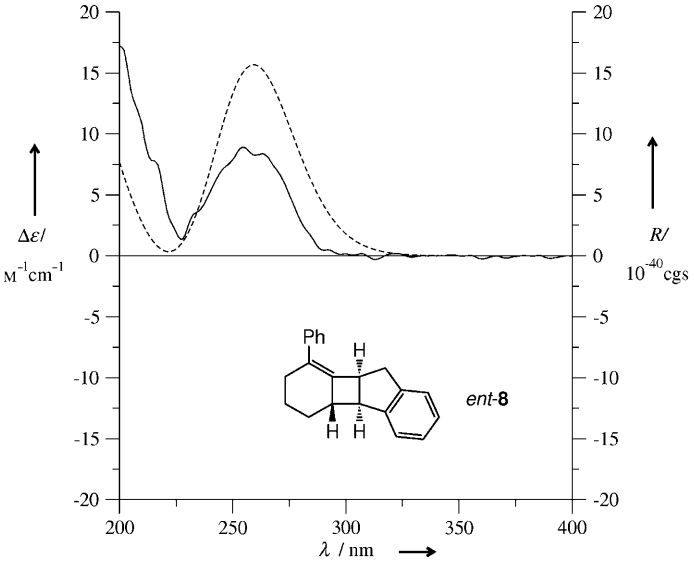


Figure 3. Comparison of the experimental (——) and calculated (B3LYP; -----) CD spectra of *ent*-**8**, which is thus proved to be the (+)-enantiomer.

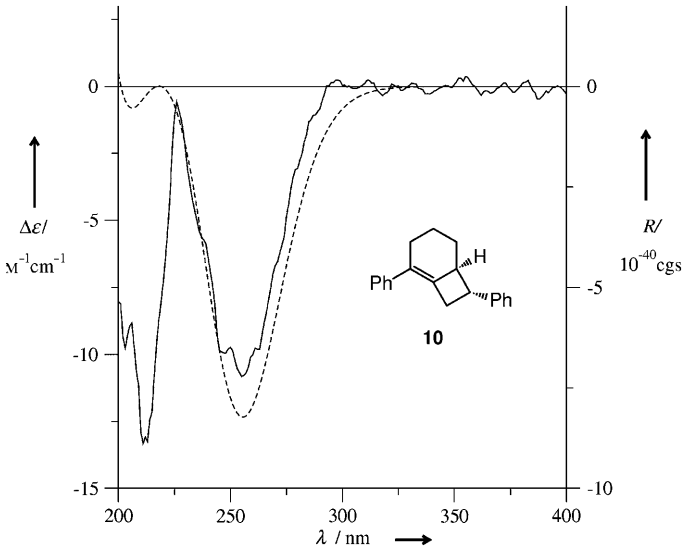


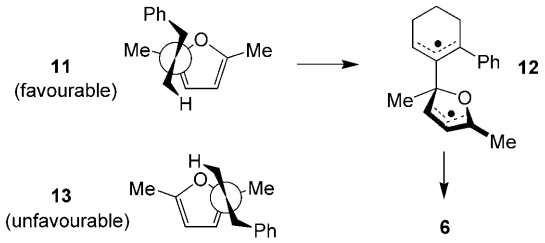
Figure 5. Comparison of the experimental (——) and calculated (B3LYP; -----) CD spectra of **10**, which is thus proved to be the (+)-enantiomer.

tiomers **10** and *ent*-**10** in the ratio of 85:15. The HPLC trace is depicted in Figure 6 (see the Experimental Section) and provided the precise ratio of **9**/*ent*-**9**/**10**/*ent*-**10** to be 50:3:40:7.

The stereochemical courses of the Doering–Moore–Skattebøl reaction of 5 and the cycloadditions of (*M*)-7: The finding that only one enantiomer of the [4+2] cycloadduct of 2,5-dimethylfuran onto the intermediate cyclic allene, namely, **6**, emerged from the pure enantiomer **5** demands the stereospecific conversion of **5** into the intermediate. The question is only whether (*M*)- or (*P*)-**7** results from **5**. On generation of the isonaphthalenes **2** from **1** (Scheme 1), one of the two bridgehead hydrogen atoms, H1a or H6b, has to change sides of the ring system, that is, H6b en route to (*M*)-**2** and H1a en route to (*P*)-**2**. Since on that move H6b experiences a stronger steric hindrance by the neighbouring aromatic CH group than H1a by a hydrogen atom of the CH_2 group, we suggested the preferential formation of (*P*)-**2** (ca. 70 %).[1] The application of this reasoning to the reaction **5**→**7** leads to an unambiguous conclusion, as this process requires the change of the ring sides either from the bridgehead hydrogen atom or the phenyl group. Owing to its size, the phenyl group should encounter a much larger restraint of its move by the proximal CH_2 group than the bridgehead hydrogen atom. Therefore we propose the exclu-

sive liberation of (*M*)-**7** from **5**. As we had anticipated,[1] the stereoselectivity of the generation of a cyclic allene is impressively improved by a phenyl group at one bridgehead position of a substrate for the Doering–Moore–Skattebøl reaction.

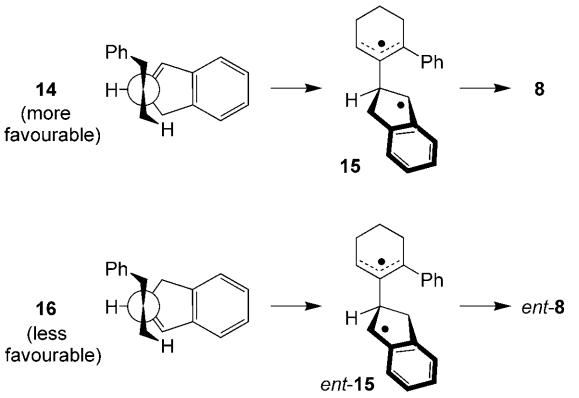
Given this assignment and the fact that (*M*)-**7** does not at all undergo the inversion to (*P*)-**7** under the reaction conditions, it has to be rationalised why (*M*)-**7** adds onto 2,5-dimethylfuran to give **6** exclusively. Quantum chemical calculations[6] as well as the experimental result of the addition of (*Z,Z*)-1,4-dideuterio-1,3-butadiene onto 1,2-cyclohexadiene[3] support a two-step mechanism through diradical intermediates even for the [4+2] cycloadditions of six-membered cyclic allenes. Scheme 3 shows the diastereomeric



Scheme 3. Possible transition states (**11**, **13**) for the addition of the central allene carbon atom of (*M*)-**7** to both enantiotropic faces of the CMe group of 2,5-dimethylfuran. Only **11** leads to diradical **12**, which should be the intermediate en route to **6**. In **11** and **13**, the cyclic allene (*M*)-**7** is represented by the PhC=C=CH subunit only and approaches the furan from above the drawing plane.

transition states **11** and **13** for the formation of the diradicals by addition of the central allene carbon atom of (*M*)-**7** to both enantiotopic faces of a CMe group of 2,5-dimethylfuran (*Re*: **11**; *Si*: **13**). Only **11** can give rise to the diradical **12**, which is the precursor of **6**, whereas **13** would produce the enantiomer of **12** (*ent*-**12**) and in consequence the enantiomer of **6** (*ent*-**6**). The phenyl group, which requires a great deal of space, is located as far away as possible from the core of the allenophile in both transition states. The crucial difference between them has to be seen in the proximity of the phenyl group to the oxygen atom in **11** and to a CH group in **13**. As the spatial demand of an oxygen atom is substantially smaller than that of a CH group, **11** is preferred over **13** to the extent that **13** has no importance at all.

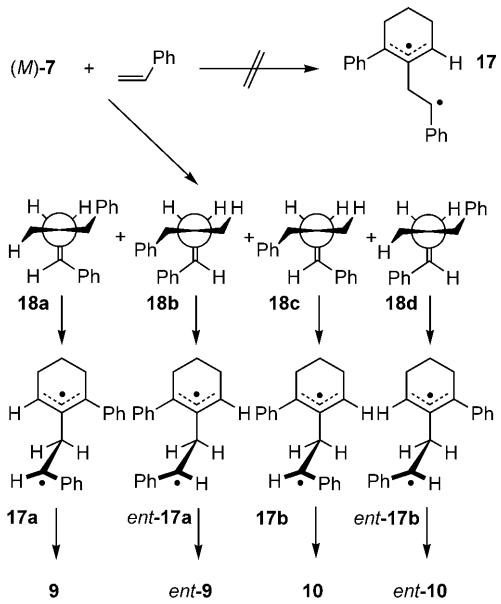
Such an exclusiveness does not hold for the cycloaddition of indene, in which the enantiomeric [2+2] cycloadducts **8** and *ent*-**8** resulted in the ratio of 95:5. Assuming that the generation of pure (*M*)-**7** from **5** also occurs, we have to take into account the transition states **14** and **16**, from which the major product **8** and the minor one *ent*-**8** emerge through the diradicals **15** and *ent*-**15**, respectively. Exhibiting the common feature that the phenyl group as the only big substituent is located as far away as possible from the core of indene, **14** and **16** differ in the arrangement of the five-membered ring relative to the phenyl group as the latter is next to the 3-CH group in **14** and to the CH_2 group in **16**. Apparently, the subtle deviation in the size of these two groups causes the preference of the attack of (*M*)-**7** at the *Re* face of indene (**14**) over that at the *Si* face (**16**) by a factor of 19 (Scheme 4).



Scheme 4. Transition states (**14**, **16**) for the addition of the central allene carbon atom of (*M*)-**7** to both enantiotopic faces of indene. The major product **8** should be formed through **14** and the diradical **15**, the minor product *ent*-**8** through **16** and *ent*-**15**. In **14** and **16**, (*M*)-**7** is represented by the PhC=C=CH subunit only and approaches indene from above the drawing plane.

Previously, we had examined the addition of indene to the isonaphthalenes **2** by using the pure enantiomer **1** as allene precursor (Scheme 1) and found only very little transfer of the stereochemical information carried by **1** to the product.[1] Possibly, (*M*)- and (*P*)-**2** are unable to clearly distinguish between the *Re* and the *Si* face of indene because of two hydrogen atoms at the allene termini. Clearly, the phenyl group of (*M*)- and (*P*)-**7** makes the difference.

Even assuming that the reaction of **5** with methyllithium in the presence of styrene liberated pure (*M*)-**7**, we were highly surprised about the relatively high enantiomeric ratios of 94:6 and 85:15 for the [2+2] cycloadducts **9**/*ent*-**9** and **10**/*ent*-**10**, respectively. Based on previous studies,[7] we had anticipated a diradical intermediate with the achiral conformation **17** (Scheme 5) for the addition of (*M*)- or (*P*)-**7** onto styrene and hence the complete loss of the stereochemical information introduced by **5**. However, the mechanism of the styrene addition onto six-membered cyclic allenes had already proven to be interesting earlier, since on use of (*Z*)-β-deuteriostyrene the stereochemical information is entirely lost in the trapping of 1,2-cyclohexadiene,[3,7,8] but partially retained in the case of 1-oxa-2,3-cyclohexadiene[3] and completely retained with a 1-thia-5-aza-2,3-cyclohexadiene derivative.[3,9] Based on their result, Elliott et al.[9] suggested the cycloaddition to be concerted and supported their view by quantum chemical calculations of a model system. A one-step course was also proposed for several [2+2] cycloadditions of 1-oxa-2,3-cyclohexadiene.[10] Probably, conclusive insight into the mechanisms will be provided only by quantum chemical calculations, which can treat equally well closed-shell transition states on one side and



Scheme 5. Possible transition states (**18a–d**) and intermediates (**17a**,**b** and *ent*-**17a**,**b**) for the addition of the central allene carbon atom of (*M*)-**7** to the methylene group of styrene. In **18a–d**, (*M*)-**7** is represented by the PhC=C=CH subunit only and approaches styrene from above the drawing plane.

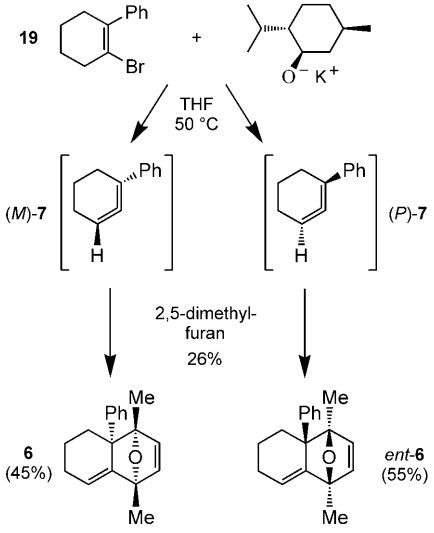
diradical intermediates on the other. Since even [4+2] cycloadditions of 1,2-cyclohexadiene are considered to proceed stepwise through diradicals,[3,6] we adhere to a general two-step course of the styrene additions onto cyclic allenes all the more, as the postulated diradical intermediates are perfectly stabilised by resonance. Thus, instead of **17**, its chiral conformers **17a**, *ent*-**17a**, **17b** and *ent*-**17b** (Scheme 5) should be intermediates en route from (*M*)-**7** to the products. Apparently, these conformers have to cyclise faster than they equilibrate. This conclusion can be drawn even from the finding that **9**+*ent*-**9** and **10**+*ent*-**10** are formed in a ratio of close to 1:1, although the equilibrium ratio is 1:10 or even smaller.[5]

As illustrated by Scheme 5, the four transition states **18a–d** are conceivable for the attack of the central allene carbon atom of (*M*)-**7** at the methylene group of styrene. Because of the mutual proximity of the two phenyl groups, **18b** should be the least favourable transition state. This is the most probable reason why *ent*-**9**, the product emerging from **18b** through the diradical *ent*-**17a**, resulted as the least abundant stereoisomer. On the other hand, **18a** and **18c** suffer from only one 1,3- and 1,4-interaction, respectively, between a phenyl group and a hydrogen atom. This would explain why **9** and **10** arise as major stereoisomers with **17a** and **17b**, respectively, being the intermediate diradicals. In **18d**, steric overcrowding due to both a 1,3- and a 1,4-interaction between a phenyl group and a hydrogen atom leads to a considerable strain energy; this accounts for the small quantity of *ent*-**10** observed, which should originate from **18d** through *ent*-**17b**. A possible alternative rationalisation for the small amounts of *ent*-**9** and *ent*-**10** is that only the energetically favourable transition states **18a** and **18c** are passed and that the resulting diradicals **17a** and **17b** undergo a conformational change to give *ent*-**17b** and *ent*-**17a** to a minor extent. The low barriers to the collapse of **17a**,**b** and *ent*-**17a**,**b** are reminiscent of the behaviour of the diradicals generated on thermolysis of 3-vinylmethylenecyclobutanes and converted into 4-methylenecyclohexenes without complete equilibration.[11]

Generation of cyclic allenes (*M*)- and (*P*)-7 from 1-bromo-2-phenylcyclohexene (19) by enantiomerically pure potassium menthoxide and trapping of the intermediates: In 1981, Balci and Jones[12] treated 3-bromobicyclo[3.2.1]octa-2,6-diene, 1-bromocyclohexene and 1-bromocycloheptene with enantiomerically pure potassium menthoxide in the presence of 1,3-diphenylisobenzofuran, which intercepted the cyclic allene intermediates bicyclo[3.2.1]octa-2,3,6-triene, 1,2-cyclohexadiene and 1,2-cycloheptadiene in [4+2] cycloadditions. Since the products were optically active, the chirality of the intermediates was thus demonstrated, although the specific rotations were tiny ($[\alpha]_D^{25} \leq 1.9$). An analysis of the ratio of the product enantiomers was not carried out and would have been very difficult at that time.

Because we now had available the analytical means, we quantitatively tested the capability of enantiomerically pure potassium menthoxide for asymmetric induction in the β elimination en route to 1-phenyl-1,2-cyclohexadiene (**7**). Accordingly, we exposed 1-bromo-2-phenylcyclohexene (**19**) to the potassium salt of (−)-menthol in the presence of 2,5-dimethylfuran. Previously, we had obtained the racemic [4+2] cycloadduct *rac*-**6** of *rac*-**7** with this furan on treatment of **19** with potassium *tert*-butoxide in 9% yield.[5] The chiral and enantiomerically pure base now brought about a 26% yield of **6** and *ent*-**6**, the ratio of which was determined from the specific rotation ($[\alpha]_D^{22} = +34$) to be 45:55 (Scheme 6).

Although the temperature of this experiment was higher by 80 °C than in the above reaction of **5** with methyllithium



Scheme 6. Reaction of 1-bromo-2-phenylcyclohexene (**19**) with the potassium salt of (−)-menthol in the presence of 2,5-dimethylfuran.

in the presence of 2,5-dimethylfuran with formation of pure **6**, we believe that the equilibration of (*M*)- and (*P*)-**7** did not proceed here, either. Given this prerequisite, the asymmetric induction of the enantiomerically pure potassium menthoxide is low, that is, the base recognised only a very small difference between the enantiotopic protons of the 6-methylene group of **19**. However, we predict that other chiral bases may be much more effective in this distinction.

Conclusion

With 1-phenyl-1,2-cyclohexadiene ((*M*)- and (*P*)-**7**) as an example, we have demonstrated that 1-substituted 1,2-cyclohexadienes can be generated with a high enantioselectivity from enantiomerically pure precursors in Doering–Moore–Skattebøl reactions and intercepted by activated olefins in [4+2] and [2+2] cycloadditions with complete or substantial retention of the stereochemical information introduced by the precursors. The mechanistic details proposed for the formation and the trapping of (*M*)- and (*P*)-**7** are a challenge for computational chemists and, if verified, will considerably extend the insight into the chemistry of strained cyclic allenes and diradical intermediates.

Experimental Section

General: See ref. [5]. CD: JASCO J-715 spectropolarimeter. Specific rotations: JASCO P-1020 polarimeter; the units of the $[\alpha]_D$ values are $deg\,10^{-1}\,cm^2\,g^{-1}$; the concentrations ($c$) are given in grams per 100 mL solution.

The racemates of all compounds described below have been fully characterised in the preceding paper.[5] The pure enantiomers and the non-racemic mixtures were identified as to their constitution and, where applicable, their diastereomeric nature by NMR spectroscopy.

Resolution of racemates and analysis of non-racemic mixtures of enantiomers: An HPLC system consisting of a Knauer HPLC pump 64, a Gynkotek UV detector (UVD), operated at 260 nm, and a Chiralcel OJ-H or OD column (each 250×21 mm) was used, with each protected by a guard column (50×21 mm) with the same stationary phase. The flow rate was maintained at a value between 12 and 18 mL min^{-1}. Before their use as eluants, the solvents were distilled through a Vigreux column (20 cm). During the chromatography, a constant stream of helium was bubbled through the solvents. The quantitative analysis of the UV signals was achieved by using a Shimadzu C-R3A Chromatopac integrator.

Resolution of *rac*-5 and determination of the absolute configuration of the enantiomers: The equipment described above was used. A Chiralcel OJ-H column was utilised and heptane/ethanol (250:1) was the eluant. Samples (100 μL) of an 0.09 M solution of *rac*-**5** in heptane were injected. The retention times were 16.5 min for the (+)-enantiomer (*ent*-**5**) and 18 min for the (−)-enantiomer (**5**). Specific rotations (heptane, $c=0.1$ and 0.25, $T=20$ °C): $[\alpha]_D=+4$ and −5. The absolute configuration was determined by comparison of the experimental with the calculated CD spectrum (Figure 1).

Resolution of *rac*-6 and determination of the absolute configuration of the enantiomers: The equipment described above was used. Both Chiralcel OD and OJ-H columns were suitable with hexane/2-propanol (200:1) and heptane/ethanol (199:1), respectively, as the eluants. Samples (100 μL) of an 0.2 M solution of *rac*-**6** in hexane/2-propanol (1:1) and heptane/ethanol (1:1), respectively, were injected. The retention times were 8 min for the (−)-enantiomer (**6**) and 10 min for the (+)-enantiomer (*ent*-**6**) using a Chiralcel OD column and 6 min for **6** and 17 min for *ent*-**6** on a Chiralcel OJ-H column. Specific rotations (methanol, $c=1$, $T=20$ °C): $[\alpha]_D=-328$ and +321. The absolute configuration was determined by comparison of the experimental with the calculated CD spectrum (Figure 2).

Reaction of the pure enantiomer 5 with methyllithium in the presence of 2,5-dimethylfuran: The reaction of **5** (60.1 mg, 0.236 mmol), dissolved in 2,5-dimethylfuran (3 mL), with methyllithium (2.0 mmol, 2.0 mL of 1.0 M in diethyl ether) was conducted as described for *rac*-**5**[5] and furnished the purified product as a colourless oil (18.2 mg, 31 %). A solution of this product in 10 mL of heptane was analysed for the enantiomeric purity by using the Chiralcel OJ-H column (see above). Only the signal of **6** appeared, whereas that of *ent*-**6** was completely missing (>98 % *ee*). Specific rotation (methanol, $c=0.6$, $T=20$ °C): $[\alpha]_D=-352$. The deviation from the above value (−328) may have its origin in the error limits of the weighing.

Resolution of *rac*-8 and determination of the absolute configuration of the enantiomers: The equipment described above was used. A Chiralcel OJ-H column was utilised and heptane/ethanol (220:1) was the eluant. Samples (500 μL) of an 0.02 M solution of *rac*-**8** in heptane were injected. The retention times were 7.7 min for the (−)-enantiomer (**8**) and 10.3 min for the (+)-enantiomer (*ent*-**8**). Specific rotations (hexane, $c=0.4$, $T=20$ °C): $[\alpha]_D=-258$ and +260. The absolute configuration was determined by comparison of the experimental with the calculated CD spectrum (Figure 3).

Reaction of the pure enantiomer *ent*-5 with methyllithium in the presence of indene: The reaction of *ent*-**5** (59.8 mg, 0.234 mmol), dissolved in indene (5 mL), with methyllithium (2.0 mmol, 2.0 mL of 1.0 M in diethyl ether) was conducted as described for 6,6-dibromo-1-phenylbicyclo-[3.1.0]hexane[5] and furnished the purified product as a colourless oil (14 mg, 22 %). A solution of this oil in heptane was analysed for the ratio of the enantiomers by HPLC with a Chiralcel OJ-H column under the conditions given above for *rac*-**8**. The ratio of **8**/*ent*-**8** turned out to be 5:95. Specific rotation of this mixture (hexane, $c=0.3$, $T=21$ °C): $[\alpha]_D=+178$. The enantiomeric ratio calculated from the specific rotation (16:84) is considered to be less reliable than that determined by HPLC.[13]

Resolution of *rac*-9 and *rac*-10 and determination of the absolute configuration of the enantiomers: The equipment described above was used. A Chiralcel OJ-H column was utilised and heptane/ethanol (250:1) was the eluant. Samples (500 μL) of an 0.04 M solution of the 1:1 mixture of *rac*-**9** and *rac*-**10** in heptane were injected. The diastereomers as well as the enantiomers were cleanly separated, with the retention times being 9.5 and 19.5 min for the (−)-enantiomers *ent*-**9** and *ent*-**10**, respectively, and 23.6 and 38.4 min for the (+)-enantiomers **10** and **9**, respectively (Figure 6). Specific rotations (heptane, $c=1$, $T=21$ °C): $[\alpha]_D=+224$ (**9**), −229 (*ent*-**9**), +35 (**10**) and −34 (*ent*-**10**). The absolute configurations were determined by comparison of the experimental with the calculated CD spectra (Figures 4 and 5).

Reaction of the pure enantiomer 5 with methyllithium in the presence of styrene: The reaction of **5** (65.0 mg, 0.255 mmol), dissolved in styrene (5 mL), with methyllithium (2.4 mmol, 1.5 mL of 1.6 M in diethyl ether) was conducted as described for 6,6-dibromo-1-phenylbicyclo-[3.1.0]hexane[5] and furnished the purified product as a colourless oil (38.2 mg, 59 %). A solution of this oil in heptane was analysed for the ratio of the enantiomers by HPLC using a Chiralcel OJ-H column under the conditions given above for *rac*-**9** and *rac*-**10**. The ratio of **9**/*ent*-**9**/**10**/*ent*-**10** turned out to be 50:3:40:7 (Figure 6). Specific rotation of this mixture (pentane, $c=1.0$, $T=21$ °C): $[\alpha]_D=+195$.

Reaction of 1-bromo-2-phenylcyclohexene (19) with enantiomerically pure potassium menthoxide in the presence of 2,5-dimethylfuran: A stirred suspension of potassium hydride (80.2 mg, 2.00 mmol) in tetrahydrofuran (10 mL) was treated dropwise with (−)-menthol (313 mg, 2.00 mmol) at 20 °C. According to the literature,[14] the mixture was stirred overnight at 20 °C and then added dropwise to a vigorously stirred solution of **19**[5] (450 mg, 1.90 mmol) in 2,5-dimethylfuran (4.50 g, 46.8 mmol) at 20 °C. Stirring was continued for 6 h at 50 °C. After having been cooled to room temperature, the mixture was hydrolysed (5 mL)

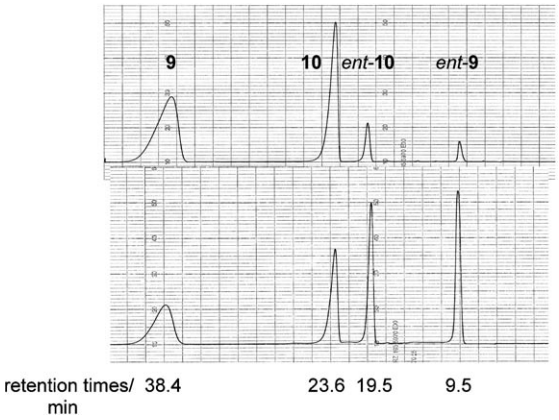


Figure 6. Diagrams of the HPLC analyses using a Chiralcel OJ-H column with heptane/ethanol (250:1), of a 1:1 mixture of *rac*-**9** and *rac*-**10** (bottom) and of the product obtained from the reaction of the pure enantiomer **5** with methyllithium in the presence of styrene (top).

and admixed with dichloromethane (10 mL). The layers were separated; the aqueous layer was extracted with dichloromethane (2×5 mL); the combined organic layers were washed with a saturated aqueous solution of NH_4Cl (2×5 mL), dried with $MgSO_4$ and concentrated in vacuo (15 mbar). The menthol was distilled off in a kugelrohr (50 °C/0.1 mbar). The residue, a colourless oil (124 mg, 26 %), was shown by NMR spectroscopy to be the [4+2] cycloadduct of 2,5-dimethylfuran onto **7**.[5] Specific rotation (hexane, $c=1.0$ $T=22$ °C): $[\alpha]_D=+34$, which afforded **6**/*ent*-**6** = 45:55 by using the specific rotations of pure **6** and *ent*-**6** (see above). However, the different solvents (hexane and methanol, respectively) may cause wide error limits.

Calculation of the CD spectra of the enantiomers of *rac*-5, *rac*-6, *rac*-8, *rac*-9 and *rac*-10: For the elucidation of the absolute configuration of a chiral compound, the simulation of its CD spectrum by quantum chemical methods and the comparison with the experimental spectrum is an established method.[13,15]

The present calculations utilised the density functional theory and its time-dependent (TD) variant by applying the TURBOMOLE programme package.[16] The geometries of the investigated compounds were optimised at the BLYP/SVP level[17–19] by applying the resolution of identity approximation[20,21] together with the matching auxiliary basis sets.[21,22] Absolute energies and Cartesian coordinates of **5**, **6**, *ent*-**8**, *ent*-**9** and **10** are given in the Supporting Information.

The electronic excitations were calculated at the TD-B3LYP[23–25] level of theory in combination with the TZVP basis sets.[26] The phenyl groups can rotate almost freely. For the calculation of the spectra, the conformation of the energy minimum was chosen. It was shown by a test that a deviation from the minimum conformation has only a small effect on the CD spectrum of the respective compound (see the Supporting Information).

For molecule **5** the first 15 excitations, for **6** and **8** the first 30 excitations, and for **9** and **10** the first 20 excitations were calculated. The UV spectra were simulated by superimposing Gauss functions, weighted according to the oscillator strength,[15] and then compared with the experimental spectra. With respect to the position of the strongest absorption, the calculated spectra of **8**, **9** and **10** showed a hypsochromic shift of 15, 16 and 13 nm, respectively. In the case of **5** and **6**, the absorption maximum at lowest energy exhibits only a shoulder in the spectra and no shift could be determined. The CD spectra were simulated by superimposing Gauss functions weighted according to the rotator strength[15] and then shifted by the number of wavelength units that corresponded to the deviation of the experimental and calculated UV spectra, given above. In Figures 1, 2, 3, 4 and 5 the simulated CD spectra of **5**, **6**, *ent*-**8**, *ent*-**9** and **10**, respectively, are compared with the matching experimental spectra, whereby the absolute configurations of the resolved samples were determined.

Acknowledgements

This work was supported by the Deutsche Forschungsgemeinschaft. We are grateful to the group of Prof. Dr. Gerhard Bringmann for help with the measurements of the CD spectra and the specific rotations.

[1] M. Christl, M. Braun, H. Fischer, S. Groetsch, G. Müller, D. Leusser, S. Deuerlein, D. Stalke, M. Arnone, B. Engels, *Eur. J. Org. Chem.* **2006**, 5045–5058.
[2] B. Engels, J. C. Schöneboom, A. F. Münster, S. Groetsch, M. Christl, *J. Am. Chem. Soc.* **2002**, *124*, 287–297.
[3] M. Christl in *Modern Allene Chemistry, Vol. 1* (Eds.: N. Krause, A. S. K. Hashmi), Wiley-VCH, Weinheim, **2004**, pp. 243–357.
[4] L. M. Tolbert, Md. N. Islam, R. P. Johnson, P. M. Loiselle, W. C. Shakespeare, *J. Am. Chem. Soc.* **1990**, *112*, 6416–6417.
[5] M. Christl, M. Schreck, T. Fischer, M. Rudolph, D. Moigno, H. Fischer, S. Deuerlein, D. Stalke, *Chem. Eur. J.* **2009**, DOI: 10.1002/chem.200900717, preceding paper in this issue.
[6] M. Nendel, L. M. Tolbert, L. E. Herring, M. N. Islam, K. N. Houk, *J. Org. Chem.* **1999**, *64*, 976–983.
[7] M. Christl, M. Schreck, *Chem. Ber.* **1987**, *120*, 915–920.
[8] S. Harnos, S. Tivakornpannarai, E. E. Waali, *Tetrahedron Lett.* **1986**, *27*, 3701–3704.
[9] R. L. Elliott, N. H. Nicholson, F. E. Peaker, A. K. Takle, C. M. Richardson, J. W. Tyler, J. White, M. J. Pearson, D. S. Eggleston, R. C. Haltiwanger, *J. Org. Chem.* **1997**, *62*, 4998–5016.
[10] R. Ruzziconi, Y. Naruse, M. Schlosser, *Tetrahedron* **1991**, *47*, 4603–4610.
[11] a) C. P. Suhrada, C. Selçuki, M. Nendel, C. Cannizzaro, K. N. Houk, P.-J. Rissing, D. Baumann, D. Hasselmann, *Angew. Chem.* **2005**, *117*, 3614–3618; *Angew. Chem. Int. Ed.* **2005**, *44*, 3548–3552; b) Y.-L. Zhao, C. P. Suhrada, M. E. Jung, K. N. Houk, *J. Am. Chem. Soc.* **2006**, *128*, 11106–11113.
[12] M. Balci, W. M. Jones, *J. Am. Chem. Soc.* **1981**, *103*, 2874–2876.
[13] E. L. Eliel, S. H. Wilen, L. N. Mander, *Stereochemistry of Organic Compounds*, Wiley, New York **1994**, Chapter 13.
[14] P. Haquette, S. Dagorne, R. Welter, G. Jaouen, *J. Organomet. Chem.* **2003**, *682*, 240–247.
[15] S. Grimme, *Rev. Comput. Chem.* **2004**, *20*, 153–218.
[16] TURBOMOLE, v5.8, R. Ahlrichs, M. Bär, H.-P. Baron, R. Bauernschmitt, S. Böcker, M. Ehrig, K. Eichkorn, S. Elliott, F. Haase, M. Häser, H. Horn, C. Huber, U. Huniar, M. Kattannek, C. Kölmel, M. Kollwitz, C. Ochsenfeld, H. Öhm, A. Schäfer, U. Schneider, O. Treutler, M. von Arnim, F. Weigend, P. Weis, H. Weiss, University of Karlsruhe, Karlsruhe, **2005**.
[17] A. D. Becke, *Phys. Rev. A* **1988**, *38*, 3098–3100.
[18] C. Lee, W. Yang, R. G. Parr, *Phys. Rev. B* **1988**, *37*, 785–789.
[19] A. Schäfer, H. Horn, R. Ahlrichs, *J. Chem. Phys.* **1992**, *97*, 2571–2577.
[20] O. Vahtras, J. Almlöf, W. M. Feyereisen, *Chem. Phys. Lett.* **1993**, *213*, 514–518.
[21] K. Eichkorn, O. Treutler, H. Öhm, M. Häser, R. Ahlrichs, *Chem. Phys. Lett.* **1995**, *242*, 652–660.
[22] K. Eichkorn, O. Treutler, H. Öhm, M. Häser, R. Ahlrichs, *Chem. Phys. Lett.* **1995**, *240*, 283–290.
[23] R. Bauernschmitt, R. Ahlrichs, F. H. Hennrich, M. M. Kappes, *J. Am. Chem. Soc.* **1998**, *120*, 5052–5059.
[24] R. Bauernschmitt, R. Ahlrichs, *Chem. Phys. Lett.* **1996**, *256*, 454–464.
[25] A. D. Becke, *J. Chem. Phys.* **1993**, *98*, 5648–5652.
[26] A. Schäfer, C. Huber, R. Ahlrichs, *J. Chem. Phys.* **1994**, *100*, 5829–5835.

Received: March 19, 2009
Published online: September 11, 2009

