# Diyne Cyclization in Camphor Derivatives – Experimental and Theoretical Investigation

Gabriele Wagner, Christian Heiß, Uwe Verfürth, Rudolf Herrmann*

Institut für Organische Chemie und Biochemie der Technischen Universität München, Lichtenbergstr. 4, D – 85747 Garching

*Dedicated to Prof. Ernest Wenkert on the occasion of his 70th birthday*

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Camphor Derivatives, Diyne Cyclization, Five-Membered Ring Annulation, Semiempirical Calculation of Intermediates

Derivatives of 3-oxo-camphorsulfonimide (**1**) with two phenylethynyl groups in the endo positions at the carbons C-2 and C-3 were prepared, and their reactivity towards halogenes and titanium chloride was studied. In every case, the two ethynyl groups led to the annulation of a five-membered ring to the bicyclo[2.2.1] system in an orientation which depends on the bulkiness of the additional substituent in position 3. NMR studies show that cationic species like **6** and **8** are the first detectable intermediates. They not only contain the fused five-membered ring but also a bond between its exocyclic methylene carbon and an oxygen atom of the sulfonyl group, thus transferring the positive charge mainly to sulfur. Semiempirical calculations (PM3) suggest two intermediates in the formation of such cations.

## Introduction

Camphor derivatives play an important role in asymmetric synthesis as chiral starting materials, auxiliaries, and catalysts[1, 2]. Having developed camphor derivatives (*e.g.* 3-hydroxycamphorsultam) as bidentate ligands for chiral Lewis acids by reduction of both double bonds of the oxoimine (**1**)[3], which showed reasonable efficiency in enantioselective Diels–Alder and ene reactions[4], we became interested in further modifications of this system by the introduction of additional substituents into the positions C-2 and C-3 of camphor. Increase in bulkiness in these positions should have a pronounced effect on reactivity and selectivity in catalytic applications. We decided to do this by the reaction of carbanions with the oxoimine (**1**) but found that most common alkyl- or aryllithium and Grignard reagents give only mixtures of compounds not of synthetic use. We succeeded, however, in preparing the corresponding phenylethynyl derivatives (**2**)-(**4**) (Fig. 1) and wish to report here on aspects of their chemistry.

* Reprint requests to Dr. Rudolf Herrmann.

## Results and Discussion

### *Synthesis and reactivity of the diynes*

The synthesis of the 2,3-bis(phenylethynyl)-camphorsultam derivatives (**2**)-(**4**) proceeds smoothly by the reaction of phenylethynyllithium with the oxoimine (**1**) followed by conventional methylation of the NH and OH groups (Fig. 1). Surprisingly, the triple bonds in these compounds are inert towards catalytic reduction (Pd and Pt) even under hydrogen pressure (50 bar), and do not react with metal carbonyls such as $Co_2(CO)_8$ either. We therefore studied their reactivity in more detail and found that they readily react with polarized or polarizable reagents, e.g. halogens. Under the reaction conditions (room temperature), alkynes are less reactive than alkenes towards halogens, but the products should be of the same type (simple addition to the multiple bond)[5].

However, we found that the expected haloalkenes did not form at all. On the basis of their NMR data, the products were identified as tetracyclic systems, having an additional five-membered ring annulated to the positions C-2 and C-3 of the camphor skeleton. The formation of five-membered rings from suitably constructed diynes

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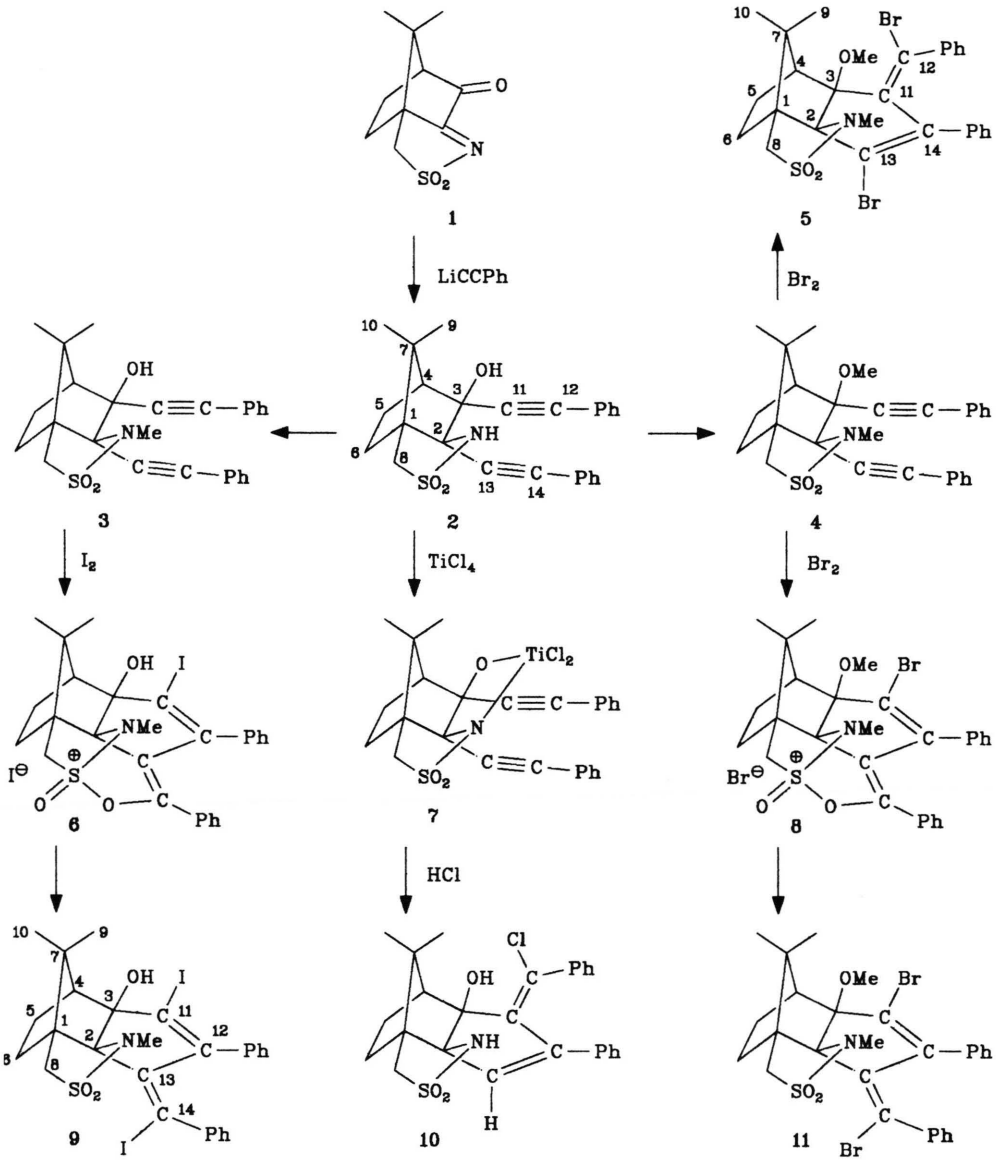



Fig. 1. Synthesis of the phenylacetylene derivatives **2-4** and their reactions with $Br_2$, $I_2$, and $TiCl_4$. Typical NMR numbering of the carbon atoms is shown in formulae **2, 5**, and **9**.

via cations seems to be a general reaction, if the alkynes can arrange such that the distance between carbon atoms which are expected to form the new bond does not exceed ≈ 4 Å, with the torsion angle between the two alkyne groups not exceeding ≈ 40° (see also the semiempirical calculations below). Thus, 1,2-bis(phenylethynyl)benzene (distance 3.65 Å , torsion angle 0°) cyclizes in a completely analogous way[6]. A larger distance cannot lead to a direct cyclization reaction; if cyclizations occur, they generally involve other carbon atoms in addition to the alkynes, which was observed in the case of phenylethynyl-substituted semibullvalenes[7].

*Mechanism of the cyclization process*

In order to get some insight in the process leading to different cyclization products, we followed

the reaction of the compounds **3** with iodine and **4** with bromine by proton and carbon NMR. Proton NMR is particularly well suited for this purpose, as starting materials, intermediates and products have well separated and easy to identify signals between $\delta$ = 2.5 and 5.0 ppm. Typical resonances in this region involve OH (broad singlet), *N*-methyl and *O*-methyl (singlets), and the diastereotopic protons 8-H (two doublets with $J$ = 11-15 Hz; for NMR numbering of the atoms, see Fig. 1). In the case of the starting materials **2** and **3**, the protons 8-H are degenerate and appear as singlets. For concentrations of 0.2 mol/l in $CDCl_3$, the kinetics can be conveniently monitored. Wherever intermediates with sufficient lifetime occurred, we confirmed our assignments by $^{13}C$ NMR and two-dimensional techniqes (COSY, HMQC, HMBC). $^1H$-NMR spectra are collected in Table I and $^{13}C$-NMR spectra in Table II.

Typical results of our NMR experiments are shown in Fig. 2 and 3. Iodine reacts comparatively slowly with the *N*-methylated compound (**3**) (Fig.2), and the signals of the starting material disappear only after more than two hours. An intermediate with a maximum intensity after 20 minutes was observed, which showed a typical 8-H pattern (doublets at $\delta$ = 4.00 and 4.94 ppm, $J$ = 15.1 Hz, spectrum 4 from bottom), but with a very large chemical shift difference, compared to the starting material (degenerate signal at 3.34 ppm; Fig. 2, bottom). This points to a severe structural change in the environment of the $SO_2$ group which strongly influences the electronic properties and the geometry of the five-membered heterocyclic ring. The $^{13}C$ spectrum clearly shows that five-membered-ring annulation by ring closure of the alkynyl groups has already occurred. Initial attack of $I^+$ at C-11 must be responsible for this change, but no carbon-centered cation can be detected. As structure for this first intermediate, we therefore suggest the cation **6**, with the positive charge localized mainly on sulfur, and a bond between one oxygen atom of the $SO_2$ group and the exocyclic carbon atom at the newly formed ring. This struc-

Table I. $^1H$ NMR data ($\delta$ values; multiplicity, integration and coupling constants (Hz) in brackets) of new compounds at 360.134 MHz in $CDCl_3$. Atom numbering follows that of the corresponding carbon atoms (Fig. 1).

| Comp. | 4-H (d) | 5,6-H (m) | 8-H (2 d) | 9,10-H (2 s) | Phenyl | Other |
|---|---|---|---|---|---|---|
| **2** | 2.23 (5.2) | 1.85 (1H), 1.94 (1H), 2.11 (1H) 2.30 (1H) | 3.38, 3.42 (13.7) | 1.04, 1.52 | 7.25 (m, 6H) 7.38 (m, 4H) | 3.15 (s, 1H) 5.20 (s, 1H) |
| **3** | 2.17 (5.1) | 1.76 (1H), 1.92 (1H), 2.11 (1H) 2.32 (1H) | 3.34[a] (2H) | 1.04, 1.62 | 7.27 (m, 6H) 7.39 (m, 4H) | 2.80 (s, 1H) 2.93 (s, 3H) |
| **4** | 2.38 (5.2) | 1.76 (1H), 1.89 (1H), 2.03 (1H) 2.32 (1H) | 3.29[a] (2H) | 1.01, 1.59 | 7.24 (m, 6H) 7.40 (m, 4H) | 2.90 (s, 3H) 3.46 (s, 3H) |
| **5** | 3.04 (4.6) | 1.65 (2H), 1.80 (1H), 2.05 (1H) | 3.36, 3.46 (13.5) | 1.09, 1.67 | 6.60 (d, 1H, 7.3) 6.90 (m, 6H) 7.28 (m, 1H) 7.40 (d, 2H, 7.4) | 2.95 (s, 3H) 3.69 (s, 3H) |
| **6** | 2.42 (4.4) | 1.48 (1H), 2.10 (2H), 2.33 (1H) | 4.00, 4.94 (15.1) | 1.19, 1.58 | 6.90–7.35 (m) | 3.33 (s, 3H) 4.10 (s, 1H) |
| **8** | 2.87 (4.4) | 1.50 (1H), 2.05 (2H), 2.40 (1H) | 4.08, 5.78 (15.4) | 1.21, 1.54 | 6.70–7.30 (m) | 3.27 (s, 3H) 3.84 (s, 3H) |
| **9** | 2.03 (4.8) | 1.48 (1H), 1.90 (2H), 1.99 (1H) | 2.66, 2.76 (13.5) | 1.03, 1.60 | 7.24 (m, 6H) 7.37 (m, 4H) | 2.61 (s, br, 1H) 2.90 (s, 3H) |
| **10**[b] | 2.73 (5.2) | 1.48 (1H), 1.54 (1H), 1.79 (1H) 1.94 (1H) | 3.26, 3.35 (13.9) | 1.03, 1.60 | 6.87 (m) | 3.66 (s, 1H) 5.21 (s, 1H) |
| **11** | 2.47 (4.6) | 1.30 (1H), 1.96 (2H), 2.61 (1H) | 2.81, 2.95 (13.6) | 1.04, 1.56 | 6.80–7.45 (m) | 2.87 (s, 3H) 3.68 (s, 3H) |

[a] Degenerate signals, appearing as singlet; [b] 13-H: 6.27 (s, 1H).

Table II. $^{13}C$ NMR data ($\delta$ values) of new compounds at 90.556 MHz in $CDCl_3$. Numbering of the carbon atoms follows Fig. 1.

| Comp. | 1 | 2 | 3 | 4 | 5, 6 | 7 | 8 | 9, 10 | 11 | 12 | 13 | 14 | Ph ($C_q$) | Ph (CH) | Others |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **2** | 62.3 | 73.0 | 82.3 | 56.7 | 24.2<br>28.6 | 49.2 | 51.5 | 23.7<br>24.1 | 87.6, | 88.3, | 89.4, | 90.4[a] | 122.0<br>122.2 | 128.4, 128.5<br>128.8, 128.9<br>132.0, 132.1 | – |
| **3** | 56.6 | 76.5 | 83.3 | 57.7 | 23.9<br>28.6 | 49.2 | 49.1 | 23.3<br>23.4 | 84.1, | 88.0, | 90.2, | 92.4[a] | 122.1<br>122.4 | 128.1, 128.2<br>128.5, 128.6<br>131.7, 131.8 | 29.1 |
| **4** | 56.2 | 76.1 | 88.9 | 50.1 | 23.3<br>28.6 | 49.0 | 48.6 | 21.7<br>23.1 | 84.2, | 87.4, | 89.4, | 91.8[a] | 122.1<br>122.2 | 127.9.128.1<br>128.3, 128.3<br>131.5, 131.6 | 28.7<br>52.4 |
| **5** | 55.5 | 89.1 | 97.3 | 54.8 | 23.4<br>27.9 | 51.6 | 49.3 | 22.8<br>24.5 | 123.5 | 147.9 | 139.8 | 134.0 | 134.2<br>138.2 | 126.7, 127.4<br>127.6, 128.3<br>129.4, 129.9 | 28.9<br>55.4 |
| **8** | 54.9 | 80.4 | 97.7 | 46.6 | 23.4<br>27.4 | 52.4 | 49.2 | 20.9<br>22.1 | 139.1 | 123.7 | 119.8 | 150.3 | 133.7<br>135.6 | 127.7, 128.2<br>129.8, 129.9<br>130.0, 130.9 | 29.9<br>55.8 |
| **9** | 57.6 | 84.7 | 94.7 | 52.5 | 24.5<br>28.6 | 52.2 | 47.9 | 24.0<br>26.1 | 122.9 | 151.6 | 145.9 | 99.7 | 138.2<br>143.9 | 126.7, 126.8<br>128.4, 129.0<br>129.1, 131.5 | 28.1 |
| **10** | 59.8 | 79.7 | 90.5 | 53.8 | 23.8<br>28.5 | 51.8 | 51.1 | 22.8<br>23.2 | 128.8 | 144.4 | 142.7 | 139.1 | 134.7<br>137.2 | 126.8, 127.1<br>127.2, 127.6<br>128.4, 129.5 | – |
| **11** | 57.0 | 86.5 | 98.2 | 47.1 | 24.8<br>28.3 | 51.8 | 47.0 | 23.6<br>24.7 | 138.3 | 146.4 | 141.5 | 127.5 | 136.2<br>137.2 | 126.9, 127.3<br>128.1, 129.1<br>130.6, 132.3 | 28.1<br>54.8 |

[a] Not assigned individually.

ture is supported by the calculations reported below. The cation then reacts with the remaining $I^-$ to the diododialkene (**9**), which was not only observed in the kinetic experiment (Fig. 2, top; 8-H doublets at $\delta$ = 2.66 and 2.76 ppm, $J$ = 13.5 Hz), but could be isolated and characterized. Although the formation of *E/Z* isomers with respect to the exocyclic double bond could be *a priori* expected, only one product was observed. The absence of NOE effects of the phenyl group at this double bond on protons of the camphor part of the molecule suggests that (**9**) is the *Z* isomer shown in Fig. 1, *i.e.* the replacement of oxygen by iodide at the double bond occurs with retention of configuration. This stereochemical result is commonly observed in vinylic nucleophilic substitution[8, 9].

The reaction of the dimethylated compound **4** with iodine is extremely slow, and kinetic experiments were therefore performed with bromine (Fig. 3). Here the starting material **4** rapidly disappeared, while the typical pattern of the sulfur-stabilized cation **8** appeared and over a period of some hours converted to the final product, the dibromodialkene **11**, in close analogy to the reaction of **3** with iodine. However, there is an additional product (about 1/3 of the total material) which formed directly from **4** and not from the cation **8**; NMR spectroscopy showed that it is the cyclized compound **5** where the initial attack of $Br^+$ occurred at C-13 (Tables I and II). This means that after cyclization the cation with the charge at C-12 has no possibility of stabilizing by charge transfer to sulfur, and hence there is no chance to observe this quite reactive ion by NMR spectroscopy. As soon as the starting material was consumed, the amount of **5** in the mixture remained constant, indicating that the pathways leading to either **5** or **11** are not interconnected. We believe that the effect of *O*-methylation on the site of the attack of the electrophile (C-11 *vs.* C-13) is mainly of steric origin.

As the products **2-4** are optically pure and of potential interest as chiral ligands, we have studied the complexation behaviour of **2** towards $TiCl_4$. We expected the formation of a chelating complex such as **7**. Due to solubility problems it was not

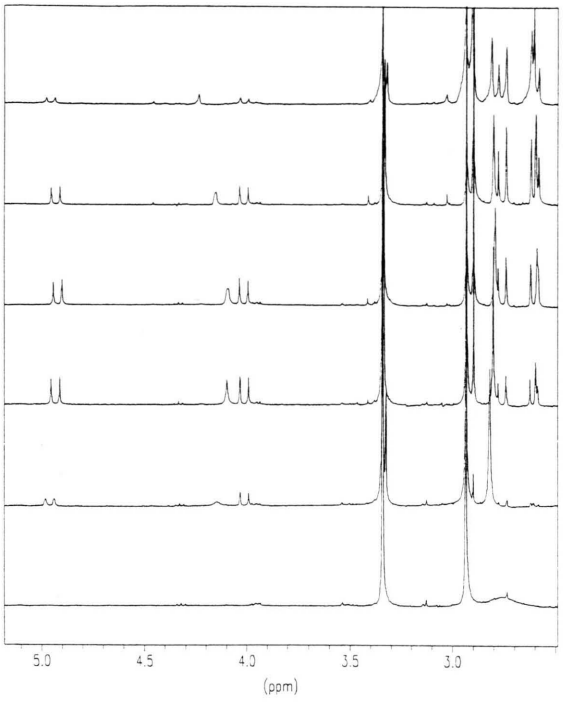



Fig. 2. Reaction of **3** with iodine. $^1$H NMR spectra (from bottom to top) after $t$ = 0, 5, 10, 20, 30, 56 min. **3**: $\delta$ = 3.34 (2H); **6**: $\delta$ = 4.94 (d), 4.00 (d); **9**: $\delta$ = 2.76 (d), 2.66 (d).

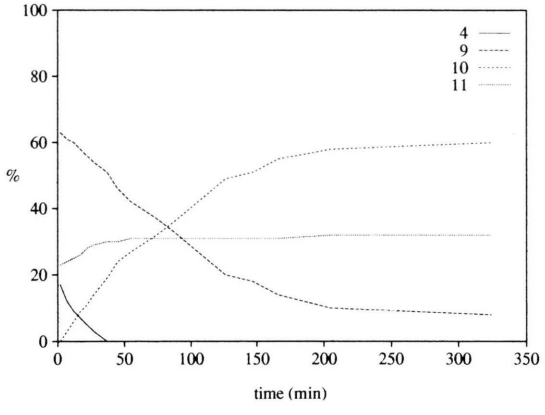



Fig. 3. Reaction of **4** with bromine. Composition of the reaction mixture according to $^1$H NMR spectra.

possible to follow the reaction by NMR spectroscopy, but after aqueous workup of the reaction mixture, an appreciable amount ($\approx$ 60%) of a new product was obtained, which we identified as the cyclized chlorinated compound **10**, together with unchanged ligand **2**. The compound is analogous to the byproduct **5** of the bromination of **4**. The rationale for its formation is that in the chelate complex **7** the attack of an electrophile at C-11 is hindered by the metal site, in analogy to the effect of *O*-methylation in **4**. As HCl is liberated during the formation of **7**, it is not surprising that it adds to the triple bonds, whereby the proton attacks C-13, leading to a reactive cation which is then trapped at C-12 by the chloride ion.

### *Semiempirical calculation of cationic intermediates*

The conclusions drawn from NMR spectra concerning the structures of the intermediate cations of the cyclization reactions might seem speculative, and we therefore carried out supporting semiempirical calculations (PM3) on the intermediates. We first checked a simple model, 1,2-diethynylbenzene, as starting material. To a geometry-optimized molecule was added a proton as the electrophile in a suitable distance to one of the triple bonds (1.0 to 1.4 Å). Geometry optimization of the ensemble led to the typical cation with the indene skeleton, as postulated in the halogenation reactions of 1,2-bis(phenylethynyl)benzene[6] with no obvious activation barrier or further intermediates as local energy minima. The optimization converged more rapidly when the proton was placed in the plane of the alkyne groups, probably because of the better overlap of the empty orbital at the (formally cationic) terminal carbon atom with the filled $\pi$-orbital of the non-protonated alkyne group. We then investigated the conditions which a starting material has to fulfill in order to cyclize analogously. We did this by constructing both *cis*- and *trans*-1,2-diethynylcycloalkanes (4- to 7-membered rings). The distances between the carbon atoms which should form bonds to give the five-membered annulated ring varied between 3.47 Å (*cis*-1,2-diethynylcyclobutane) and 4.06 Å (*trans*-1,2-diethynylcycloheptane). The corresponding torsion angles varied between 1.2° (almost in plane) and 83.0° (for *trans*-1,2-diethynylcyclobutane). After the addition of a proton in a similar position as described before, the geometry optimization was performed. Cyclization was observed for all compounds where the distance between the carbon atoms to be connected did not exceed the limit of 3.8 Å, whereas for *trans*-1,2-diethynylcyclobutane (4.71 Å), *trans*-1,2-diethynylcyclopentane (4.05 Å), and *trans*-1,2-diethynyl-

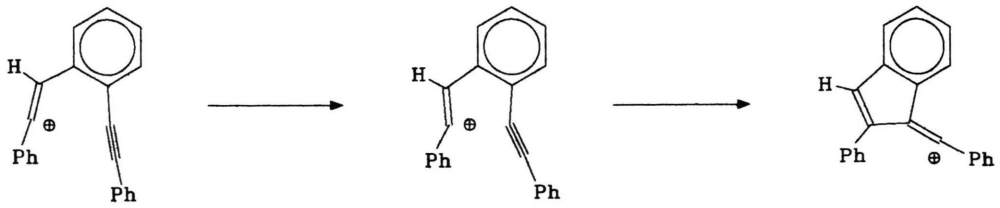
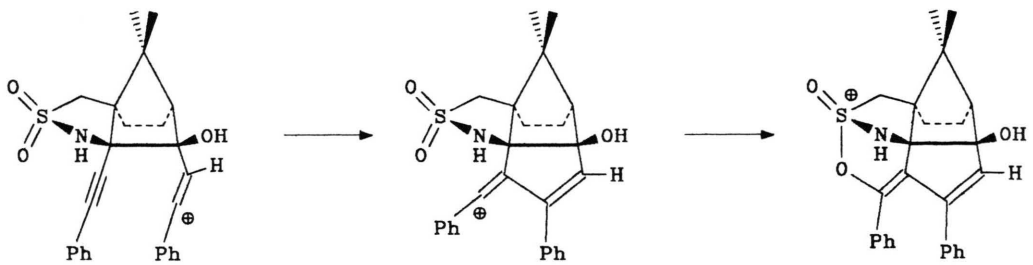



Fig. 4. Calculated intermediate (left), transition state (middle), and final product (right) of the protonation reaction of 1,2-bis(phenylethynyl)benzene. The relative heats of formation are 0, +5.2, and -23.6 kcal/mol. The planes through the phenyl groups are almost perpendicular to the plane of the disubstituted benzene in all cases.

cycloheptane (4.06 Å), no cyclization was observed. The compounds which did not cyclize showed higher torsion angles as well (83.0, 41.2, and 45.0°, respectively). We therefore propose as a rule-of-thumb that formation of a five-membered ring from a 1,2-dialkyne should occur in all cases where a conformation can be achieved which shows a distance between the carbon atoms to be connected below ≈ 4 Å, together with a torsion angle between the alkyne groups below ≈ 40°. The experimentally studied 1,2-bis(phenylethynyl)-benzene[6] (distance 3.65 Å, torsion angle 0°) obeys this rule-of-thumb. However, it did not cyclize during the geometry optimization, but gave a local minimum with a distance of 2.92 Å between the carbon atoms to be connected (Fig. 4, left), although we calculated the cyclized cation (Fig. 4, right) to be ≈ 24 kcal/mol more stable than this intermediate. We therefore estimated the activation barrier for the transition between the two cations using MOPAC's transition state ability (saddle point calculation (keyword SADDLE) followed by optimization of the transition state (keyword TS)). We found that the transition state is approximately 5 kcal/mol higher in energy than the intermediate cation. The distance between the carbons to be connected is shortened considerably (2.20 *vs.* 2.92 Å.) The low barrier is in accord with the conclusions drawn earlier from the experimental data concerning the high degree of concertedness of this cyclization reaction[6].

Next, we optimized the geometry of the camphor derivative **2** and found the distances between the carbon atoms which could potentially be connected to be 3.23 Å (C-11 – C-14) and 3.27 Å (C-12 – C-13) (we use the NMR numbering for the carbon atoms shown in Fig. 1). Together with a torsion angle of 9.3° such camphor derivatives are almost ideal substrates for the cyclization. However, the direction of the cyclization (*i.e* the question if the primary attack of the electrophile occurs at C-11 or C-13) cannot be predicted from these geometric considerations, as both distances are almost the same. Addition of a proton to C-11 followed by geometry optimization led to the first intermediate **12** (Fig. 5) as a local minimum, in close analogy to the intermediate in the protonation of 1,2-bis(phenylethynyl)benzene. The distance between the carbon atoms to be connected (C-12 and C-13) is shortened compared with the




**12** **13** **14**

Fig. 5. Calculated intermediates in the protonation of **2** (PM3). Heats of formation relative to **12** (0 kcal/mol): **13**: -38.2; **14**: -64.2 kcal/mol.

starting material (2.85 *vs.* 3.23 Å). The next step in the reaction should be the annulation of the five-membered ring, leading to a second intermediate **13**. This cation is indeed another local energy minimum (38.2 kcal/mol more stable). The distance C-12 – C-13 is typical for a single bond (1.48 Å). In the final cation **14** the positive charge is stabilized considerably by transfer to the sulfur atom. This is reflected in an additional decrease of the heat of formation (64.2 kcal/mol more stable than **12**, 26.0 kcal/mol more stable than **13**). The stabilization effect is also reflected in the decrease of the calculated dipole moments (**12**: 8.0 D, **13**: 8.0 D, **14**: 5.1 D). The S-O distance was calculated as 1.69 Å (typical S-O single bond, compared with the double bond of 1.42 Å to the second oxygen), and the newly formed C-O bond as 1.41 Å(single bond). Attempts to localize the transition states failed, probably due to the high complexity of the molecules. Energy minima lower than **14** were not detected. Thus, these calculations support strongly our conclusions drawn from NMR measurements concerning the structures of the intermediates.

## Experimental

NMR spectra were obtained with a Bruker AM 360 instrument ($^1$H: 360.13 MHz, $^{13}$C: 90.56 MHz). Optical rotations were measured with a Perkin Elmer 241 M polarimeter and mass spectra with a Varian CH5 instrument (EI mode, 70 eV).

Semiempirical calculations were performed with PM3 using the standard parametrization as implemented in the HYPERCHEM (release 3) and MOPAC (version 7.0 for DOS) software packages. HYPERCHEM was used for geometry optimizations (Polak-Ribiere algorithm) followed by single-point calculations and MOPAC for the localization of transition states.

### *Starting materials* **2**-**4**

*(1aS,3aS,7R)-7-Hydroxy-8,8-dimethyl-1a,7-bis(phenylethynyl)-1,1a,4,5,6,7-hexahydro-3H-3a,6-methano-2,1-benzisothiazole 2,2-Dioxide* (**2**): To a solution of phenylacetylene (2.6 g, 25 mmol) in dry diethyl ether (50 ml), 25 mmol of butyl lithium (2.5 M solution in hexane, 10 ml) was added dropwise at room temperature. After stirring for 30 min the oxoimine **1** (2.3 g, 10 mmol) was added in five portions over a period of 10 min. The mixture was heated at reflux for 12 h and then hydrolyzed with 25 ml of water. The organic layer was separated and the aqueous layer extracted with dichloromethane (3×50 ml). The combined organic layers were dried ($Na_2SO_4$), the solvents were evaporated, and the residue was recrystallized from dichloromethane/hexane (1:1). Yield 3.9 g (90%), m.p. 224–225 ° C; $[\alpha]_D^{22}$ = -30.0 (*c* = 1.0 in acetone); $[\alpha]_D^{24}$ = -34.2 (*c* = 1.0 in ethanol); *m/z*: 431 [M$^+$].

$C_{26}H_{25}NO_3S$ (431.56)
Calcd C 72.4 H 5.8 N 3.1%,
Found C 71.9 H 5.9 N 3.1%.

*(1aS,3aS,7R)-7-Hydroxy-1,8,8-trimethyl-1a,7-bis(phenylethynyl)-1,1a,4,5,6,7-hexahydro-3H-3a,6-methano-2,1-benzisothiazole 2,2-Dioxide* (**3**): To a solution of **2** (0.30 g, 0.70 mmol) in 3 ml of dry THF, sodium hydride (60% in mineral oil, 28 mg, 0.70 mmol) was added. After stirring for 30 min at room temperature, dimethyl sulfate (67 $\mu$l, 0.70 mmol) was added, and stirring was continued for 12 h. After workup with dichloromethane/water, the residue was recrystallized from dichloromethane/hexane (1:1). Yield: 0.30 g (97%), m.p. 166–168 ° C; $[\alpha]_D^{23}$ = -16.9 (*c* = 0.6 in ethanol); *m/z*: 445 [M$^+$].

$C_{27}H_{27}NO_3S$ (445.59)
Calcd C 72.8 H 6.1 N 3.1%,
Found C 72.5 H 6.0 N 3.2%.

*(1aS,3aS,7R)-7-Methoxy-1,8,8-trimethyl-1a,7-bis(phenylethynyl)-1,1a,4,5,6,7-hexahydro-3H-3a,6-methano-2,1-benzisothiazole 2,2-Dioxide* (**4**): The compound was prepared as described for **3**, except that the amounts of sodium hydride and dimethyl sulfate were doubled. The crude product was purified by chromatography (silicagel/dichloromethane). $R_f$: 0.32, yield: 0.31 g (98%), m.p. 62–65 ° C; $[\alpha]_D^{23}$ = +16.4 (*c* = 0.9 in ethanol); *m/z*: 459 [M$^+$].

$C_{28}H_{29}NO_3S$ (459.61)
Calcd C 73.2 H 6.4 N 3.1%,
Found C 73.5 H 6.2 N 3.0%.

### *Reaction of* **2** *with* $TiCl_4$:

*(3aS,6aS,9aS)-7-(Z-2-Chloro-2-phenylmethylene)-6a-hydroxy-10,10-dimethyl-8-phenyl-3a,4,5,6,6a,7-hexahydro-1H,3H-3a,6-methano-indeno[3a,4-c]isothiazole 2,2-Dioxide* (**10**): To a solution of $TiCl_4$ (55 $\mu$l, 0.50 mmol) in 3 ml of dichloromethane, a solution of the sulfonamide **2** (0.22 g, 0.50 mmol) in 12 ml of dichloromethane was added under nitrogen at 0 °C. The mixture was stirred for 5 h. Water (10 ml) was added, and the aqueous layer was extracted with

dichloromethane (2×10 ml). The combined organic layers were dried ($MgSO_4$), and the solvent was evaporated. The crude product was purified by chromatography (silicagel, dichloromethane) followed by recrystallization from chloroform. $R_f$: 0.13, yield 0.14 g (60%), m.p. 156–160 °C; $[\alpha]_D^{23}$ = -21.9 (*c* = 0.8 in chloroform); *m/z*: 468 [M+1$^+$] (rel. $^{35}$Cl, FAB spectrum).

$C_{26}H_{26}ClNO_3S$ (468.02)
Calcd C 66.7 H 5.6 N 3.0%,
Found C 66.5 H 5.6 N 3.1%.

*Kinetic NMR measurements*

The sulfonamide **3** or **4** (0.10 mmol) was dissolved in $CDCl_3$ (0.3 ml), and the solution transfered to an NMR tube, and a solution of iodine or bromine (0.10 mmol) in $CDCl_3$ (0.2 ml) was added to it. NMR measurements were started immediately afterwards and repeated first every 5 min and later at larger intervals, until no further changes of the spectrum occurred during a period of 1 h.

*Compounds* **5**, **9**, *and* **11**

For preparative variants of the NMR experiments, the tenfold amounts of starting materials were used, and the solvent $CDCl_3$ was replaced by dichloromethane, maintaining the same concentrations as in the experiments. At the end of the reaction, a 10% aqueous solution of sodium thiosulfate (10 ml) was added, and the organic layer washed with water (2×10 ml). After drying of the organic layer ($MgSO_4$) and evaporation of the solvent, the crude product was purified as described below.

*(3aS,6aS,9aR)-6a-Hydroxy-7-iodo-9-(Z-2-iodo-2-phenylmethylene)-1,10,10-trimethyl-8-phenyl-3,3a,4,5,6,6a-hexahydro-1H,9H-3a,6-methano-indeno[*3a,4-*c]isothiazole 2,2-Dioxide* (**9**): The product was purified by recrystallization from dichloromethane/hexane 1:1. Yield: 0.68 g (97%), m.p. 95 °C (dec.); $[\alpha]_D^{23}$ = +25.4 (*c* = 1.1 in ethanol); no mass spectrum obtained due to decomposition.

$C_{27}H_{27}I_2NO_3S$ (699.39)
Calcd C 46.4 H 3.9 N 2.0%,
Found C 46.2 H 3.7 N 2.0%.

*(3aS,6aS,9aS)-9-Bromo-7-(Z-2-bromo-2-phenylmethylene)-6a-methoxy-1,10,10-trimethyl-8-phenyl-3a,4,5,6,6a,7-hexahydro-1H,3H-3a,6-methano-indeno[3a,4-c]isothiazole 2,2-Dioxide* (**5**) *and (3aS,6aS,9aR)-7-bromo-9-(Z-2-bromo-2-phenylmethylene)-6a-methoxy-1,10,10-trimethyl-8-phenyl-3,3a,4,5,6,6a-hexahydro-1H,9H-3a,6-methano-indeno[3a,4-c]isothiazole 2,2-Dioxide* (**11**): The products were separated by chromatography (silicagel, hexane/ethyl acetate 4:1). **5**: $R_f$: 0.66, yield 0.16 g (24%), m.p. 250–254 °C (dec.); $[\alpha]_D^{23}$ = -163 (*c* = 0.1 in ethanol/dichloromethane 1:1); *m/z*: 617 [M$^+$] (rel. $^{79}$Br).

$C_{28}H_{29}Br_2NO_3S$ (619.43)
Calcd C 54.3 H 4.7 N 2.3%,
Found C 54.0 H 4.6 N 2.2%.

**11**: $R_f$: 0.55, yield 0.25 g (40%), m.p. 200–201 °C; $[\alpha]_D^{23}$ = -12.8 (*c* = 0.1 in ethanol); *m/z*: 617 [M$^+$] (rel. $^{79}$Br).

$C_{28}H_{29}Br_2NO_3S$ (619.43)
Calcd C 54.3 H 4.7 N 2.3%,
Found C 54.1 H 4.6 N 2.3%.

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