Synthesis of α,β-Unsaturated *Pseudogeminal* [2.2]Paracyclophane Bisketones

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Abstract: An unexpected synthesis of α,β-unsaturated *pseudogeminal* [2.2]paracyclophane bisketones has been realized via a dyotropic-type rearrangement of the corresponding bisallenyl *o*-nitrophenyl sulfoxides.

Key words: [2.2]paracyclophanes, sulfoxides, allenes, rearrangement

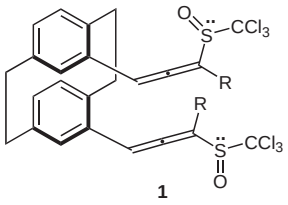

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Figure 1

Because of the rigid molecular framework provided by the paracyclophane unit and its short interannular distance, functional groups in pseudogeminally substituted [2.2]paracyclophanes are often held in such a position as to allow highly specific reactions to take place between them. In one such application unsaturated cyclophane bisesters undergo intramolecular photocyclization to the corresponding ladderane isomers.[1–3]

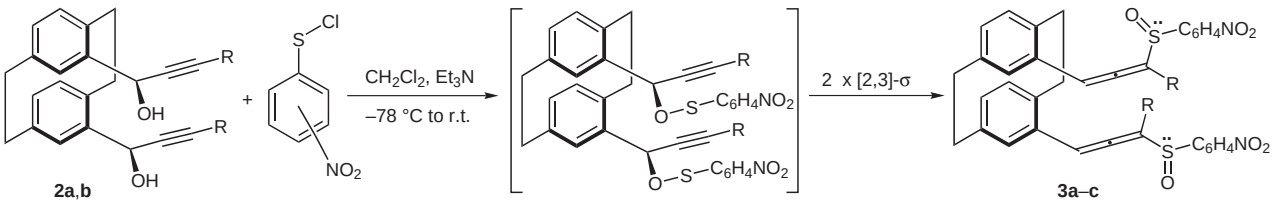
Using pseudogeminally substituted [2.2]paracyclophanes as spacers for bisallenic moieties, interesting starting materials for intra- or intermolecular reactions can be realized. In a recent paper we have reported on the synthesis of first bisallenyl-substituted pseudogeminal [2.2]paracyclophanes **1**.[4] Although the distance between two allenic moieties should allow intramolecular interactions, none of these have been observed under various conditions.

The lack of reactivity of these unsaturated systems could be due to both electronic and steric effects of the trichloromethyl sulfoxide or sulfone substituents, respectively. In order to get a deeper insight into this phenomenon we decided to replace the trichloromethyl group with a nitrophenyl substituent. This was accomplished by the reaction of bispropargylic alcohols **2a**,**b** with nitrobenzenesulfenyl chloride via a double [2,3]-sigmatropic rearrangement of the corresponding sulfenyl esters (Scheme 1).[5,6]

Following the above protocol, *o*- and *p*-nitrophenyl sulfoxides were obtained in good yields (50–55%) as bright yellow solids.[7] As expected, a mixture of four diastereoisomers was isolated in all cases.

Mass spectrometric analysis of the above compounds revealed an unexpected sensitivity of the *o*-nitrophenyl sulfoxide derivatives towards EI conditions. In both cases (**3a** and **3b**) a molecular ion of m/z = 308 ($C_{12}H_8N_2O_4S_2$) was recorded. However under ESI conditions the molecular mass of the above sulfoxides ($C_{40}H_{38}N_2O_6S_2$ and $C_{36}H_{30}N_2O_6S_2$, respectively) was confirmed.

In order to elucidate the chemical process that took place under thermal conditions, we gently heated a solution of **3** at 40 °C. After 18 hours the starting material was consumed and from the mixture of diastereoisomers a symmetrical compound could be isolated. Valuable information was obtained by NMR monitoring. The spectra of the crude product showed a clean and symmetrical aliphatic area, a doublet with J = 12 Hz (δ = 6.05 ppm), and a complex aromatic area in comparison with the *o*-nitrophenyl pattern. Separation by silica gel column chromatography indicated the formation of two major



2a,**b**

2a R = *n*-Pr
2b R = Me

3a–**c**

3a R = *n*-Pr, $C_6H_4NO_2$ (*ortho*)
3b R = Me, $C_6H_4NO_2$ (*ortho*)
3c R = *n*-Pr, $C_6H_4NO_2$ (*para*)

Scheme 1

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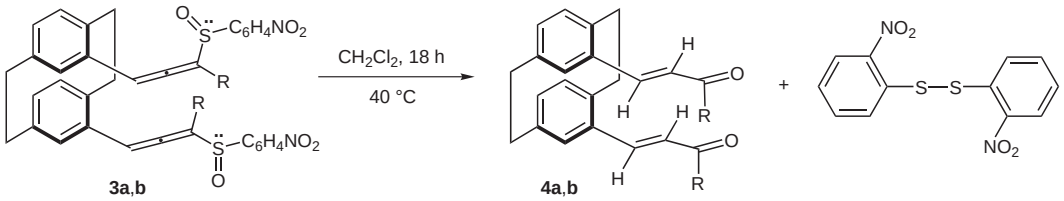


3a R = *n*-Pr, $C_6H_4NO_2$ (*ortho*)
3b R = Me, $C_6H_4NO_2$ (*ortho*)

4a R = *n*-Pr
4b R = Me

Scheme 2

compounds, an α,β-unsaturated ketone **4** and bis(*o*-nitrophenyl) disulfide **5** (MW = 308, ca. 15% isolated yield; Scheme 2). The formation of disulfide **5**, a known compound, was unambiguously proven by X-ray structural analysis. Although the spectra of the crude mixture revealed the formation of the *cis* isomer only, during purification isomerization took place and the thermodynamically more stable *trans* isomer **4** was isolated.[8]

Interestingly, under the same experimental conditions the corresponding *p*-nitrophenyl sulfoxide **3c** was found to be stable. This observation indicates that the above reaction may be a special case due to the *ortho* orientation of the nitro group towards the sulfoxide unit. In order to elucidate some mechanistic aspects we decided to investigate whether the reaction took place only in case of the *o*-nitrophenyl sulfoxide pattern, whether the *pseudogeminal* substitution favored an intramolecular interaction, and whether the process involved radical or anionic intermediates.

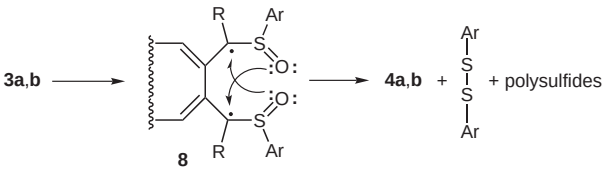
Thus, we oxidized the *o*-nitrophenyl sulfoxide **3a** to the corresponding sulfone, using dimethyldioxirane (DMDO) as the oxidant. The sulfone was obtained as a single isomer in 20% isolated yield. Despite of the low yield obtained, no reaction or decomposition was observed during two weeks.

Moreover, in order to check whether the α,β-unsaturated ketone had been formed by an intramolecular interaction or from independent interactions between allenic and sulfoxide units we investigated the chemical behavior of allenyl sulfoxide **7** under the same experimental conditions. This compound was prepared from 1-hydroxy-1-phenylbut-2-yne (**6**) following the procedure described above (Scheme 3). Sulfoxide **7** was obtained as a mixture of two diastereoisomers.[9]

Indication for an intramolecular interaction in bisallenyl sulfoxides **3a**,**b** is supported by the fact that no chemical reaction of **7** was observed under the same experimental conditions. A survey of literature data on *ortho*-substituted phenyl sulfoxides revealed that mono-*ortho*-substitution prevents free rotation of the S(O)R group.[10] Consequently, it is reasonable to assume that the formation of α,β-unsaturated ketone is initiated by an interaction between the electron pairs of the sulfur and nitrogen atoms, making the system flat and inducing a high rotational barrier around the S–C_{Ar} bond (Figure 1).

No deuterium incorporation was observed when *pseudogeminal* bisallenyl sulfoxides were heated in $CDCl_3$ at 40 °C. Finally, a radical mechanism appeared reasonable after an experiment in the presence of the free radical inhibitor hydroquinone. No reaction was observed during two days.

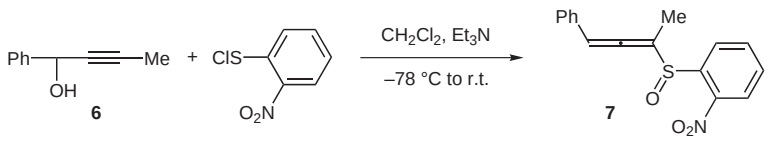
Taking these results into account, we postulate the following mechanism for the conversion of **3a**,**b** into **4a**,**b**. In the first step **3** closes to the diradical **8**, which then undergoes a dyotropic rearrangement[11,12] as shown in Scheme 4.



Scheme 4

The formation of **4** requires two additional hydrogen atoms. Corroborating that with the low yield for the disulfide (ca. 15%) one can assume that the aromatic ring of the *o*-nitrophenyl sulfoxide unit may be the source of hydrogen atoms. The formation of polymeric sulfides is indicated by the crowded aromatic area in the spectra of crude reaction products.

In conclusion, we have discovered an interesting intramolecular reaction of *pseudogeminal* bisallenyl *o*-nitrophenyl sulfoxide systems that is presumably caused by an interaction between nitro and sulfoxide groups. Evidence for a radical mechanism via a dyotropic-type rearrangement has been presented. The formation of the *pseudogeminal* α,β-unsaturated ketone **4** has opened a way towards ladderane-type compounds.



Scheme 3

Acknowledgment

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References and Notes

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(7) Compound **3a** (0.35 g, 50%); mp 118–119 °C. IR (neat): 2927, 1960, 1515, 1337, 1063, 733 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$, TMS): δ = 1.05 (t, ^3J = 7 Hz, 6 H, 2 × Me), 1.62 (sext., ^3J = 7 Hz, 4 H, 2 × CH_2), 2.47 (dt, ^3J = 7, ^5J = 3 Hz, 4 H, 2 × CH_2), 2.95 (m, 6 H, 3 × CH_2), 3.05 (m, 1 H, CH_2), 3.42 (m, 1 H, CH_2), 6.38 (m, 6 H, 6 × CH_{Ar}), 6.58 (t, ^5J = 3 Hz, 2 H, 2 × CH_{allene}), 7.40 (m, 2 H, 2 × CH_{Ar}), 7.65 (m, 2 H, 2 × CH_{Ar}), 7.88 (m, 2 H, 2 × CH_{Ar}), 8.35 (m, 2 H, 2 × CH_{Ar}) (selected NMR data for one isomer). ^{13}C NMR (50 MHz, $CDCl_3$, TMS): δ = 13.9 (q), 21.5 (t), 30.1 (t), 32.3 (t), 34.7 (t), 101.6 (d), 115.9 (s), 124.1 (d), 125.2 (d), 126.4 (d), 131.0 (d), 132.9 (d), 133.2 (d), 133.5 (d), 135.2 (s), 137.8 (s), 140.0 (s), 142.1 (s), 144.3 (s), 204.6 (s) (selected NMR data for one isomer). MS–ESI: *m*/*z* = 729 [M^+ + 23]. Anal. Calcd for $C_{40}H_{38}N_2O_6S_2$: C, 67.97; H, 5.42; N, 3.96; S, 9.07. Found: C, 67.79; H, 5.24; N, 3.77; S, 9.17.

(8) Compound **4a** (0.17 g, 85%); viscous oil. IR (neat): 2960, 1683, 1655, 1584, 1366, 1183, 728 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$, TMS): δ = 0.97 (t, ^3J = 7 Hz, 6 H, 2 × Me), 1.62 (sext, ^3J = 7 Hz, 4 H, 2 × CH_2), 2.54 (t, ^3J = 7 Hz, 4 H, 2 × CH_2), 3.05 (m, 6 H, 3 × CH_2), 3.09 (m, 1 H, CH_2), 3.61 (m, 1 H, CH_2), 6.37 (d, ^3J = 16 Hz, 2 H, 2 × CH), 6.56 (m, 4 H, 4 × CH_{Ar}), 6.74 (m, 2 H, 2 × CH_{Ar}), 7.60 (d, ^3J = 16 Hz, 2 H, 2 × CH). ^{13}C NMR (50 MHz, $CDCl_3$, TMS): δ = 13.7 (q), 17.5 (t), 32.6 (t), 34.8 (t), 42.5 (t), 126.4 (d), 130.2 (d), 134.7 (s), 134.8 (d), 135.1 (d), 139.4 (d), 139.9 (s), 140.0 (s), 200.1 (s). MS–EI: *m*/*z* (%) = 400 (20) [M^+], 383 (15), 329 (25), 187 (21), 129 (100). Anal. Calcd for $C_{28}H_{32}O_2$: C, 83.96; H, 7.99. Found: C, 83.64; H, 7.70.

(9) Compound **7** (0.25 g, 85%); viscous oil. IR (neat): 2954, 1974, 1534, 1342, 1052, 729 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$, TMS): δ = 2.05 (t, ^5J = 3.3 Hz, 3 H, Me), 6.15 (t, ^5J = 3.3 Hz, 1 H, CH_{allene}), 7.00 (m, 2 H, 2 × CH_{Ar}), 7.15 (m, 3 H, 3 × CH_{Ar}), 7.31 (m, 1 H, CH_{Ar}), 7.52 (m, 1 H, 2 × CH_{Ar}), 7.75 (m, 1 H, CH_{Ar}), 8.22 (m, 1 H, CH_{Ar}) (selected NMR data for one isomer). ^{13}C NMR (50 MHz, $CDCl_3$, TMS): δ = 13.0 (q), 100.4 (d), 112.5 (s), 125.0 (s), 126.3 (d), 126.9 (d), 127.0 (d), 127.1 (d), 127.3 (d), 128.1 (d), 128.6 (d), 128.7 (d), 131.3 (s), 134.5 (d), 134.8 (s), 203.6 (s) (selected NMR data for one isomer). MS (ESI): *m*/*z* = 322 [M^+ + 23]. Anal. Calcd for $C_{16}H_{13}NO_3S$: C, 64.20; H, 4.38; N, 4.68; S, 10.71. Found: C, 63.94; H, 4.19; N, 4.54; S, 10.48.

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