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[2.2]Paracyclophanes: The Interaction of *Pseudo-Geminal* Bispropargylic Alcohols with Sulfur Halides

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Abstract: The interaction of *pseudo-geminally* substituted bispropargylic alcohols with disulfur dichloride and sulfur dichloride leads to a mixture of cyclic eters. These compounds are formed under mild acidic condition provided by the organic ammonium chlorides or silica gel. The corresponding dipropargyloxy sulfides have been identified as reaction intermediates.

Keywords: [2.2]Paracyclophane; Propargylic alcohols; Disulfur dichloride; Sulfur dichloride.

Introduction

The sigmatropic rearrangements of allylic and propargylic esters of sulfur acids at various oxidation states has proven to be a rich source of

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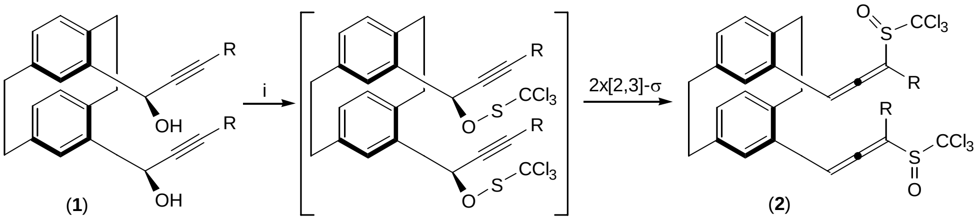
synthetically valuable and mechanistically intriguing reactions, often yielding novel and surprising products.[1-4] On the other hand, due to of the rigid molecular framework provided by the paracyclophane unit and its short interannular distance, functional groups in *pseudo-geminally* substituted [2.2]paracyclophanes 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.[5-8] Following our interest in the synthesis of new unsaturated *pseudo-geminally* substituted [2.2]paracyclophanes, we recently have reported the synthesis of the first *pseudo-geminal* bisallenyl[2.2]paracyclophanes.[9] This was accomplished by the reaction of the corresponding bispropargylic alcohols **1** with perchloromethylmercaptane via a double [2,3]sigmatropic rearrangement (Scheme 1).

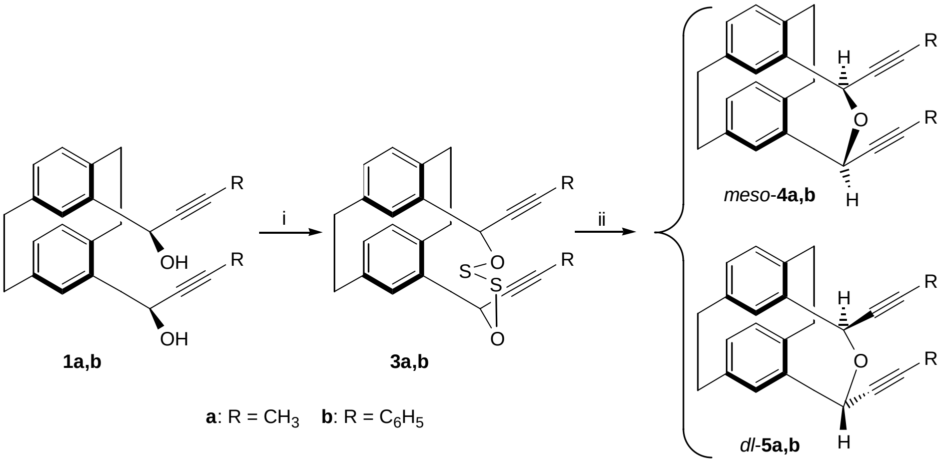


Scheme 1. Conditions: (i) PCMM (2 equiv.), Et_3N (2 equiv.), CH_2Cl_2, -78 °C

In view of our past experience with the use of electrophilic sulfur reagents with hydroxyalkynes,[10] we decided to examine the reactivity of the disulfur dichloride and sulfur dichloride towards *pseudo-geminally* substituted propargylic alcohols.

Results and Discussion

The reactions of *pseudo-geminal* bispropargylic alcohols **1a,b** with disulfur dichloride have been performed under high dilution conditions in the presence of triethylamine at -78 °C (Scheme 2). The NMR spectra of the crude reactions product have indicated a major symmetrical compound. However, the purification on silica gel has always provided a mixture of two compounds with an NMR pattern completely different of that of the crude product. Traces of these compounds have been identified in crude mixture when the reaction was performed in methylene chloride. In order to characterize the first reaction product the conditions was changed to give the minimum amount of side products. By using diethyl ether as solvent at -78 °C compounds **3a,b** were obtained more than 90% purity (determined by NMR). Mass spectrometric analysis of compound **3a** using ESI technique has indicated a molecular ion (*m/z* = 434) consistent with molecular formula of a dipropargyloxy disulfide ($C_{26}H_{26}O_2S_2$). The 2D NMR analysis supports the structure of compound **3a**.

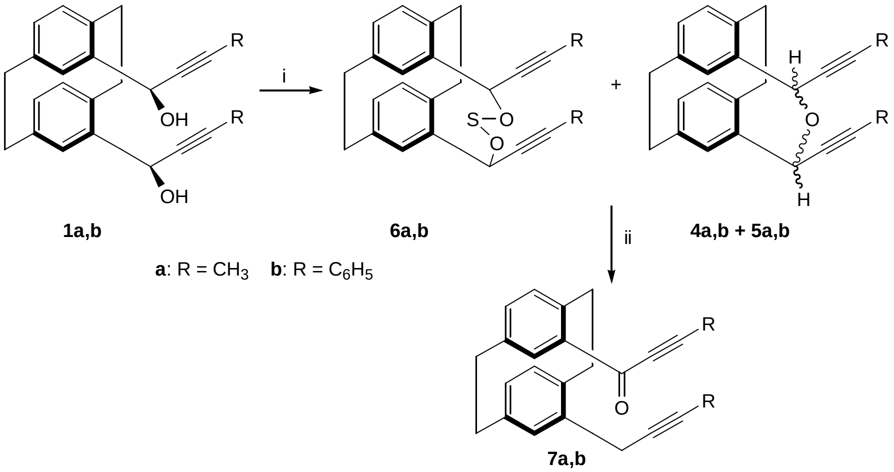


Scheme 2. Conditions: (i) S_2Cl_2, NEt_3 (2 eq.), Et_2O, -78 °C; (ii) silica gel

Similar results support the structure of **3b**. As mentioned above, purification of compounds **3** on silica gel was always accompanied of sulfur extrusion, most likely as polysulfides, and of formation of cyclic ethers **4** and **5**. This process is triggered by the mild acidic conditions provided by silica. The formation of cyclic ether from bispropargylic alcohols in the presence of pyridinium chloride has been previously reported by us.[11] The fact that traces of compounds **4** and **5** have been identified in crude mixture when the reaction was performed in methylene chloride comes in support to the above mechanism. The triethylammonium chloride precipitates in Et_2O whereas in CH_2Cl_2 it is soluble. According to NMR analysis, compounds **4** possess the symmetrically *meso*-structure and **5** are the *d,l* diastereomer; the ratio of the two compounds was found 2.5 : 1. The structural data of compounds **4b** and **5b** proved to be identical to those previously reported and detailed by X-ray analysis.[11]

The formation of cyclic ethers from dipropargyloxy disulfides **3** competes the expected double and concerted [2,3]sigmatropic rearrangement to the corresponding vicinal bis sulfoxides. Apparently, the first process is kinetically favored.

The reactions of *pseudo-geminal* bispropargylic alcohols **1a,b** with sulfur dichloride have been performed under various experimental conditions using methylene chloride as solvent and triethylamine as scavenger for hydrochloric acid (Scheme 3). Regardless of the concentration (10^{-4} or 10^{-2} M) and reaction temperature (-78 or 0 °C) a complex mixture of products was obtained. The NMR spectra have revealed that major constituents of the crude mixture are cyclic ethers **4** and **5**, and a compound related to disulfide **3**. The latter should correspond to the structure of dipropargyloxy sulfides **6**, as the NMR spectra revealed an identical pattern for the bridge hydrogens. The ratio cyclic ethers / monosulfide **6** was always ca. 1 : 1. Even in Et_2O the amount of cyclic ethers was considerable. Most likely the dipropargyloxy sulfides **6** are more sensitive to acidic conditions than the corresponding disulfides. This assumption is supported by an unexpected conversion of the crude reaction mixture to a single compound, process that involves an intramolecular hydride transfer. In contact with silica the pinacolone type compounds **7a,b** were formed in 75-78% isolated yield (Scheme 3).



Scheme 3. Conditions: (i) SCl_2, NEt_3 (2 eq.), CH_2Cl_2, -78 °C; (ii) silica gel

These structures have been previously reported as a result of interactions between various *pseudo-geminally* substituted diols and stronger acids than PyHCl, such as TsOH at 55 °C or H_2SO_4 at 0 °C.[11] Detailed mechanistic aspects have been presented. The above transformation appears to be catalyzed by a sulfur acid as a result of sulfur elimination from compounds **6**. The analytical data of pinacolone type compound **7b** are in agreement with those reported for the same compound synthesized by an alternative method.[11] Again the acid catalyzed rearrangement of dipropargyloxy sulfide to pinacolone type compounds appears to be kinetically favored against the double sigmatropic rearrangement to the bisallenyl sulfone derivatives.

Conclusions

The interactions between *pseudo-geminally* substituted bispropargylic alcohols and sulfur chlorides have been studied under various experimental conditions. The dipropargyloxy disulfides have been demonstrated as reaction intermediates of disulfur dichloride. Under mild acidic conditions provided by $Et_3N{\cdot}HCl$ or silica these compounds undergo sulfur elimination providing a mixture of *meso* and *d,l* cyclic ethers in a 2.5 : 1 ratio. The sulfur dichloride has provided dipropargyloxy sulfides, compounds that were found responsible for a vinylogous pinacol rearrangement.

Acknowledgments

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Experimental

Disulfur dichloride was purchased from commercial sources and distilled before use. Sulfur dichloride was prepared according to literature data and distilled prior use in the presence of phosphorus trichloride.[12] Melting points were obtained on a Mel-Temp II apparatus. IR spectra were recorded on a Bruker Tensor 27 instrument. NMR spectra were recorded on a Bruker DPX-300 spectrometer. Chemical shifts are reported in ppm downfield from TMS. Elemental analyses (C, H, N, S) were conducted using the CE440 Elemental Analyser. Mass spectra were recorded on a Finnigan MAT 90X spectrometer.

Reaction of disulfur dichloride with bispropargylic alcohol **1a***; Typical Procedure*

To a solution of bispropargylic alcohol (**1a**, 86 mg, 0.25 mmol) in diethyl ether (30 mL) triethyl amine (0.07 mL, 0.5 mmol) was added and reaction mixture cooled to -78 °C. A solution of disulfur dichloride (0.02 mL, 0.25 mmol) in diethyl ether (15 mL) was added dropwise. After 1 h the reaction mixture was allowed to warm to room temperature and stirred for additional 2 h. After the usual work-up (H_2O, $NaHCO_3$, $MgSO_4$) evaporation of the solvent gave the crude product as brown viscous oil (92 mg). NMR data of dipropargyloxy disulfide **3a** were selected from the spectrum of this oil. Purification by column chromatography on silica gel using CH_2Cl_2/pentane 1:1 as eluent provided *meso*-ether **4a** and *d,l*-ether **5a** in a 2.5 : 1 ratio.

Dipropargyloxy disulfide 3a: Selected NMR data: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.70 (d, ^5J = 2 Hz, 6 H, $2CH_3$), 3.0 (m, 2H, CH_2), 3.09 (s, 4H, $2CH_2$), 3.45 (m, 2H, CH_2), 5.64 (q, ^5J = 2 Hz, 2 H, 2CH), 6.51 (m, 4H, 4CHar), 6.78 (m, 2H, 2CHar). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 3.2 (q), 31.6 (t), 36.1 (t), 61.5 (d), 78.9 (s), 82.0 (s), 127.6 (d), 133.0 (d), 134.8 (s), 135.4 (d), 139.2 (s), 140.3 (s).

Dipropargyloxy disulfide 3b: Selected NMR data: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.02 (m, 2H, CH_2), 3.12 (s, 4H, $2CH_2$), 3.47 (m, 2H, CH_2), 5.68 (s, 2 H, 2CH), 6.49 (m, 4H, 4CHar), 6.82 (m, 2H, 2CHar), 7.24 (m, 4H, 4CHar), 7.38 (m, 6H, 6CHar). ^{13}C NMR (75 MHz, CDCl$_3$): δ = 31.8 (t), 35.8 (t), 61.7 (d), 78.7 (s), 82.1 (s), 122.9 (s), 127.6 (d), 128.1 (d), 132.4 (d), 133.0 (d), 134.5 (d), 134.8 (s), 135.0 (d), 138.8 (s), 140.3 (s).

*meso-Ether **4a***: white crystals, 44 mg (54%); Mp 174-175 °C. IR (ATR): 3310, 3025, 2947, 2210, 1654, 1592, 1478, 1410, 1357, 1254, 1068, 1012, 741, 642 cm^{-1}. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.81 (d, ^5J = 2.2 Hz, 6 H, 2CH$_3$), 2.95 (m, 2H, CH$_2$), 3.05 (m, 4H, 2CH$_2$), 3.47 (m, 2H, CH$_2$), 5.36 (q, ^5J = 2.2 Hz, 2H, 2CH), 6.36 (m, 4H, 4CHar), 6.98 (m, 2H, 2CHar). ^{13}C NMR (75 MHz, CDCl$_3$): δ = 3.9 (q), 32.0 (t), 35.6 (t), 68.1 (d), 78.1 (s), 82.4 (s), 132.5 (d), 134.5 (d), 135.2 (d), 137.0 (s), 138.2 (s), 141.3 (s). MS (ESI): m/z = 326 (M$^+$). Calcd for $C_{24}H_{22}O$: C, 88.31; H, 6.79. Found: C, 88.58; H, 6.98.

*d,l-Ether **5a***: white crystals, 18 mg (22%); Mp 138-139 °C. IR (ATR): 3307, 3023, 2214, 1650, 1584, 1471, 1417, 1354, 1252, 1014, 743, 648 cm^{-1}. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.84 (d, ^5J = 2 Hz, 3 H, CH$_3$), 2.08 (d, ^5J = 2 Hz, 3H, CH$_3$), 2.99 (m, 2H, CH$_2$), 3.14 (m, 4H, 2CH$_2$), 3.52 (m, 1H, CH$_2$), 3.93 (m, 1H, CH$_2$), 5.56 (q, ^5J = 2 Hz, 1H, CH), 5.94 (q, ^5J = 2 Hz, 1H, CH), 6.34 (m, 4H, 4CHar), 6.98 (m, 2H, 2CHar). ^{13}C NMR (75 MHz, CDCl$_3$): δ = 3.9 (q), 4.0 (q), 31.9 (t), 35.0 (t), 35.8 (t), 69.2 (d), 69.8 (d), 75.1 (s), 78.2 (s), 82.0 (s), 86.8 (s), 132.1 (d), 132.6 (d), 135.3 (d), 136.5 (d), 136.9 (d), 139.2 (s), 139.3 (s), 139.5 (s), 140.1 (s). MS (ESI): m/z = 326 (M$^+$). Calcd for $C_{24}H_{22}O$: C, 88.31; H, 6.79. Found: C, 88.62; H, 7.03.

Reaction of sulfur dichloride with bispropargylic alcohol **1a***; Typical Procedure*

To a solution of bispropargylic alcohol (**1a**, 172 mg, 0.5 mmol) in CH_2Cl_2 (700 mL) triethyl amine (0.14 mL, 0.5 mmol) was added and reaction mixture cooled to -78 °C. A solution of sulfur dichloride (0.032 mL, 0.5 mmol) in CH_2Cl_2 (50 mL) was added dropwise. After 1 h the reaction mixture was allowed to warm to room temperature and stirred for additional 2 h. After the usual work-up (H_2O, $NaHCO_3$, $MgSO_4$) evaporation of the solvent gave the crude product that was purified by column chromatography on silica gel using CH_2Cl_2/pentane 1:1 as eluent. The pinacolone **7a** was obtained as white crystals (100 mg, 61%); Mp 153-154 °C. IR (ATR): 2930, 2215, 1621, 1421, 1288, 1262, 1189, 894, 757, 650, 528 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.78 (t, ^5J = 2.4 Hz, 3 H, CH_3), 2.13 (s, 3H, CH_3), 2.92-3.16 (m, 6H, $3CH_2$), 3.19- 3.31 (tABq, ^2J = 19, ^5J = 2.4 Hz, 2H, CH_2), 3.36 (m, 1H, CH_2), 4.32 (m, 1H, CH_2), 6.50 (m, 4H, 4CHar), 6.68 (dd, ^3J = 7.8, ^4J = 2 Hz, 1H, CHar), 7.39 (d, ^4J = 2 Hz, 1H, CHar). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 3.7 (q), 4.4 (q), 23.5 (t), 32.0 (t), 33.2 (t), 34.7 (t), 34.8 (t), 80.2 (s), 91.1 (s), 130.8 (d), 132.2 (d), 134.3 (d), 135.5 (s), 136.5 (d), 136.9 (d), 137.5 (d), 137.6 (s), 138.0 (s), 139.4 (s), 139.5 (s), 142.8 (s), 180.0 (s). MS (ESI): m/z = 326 (M^+). Calcd for $C_{24}H_{22}O$: C, 88.31; H, 6.79. Found: C, 88.60; H, 7.06.

References

1. Braverman, S. In *Chemistry of Sulfones and Sulfoxides*, Patai, S., Rappoport, Z., Stirling, C. J. M., Eds., Wiley: New York, 1988, Chapter 13.

2. Braverman, S. In *Chemistry of Sulfones and Sulfoxides*, Patai, S., Rappoport, Z., Stirling, C. J. M., Eds., Wiley: New York, 1988, Chapter 14.
3. Braverman, S. In *The Chemistry of Sulfinic Acids, Esters and Their Derivatives*, Patai, S. Ed., Wiley: New York, 1990, Chapter 11.
4. Braverman, S. in *The Chemistry of Sulfenic Acids and Their Derivatives*, Patai, S. Ed., Wiley: New York, 1990, Chapter 8.
5. Greiving, H., Hopf, H., Jones, P. G., Bubenitschek, P., Desvergne, J.-P., and Bouas-Laurent, H. *Eur. J. Org. Chem.* **2005**, 558.
6. Hopf, H., Greiving, H., Beck, C., Dix, I., Jones, P. G., Desvergne, J.-P., and Bouas-Laurent, H. *Eur. J. Org. Chem.* **2005**, 567.
7. Hopf, H. *Angew. Chem.* **115**, 2928 (2003); *Angew. Chem. Int. Ed.* **42**, 2822 (2003).
8. Hopf, H. In *Modern Cyclophane Chemistry,* Gleiter, R. and Hopf, H. Eds., Wiley-VCH: Weinheim, 2004, Chapter 7.
9. Birsa, M. L., Jones, P. G., Braverman, S., and Hopf H. *Synlett* **2005**, 640.
10. Birsa, M. L. and Hopf H. *Synlett* **2007**, 2753.
11. Birsa, M. L., Jones, P. G., and Hopf, H. *Eur. J. Org. Chem.* **2005**, 3263.
12. *Handbook of Preparative Inorganic Chemistry* 2nd English Ed., Brauer, G., Ed., Academic Press: New York, 1963, Vol. 1, p. 370.