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Synthesis and cascade reactions of diallenyl α-disulfones and sulfinyl sulfones

Samuel Braverman,[a,*] Marina Cherkinsky,[a] Israel Goldberg[b] and Milon Sprecher[a]

[a]*Department of Chemistry, Bar-Ilan University, Ramat-Gan 52900, Israel*
[b]*School of Chemistry, Tel-Aviv University, Ramat-Aviv 69978, Israel*

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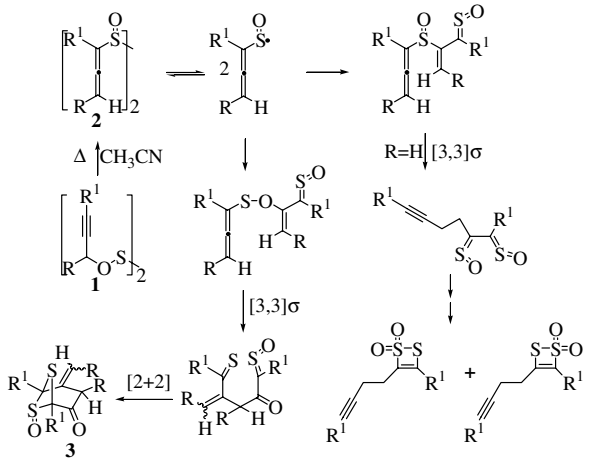
Abstract—The synthesis and reactivity of diallenic α-disulfones and diallenic sulfinyl sulfones are described. Both types of compound exhibit enhanced reactivity relative to their saturated counterparts, and react spontaneously at low temperature, upon preparation, to yield novel and functionalized bicyclic products. Possible mechanisms for their multi-step rearrangements are suggested.

The increasing awareness of environmental issues in our society and the fear that chemistry could negatively influence the ecological balance, impart an uncompromising demand for high efficiency on any modern synthetic design. Such efficiency is examined in terms of the atom-economy[1] of the reactions used. Clearly, both catalytic reactions[2] and tandem processes[3–6] can make a crucial contribution to the achievement of the desired goal. Our first encounter with tandem reactions was some three decades ago following our discovery of the [2,3]-sigmatropic rearrangement of propargylic sulfenates[7] and sulfinates[8,9] to allenic sulfoxides and sulfones, respectively. We then found that thiophene dioxide derivatives such as 3-isopropenyl-4-isopropylthiophene 1,1-dioxide were readily accessible by a tandem double [2,3]-sigmatropic rearrangement of the appropriate dipropargylic sulfoxylates, followed by cyclization of the generated diallenyl sulfone via a diradical intermediate.[10] Subsequently, we reported the synthesis of diallenic disulfides and their spontaneous rearrangement to thienothiophene derivatives,[11,12] via tandem [3,3]-sigmatropic rearrangement and double intramolecular Michael-type addition. More recently, some interesting tandem reactions have also been observed for bis-allenyl thiosulfonates,[13] which were obtained by disproportionation of the appropriate sulfinic acids.

A most impressive example of tandem reactions of dipropargylic systems is the unprecedented transformations of dipropargylic dialkoxy disulfides (**1**) (Scheme 1).[14] These mechanistically fascinating multi-step reactions lead in an atom economic manner, via highly unstable diallenic *vic*-disulfoxide intermediates (**2**), to novel bicyclic products (**3**) of synthetic, and perhaps medicinal interest, since they are related to the naturally occurring zwiebelanes.[15–17]

In continuation of these studies and in view of the variety of novel products obtained, it was decided to investigate the synthesis and reactivity of diallenic α-disulfones and diallenic sulfinyl sulfones. Unlike the



Scheme 1.

Keywords: Allenes; α-Disulfones; Sulfinyl sulfones; γ-Sultines; γ-Sultones; Tandem reaction.
* Corresponding author. Tel.: +972 3 5318322; fax: +972 3 7384053; e-mail: bravers@mail.biu.ac.il

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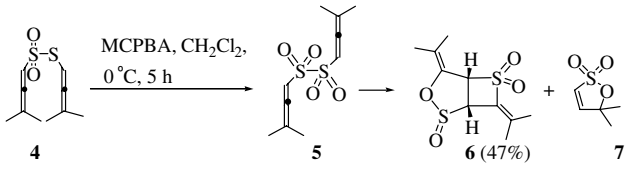
corresponding *vic*-disulfoxides, which are well-known for their high instability, simple α-disulfones are quite stable compounds.[18,19] On the one hand, with only few exceptions,[20,21] oxidation of disulfides generally affords the corresponding thiosulfonates due to spontaneous free radical cleavage and recombination of the unstable *vic*-disulfoxide intermediates.[22,23] In contrast, α-disulfones, usually prepared by oxidation of thiosulfonates with MCPBA,[24,25] are easily isolable and undergo sulfur–sulfur bond cleavage only on heating or irradiation.[26–29]

Due to the instability of the diallenyl disulfides mentioned above,[11] we were precluded from using their oxidation to thiosulfonate as the first stop towards our goal. The thiosulfonates were therefore prepared via disproportionation of the corresponding allenesulfinic acids.[13] Interestingly, while oxidation of dialkyl thiosulfonates to disulfones with MCPBA at room temperature has been reported to proceed rather slowly,[25] the oxidation of *S*-(3-methylbuta-1,2-dienyl)-3-methylbuta-1,2-diene-1-sulfonothioate (**4**) proceeds quite rapidly at 0 °C as judged by the disappearance of the starting material on TLC. Furthermore, after the putative oxidation, product **5** was found to rearrange and cyclize to the novel bicyclic multifunctional product **6** containing *exo*-methylene double bonds, γ-sultine and sulfone functionalities (Scheme 2).[30] The structure of this new compound was unequivocally confirmed by X-ray determination (Fig. 1). Starting from *S*-(2-cyclohexylidenevinyl) 2-cyclohexylideneethylenesulfonothioate,[13] the corresponding cyclohexylidene derivative of product **6** has also been obtained, although not fully purified.



Scheme 2.

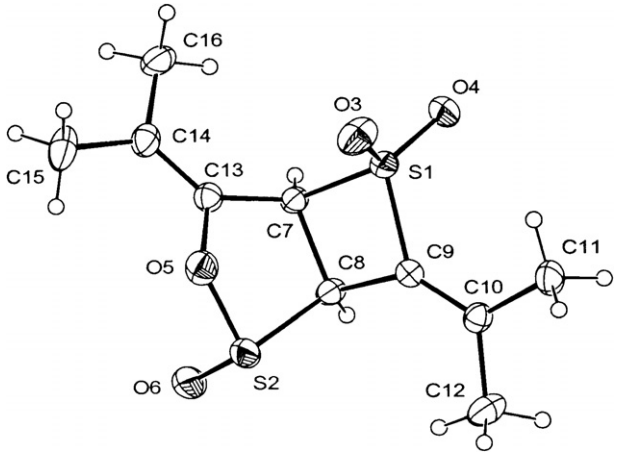
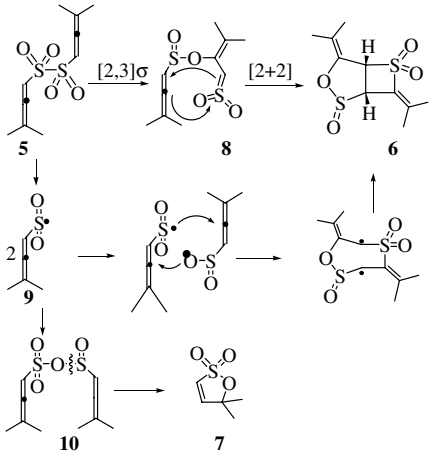


Figure 1. X-ray structure of *cis*-4,7-bis(1-methylethylidene)-3-oxa-2,6-dithiabicyclo[3.2.0]heptane 2,6,6-trioxide, **6**.

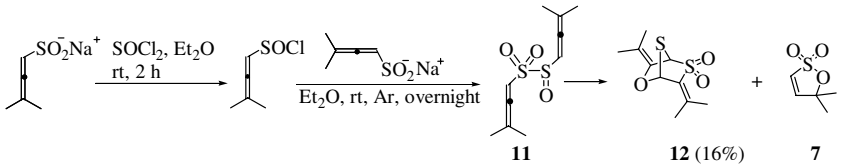
Two alternative mechanisms can be tentatively suggested to explain the formation of **6** from **5**. The first mechanism postulates a [2,3]-sigmatropic rearrangement of **5** to the sulfene-sulfinate intermediate **8**, followed by an intramolecular [2+2]-cycloaddition of the sulfene moiety[31–35] to the α,β-double bond of the allenyl group (Scheme 3). Alternatively, a free radical cascade reaction may be suggested involving cleavage of the disulfone **5** to two allenesulfonyl radicals **9** followed by their 'head to tail' recombination and cyclization to **6**, as shown in Scheme 3. The formation of α,β-unsaturated γ-sultone **7** as a minor product (not isolated) was detected by NMR analysis of the crude mixture. Formation of this compound, which we have encountered in previous studies[36] can be explained by a recombination of two allenesulfonyl radicals to yield a mixed sulfinic-sulfonic anhydride **10** which can undergo further cleavage and cyclization to the γ-sultone **7** (Scheme 3). Such a type of recombination of sulfonyl radicals to an intermediate **10**, the decomposition of which may yield a sulfinyl radical and an oxygen-centered radical $RSO_2O^{\cdot}$ has been reported before.[37] In the present instance, in the presence of MCPBA, the formation of **7** may follow an ionic pathway.

Although sulfinyl sulfones are expected intermediates in the conversion of thiosulfonates to α-disulfones,[38] these compounds are usually prepared by nucleophilic reactions of sulfinyl chlorides with sodium sulfinate salts.[39] Therefore, we used this procedure to prepare the diallenyl sulfinyl sulfone **11** by treatment of sodium allenesulfinate with the corresponding sulfinyl chloride. In view of the reduced stability of sulfinyl sulfones as compared to α-disulfones in general,[19,40] it was not surprising that these compounds could not be isolated. However, we were able to isolate bicyclic product **12** (along with γ-sultone **7** (Scheme 4)). The former product is similar to that isolated by us from the rearrangement of α-*t*-butyl- and α-adamantyl dipropargyloxy disulfides[14] and identical to the one unexpectedly obtained by Baudin[41] from the acidic hydrolysis of allenesulfinamides.

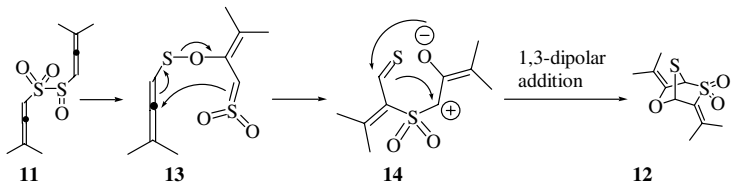
A tentative mechanism for the conversion of sulfinyl sulfone **11** to product **12** is presented in Scheme 5. This mechanism is reminiscent of that suggested before for



Scheme 3.



Scheme 4.



Scheme 5.

the rearrangement of α-*t*-butyl- and α-adamantyl dipropargyloxy disulfides.[14] Intermediate **13** can arise by either a [2,3]σ shift or a free radical pathway. Finally, formation of γ-sultone **7** parallels its formation from the corresponding α-disulfone shown in Scheme 3.

Acknowledgment

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30. Structural assignments for compound **6** were made on the basis of 2D ^{1}H and ^{13}C NMR techniques, including COSY, HMQC, HMBC and NOESY. ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.49 (d, 1H, $J = 7.0$ Hz, H-5), 4.49 (dsept, 1H, $J = 7.0$, 1.9 Hz, H-1), 2.12 and 2.02 (2d, 3H each, $J = 1.9$ Hz, $C(CH_3)_2$–C-7), 1.92 and 1.89 (2s, 3H each, $C(CH_3)_2$–C-4); ^{13}C NMR (150 MHz, $CDCl_3$): δ 148.40 (C-7), 143.52 (C-4), 142.56 (*C*=C-7), 124.07 (*C*=C-4), 75.18 (C-5), 66.87 (C-1), 22.32 and 21.68 ((*C*H$_3$)$_2$C=C-7), 20.55 and 18.27 ((*C*H$_3$)$_2$C=C-4). CIHRMS *m/z* Calcd for $C_{10}H_{14}O_4S_2$: 262.0334; found, 262.0326. IR ν_{max} (KBr): 1677, 1442, 1312, 1177, 1131 cm^{-1}. X-ray crystallographic data (excluding structure factors) for **6** have been deposited with the Cambridge Crystallographic Data Centre as a Supplementary Publication Number CCDC 645208. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ [fax: +44 0 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].
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