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Facile preparation and rearrangement of allylic dialkoxy disulfides

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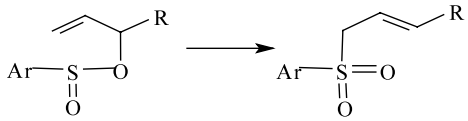
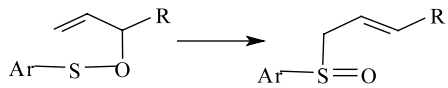
Abstract—Allylic dialkoxy disulfides were obtained in good yields and their reactivity has been investigated. Similarly to allylic sulfoxylates, these esters undergo double [2,3]-sigmatropic rearrangement to the appropriate *vic*-disulfoxides. The latter, being unstable, undergoes spontaneous rearrangement to the corresponding thiosulfonates. © 2002 Elsevier Science Ltd. All rights reserved.

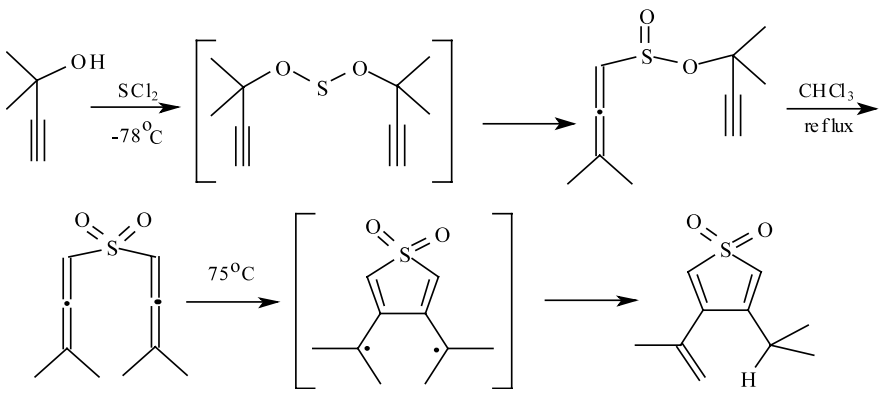
The [2,3]-sigmatropic rearrangement of allylic arenesulfinates to allylic aryl sulfones (Eq. (1)), discovered by us more than three decades ago,[1a] has served as a model for the analogous and well known rearrangement of allylic sulfenates to sulfoxides (Eq. (2)),[1b] as well as for the related rearrangements of propargylic sulfenates[1c] and sulfinates[1d] to allenic sulfoxides and sulfones, respectively. Due to their high stereoselectivity and efficiency, these rearrangements have found extensive application in organic synthesis since their publication.[2,3]



(1)



(2)



Scheme 1.

Keywords: allylic dialkoxy disulfides; thiosulfonates; *vic*-disulfoxides; sigmatropic rearrangement.

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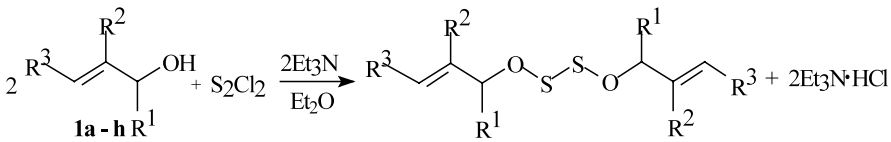
In one such application from our own laboratory, a combination of the last two rearrangements was used to prepare bis-γ,γ-dimethylallenyl sulfone. Furthermore, this sulfone underwent a facile and quantitative cyclization via a diradical intermediate on heating, to a thiophene 1,1-dioxide derivative (Scheme 1).[4] More recently, this reaction has also been used as a model for the design of a new class of DNA cleaving molecules which could mimic the biological activity of the naturally occurring enediynes.[5,6] Interestingly, shortly after the publication of our report on the double [2,3]-sigmatropic rearrangement of propargylic sulfoxylates the analogous transformation of allylic sulfoxylates was also reported.[7]

Our past experience with [2,3]-sigmatropic rearrangements of various types of allylic and propargylic thioesters led us to the discovery and study of the double [2,3]-sigmatropic rearrangement of allylic and propargylic dialkoxy disulfides. Until recently, dialkoxy disulfides have been little studied.[8–10] In 1965, Thompson and co-workers[8] investigated the preparation and reactions of such compounds. However, Thompson reported[8] failure in his attempts to prepare allylic and propargylic dialkoxy disulfides.

Notwithstanding these previous unsuccessful attempts, we have recently succeeded in the preparation of a series of various allylic and propargylic dialkoxy disulfides in good to excellent yields.[11,12] The present report describes the synthesis and rearrangement of allylic dialkoxy disulfides. The results obtained with the propargylic esters[12] will be described separately. Allylic esters **2a–h** were obtained in high yields and have been found to be stable in $CHCl_3$ solution at −18°C for extended periods (Eq. (3), Table 1).[11] Our success is attributable to a modified preparative procedure (ROH, S_2Cl_2, Et_3N, diethyl ether as solvent, 0°C, low temperature work-up) in the course of which the chloride ion produced is removed from the reaction mixture as precipitated triethylamine hydrochloride. Cleavage of the S–S bond in the product and subsequent washings are thus avoided. Due to its high reactivity, compound **2b** was difficult to isolate. However, by shortening the reaction time to only 30 min and lowering the temperature to −12°C, we were able to isolate **2b** as well, though in a lower yield. Most of the new compounds have a strong pungent smell of crushed onion. All new compounds were easily identified by their spectral data, which in the case of primary esters exhibits the characteristic NMR splitting pattern of diastereotopic α-methylene protons due to restricted rotation around the S–S bond.[8,10b]

Our first attempts to test the reactivity of the new compounds at room temperature were rather disap-



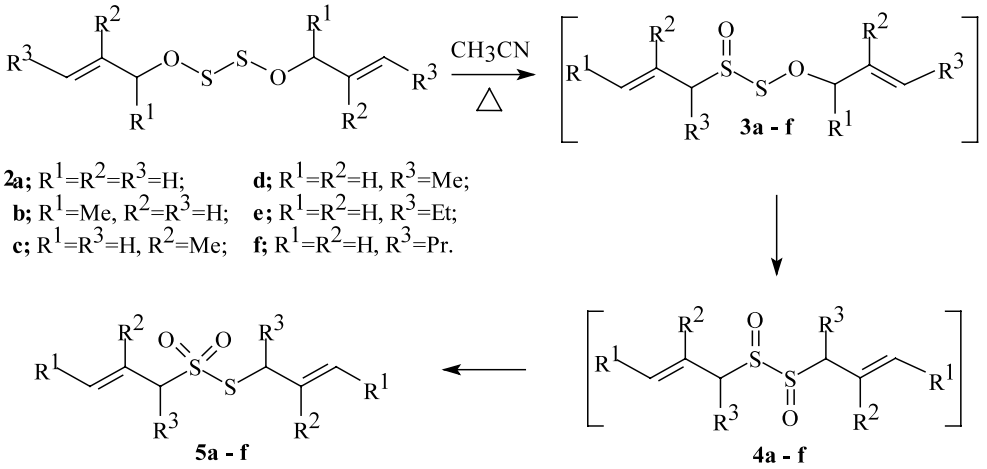
1a - h

(3)

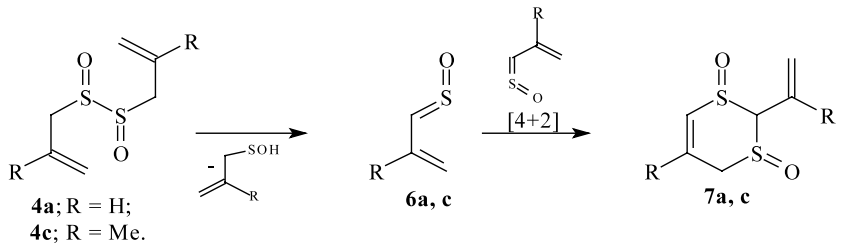
2a; $R^1=R^2=R^3=H$; **2e;** $R^1=R^2=H$, $R^3=Et$;
b; $R^1=Me$, $R^2=R^3=H$; **f;** $R^1=R^2=H$, $R^3=Pr$;
c; $R^1=R^3=H$, $R^2=Me$; **g;** $R^1=R^2=H$, $R^3=Ph$,
d; $R^1=R^2=H$, $R^3=Me$; **h;** $R^1=H$, $R^2=Me$, $R^3=Ph$.

Table 1. ^1H NMR data and yields of allylic dialkoxy disulfides

Compound	^1H NMR (300 MHz, $CDCl_3$)	Yield (%)
2a	δ 5.93 (ddt, $J=17.1$, 10.3, 6.0 Hz, 2H), 5.32 (ddt, $J=17.1$, 1.5, 1.2 Hz, 2H), 5.26 (ddt, $J=10.3$, 1.5, 1.2 Hz, 2H), ABq system: 4.40 (ddt, $J=12.2$, 6.0, 1.2 Hz, 2H) and 4.29 (ddt, $J=12.2$, 6.0, 1.2 Hz, 2H).	87
2b	As a mixture of four diastereoisomers: δ 5.83 (m, 2H for four isomers), 5.27 (dm, $J=10.5$ Hz, 4H for one isomer) and 5.21 (dm, $J=10.5$ Hz, 4H for three isomers), 4.40 (quint, $J=6.4$ Hz, 2H for four isomers), 1.370, 1.365, 1.360 and 1.355 (d, $J=6.4$ Hz, 3H each).	62
2c	δ 5.00 (s, 2H), 4.97 (s, 2H), ABq system: 4.31 (d, $J=12.0$ Hz, 2H) and 4.20 (d, $J=12.0$ Hz, 2H), 1.77 (s, 6H).	95
2d	ABq system: δ 5.79 (dqt, $J=15.2$, 6.5, 1.0 Hz, 2H) and 5.61 (dqt, $J=15.2$, 6.7, 1.0 Hz, 2H), ABq system: 4.33 (ddquint, $J=11.2$, 6.7, 1.0 Hz, 2H) and 4.21 (ddquint, $J=11.2$, 6.7, 1.0 Hz, 2H), 1.74 (ddt, $J=6.5$, 1.5, 1.0 Hz, 6H)	98
2e	δ 5.68 (dtt, $J=10.6$, 7.5 1.0 Hz, 2H), 5.53 (dtt, $J=10.6$, 6.8, 1.0, 2H), ABq system: 4.44 (dd, $J=11.5$, 6.8 Hz, 2H), and 4.34 (dd, $J=11.5$, 6.8 Hz, 2H), 2.10 (dquint., $J=7.5$, 1 Hz, 4H), 0.98 (t, $J=7.5$ Hz, 6H).	87
2f	δ 5.75 (dtt, $J=15.4$, 6.8, 0.8 Hz, 2H), 5.57 (dtt, $J=15.4$, 6.5, 1.0 Hz, 2H), ABq system: 4.32 (ddd, $J=11.5$, 6.5, 0.8 Hz, 2H) and 4.21 (ddd, $J=11.5$, 6.5, 0.8 Hz, 2H), 2.03 (q, $J=7.0$ Hz, 4H), 1.40 (sextet, $J=7.5$ Hz, 4H), 0.90 (t, $J=7.3$ Hz, 6H).	90
2g	δ 7.31 (m, 10H), 6.60 (d, $J=15.9$ Hz, 2H), 6.27 (dt, $J=15.9$, 6.5 Hz, 2H), ABq system: 4.55 (ddd, $J=12.1$, 6.5, 1.2 Hz, 2H) and 4.44 (ddd, $J=12.1$, 6.5, 1.2 Hz, 2H).	95
2h	δ 7.27 (m, 10H), 6.51 (br. s, 2H), ABq system: 4.44 (dd, $J=11.5$, 1.0 Hz, 2H) and 4.34 (dd, $J=11.5$, 1.0 Hz, 2H), 1.92 (d, $J=1.5$ Hz, 6H).	93



Scheme 2.



Scheme 3.

pointing due to the formation of allylic sulfinates resulting from [2,3]-sigmatropic rearrangements of the corresponding sulfoxylates. The latter may arise by attack of liberated alcohol on a sulfur atom of ROSSOR. However, when the reaction is carried out in refluxing acetonitrile solution, allylic dialkoxy disulfides undergo double [2,3]-sigmatropic rearrangements to the expected *vic*-disulfoxides **4a**–**f**, which due to their well known instability,[13] rearrange further to the corresponding thiosulfonates **5a**–**f** (Scheme 2).[11] Reaction times depend on substitution and vary between 5 min for α-methylallyl to several hours for the unsubstituted and γ-alkylsubstituted allylic dialkoxy disulfides. Not surprisingly, the γ-phenylallyl esters **2g**,**h** do not undergo the [2,3]-sigmatropic rearrangement, but rather disproportionate to the corresponding aldehydes, alcohols and elemental sulfur. The lack of rearrangement of these esters is reminiscent of the lack of rearrangement of cinnamyl sulfenates[1b,2] and is caused by the loss of conjugation of the allylic double bond with the benzene ring during the allylic shift. The cost of the latter exceeds the gain in free energy accompanying the sulfenate to sulfoxide rearrangement.[2] We should also note that so far we have not been able to eliminate completely the accompanying ROSSOR to ROSOR transformation. Therefore, the yields of thiosulfonates **5a**–**f** are only moderate and range between 30 and 65%.

It is interesting to note that in addition to thiosulfonates **5a**–**f**, small amounts of 2-vinyl-2,4-dihydro-1,3-dithiin 1,3-dioxides (**7a**, **c**) have also been obtained in the case of **2a** and **2c**. These products may arise by the intermolecular self [4+2]-cycloaddition of the corresponding conjugated vinyl sulfine **6** generated by either H-abstraction from a sulfinyl radical by another such radical, or by a cycloelimination reaction of **4** (Scheme 3). The structure of this compound was confirmed by 2D NMR experiments. Although the rare [4+2] reaction of conjugated vinyl sulfines has already been observed in our laboratory,[14] it is apparently the first known example of a self-cycloaddition of such sulfines. The parent 1,3-dithiin of **7a** was reported by Block[15] as a decomposition product of allicin (diallyl thiosulfinate) via thioacrolein.

Finally, we intend to use chiral and optically active allylic alcohols to prepare previously unreported, optically active dialkoxy disulfides. Rearrangement of the latter should yield chiral thiosulfonates. Such results would be of both chemical and biological interest since thiosulfonates in general show various biological activities.[15,16]

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11. All new compounds showed spectral data in accord with assigned structures. Selected data: diallyloxy disulfide **2a**: ^{1}H NMR see Table 1, ^{13}C NMR (300 MHz, $CDCl_3$): δ 133.11 (=**C**H–), 119.03 (=**C**H_2), 75.56 (–**C**H_2–), IR (neat): 1053, 1165, 1646 cm^{-1}, MS (CI/CH_4): m/z 179 (MH^+, 5.25%), 160 (100%), 89 ($M^+/2$, 51%), HRMS (elemental composition): calcd ($C_6H_{11}O_2S_2$) 179.020048; found 179.016563, diallyl thiosulfonate **5a** (yield 46%): ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.92 (m, 1H+1H for both protons), 5.56 (dq, J=10.0, 1.1 Hz, 1H), 5.50 (dq, J=17.0, 1.2 Hz, 1H), 5.36 (dq, J=17.0, 1.2 Hz, 1H), 5.26 (dq, J=10.0, 1.2 Hz, 1H), 4.00 (ddd, J=7.2, 1.1, 0.8 Hz, 2H), 3.80 (ddd, J=7.2, 1.2, 0.8 Hz, 2H), ^{13}C NMR (300 MHz, $CDCl_3$): δ 131.78 (=**C**H–), 126.02 (=**C**H_2), 124.57 (=**C**H–), 120.21 (=**C**H_2), 67.30 (–**C**H_2–SO_2), 39.49 (–**C**H_2–S), IR (neat): 1127, 1324, 1637, 3416 cm^{-1}, MS (CI/CH_4): m/z 179 (MH^+, 14.99%), 177 ($(M-H)^+$, 100.00%), 137 (M^+/2+'O', 10.38%), 105 (M^+/2-'O', 24.50%), HRMS (elemental composition): calcd ($C_6H_{11}O_2S_2$) 179.020048; found 179.019867, bis-α-methylallyl thiosulfonate **5d** (yield 45%) as a mixture of two diastereoisomers: ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.91 (m, 2H for both isomers), 5.48 (m, 2H for both isomers), 5.305 and 5.296 (dt, J=17.0, 1.0 Hz, 1H each), 5.19 and 5.18 (dt, J=10.0, 1.0 Hz, 1H each), 4.15 (m, 1H for both isomers), 3.90 (m, 1H for both isomers), 1.56 and 1.55 (d, J=7 Hz, 3H each), 1.54 and 1.53 (d, J=7 Hz, 3H each), ^{13}C NMR (300 MHz, $CDCl_3$): δ 138.14 and 137.92 (=**C**H– each), 131.25 and 130.51 (=**C**H– each), 123.20 and 123.06 (=**C**H_2 each), 116.89 and 116.78 (=**C**H_2 each), 71.30 and 71.18 (–**C**H_2–SO_2 each), 49.59 and 49.55 (–**C**H_2–S each), 20.84 and 20.76 (**C**H_3–CH–SO_2 each), 14.10 and 13.62 (**C**H_3–CH–S each), IR (neat): 1125, 1321, 1451, 1637, 2980 cm^{-1}, MS (CI/CH_4): m/z 207 (MH^+, 4%), 205 ($(M-H)^+$, 25.50%)), 141 (100%). HRMS (elemental composition): calcd ($C_8H_{15}O_2S_2$) 207.051348; found 207. 048168.
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