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Expeditious synthesis of β-cycloacetalic sulfoxides. Introducing 1-phenylsulfinyl-2-phenylsulfanylethylene (SOSE), a promising new alkenylsulfur reagent

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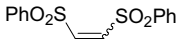
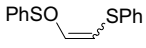
Abstract—In similarity with the strongly electrophilic BPSEs and despite its more electron-rich character, 1-phenylsulfinyl-2-phenylsulfanylethylene (SOSE) reacts with nucleophiles with displacement of the phenylthio moiety. Specifically it reacts with diols under basic conditions to produce β-cycloacetalic sulfoxides. The reaction has been amply developed in carbohydrate chemistry.

The two isomeric *Z*- and *E*-bis-1,2-(phenylsulfonyl)ethylenes (BPSE) enjoy a large number of applications in organic synthesis.[1] They can be used either as ethylene or acetylene surrogates in cycloaddition reactions or as powerful Michael acceptors with substitution of a phenylsulfonyl group.[1]



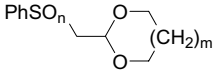
BPSE



SOSE

Recently, we have developed the use of commercial BPSE to access various types of alkoxyvinyl sulfones[2,3] and simple or more complex phenylsulfonylethylidene (PSE) acetals.[4,5] Especially in carbohydrate chemistry, it can be taken advantage of the remarkable reluctance of PSE acetals of type **3** to undergo hydrolysis in acidic media. In this respect, our concern has constantly been to develop an alternative, possibly more convenient reagent offering similar behaviour and reactivity. Anterior and current studies in our group[5,6] have demonstrated that while sulfides **1** ($n = 0$) behave similarly to standard cyclic acetals with regard to acid-catalyzed hydrolysis, sulfoxides **2** ($n = 1$) show a behaviour comparable to that observed for the previously described sulfones **3** ($n = 2$) prepared from BPSE. Hence, a logical first choice was to test the reactivity of 1-phenylsulfinyl-2-phenylsulfanylethylene (SOSE).

One major advantage in using SOSE as a reagent rather than BPSE (and sulfones in general) is its lower molecular weight : indeed, if on one hand it allows crystallinity because of its high molecular weight, the $PhSO_2$ functional group appears on the other hand as a patent 'oxygen-squanderer'. In contrast with BPSE, SOSE offers a better atom-economy associated with a lower oxidation state of the sulfur atoms involved. In other respects, the sulfinyl group constitutes a stable stereocentre and therefore SOSE could be further considered in enantiopure form to be used in asymmetric synthesis. Altogether, the sulfinyl moiety allows to anticipate a wider range of synthetic transformations of its own.



1 n = 0 m = 0-2
2 n = 1 m = 0-2
3 n = 2 m = 0-2

Keywords: Cyclic acetals; Carbohydrates; Sulfoxides; Protecting groups.
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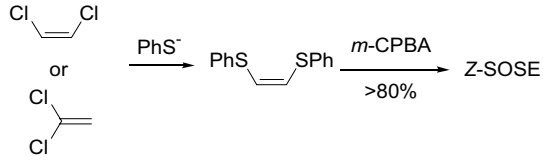
Obviously, the dramatically different stereoelectronic features between BPSE and SOSE call for an in-depth study aimed at verifying the reactivity of SOSE and if indeed it can be considered as an alternative, more convenient reagent compared with BPSE.

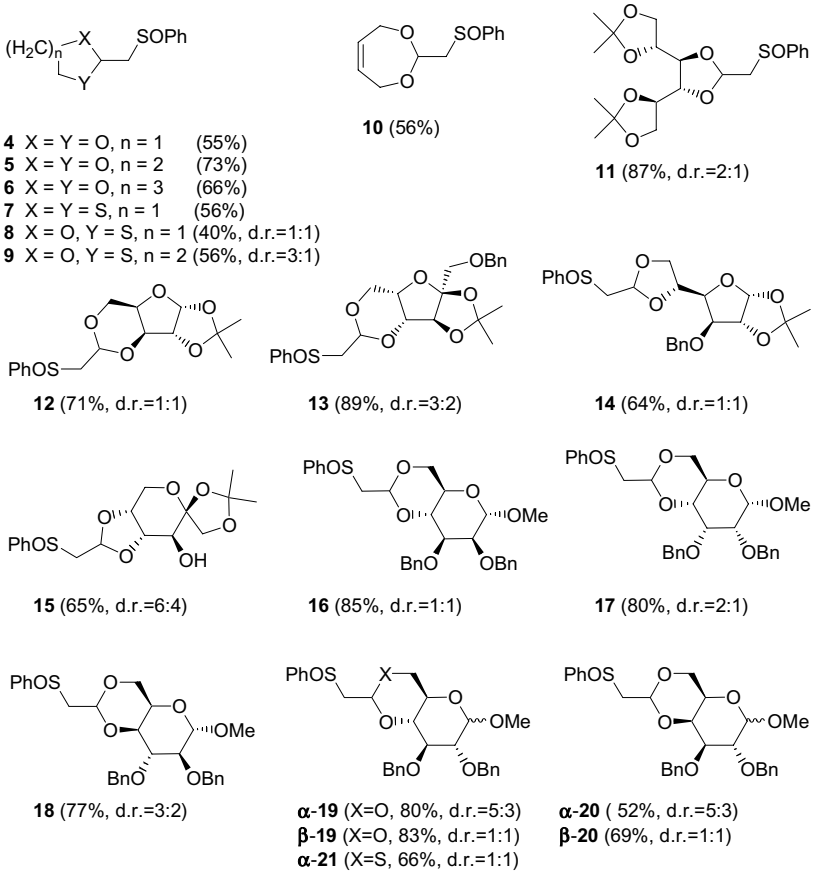
Z-SOSE can be readily obtained from inexpensive (*Z*)-1,2-bis(phenylsulfanyl)ethylene which in turn is readily available in stereopure form via substitution of *cis*-1,2-dichloroethylene[7] or even more economically via 1,1-dichloroethylene.[8] *Z*-1,2-Bis(phenylsulfanyl)ethylene is then submitted to monooxidation with *m*-CPBA in dichloromethane to produce racemic *Z*-SOSE in more than 80% yield.[9,10]

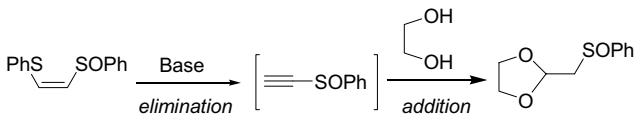


With a view to providing an introductory evaluation of SOSE's potential, the base-promoted synthesis of cyclic acetals from simple or complex diols undoubtedly was the test reaction of choice. Application to a broad range of structurally diverse diols of the protocol established before[5] actually furnished the respective phenylsulfinylethylidene acetals in moderate to excellent yields. Hydroxythiols (and dithiols) reacted in a similar manner to produce the corresponding cyclic thioacetals (and dithioacetals). The table below displays the results[11,12] obtained both with simple molecules and carbohydrate-derived chiral substrates, for which the stereoisomeric ratio (d.r.) observed in connection with the introduction of the sulfoxide stereocentre ranged from 1:1 to 2:1.

At variance with *Z*-SOSE, which proved reactive in most cases, *E*-SOSE[13] showed a much reduced reactivity, such as it was recovered largely unchanged under the conditions where its *Z* isomer was completely converted. Such a result was not really unexpected: indeed, a number of related alkenes do behave similarly. As a pertinent example, *Z*-1,2-dichloroethylene reacts with thiols under basic conditions, while the *E*-isomer does not.[7,8]

It should be pointed out here that in apparent contrast with SOSE, BPSE reacts with an addition–elimination mechanism, the double bond displaying a highly electrophilic character due to the strongly electron-withdrawing phenylsulfonyl groups. For this reason *Z*- and *E*-BPSE do not exhibit appreciable differences in reactivity as the elimination of the phenylsulfinate anion is not the rate-determining step. In return, the marked difference of reactivity between *E*- and *Z*-SOSE might indicate an elimination–addition mechanism. Under basic conditions, *Z*-SOSE would expel a thiophenolate ion to produce transient ethynyl phenyl sulfoxide, which in turn could act as the double Michael acceptor.





Miscellaneous reaction conditions are under current concerted investigation to complete our mechanistic knowledge of SOSE's reactivity against diverse nucleophiles.

In summary, in this communication we have introduced the new doubly thio-functionalized reagent SOSE which, besides its electron-rich character, displays a marked reactivity towards nucleophiles similar to that of the strongly electrophilic BPSEs. The electrophilicity of SOSE was tested in combination with various diols—particularly carbohydrate derivatives, affording good yields of β-cycloacetalic sulfoxides, which are amenable to the many transformations proper to the sulfinyl group.[14]

Acknowledgements

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9. Aryl monosulfoxides of the SOSE-type were once mentioned as side-products by Montanari & coll., see Farina, G.; Montanari, F.; Negrini, A. *Gazz. Chim. Ital.* **1959**, *89*, 1548–1563.
10. All new compounds gave satisfactory analytical data. Selected spectroscopy data for *Z*-SOSE: ^{1}H NMR ($CDCl_3$) δ 6.38 (d, 1H, J_{vic} = 8.8, H-1), 7.02 (d, 1H, H-2), 7.33–7.58 (m, H-Ar), 7.68–7.76 (br d, 2H, *ortho*-H-PhSO). ^{13}C NMR ($CDCl_3$) δ 123.9 (2*CH–*ortho*-PhSO), 128.3 (C-1), 129.1 (CH–*para*-PhS), 129.3 (2*CH–*meta*-PhS), 130.3 (2*CH–*meta*-PhSO), 130.7 (CH–*para*-PhSO), 132.7 (2*CH–*ortho*-PhS), 133.3 (C_{IV}-PhS), 138.5 (C-2), 144.1 (C_{IV}-PhSO). MS: *m*/*z* 261.3 $[M + H]^+$, 283.3 $[M + Na]^+$. HRMS: $C_{14}H_{12}OS_2$: calcd 260.0330; found 260.0343.
11. *General procedure*. 2.2 equiv of NaH were added at 0 °C to a THF solution of the diol; after 15 min, 1 equiv of *Z*-SOSE and a few crystals of Bu_4NBr were added. After 12 h stirring at room temperature, the mixture was treated with brine and extracted with AcOEt. The combined organic phases were dried over $MgSO_4$, concentrated under reduced pressure and the crude product was purified by silica gel column chromatography.
12. Selected data for the dioxolane **1**: ^{1}H NMR ($CDCl_3$) δ 3.00 (dd, 1 H, $J_{2,6b}$ = 5.6, $J_{6a,6b}$ = 13.4, H-6b), 3.24 (dd, 1H, $J_{2,6a}$ = 3.6, H-6a), 3.9–4.1 (m, 4H, CH_2O), 5.25 (dd, 1H, H-2), 7.50–7.56 (m, 3H, H-Ar), 7.67–7.71 (m, 2H, *ortho*-H-PhSO). ^{13}C NMR ($CDCl_3$) δ 62.1 (C-6), 65.4 (C-4, C-5), 99.5 (C-2), 124.0 (2*CH–*ortho*-PhSO), 129.4 (2*CH–*meta*-PhSO), 131.3 (CH–*para*-PhSO), 144.1 (C_{IV}-PhSO). MS: *m*/*z* 235 $[M+Na]^+$. HRMS: $C_{10}H_{12}O_3S$: calcd 212.0507; found 212.0498. Selected data for the xylofurano derivative **12**: ^{1}H NMR ($CDCl_3$) δ 1.31, 1.33, 1.48, 1.49 (4s, 6H, *i*-Prd), 2.91–3.01 (m, 1H, H-7b), 3.07–3.17 (m, 1H, H-7a), 3.94 (dd, J_{3-4} = 1.9, J_{4-5} = 13.4, H-4′), 4.08 (m, H-4″, H-5b), 4.22–4.40 (m, 2H, H-3, H-5a), 4.45 (d, H-2′), 4.64 (d, H-2″), 4.94 (m, 1H, H-6), 5.98 (d, 0.5H, J_{1-2} = 3.7, H-1′), 6.04 (d, 0.5H, J_{1-2} = 3.6, H-1″), 7.51–7.55 (m, 3H, H-Ar), 7.62–7.67 (m, 2H, *ortho*-H-PhSO). ^{13}C NMR ($CDCl_3$) δ 26.1, 26.7 (2*i*-Prd), 61.7, 61.9 (C-7), 66.4 (C-5), 72.0 (C-4), 78.6 (C-3), 83.5, 83.6 (C-2), 94.7 (C-6), 105.5 (C-1), 111.9 (C_{IV}, *i*-Prd), 123.8. (2*CH–*ortho*-PhSO), 129.4 (2*CH–*meta*-PhSO), 131.3 (CH–*para*-PhSO), 143.7 (C_{IV}-PhSO). MS: *m*/*z* 341 $[M+H]^+$, 358 $[M+NH_4]^+$, 363 $[M+Na]^+$. HRMS: $C_{16}H_{20}O_6S$: calcd 340.0981; found 340.0969.
13. *E*-SOSE was similarly prepared via controlled oxidation of (*E*)-1,2-bis(phenylthio)ethylene. Selected spectroscopy data: ^{1}H NMR ($CDCl_3$) δ 6.11 (d, 1H, J_{vic} = 14.6, H-1), 7.44 (d, 1H, H-2), 7.35–7.50 (m, H-Ar), 7.53–7.60 (br d, 2H, *ortho*-H-PhSO). ^{13}C NMR ($CDCl_3$) δ 124.3 (2*CH–*ortho*-PhSO), 128.9 (C-1), 129.0 (CH–*para*-PhS), 129.2 (2*CH–*meta*-PhS), 129.5 (2*CH–*meta*-PhSO), 130.5 (C_{IV}-PhS), 130.9 (CH–*para*-PhSO), 132.4 (2*CH–*ortho*-PhS), 137.7 (C-2), 143.8 (C_{IV}-PhSO). MS: *m*/*z* 261.3 $[M+H]^+$, 283.3 $[M+Na]^+$. HRMS: $C_{14}H_{12}OS_2$: calcd 260.0330; found 260.0346.
14. See for example: De Lucchi, O.; Miotti, U.; Modena, G. *Org. React.* **1991**, *40*, 157–405.