Chemoselective Synthesis of Isomerical Pair of (*E*),(*Z*)-Mono-sulfones and Bis-sulfones

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Received May 28, 2008

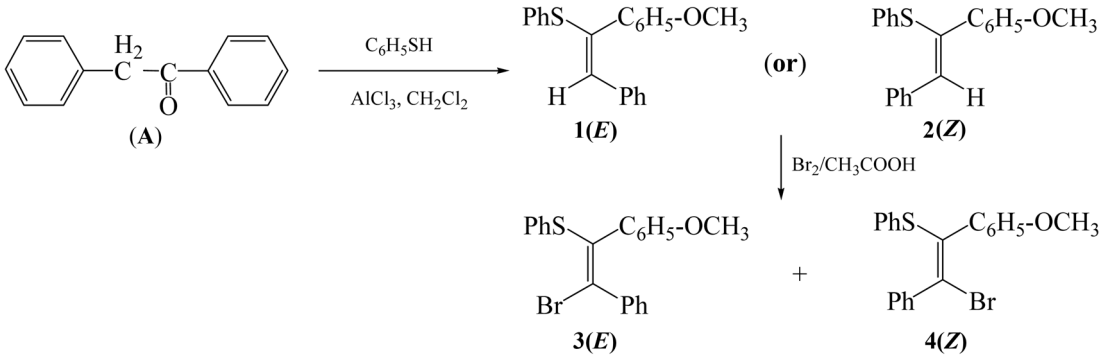
Key Words : *E*,*Z*-Mono-sulfones, Bis-sulfones, Isomerisation, Chemoselectivity

Organosulfur compounds containing sulfides, sulfoxides, and sulfones are important group of heterocyclic compounds, because of their wide range of biological and pharmacological activities such as insecticidal, scabicidal, anti-ulcer, anti-leprosy, anti-tumor, fungicidal and purgative properties.[1-5] Their properties turn organosulfur compounds very interesting targets to organic chemists and several strategies for their synthesis were already developed. Organosulfur compounds can be synthesized by various methods for example, the addition of thiols to acetylene was considered as an important route for the preparation of α,β-ethylenic sulfones[6] and their *Z*-isomers.[7] The addition of benzylthiols with phenyl acetylene has been utilized to obtain Z-styrylbenzylsulfones,[8] *Z*-styryl thioacetic acid, and it's esters by the *trans*-addition rule.[9] Idosufonization of 1-alkynes were found to be the useful intermediates for the stereoselective preparation of *Z*-vinyl and *Z*-allyl sulfones.[10] However, alkoxy carbonyl vinylsulfones were usually synthesized by refluxing in the presence of organic solvents and reagents.[11] *E*-γ-Hydroxy α,β-unsaturated sulfones can be obtained selectively by reacting enolizable aldehydes with *p*-tolylsulfinyl methylphenyl sulfones.[12] In addition, α,β-unsaturated sulfones and sulfoxides were synthesized in the presence of molybdenum and ruthenium precatalysts via cross-metathesis.[13,14] Recently the preparation of (*E*) and (*Z*)-isomers and their corresponding sulphones from *p*-chlorophenylphenylacetylene were reported.[15] In the present investigation we address a new method for the synthesis of both containing (*E*) and (*Z*) mono-sulfones and bis-sulfones from 1-(4-methoxyphenyl)-2-phenyl ethanone.

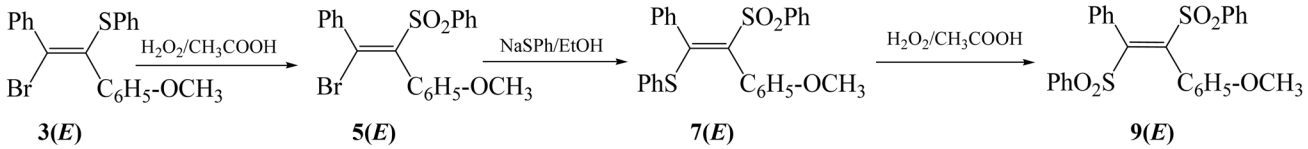
Compound (**A**) was treated with thiophenol in the presence of anhydrous $AlCl_3$ and a mixture of both (*E*)-1-(4-methoxyphenyl)-2-phenyl-1-(phenylthio)-ethene (**1*E***) and (*Z*)-1-(4-methoxyphenyl)-2-phenyl-1-(phenylthio)-ethene (**2*Z***). These compounds are separated on the basis of solubility using *n*-Heptane and purified by column chromatography. The formation of products indicates that the reaction proceeds in a chemoselective manner. On bromination of compound **1*E*** or **2*Z***, they undergo chemoselection to furnish a mixture containing both isomers (*E*) and (*Z*)-1-bromo-2-(4-methoxyphenyl)-1-phenyl-2-(phenylthio)-ethenes (**3*E*** and **4*Z***). The resulting isomers are easily separated by using ethanol; this reaction is represented by Scheme 1.[15]

Compound **3*E*** were treated with 30% H_2O_2 in the presence of acetic acid, this was refluxed for 2-3 h to afford 82% yield of (*E*)-1-bromo-2-(4-methoxyphenyl)-1-phenyl-2-(phenylsulfonyl)-ethene (**5*E***). Compound **5*E*** when treated with sodiumbenzenethiolate in dry ethanol, the colorless (*E*)-1-(4-methoxyphenyl)-2-phenyl-1-(phenylsulfonyl)-2-(phenylthio)-ethene (**7*E***) was obtained with an yield of 70%. On oxidation of compound **7*E*** with 30% H_2O_2 to afford 78% yield of (*E*)-1,2-bis-(phenylsulfonyl)-1-(4-methoxyphenyl)-2-(phenyl)-ethene (**9*E***) in the corresponding product as shown in Scheme 2.

Similarly, the reaction of the Scheme 3 was carried out under the same conditions for the synthesis of (*Z*)-1-bromo-2-(4-methoxyphenyl)-1-phenyl-2-(phenylsulfonyl)-ethene (**6*Z***), (*Z*)-1-(4-methoxyphenyl)-2-phenyl-1-(phenylsulfonyl)-2-(phenylthio)-ethene (**8*Z***), (*Z*)-1,2-bis (phenylsulfonyl)-1-(4-methoxyphenyl)-2-(phenyl)-ethene (**10*Z***).

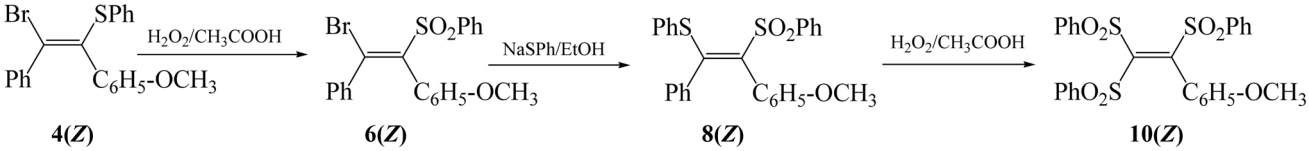


Scheme 1



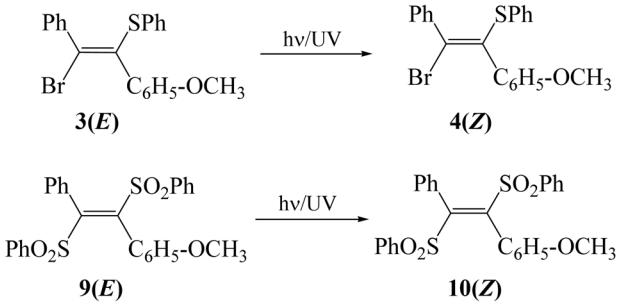
3(*E*) **5(*E*)** **7(*E*)** **9(*E*)**

Scheme 2



4(*Z*) **6(*Z*)** **8(*Z*)** **10(*Z*)**

Scheme 3



3(*E*) **4(*Z*)** **9(*E*)** **10(*Z*)**

Scheme 4

For the conversion of *E*-isomer to *Z*-isomer about 1 g of compound 3*E* was taken in 500 mL of benzene and the resulting solution was irradiated with UV rays for 20 h. After evaporation of solvent under reduced pressure, the residue was chromatographed on silica gel to afford 75% yield of *Z* isomer and it's b.p.180-181 °C; λ_{max} 307, 230, 204 nm; identified as (*Z*)-1-bromo-2-(4-methoxyphenyl)-1-phenyl-2-(phenylthio)-ethene (**4*Z***). Similar procedure used for (*E*)-1,2-bis-(phenylsulfonyl)-1-(4-methoxyphenyl)-2-(phenyl)-ethene (**9*E***) isomerised to (*Z*)-1,2-bis-(phenylsulfonyl)-1-(4-methoxyphenyl)-2-(phenyl)-ethene (**10*Z***) m.p. 203-205 °C; λ_{max} 259, 223, 205 nm; **9*E***; m.p. 191-192 °C; λ_{max} 251, 207 nm; **10*Z***. The reaction sequence is shown in Scheme 4.

The *E*-isomers absorbed slightly longer wavelength than the corresponding *Z*-isomers, it may be attributed to the steric crowding and steric inhibition of resonance in crystal lattice of the corresponding *Z*-isomer. When bulky groups are on the same side of the ethylinic double bond, there may be repulsion between the non bonding electrons on the non bonded atoms or repulsion between two bulky benzene moieties. As a consequence of steric repulsion, the two bulky benzene groups are not coplanar and the molecules can not have planar configuration, as a result, the existed state of the molecule has higher energy and its life time also decreases when compared to the planar *E*-isomer. These compounds exhibited UV region, shows longer wave length band around 250-275 nm and a second band occurred around 207-225 nm. This may be attributed to hyposchromic shift of the longer wave length band from 310-320 nm to 250-275 nm. The loss of vibrational fine structure and hyposchromic shift of the longer wave length band may be due to the interference of groups, which prevent the conjugated system from assuming a planar configuration. The structures of the products were established from their spectral (UV, IR, ^{1}H NMR and MS) data given below.

Experimental Section

General procedure for the synthesis of both E and Z-isomers:

(*E*) and (*Z*)-1-(4-methoxyphenyl)-2-phenyl-1-(phenylthio)-ethenes (1*E* and 2*Z*). A solution of 50 mmol of 1-(4-methoxyphenyl)-2-phenyl ethanone and 125 mmol of thiophenol in 100 mL of CH_2Cl_2 was taken in a round-bottomed flask, fitted with an air condenser guarded with a calcium chloride tube. The solution was stirred at room temperature and 17 mmol anhydrous $AlCl_3$ was added over a period of 10 minutes, stirring was continued for another 30 minutes and was then poured into 75 mL of water. The resulting mixture was extracted with 100 mL of CH_2Cl_2. The aqueous layer was washed with brine (2 × 10 mL), dried over anhydrous $MgSO_4$, and the solvent was evaporated to give light yellow oil. This was treated with *n*-heptane and the solid was separated by filtration and recrystallized from acetic acid to yield 45% of (*E*)-1-(4-methoxyphenyl)-2-phenyl-1-(phenylthio)-ethene (**1*E***). m.p. 72-74 °C. Then the filtrate was evaporated to yield 40% of (*Z*)-1-(4-methoxyphenyl)-2-phenyl-1-(phenylthio)-ethene (**2*Z***) as yellow liquid. Compounds **1*E*** and **2*Z*** were purified by flash chromatography on silica gel.

Compound **1*E*:** m.p. 72-74 °C; λ_{max}, 317, 225, 203 nm; IR (KBr) 1673 (C=C), 1090 (S-Ar) cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 3.76 (s, 3H, CH_3), 6.38 (s, 1H, C=C-H), 6.83-7.14 (m, 5H, Ar-H), 7.16-7.39 (m, 5H, Ar-H), 7.56-7.60 (d, 2H, Ar-H), 7.62-7.94 (d, 2H, Ar-H); LCMS: *m/z* 318 [M]$^+$. Anal. Calcd for $C_{21}H_{18}OS$: C, 79.21; H, 5.7; S, 10.07%. Found: C, 79.18; H, 5.48; S, 9.84%.

Compound **2*Z*:** b.p. 195-197 °C; λ_{max}, 308, 230, 204 nm; IR (KBr) 1636 (C=C), 1083 (S-Ar) cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 3.74 (s, 3H, CH_3), 6.55 (s, 1H, C=C-H), 6.77-6.15 (m, 5H, Ar-H), 7.21-7.32 (m, 5H, Ar-H), 7.57-7.61 (d, 2H, Ar-H), 7.70-7.98 (d, 2H, Ar-H); LCMS: *m/z* 318

$[M]^+$. Anal. Calcd for $C_{21}H_{18}OS$: C, 79.21; H, 5.7; S, 10.07%. Found: C, 78.98; H, 5.5; S, 9.86%.

(*E*) and (*Z*)-1-bromo-2-(4-methoxy phenyl)-1-phenyl-2-(phenylthio)-ethenes (3*E* and 4*Z*). To the solution of 10 mmol of **1*E*** or **2*Z*** and 100 mL of glacial acetic acid taken in round-bottomed flask, 10 mmol of bromine in acetic acid was added drop wise over a period of 30 minutes and the stirring was continued for another 30 minutes. The solid was separated by filteration and recrystallized from ethanol to yield 60% of (*Z*)-1-bromo-2-(4-methoxyphenyl)-1-phenyl-2-(phenylthio)-ethene (**4*Z***). The filtrate was diluted with water to yield 32.3% of (*E*)-1-bromo-2-(4-methoxyphenyl)-1-phenyl- 2-(phenylthio)-ethene (**3*E***) as viscous liquid.

Compound **3*E*:** m.p. 125-127 °C; λ_{max} 312, 226, 203 nm; IR (KBr) 1682 (C=C), 1080 (S-Ar) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ: 3.73 (s, 3H, CH_3), 6.63-7.10 (m, 5H, Ar-H), 7.16-7.36 (m, 5H, Ar-H), 7.51-7.52 (d, 2H, Ar-H), 7.95-8.01 (d, 2H, Ar-H); LCMS: *m/z* 396 $[M]^+$. Anal. Calcd for $C_{21}H_{17}BrO$ S; C, 63.26; H, 4.11; S, 7.85%. Found: C, 63.26; H, 4.11; S, 7.85%.

Compound **4*Z*:** b.p. 180-181 °C; λ_{max} 307, 230, 204 nm; IR (KBr) 1605 (C=C), 1075 (S-Ar) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ: 3.86 (s, 3H, CH_3), 6.92-7.12 (m, 5H, Ar-H), 7.15-7.42 (m, 5H, Ar-H), 7.47-7.49 (d, 2H, Ar-H), 7.50-7.51 (d, 2H, Ar-H); LCMS: *m/z* 396 $[M]^+$. Anal. Calcd for $C_{21}H_{17}BrO$ S; C, 63.48; H, 4.31; S, 8.07%. Found: C, 63.27; H, 4.09, S, 7.86%.

(*E*)-1-Bromo-2-(4-methoxyphenyl)-1-phenyl-2-(phenylsulfonyl)-ethene (5*E*). A solution of 5 mmol of **3*E*** in 60 mL of glacial acetic acid was taken in round bottomed flask fitted with a reflux condenser and heated. To this solution 20 mL of 30% H_2O_2 was added and refluxed for 2 h. The resulting product separated, followed by filtration and recrystallization from ethanol to yield 82% of **5*E***. Similar procedure was adopted in the synthesis of (*Z*)-1-bromo-2-(4-methoxyphenyl)-1-phenyl-2-(phenylsulfonyl)-ethene (**6*Z***) from **4*Z***.

Compound **5*E*:** m.p. 201-203 °C; λ_{max} 311, 217, 200 nm; IR (KBr) 1634 (C=C), 1167 & 1325 (S=O), 1088 (S-Ar) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ: 3.69 (s, 3H, CH_3), 7.14-7.26 (m, 5H, Ar-H), 7.39-7.45 (m, 5H, Ar-H), 7.49-7.51 (d, 2H, Ar-H), 7.58-7.6 (d, 2H, Ar-H); LCMS: *m/z* 430 $[M]^+$. Anal. Calcd for $C_{21}H_{17}BrO_3S$; C, 58.75; H, 3.99; S, 7.47%. Found: C, 58.54; H, 3.76, S, 7.26%.

Compound **6*Z*:** m.p. 180-182 °C; λ_{max} 305, 226, 202 nm; IR (KBr) 1630 (C=C), 1161 & 1327 (S=O), 1078 (S-Ar) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ: 3.72 (s, 3H, CH_3), 7.04-7.18 (m, 5H, Ar-H), 7.29-7.36 (m, 5H, Ar-H), 7.39-7.41 (d, 2H, Ar-H), 7.48-7.50 (d, 2H, Ar-H); LCMS: *m/z* 430 $[M]^+$. Anal. Calcd for $C_{21}H_{17}BrO_3$; C, 58.75; H, 3.99; S, 7.47%. Found: C, 58.56; H, 3.84; S, 7.35%.

(*E*)-1-(4-Methoxyphenyl)-2-phenyl-1-(phenylsulfonyl)-2-phenylthio)-ethene (7*E*). A solution of 1.30 g of (*E*)-1-bromo-2-(4-methoxyphenyl)-1-phenyl-2-(phenylsulfonyl)-ethene (**5*E***) in 160 mL of dry ethanol was taken in a round bottomed flask fitted with a reflux condenser and guarded with calcium chloride tube. To this reaction solution, Sodium benzenethiolate prepared from 69.2 mg (3 mg atom) of sodium, 10 mL of dry ethanol and 0.33 g (3 mmol) of thiophenol was added. The mixture was refluxed for 7 h, then cooled, and filtered to get colorless product. This was recrystallized from ethanol to yield 70% of **7*E***. Similar procedure was adopted in the synthesis of (*Z*)-1-(4-methoxyphenyl)-2-phenyl-1-(phenylsulfonyl)-2-(phenylthio)-ethene (**8*Z***) from **6*Z***.

Compound **7*E*:** m.p. 167-169 °C; λ_{max} 310, 238, 206 nm; IR (KBr) 1635 (C=C), 1163 & 1358 (S=O), 1094 (S-Ar) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ: 3.72 (s, 3H, CH_3), 7.38-7.52 (m, 5H, Ar-H), 7.58-7.69 (m, 5H, Ar-H), 7.71-7.90 (m, 5H, Ar-H) 7.94-7.95 (d, 2H, Ar-H), 7.96-8.10 (d, 2H, Ar-H); LCMS: *m/z* 458 $[M]^+$. Anal. Calcd for $C_{27}H_{22}O_3S_2$; C, 70.01; H, 4.84; S, 13.98%. Found: C, 69.9; H, 4.75; S, 13.87%.

Compound **8*Z*:** m.p. 156-157 °C; λ_{max} 306, 201 nm; IR (KBr) 1622 (C=C), 1162 & 1363 (S=O), 1085 (S-Ar) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ: 3.75 (s, 3H, CH_3), 7.29-7.57 (m, 5H, Ar-H), 7.58-7.71 (m, 5H, Ar-H), 7.79-7.83 (m, 5H, Ar-H) 7.84-7.86 (d, 2H, Ar-H), 7.86-7.91 (d, 2H, Ar-H); LCMS: *m/z* 458 $[M]^+$. Anal. Calcd for $C_{27}H_{22}O_3S_2$; C, 70.01; H, 4.84; S, 13.98%. Found: C, 69.86; H, 4.78; S, 13.86%.

(*E*)-1,2-Bis-(phenylsulfonyl)-1-(4-methoxyphenyl)-2-(phenyl)-ethene (9*E*). A solution of 3 mmol of **7*E*** in 70 mL glacial acetic acid was taken in a round bottomed flask fitted with a reflux condenser and guarded with calcium chloride tube. The solution was heated and to this 15 mL of 30% H_2O_2 was added, the mixture was refluxed for 1 h, then cooled and filtered to get a colorless product. This was recrystallized from ethanol to yield 78% of **9*E***. Similar procedure was adopted in the synthesis of (*Z*)-1,2-bis-(phenylsulfonyl)-1-(4-methoxyphenyl)-2-(phenyl)-ethene (**10*Z***) from **8*Z***.

Compound **9*E*:** m.p. 203-205 °C; λ_{max} 259, 223, 205 nm; IR (KBr) 1642 (C=C), 1149 & 1322 (S=O), 1089 (S-Ar) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ: 3.72 (s, 3H, CH_3), 6.79-7.02 (m, 5H, Ar-H), 7.03-7.17 (m, 5H, Ar-H), 7.23-7.41 (m, 5H, Ar-H), 7.42-7.43 (d, 2H, Ar-H), 7.55-7.57 (d, 2H, Ar-H); LCMS: *m/z* 490 $[M]^+$. Anal. Calcd for $C_{27}H_{22}O_5S_2$; C, 66.10; H, 4.52; S, 13.07%. Found: C, 65.98; H, 4.43; S, 12.96%.

Compound **10*Z*:** m.p. 191-192 °C; λ_{max} 251, 207 nm; IR (KBr) 1637 (C=C), 1142 & 1317 (S=O), 1068 (S-Ar) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ: 3.73 (s, 3H, CH_3), 6.91-7.13 (m, 5H, Ar-H), 7.21-7.38 (m, 5H, Ar-H), 7.39-7.48 (m, 5H, Ar-H) 7.52-7.54 (d, 2H, Ar-H), 7.67-7.72 (d, 2H, Ar-H); LCMS: *m/z* 490 $[M]^+$. Anal. Calcd for $C_{27}H_{22}O_5S_2$; C, 66.10; H, 4.52; S, 13.07%. Found: C, 65.96; H, 4.47; S, 12.98%.

Acknowledgments. The authors gratefully acknowledge the support by the Korea Research Foundation (Grant No. KRF-C00168).

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