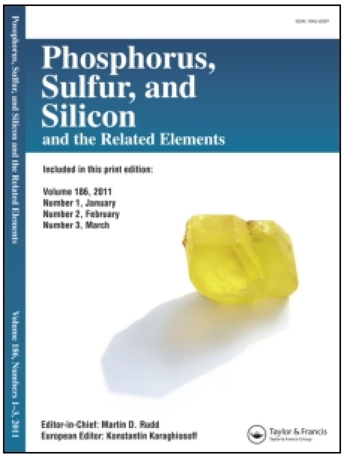

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ANIONIC ADDITIONS TO CONJUGATED ENYNES—UNUSUAL DISPLACEMENTS OF VINYLIC SULFONES

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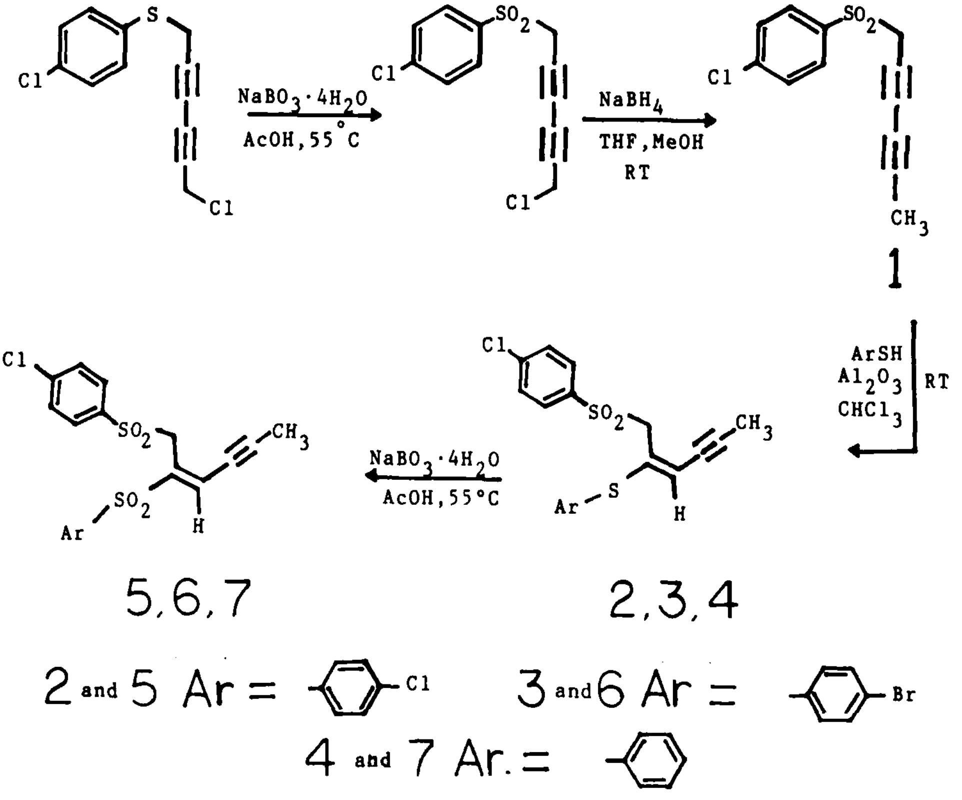
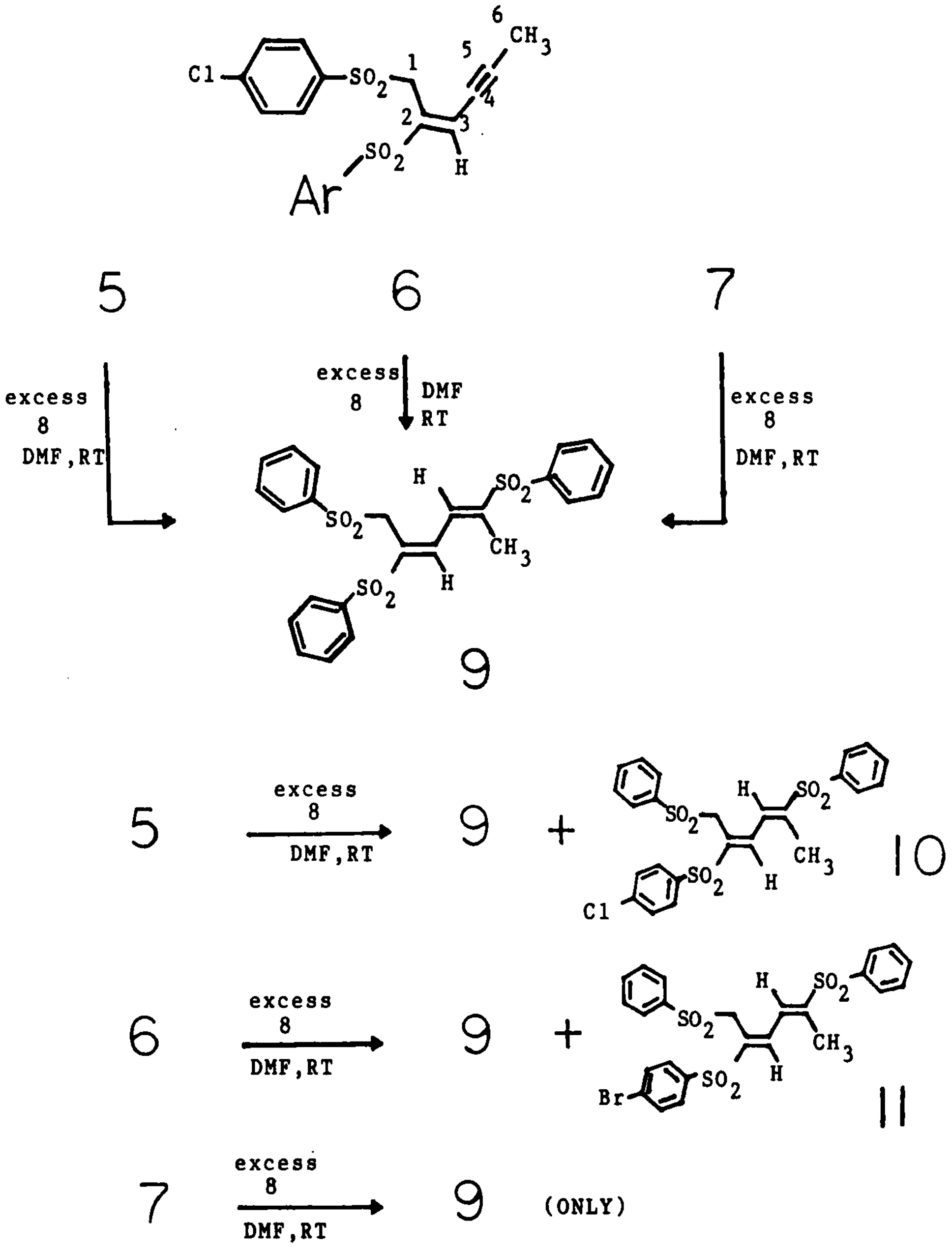
Reaction of sodium benzenesulfinate with 1,2-di(4-chloro-benzenesulfonyl)-2-hexen-4-yne affords not only the regiospecific addition of the nucleophile at Carbon-5 but also effects concomitant vinylic *and* allylic displacements at Carbons-1 and 2.

Additions to conjugated enynes have been studied extensively.[1,2,3,4] None such has been concerned with additions to enynes that carry a vinyl sulfone. We report herein *unusual* nucleophilic displacements of vinylic and allylic sulfone functions *accompanying* regiospecific addition of benzene sulfinate as a nucleophile. The different enynes (**5**, **6** and **7**) were synthesized[5] as shown in Scheme I.



SCHEME I

Sodium benzenesulfinate (**8**) was added at ambient temperature to all three enynes (in separate reactions) using DMF as solvent. All reactions were complete *within 20 minutes*! Surprisingly, the trisulfone **9** was a common product from all three reactions! In addition to **9**, the enynes **5** and **6** also gave the trisulfones **10** and **11**. Scheme II outlines the relationships among **9**, **10** and **11**. Table I shows the spectral characteristics of the compounds **5** through **11**.



SCHEME II

TABLE I

The spectral characteristics of compounds **5** through **11**

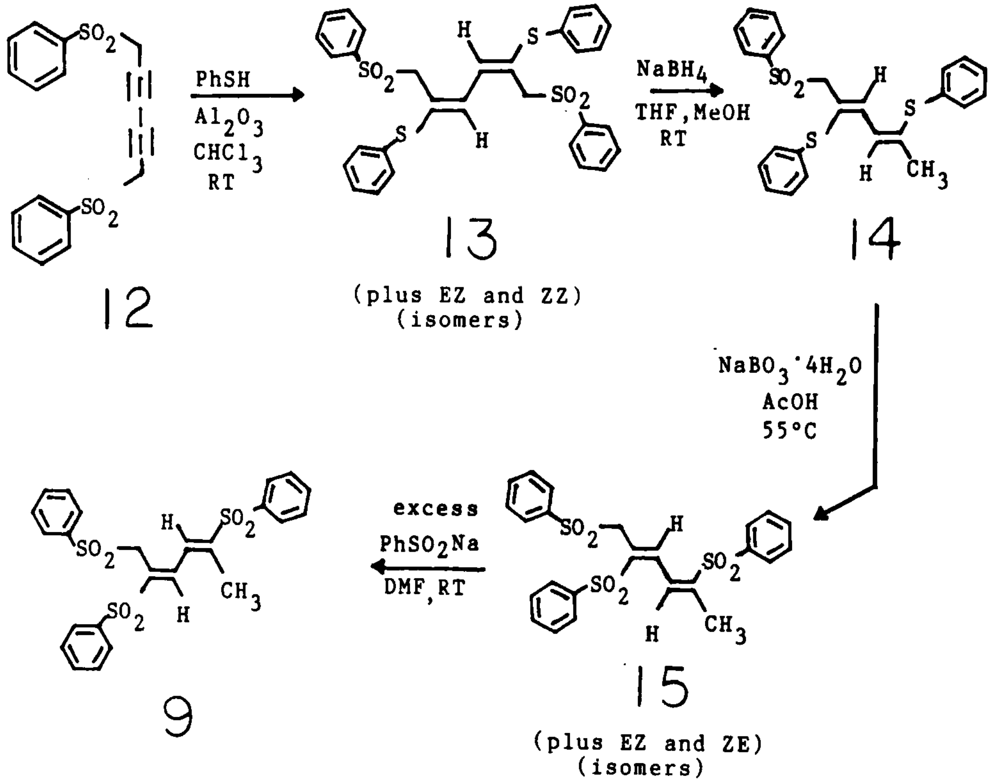
Cmpd.	IR (KBr) cm^{-1}	^{1}H-NMR (ppm $CDCl_3$)
5	3085, 2939, 2913, 2214, 1583, 1322s, 1147vs, 1088vs, 1013, 767	7.81(d, 2H), 7.65(d, 2H), 7.53(d, 2H), 7.48(d, 2H), 6.96(q, 1H), 4.34(d, 2H), 2.01(d, 3H)
6	3092, 2980, 2929, 2216, 1574, 1329s, 1148vs, 1087s, 1010, 751	7.73–7.70(q, 4H), 7.65(d, 2H), 7.49(d, 2H), 6.9(q, 1H), 4.37(s, 2H), 1.99(d, 3H)
7	3091, 2960, 2913, 2213, 1582, 1330vs, 1314s, 1147vs, 1087s, 1014, 740	7.86(d, 2H), 7.68–7.45(m, 7H), 6.94(q, 1H), 4.33(s, 2H), 2.01(d, 3H)
9	3065, 2929, 1584, 1447s, 1301vs, 1150vs, 1084s, 898, 729s, 586s	7.95(d, 2H), 7.86(t, 3H), 7.74–7.53(m, 12H), 4.35(s, 2H), 2.11(s, 3H)
10	3062, 2921, 2850, 1584, 1447, 1324vs, 1301vs, 1152vs, 1083s, 899, 726s, 616s	7.94(d, 2H), 7.85(t, 3H), 7.73–7.52(m, 11H), 4.36(s, 2H), 2.12(s, 3H)
11	3065, 2929, 1584, 1447, 1322vs, 1301vs, 1151vs, 1084s, 899, 729s, 586s	7.94(d, 2H), 7.86(d, 2H), 7.76–7.52(m, 12H), 4.37(s, 2H), 2.12(s, 3H)

The structure of **9** was confirmed by an independent synthesis[6] starting from 1,6-di(benzenesulfonyl)-2,4-hexadiyne as shown in Scheme III. The regiospecificity of additions to 1,6-di(benzenesulfonyl)-2,4-hexadiyne and the borohydride reduction thereof have been described elsewhere.[7]

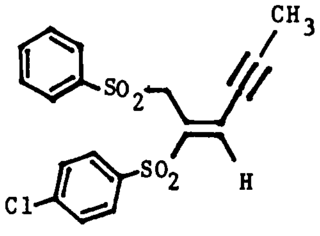
The formation of **10** and **11** reveals that the displacement of the allylic sulfone at Carbon-1 *precedes* the displacement of the vinylic sulfone. But the displacement of the allylic sulfone even precedes the addition of the sulfinate at Carbon-5. This we have shown by interrupting the addition of **8** to **5** before completion and examining the mixture for the unchanged enyne. Compound **16** was isolated from the reaction mixture-confirming our expectation stated above.

The displacement of the vinylic sulfone occurs subsequent to the formation of **10** and **11**. This is readily proven by the fact that both **10** and **11** can be converted to **9** by further reaction with Sodium benzenesulfinate. Interestingly, such conversions of **10** and **11** into **9** are not *quantitative* but they attain an invariant composition[8] wherein the ratio of **10** to **9** and **11** to **9** is a constant 3 to 1. *Even when a four- or five fold excess of sodium benzenesulfinate is employed, the ratio remained the same.* An explanation for the feature might be found in the following possibility. The trisulfones **10** and **11** can undergo addition of **8** at either end of the diene system viz. Carbon-2 or Carbon-5. Of these two possibilities, only the former can lead to a change in structure. Even then, ejection of the aryl sulfonyl vs. the benzenesulfonyl moiety would determine the extent of formation of **9**. The appropriate intermediates **17** and **18** are shown below:

Thus, incorporation of the vinyl sulfone moiety into an enyne such as in **5**, **6** and **7** not only ensures a regiospecific addition of the sulfinate but also effects hitherto unreported modes of displacement of a vinylic sulfone through an elimi-



SCHEME III

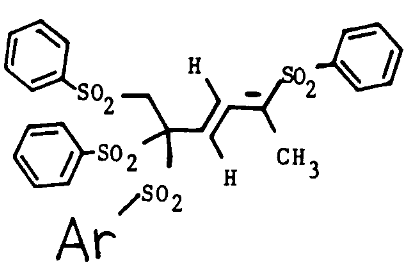


16

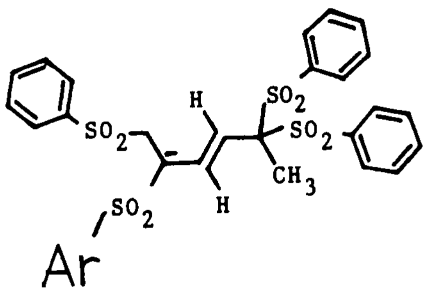
nation-addition pathway. The location of the aryl sulfone moieties at the termini of the conjugated diene provides an electron-deficient diene of some synthetic value. It also raises the prospects of displacing either sulfone by other nucleophiles. These possibilities are currently under study.

EXPERIMENTAL

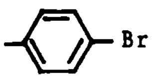
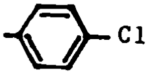
General Comments. Nuclear magnetic resonance spectra were recorded on a General Electric QE-300 spectrometer, in $CDCl_3$ solution. Mass spectral data was obtained by Dr. Susan Weintraub, Uni-



17



18

Ar =  OR Ar = 

versity of Texas at San Antonio Health Science Center, San Antonio, Texas. Elemental analyses were determined by Midwest Microlabs, of Indianapolis, Indiana.

General procedure for addition of arene thiols to **1**. A solution of the sulfone **1** (0.00396 moles) in $CHCl_3$ (70 ml), and the appropriate thiophenol (0.00416 moles) were added to neutral alumina (50 g) in $CHCl_3$ (30 ml) in a separatory funnel. The mixture was shaken under N_2. The reaction was complete in 15 minutes. The alumina was filtered and washed with $CHCL_3$ (300 ml). The combined filtrates were evaporated to dryness yielding a mostly solid residue (95–98% recovery). The ^{1}H-NMR spectrum of the residue showed presence of only the E and Z isomers of the mono addition products. The ratio of E/Z was 80/20. The solid E isomer was crystallized from benzene/pet ether (60% recovery). Further separation of the two isomers required column chromatography [silica gel-1" × 6", eluted with hexanes/EtOAc (7/3)]. The compounds **1**, **2** and **3** have been described earlier.[5]

4: m.p. 114–115°C; calculated for $C_{18}H_{15}S_2O_2Cl$, %: C, 54.75; H, 3.83; found: C, 54.57; H, 3.70. ^{1}H-NMR δ 7.86(d, 2H), 7.56(d, 2H), 7.54–7.46(m, 5H), 5.50(q, 1H), 4.20(s, 2H) and 1.83(d, 3H).

General procedure for the oxidation of **2**, **3** *and* **4**. The appropriate vinyl sulfide was dissolved in AcOH (60 ml/g) containing conc. H_2SO_4 (3 drps/g) and heated to 55°C. The $NaBO_3 \cdot 4H_2O$ (5 eqv) was then added to the solution and heating continued. After 1 hour additional perborate (2 eqv) was added. The oxidation proceeded for a total of 5 hours. The reaction mixture was poured over ice and water. The solid vinyl sulfone precipitated, was filtered, washed and dried (85% recovery).

5: m.p. 132–133°C; calculated for $C_{18}H_{14}O_4S_2Cl_2$, %: C, 50.35; H, 3.29; found: C, 50.35; H, 3.30.

6: m.p. 135–136°C; calculated for $C_{18}H_{14}O_4S_2ClBr$, %: C, 45.63; H, 2.98; found: C, 45.59; H, 2.85.

7: m.p. 114–115°C; calculated for $C_{18}H_{14}O_4S_2Cl$, %: C, 54.75; H, 3.83; found: C, 54.57; H, 3.70. See Table I for spectral data for **5**, **6** and **7**.

Sodium benzenesulfinate addition to **5**. Sodium benzenesulfinate (0.00233 moles) in DMF (15 ml) was added with stirring to the vinyl sulfone **5** (0.00047 moles) in DMF (15 ml) over one minute. The reaction was complete by 15 minutes (TLC). The reaction mixture was diluted with benzene (300 ml), washed (H_2O 12 × 75 ml), dried (Na_2SO_4) and evaporated to dryness giving a near quantitative recovery. The ^{1}H-NMR of the reaction mixture showed the presence of major product **10** (75%) with the minor product **9** (25%). This mixture was purified by flash column chromatography [silica gel 1" × 7" eluted with pet ether/benzene/acetone (6/3/1)]. A clean separation of **10** (60%) and **9** (20%) was achieved.

9: m.p. 199–200°C; calculated for $C_{24}H_{22}S_3O_6$, %: C, 57.35; H, 4.41; found: C, 57.27; H, 4.36. Mass spectrum: molecular ion m/e 503 (40%), 361 (10%), 221 (20%), 143 (20%) and 125 (100%).

10: m.p. 198–199°C; calculated for $C_{24}H_{21}S_3O_6Cl$, %: C, 53.67; H, 3.94; found: C, 53.76; H, 3.99. Mass spectrum: molecular ion m/e 537 (10%), 395 (70%), 361 (15%), 219 (12%), 159 (25%), 125 (100%), 111 (15%) and 77 (70%).
See Table I for additional spectral data for **9** and **10**.

Sodium benzenesulfinate addition to **6**. Sodium benzenesulfinate (0.0042 moles) in DMF (35 ml) was added over one minute to the vinyl sulfone **6** (0.0011 moles) in DMF (35 ml) solution. The reaction was over in 15 minutes and worked up the same way as the previous reaction 5. The ^{1}H-NMR of the reaction mixture showed the presence of **11** (75%),and **9** (25%). The reaction mixture was again purified by flash column chromatography [silica gel 1" × 7") eluted with pet ether/benzene/acetone (6/3/1)] giving 10 (65%) and 11 (20%).

11: m.p. 94–195°C; calculated for $C_{24}H_{21}S_3O_6Br$, %: C, 49.57; H, 3.64; found: C, 49.51; H, 3.61. Mass spectrum: molecular ion 583 (25%), 441 (5%), 221 (20%), 205 (15%), 143 (30%) and 125 (100%).

9: (vide supra)
See Table I for additional spectral data for **11**.

Sodium benzenesulfinate addition to **7**. Sodium benzenesulfinate (0.0051 moles) in DMF (20 ml) was added to the vinyl sulfone **7** (0.00051 moles) in 10 ml DMF over a minute. The reaction was complete by 18 minutes. The work up procedure was identical to the previous two reactions. The ^{1}H-NMR of the reaction showed a single product **9**. The pure solid **9** was obtained in 80% yield without chromatographic purification.

9: (vide supra)

Thiophenol addition to **12**. The bissulfone **12** (0.0056 moles) in $CHCl_3$ (100 ml) was added to a slurry of 20 g alumina in 25 ml $CHCl_3$ followed by rapid addition of the thiophenol (0.011 moles) within 20 seconds. The reaction was complete by 10 minutes. The mixture was filtered, the alumina washed with $CHCl_3$ (300 ml) and the combined filtrates were evaporated to dryness. The expected vinyl sulfide **13** was obtained in quantitative yield. The ^{1}H-NMR of the reaction mixture consisted of the three isomers[7] in ratio EE (65%), EZ (23%) and ZZ (12%).[6]

Sodium borohydride reduction of **13**. The isomer mixture **13** (0.0035 moles) was partially suspended in THF/MeOH (400/200 ml) and heated to 55°C. The $NaBH_4$ (0.014 moles) was then added. Additional borohydride (0.00692 moles) was added after 15 and 30 minutes. The reaction was allowed to proceed for 1.5 hours. The reaction mixture was concentrated to 100 ml diluted with $CHCl_3$ (500 ml), washed (H_2O 12 × 100 ml), dried (Na_2SO_4) and evaporated to dryness for a near quantitative recovery. The pure solid **14** was isolated by crystallization from benzene/pet ether solvent mixtures.

14: m.p. 140–141°C; calculated for $C_{24}H_{22}S_3O_2$, %: C, 65.72; H, 5.06; found: C, 65.72; H, 5.13. ^{1}H-NMR δ 7.80(d, 2H), 7.65(t, 1H), 7.52(d, 2H), 7.35–7.30(m, 10H), 6.92(d, 1H), 6.78(d, 1H), 4.87(s, 2H) and 1.95(s, 3H).

Oxidation of **14** *to* **15**. The disulfide **14** (0.00344 moles was dissolved in AcOH (100 ml) containing conc. H_2SO_4 (8 drps) and heated to 55°C. $NaBO_3{\cdot}4H_2O$ (0.021 moles) was added. More perborate was added after 1 hour (0.010 moles) and 2 hours (0.00688 moles) with a total reaction time of 5 hours. The reaction mixture was diluted with $CHCl_3$ (500 ml), washed (H_2O 15 × 100 ml), dried (Na_2SO_4) and evaporated to dryness resulting in an oily residue (85% recovery). The ^{1}H-NMR of the reaction mixture showed a mixture of the geometrical isomers of the trisulfones.[6]

Equilibration of **15** *in the presence of sodium benzenesulfinate*. Sodium benzenesulfinate (0.011 moles) was added to the isomer mixture **15** (0.00139 moles) in DMF (70 ml) with stirring. The reaction mixture was stirred at room temperature for 6 hours by which time equilibration was reached. The ^{1}H-NMR of the reaction mixture showed the single isomer **9** (95%) and a trace impurity (5%). The reaction mixture was diluted with benzene (400 ml) washed (H_2O 12 × 75 ml), dried and evaporated to dryness for a near quantitative recovery. The solid **9** was crystallized from pet ether/benzene for a 75% yield, with further isolation of **9** by column chromatography [silica gel 1" × 6" eluted with pet ether/benzene/acetone (6/3/1)].

Procedure for the isolation of **16**. Sodium benzenesulfinate (0.00233 moles) in DMF (15 ml) was added to the vinyl sulfone **5** (0.00047 moles) in DMF (15 ml) over one minute. The reaction was stopped after 7 minutes. The reaction mixture was worked up as in the previous benzenesulfinate addition reactions for **5**, **6** and **7**. The mixture was purified by flash column chromatography [silica gel- 1" × 7" eluted with pet ether/benzene/acetone (6/3/1)] with separation of **16** as well as **9** and **10**.

16: m.p. 166–167°C; calculated for $C_{18}H_{15}S_2O_4Cl$, %: C, 54.75; H, 3.83; found C, 54.82; H, 3.71. ^{1}H-NMR δ 7.83(d, 2H), 7.72(d, 2H), 7.64(t, 1H), 7.54–7.49(m, 4H), 6.97(q, 1H), 4.36(s, 2H) and 2.00(d, 3H). Mass spectrum: molecular ion m/e 394(25%), 269(25%), 255(40%), 219(20%), 189(40%), 175(35%), 154(35%), 111(80%) and 77 (100%).

General procedure for the equilibration of **10** *or* **11** *in the presence of sodium benzenesulfinate.* The appropriate product **10** or **11** (0.00021 moles) was dissolved in DMF (20 ml) followed by the addition of the sodium benzenesulfinate (0.00165 moles). In monitoring the reaction by ^{1}H-NMR equilibration was complete by 30 minutes with composition **10/9** or **11/9** = 3/1. The identity of the compounds from each of these equilibrations was confirmed by superimposable IR spectra with authentic samples. Similarly the structures of **10** and **11** after the equilibration were also confirmed by superimposability of their IR spectra with the appropriate starting compounds.

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6. Compounds **13** and **15** were used as unseparated stereoisomeric mixtures which led to stereochemically homogeneous **14** and **9** respectively.
7. B. S. Thyagarajan and R. A. Chandler, *J. Chem. Soc., Chem. Commun.*, 328–330 (1990).
8. The E,E geometry for **9, 10** and **11** are assigned on the basis of earlier established evidence. See B. S. Thyagarajan, B. F. Wood and J. A. Glowienka, *Phosphorus and Sulfur*, **26**, 275–284 (1986).

Note: A preliminary communication of this work is in press. J. Chem. Soc., CHEM. COMMUN. in 1990.