Stereoselective Synthesis of Alkynyl Vinyl Chalcogenides via Horner–Wittig Reaction

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Abstract: New (diphenylphosphoryl)methyl phenylethynyl sulfides, selenides, or tellurides were prepared by the reaction of (diphenylphosphoryl)methyl p-toluenesulfonate with alkynethiols, -selenols, or -tellurols at room temperature. The (diphenylphosphoryl)methyl phenylethynyl sulfides, selenides, or tellurides reacted with aldehydes and cyclic ketones to give the corresponding alkynyl vinyl sulfides, selenides, or tellurides, with preferential E-stereoselectivity, in a Horner–Wittig-type reaction.

Key words: Wittig reaction, alkynyl vinyl chalcogenides, vinyl chalcogenides, chalcogenium, olefination

Organochalcogenium compounds have become the key component of a variety of versatile and useful reagents for organic synthesis. The multiple applications of organochalcogenium chemistry have been well described in a number of review articles and books. Functionalized alkynyl and alkenyl chalcogenides have a great potential in organic synthesis, since they are valuable intermediates for the selective preparation of several organic compounds. Furthermore, methods for the synthesis of chalcogenyl-substituted acetylenes have also been described in recent years, although in a reduced number compared to their vinylic counterparts. The most common approach to alkynyl chalcogenides employs the reaction of a metal alkynide with elemental chalcogenium followed by reaction with an alkyl halide or an appropriate electrophilic reagent.

Among the many applications of vinyl selenides, divinyl selenides, and vinyl sulfides, the cross-coupling reaction with Grignard reagents catalyzed by nickel or palladium has been described. On the other hand, palladium and nickel-catalyzed cross-coupling reactions and tellurium–metal exchange reactions demonstrate the usefulness of vinyl tellurides.

Except for alkynyl vinyl sulfides, alkynyl vinyl chalcogenides constitute a nearly unexplored class of unsaturated chalcogenides. Their preparation include multistep sequences employing aldehydes or 2-chloroethyl thiocyanate and the reaction of lithium acetyldide with β-chlorovinyl sulfenamides. The sulfur derivatives, as the corresponding sulfoxides and sulfones, were converted into sulfur, selenium, or nitrogen heterocycles by reaction with sodium sulfide, sodium selenide, or methylamine. Alkynyl vinyl sulfides were also claimed to have pesticide and bactericide activity.

In light of the above comments and from our continuous interest in the development of new vinyl chalcogenides based on Horner–Wittig reaction, we became interested in the development of practical stereoselective synthetic methods for alkynyl vinyl chalcogenides. For instance, we have recently described a detailed study of the synthesis of symmetrical and unsymmetrical divinyl sulfides, selenides, and tellurides from chalcogenyl phosphonates and phosphine oxides, by reaction with arylaldehydes and cyclic ketones. Thus, as a continuation of this study, we planned the preparation of alkynyl vinyl sulfides, selenides, and tellurides by a similar route, starting from (diphenylphosphoryl)methyl phenylethynyl chalcogenides. The alkynylphosphine oxides were prepared in 68–89% isolated yield by the reaction of phenylacetylene with butyllithium at 0 °C, followed by addition of elemental sulfur, selenium, or tellurium to the lithium acetylide and (diphenylphosphoryl)methyl p-toluenesulfonate (Scheme 1). The compounds can be easily purified by column chromatography and are quite stable compounds. The Horner–Wittig reaction of 2c was subsequently performed, initially by reaction of the sulfur derivative 2a with benzaldehyde in tetrahydrofuran at 0 °C and using sodium hydride as the base; the corresponding product 3a was obtained in 70% yield after one hour of reaction (TLC monitoring). Next, a detailed study was performed with aldehydes and ketones and the reaction was showed to be effective also with selenium and tellurium derivatives. The corresponding alkynyl vinyl chalcogenides 3–5 were isolated in good yields (Table 1), the only exception was the reaction of tellurium derivative 2c with isobutyraldehyde (entry 21).

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Scheme 1
Concerning stereochemistry of the reaction, a very high preference for the E-isomer could be detected by GC and 1H NMR from the reactions with aromatic aldehydes. This result could be expected from the known behavior of the Horner–Wittig reaction of the diphenylphosphoryl group in stabilized ylides. However, aliphatic aldehydes furnished lower yields with a small preference for the Z-isomer, based on the coupling constant values for the vinylic hydrogen.

When the reaction was performed with 4-tert-butylcyclohexanone and benzophenone, good yields of the corresponding trisubstituted alkynyl vinyl chalcogenides were obtained with 2a and 2b (Table 1, entries 7, 8, 15, and 16). A small amount of hexamethylphosphoramide as a co-solvent for the Z-isomer, based on the coupling constant values for the vinylic hydrogen.

In summary, we described a highly convenient method for the preparation of alkynyl vinyl chalcogenides through the reaction of (diphenylphosphoryl)methyl phenylethynyl chalcogenides with ketones and aromatic and aliphatic aldehydes by a Horner–Wittig route.

The product ratios were analyzed by gas chromatography using a Shimadzu 14A gas chromatograph, capillary column, equipped with an FID. IR data were collected on a Bruker FT Tensor 27 spectrophotometer. NMR spectroscopy was performed on Bruker 200 MHz and 400 MHz spectrometers, with TMS and CDCl3 as internal standards. Melting points were obtained on a Microquimica MQAPF-301 melting point apparatus. Mass spectrometry was carried out on a Shimadzu QP2010 Plus instrument. Elemental analyses were obtained from Central Analítica, Instituto de Química, Universidade de São Paulo. All new compounds were adequately characterized; detailed data for representative compounds are given below.

### Table 1 Alkynyl Vinyl Chalcogenides Prepared

<table>
<thead>
<tr>
<th>Entry</th>
<th>R¹</th>
<th>R²</th>
<th>Y</th>
<th>Compound</th>
<th>Ratio E/Z</th>
<th>Time (min)</th>
<th>Yield (%)</th>
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<td>Ph</td>
<td>H</td>
<td>S</td>
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<td>70</td>
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<td>S</td>
<td>3b</td>
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<td>78</td>
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<tr>
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<td>4-MeC₆H₄</td>
<td>H</td>
<td>S</td>
<td>3c</td>
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<td>S</td>
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<td>S</td>
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<td>H</td>
<td>S</td>
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<td>–</td>
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<td>26</td>
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</table>

*a Determined by GC and 1H NMR.

ᵇ HMPA was used as a co-solvent (1 mL/mmol).
(11 mmol) was added and the mixture was further stirred at r.t. until consumption of the chalcogen. Then, a soln of (diphenylphosphoryl) methyl p-toluenesulfonate (1, 3.86 g, 10 mmol) in THF (20 mL) was added at 0 °C and the mixture was stirred at r.t. for 2 h (3.5 h for the sulfur derivative). H₂O (50 mL) was added, the mixture was extracted with EtOAc (3 × 50 mL), and the combined organic layers were washed with brine (50 mL). The organic layer was dried (MgSO₄) and the solvent was removed under reduced pressure. The residue was purified by column chromatography (hexanes–EtOAc, 7:3).

**Phenylethyl Styryl Sulfide (3a)**


IR (KBr): 1603, 2166 cm⁻¹.

1H NMR (200 MHz, CDCl₃): δ = 6.57 (d, J = 15.0 Hz, 1 H), 6.86 (d, J = 15.0 Hz, 1 H), 7.18–7.36 (m, 8 H), 7.47–7.53 (m, 2 H).

1³C NMR (50 MHz, CDCl₃): δ = 74.5, 98.7, 118.6, 122.7, 126.0, 127.6, 128.4, 128.7, 129.6, 131.6, 135.9.

MS (EI): m/z (%) = 236 (58, M⁺).


**4-Methylstyryl Phenylethynyl Sulfide (3c)**


IR (KBr): 1595, 2172 cm⁻¹.

1H NMR (400 MHz, CDCl₃): δ = 2.30 (s, 3 H), 6.47 (d, J = 15.0 Hz, 1 H), 6.81 (d, J = 15.0 Hz, 1 H), 7.09 (d, J = 8.0 Hz, 2 H), 7.20 (d, J = 8.0 Hz, 2 H), 7.29–7.31 (m, 3 H), 7.46–7.49 (m, 2 H).

1³C NMR (100 MHz, CDCl₃): δ = 74.1, 74.9, 98.3, 117.4, 122.8, 125.9, 128.3, 129.3, 129.8, 131.6, 133.2, 137.5.

MS (EI): m/z (%) = 250 (68, M⁺), 249 (29), 235 (36), 234 (73), 205 (25), 202 (38), 121 (100), 115 (35), 91 (21), 89 (41), 65 (26), 63 (24).


**4-Chlorostyryl Phenylethynyl Sulfide (3d)**


IR (KBr): 1603, 2166 cm⁻¹.

1H NMR (400 MHz, CDCl₃): δ = 6.53 (d, J = 15.0 Hz, 1 H), 6.78 (d, J = 15.0 Hz, 1 H), 7.22 (d, J = 8.7 Hz, 2 H), 7.26 (d, J = 8.7 Hz, 2 H), 7.31–7.34 (m, 3 H), 7.48–7.50 (m, 2 H).

1³C NMR (100 MHz, CDCl₃): δ = 74.2, 99.0, 119.6, 122.6, 127.2, 128.1, 128.4, 128.8, 131.7, 133.2, 134.5.

MS (EI): m/z (%) = 270 (37, M⁺), 235 (30), 234 (82), 225 (17), 202 (36), 121 (100), 117 (19), 102 (20), 101 (29), 89 (37), 75 (28), 63 (17), 51 (20).


**Pent-1-enyl Phenylethynyl Sulfide (3f)**

Mp 131–132 °C.

IR (KBr): 1591, 2171 cm⁻¹.

1H NMR (400 MHz, CDCl₃): δ = 1.44 (sext, J = 7.3 Hz, 2 H), 2.12 (dq, J = 14.7, 6.8 Hz, 1 H), 5.75 (dt, J = 7.3, 1.2 Hz, 2 H), 5.87 (dt, J = 7.3, 1.4 Hz, 2 H), 7.26 (d, J = 8.7 Hz, 2 H), 7.31–7.34 (m, 3 H), 7.48–7.50 (m, 2 H).

1³C NMR (100 MHz, CDCl₃): δ = 74.2, 99.0, 119.6, 122.6, 127.2, 128.1, 128.4, 128.8, 131.7, 133.2, 134.5.

MS (EI): m/z (%) = 270 (37, M⁺), 235 (30), 234 (82), 225 (17), 202 (36), 121 (100), 117 (19), 102 (20), 101 (29), 89 (37), 75 (28), 63 (17), 51 (20).


**Phenylethynyl Styryl Sulfide (3a)**

Mp 51–52 °C.

IR (KBr): 1591, 2171 cm⁻¹.

1H NMR (400 MHz, CDCl₃): δ = 0.92 (t, J = 7.3 Hz, 3 H), 1.44 (sext, J = 7.3 Hz, 2 H), 2.13 (dq, J = 7.3, 1.2 Hz, 2 H), 5.87 (dt, J = 14.7, 1.2 Hz, 1 H), 5.99 (dt, J = 14.7, 6.8 Hz, 1 H), 7.28–7.31 (m, 3 H), 7.40–7.47 (m, 2 H); δ (Z form) = 0.94 (t, J = 7.3 Hz, 3 H), 1.45 (sext, J = 7.3 Hz, 2 H), 2.12 (dq, J = 7.3, 1.4 Hz, 2 H), 5.75 (dt, J = 9.0, 1.3 Hz, 1 H), 6.12 (dt, J = 9.0, 1.4 Hz, 1 H), 7.28–7.31 (m, 3 H), 7.40–7.47 (m, 2 H).

1³C NMR (100 MHz, CDCl₃): δ = 13.5, 13.6, 21.9, 22.1, 30.6, 34.7, 76.1, 77.7, 92.9, 96.7, 117.3, 121.8, 123.0, 123.1, 128.2, 128.2, 128.3, 131.4, 131.5, 132.7, 132.9.

MS (EI): m/z (%) = 202 (54, M⁺).


**2,2-Diphenylvinyl Phenylethynyl Sulfide (3h)**

Mp 51–52 °C.

IR (KBr): 1591, 2171 cm⁻¹.
1H NMR (200 MHz, CDCl3): δ = 6.77 (s, 1 H), 7.19–7.45 (m, 15 H).
13C NMR (50 MHz, CDCl3): δ = 77.8, 93.8, 121.9, 123.8, 127.0, 127.6, 128.1, 128.3, 128.3, 128.5, 129.5, 131.5, 137.9, 140.4, 141.9.
MS (EI): m/z (%) = 312 (57, M+).

Phenylethynyl Styryl Selenide (4a)
IR (KBr): 1591, 2156 cm–1.

4-Chlorostyryl Phenylethynyl Selenide (4d)
IR (KBr): 1591, 2156 cm–1.

1H NMR (200 MHz, CDCl3): δ = 3.88 (s, 3 H), 6.81 (d, J = 15.3 Hz, 1 H), 6.88 (d, J = 8.8 Hz, 1 H), 7.11 (d, J = 8.1 Hz, 2 H), 7.22 (d, J = 8.1 Hz, 2 H), 7.31–7.33 (m, 2 H), 7.47–7.49 (m, 2 H).
13C NMR (100 MHz, CDCl3): δ = 55.2, 68.3, 102.9, 114.1, 123.1, 124.1, 128.3, 128.4, 131.6, 133.7, 159.4.
MS (EI): m/z (%) = 314 (17, M+).

4-Methoxystyryl Phenylethynyl Selenide (4b)
Mp 119–121 °C; ratio E/Z 12:1.
IR (KBr): 1602, 2151 cm–1.

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References