Synthesis and Reactions of (Aroylthiomethyl)-triphenylphosphonium Bromides

Masaru ISHIDA, Taketoshi IWATA, Masato YOKOI, Kohichi KAGA, Shinzi KATO*

Department of Chemistry, Faculty of Engineering, Gifu University, Yanagido, Gifu, 501-11, Japan

The synthesis of (arylmethylthio)-triphenylphosphonium bromides and the application as an equivalent of (mercaptoethyl)-triphenylphosphonium bromide in the synthesis of aryl vinyl sulfides (thioenolates) are described.

Synthesis of thioenolates and their precursors have been the subject of our research, because of their synthetic applications. Wittig reaction of phosphonium ylids having an arylthiol group with aldehydes seems to be a method for the synthesis of such species. However, direct generation of the ylid has been quite difficult. In this paper, we describe a synthesis and some reactions of the new phosphonium salts, (arylmethylthio)-triphenylphosphonium bromides 3, as an equivalent of (mercaptoethyl)-triphenylphosphonium bromide 4.

\[
\begin{align*}
\text{Ar}-\text{C}^-\text{S}-\text{CH}_2-\text{P(Ph)H}_3\text{Br}^- \quad & \quad \text{HS}-\text{CH}_2-\text{P(Ph)H}_3\text{Br}^- \\
\end{align*}
\]

The salt 3 was easily prepared by addition of potassium arylethenecarboxylate to a chloroform suspension of (bromomethyl)-triphenylphosphonium bromide (2) followed by refluxing for 4 h (Table 1). The salt 3 is dried in vacuo and can be employed in the following reactions without further purifications.

The salt 3, suspended in dry tetrahydrofuran, was cooled to \(-70^\circ\text{C}\) and treated with an equimolar amount of potassium \(t\)-butoxide to give a yellow solution of the ylid. Subsequently, the aryl aldehyde 6 was added and the mixture was warmed to \(-5\) to \(-10^\circ\text{C}\) within 3 h. In the case of the reaction with the alkyl aldehyde, the mixture was stirred for 0.5 h at \(-30^\circ\text{C}\) after addition of aldehyde. After the usual work-up, the corresponding aryl vinyl sulfide 7 was obtained in moderate to good yield (Table 2).

These sulfides 7 can be regarded as the corresponding thioenolates. For example, the treatment of the sulfide 7d with methanolic potassium methoxide gave a dark brown solution of the potassium thioenolate 8. Subsequent

\[
\begin{align*}
\text{7a-j} \quad \text{R}^-\text{CHO} \quad \text{Ar}-\text{C}^-\text{S}-\text{CH}==\text{CH}-\text{R}^\prime \\
\end{align*}
\]

Table 1. (Aroylthiomethyl)-triphenylphosphonium Bromides 3a-c prepared

<table>
<thead>
<tr>
<th>Product</th>
<th>Yield [%]</th>
<th>m.p. [°C]</th>
<th>Molecular Formula*</th>
<th>I.R. (KBr) ν [cm(^{-1})]</th>
<th>(^{1})H-N.M.R. (CDCl(_3)/TMS) δ [ppm]</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>68</td>
<td>207–209°</td>
<td>C(_2)H(_4)BrOPS (493.4)</td>
<td>1670 (C=O)</td>
<td>5.70 (d, J = 7.5 Hz, 2H, CH(<em>2)); 7.1–8.1 (m, 20H, H(</em>{\text{Ar}}))</td>
</tr>
<tr>
<td>3b</td>
<td>64</td>
<td>215–217°</td>
<td>C(_2)H(_4)BrOPS (507.4)</td>
<td>1665 (C=O)</td>
<td>2.35 (s, 3H, CH(_3)); 5.73 (d, J = 7.5 Hz, 2H, CH(<em>2)); 7.0–8.1 (m, 19H, H(</em>{\text{Ar}}))</td>
</tr>
<tr>
<td>3c</td>
<td>67</td>
<td>193–195°</td>
<td>C(_2)H(_4)BrO(_2)PS (523.4)</td>
<td>1670 (C=O)</td>
<td>3.80 (s, 3H, CH(_3)); 5.66 (d, J = 7.5 Hz, 2H, CH(<em>2)); 6.7–8.1 (m, 19H, H(</em>{\text{Ar}}))</td>
</tr>
</tbody>
</table>

* Satisfactory microanalyses were obtained: C ± 0.38, H ± 0.06; exception 3a: C ± 0.5, H ± 0.01.
Table 2. Aryl Vinyl Sulfides 7a–j prepared

<table>
<thead>
<tr>
<th>Product</th>
<th>Yield [%]a</th>
<th>Molecular Formulab</th>
<th>trans/cis Ratioc</th>
<th>Isomer (m.p. [°C] (solvent))</th>
<th>M.S. (20 eV) m/e (M+)</th>
<th>I.R. (KBr) νC=O [cm⁻¹]</th>
<th>1H-N.M.R. (CDCl3/TMS) δ [ppm]</th>
</tr>
</thead>
<tbody>
<tr>
<td>7a</td>
<td>84</td>
<td>C₁₅H₁₄NO₂S</td>
<td>3:4 trans</td>
<td>154–156°C (CH₂Cl₂, n-C₆H₁₄)</td>
<td>285 1665 6.86 (d, 1H, J = 16.5 Hz, H₁₅ν)</td>
<td>7.2–8.4 (m, 10H, H₁₆–H₁₉ν)</td>
<td>8.44 (d, 2H, H₂ν)</td>
</tr>
<tr>
<td>7b</td>
<td>95d</td>
<td>C₁₅H₁₄OS</td>
<td>4:5 mixture</td>
<td>119–121°C (CH₂Cl₂, n-C₆H₁₄)</td>
<td>325 1660 2.35 (s, 3H, CH₃)</td>
<td>6.5–8.0 (m, 12H, H₁₆–H₁₉ν)</td>
<td>7.2–8.0 (m, 10H, H₁₆–H₁₉ν)</td>
</tr>
<tr>
<td>7c</td>
<td>46</td>
<td>C₁₅H₁₄OS</td>
<td>1:1 mixture</td>
<td>121–123°C (CH₂Cl₂, n-C₆H₁₄)</td>
<td>254 1660 2.35 (s, 3H, CH₃)</td>
<td>6.5–8.0 (m, 12H, H₁₆–H₁₉ν)</td>
<td>7.2–8.0 (m, 10H, H₁₆–H₁₉ν)</td>
</tr>
<tr>
<td>7d</td>
<td>90</td>
<td>C₁₅H₁₄NO₂S</td>
<td>– mixture</td>
<td>95–98°C (CH₃OH)</td>
<td>278 1665 2.40 (s, 3H, CH₃)</td>
<td>6.00 (d, 1H, J = 10.0 Hz, H₁₅ν)</td>
<td>7.15–7.90 (m, 10H, H₁₆–H₁₉ν)</td>
</tr>
<tr>
<td>7e</td>
<td>62d</td>
<td>C₁₅H₁₄OS</td>
<td>1:1 trans</td>
<td>172–176°C (CH₂Cl₂, n-C₆H₁₄)</td>
<td>315 1665 2.35 (s, 3H, CH₃)</td>
<td>6.5–8.0 (m, 12H, H₁₆–H₁₉ν)</td>
<td>7.2–8.0 (m, 10H, H₁₆–H₁₉ν)</td>
</tr>
<tr>
<td>7f</td>
<td>96</td>
<td>C₁₅H₁₄NO₂S</td>
<td>1:2 mixture</td>
<td>111–120°C (CH₂Cl₂, n-C₆H₁₄)</td>
<td>341 1665 2.35 (s, 3H, CH₃)</td>
<td>6.3–8.1 (m, 12H, H₁₆–H₁₉ν)</td>
<td>7.0–8.0 (m, 4H, H₁₅ν)</td>
</tr>
<tr>
<td>7g</td>
<td>39</td>
<td>C₁₅H₁₄OS</td>
<td>1:3 mixture</td>
<td>111–115°C (CH₂Cl₂, n-C₆H₁₄)</td>
<td>270 1665 2.00 (s, 3H, CH₃)</td>
<td>6.3–8.1 (m, 12H, H₁₆–H₁₉ν)</td>
<td>7.0–8.0 (m, 4H, H₁₅ν)</td>
</tr>
<tr>
<td>7h</td>
<td>71</td>
<td>C₁₅H₁₄NO₂S</td>
<td>– mixture</td>
<td>111–120°C (CH₂Cl₂, n-C₆H₁₄)</td>
<td>208 1660 2.00 (s, 3H, CH₃)</td>
<td>6.3–8.1 (m, 12H, H₁₆–H₁₉ν)</td>
<td>7.0–8.0 (m, 4H, H₁₅ν)</td>
</tr>
<tr>
<td>7i</td>
<td>78</td>
<td>C₁₅H₁₄OS</td>
<td>2:3 mixture</td>
<td>2.1–2.4 (m, 2H, CH₂)</td>
<td>3.84 3.85 (2s, 3H, CH₃ν)</td>
<td>5.90 (dt, 1H, J = 15.8 Hz, CH₂ν)</td>
<td>7.0–8.0 (m, 4H, H₁₅ν)</td>
</tr>
<tr>
<td>7j</td>
<td>38</td>
<td>C₁₅H₁₄OS</td>
<td>1:1 mixture</td>
<td>2.1–2.4 (m, 2H, CH₂)</td>
<td>3.84 3.85 (2s, 3H, CH₃ν)</td>
<td>5.90 (dt, 1H, J = 15.8 Hz, CH₂ν)</td>
<td>7.0–8.0 (m, 4H, H₁₅ν)</td>
</tr>
</tbody>
</table>

a Yield of trans/cis-mixture.
b Satisfactory microanalyses obtained: C ± 0.35, H ± 0.32, N ± 0.22; exception 7h, C = 0.47. Because of their lability cis-7b and cis-7c were characterized by H.R.M.S.; cis-7b, m/e = 264.0605 (calc. for M⁺: 264.0608); cis-7c, m/e = 278.0751 (calc. for M⁺: 278.0765).
c Determined by 1H-N.M.R. spectrometry.
d Yield of crude product.
* Neat.
addition of 2,4-dinitrophenyl chloride 9a gave the dienyl sulfide 10a in quantitative yield. Similar treatment of the sulfide 7f followed by the reaction with phenacyl bromide 9b gave the corresponding sulfide 10b in 77% yield. Some applications of this reaction are now being studied.

[(4-Methylbenzothio)-methyl]triphenylphosphonium Bromide (3b); Typical Procedure:
Potassium 3-oluenethiocarboxylate (1b; 1.43 g, 7.5 mmol) is added to a suspension of (bromomethyl)-triphenylphosphonium bromide (2; 3.26 g, 7.5 mmol) in chloroform (50 ml). The mixture is refluxed for 4 h, washed with water (3 x 20 ml), and then dried with anhydrous sodium sulfate. After removal of the solvent, the residue is added dropwise to dry ether (100 ml) at 0°C with stirring to give 3b as white precipitates; yield: 2.44 g (64%). A pure sample is obtained by recrystallization from hot acetone; m.p. 215–217°C.

C₂₄H₂₄Br₂OSP calc. C 63.91 H 4.77
(507.4) found 63.71 4.82

S-(2-Phenylvinyl)-p-Toluenethiocarboxylate (7c); Typical Procedure:
To the salt 3b (0.406 g, 0.80 mmol) suspended in dry tetrahydrofuran (30 ml) is added potassium t-butoxide (0.09 g, 0.8 mmol) under argon at −78°C. The mixture is stirred at that temperature for 1 h. Then benzenediazide (0.077 g, 0.72 mmol) in tetrahydrofuran (5 ml) is added and warmed to −7°C within 1.5 h. After quenching by addition of ammonium chloride (0.5 mol) followed by evaporation of the solvent, the residue is diluted with dichloromethane (30 ml) and washed with water (3 x 20 ml). The organic layer is dried with anhydrous sodium sulfate. After removal of the solvent, the residue is chromatographed on silica gel (benzene as eluant). The white syrup liquid obtained is purified by preparative TLC (Wako-gel B-5F, benzene/n-hexane, 1/1) to give 7c; yield: 0.093 g (46%). A pure sample is obtained by recrystallization from dichloromethane/n-hexane; m.p. 121–123°C.

C₁₄H₁₄OS calc. C 75.56 H 5.48
(254.4) found 75.21 5.58

S-[2-(4-Nitrophenyl)-vinyl]-4-Methoxythiobenzonate (7f); Large Scale Preparation:
Similar to the synthesis of 7c, a yellow solution of the ylid (11 mmol) is generated from the salt 3c (5.75 g, 11.0 mmol) and potassium t-butoxide (1.23 g, 11.0 mmol) in dry tetrahydrofuran (200 ml) at −70°C. Then, 4-nitrobenzaldehyde (1.51 g, 10 mmol) is added. After work-up as described above, the residue is treated with dichloromethane to give the crude ester 7f as yellow needles; yield: 2.45 g (78%). Recrystallization from dichloromethane gives pure 7f; yield: 1.88 g (60%); m.p. 169–175°C.

S-(1-Propenyl)-4-Methoxythiobenzonate (7g); Typical Procedure:
To the salt 3e (0.263 g, 0.5 mmol) suspended in dry tetrahydrofuran (20 ml) is added potassium t-butoxide (0.056 g, 0.5 mmol) under argon at −30°C. The mixture is stirred for 10 min. Then acetaldehyde (0.022 g, 0.5 mmol) in tetrahydrofuran (5 ml) is added and the mixture is stirred at the same temperature for 0.5 h. After work-up similarly to the synthesis of 7c, the ester 7f is obtained; yield: 81 mg (75%). An analytical sample is obtained by bulb-to-bulb distillation; b.p. 80°C/4–5 torr.

C₁₄H₁₇O₂S calc. C 63.44 H 5.81
(208.3) found 63.59 5.01

2,4-Dinitrophenyl 4-(2-Nitrophenyl)-1,3-butadienyl Sulfide (10a):
The sulfide 7d (41 mg, 0.126 mmol) in tetrahydrofuran (10 ml) is added dropwise to methanol (2.5 ml) containing potassium t-butoxide (15 mg, 0.13 mmol) under argon at −73°C. The reaction mixture is warmed to −20°C with n 50 min. Then 2,4-dinitrophenyl chloride (9a; 26.5 mg, 0.13 mmol) in tetrahydrofuran (5 ml) is added dropwise. After warming to room temperature, the solvent is removed. The residue is extracted with dichloromethane (50 ml), washed with water (3 x 20 ml), and dried with anhydrous sodium sulfate. After removal of the solvent, the residue is recrystallized from dichloromethane/n-hexane to give the sulfide 10a; yield: 47 mg (100%); m.p. 125–128°C.

C₁₈H₁₃N₂O₅S calc. C 51.47 H 2.97 N 11.26
(373.3) found 51.15 3.15 10.89

I.R. (KBr): ν = 1510, 1340 cm⁻¹ (NO₂)

H-N.M.R. (CDCl₃): δ = 6.2–7.8 (m, 8 H, H₈mono and H₈vinyl); 5.9 (d, J = 8.5 Hz, 1 H, H₈α); 8.5 (dd, J = 2.5 Hz, 8.5 Hz, 1 H, H₈α); 10.9 (9.0 ppm (d, J = 2.5 Hz, 1 H, H₈α)

[2-(4-Nitrophenylvinyl) Phenacyl Sulfide (10b):
The sulfide 7f (158 mg, 0.5 mmol) in tetrahydrofuran (30 ml) is added dropwise to methanol (10 ml) containing potassium t-butoxide (56 mg, 0.5 mmol) at −20°C. The mixture is stirred for 50 min at the same temperature. To the resulting deep purple mixture, a solution of phenacyl bromide (9b; 104 mg, 0.52 mmol) in tetrahydrofuran (10 ml) is added and the mixture is warmed to 20°C within 20 min. After removal of the solvent, the residue is extracted with dichloromethane (3 x 25 ml). Then the extract is washed with water (3 x 20 ml) and dried with anhydrous sodium sulfate. After concentration, the residue is treated with methanol to give the sulfide 10b as pale yellow plates; yield: 104 mg (77%). A sample is recrystallized from dichloromethane/n-hexane; m.p. 150–153°C.

C₁₈H₁₅NO₃S calc. C 64.20 H 4.38 N 4.68
(299.3) found 63.97 4.32 4.60

I.R. (KBr): ν = 1680 cm⁻¹ (C=C=O)

H-N.M.R. (CDCl₃): δ = 4.10 (s, 2H, CH₂); 6.47 (d, J = 11 Hz, 1H, H₈α); 6.6 (d, J = 11 Hz, 1H, H₈α); 7.20–8.20 ppm (m, 9 H, H₈α)

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* Address for correspondence.
8 The stabilized ylid, 1-(benzothio-phenacylidienethiophosphorane was prepared by us; Kato, S., Imamura, S., Mizuta,
10 The ylids 5a–e were generated at −30°C for the syntheses of the sulfides 7b, e, i, and j.
13 The sulfide 7f used is a mixture (cis:trans = 3:1).
14 The reaction is carried out at −20°C, because of the low solubility of the sulfide 7f at −70°C.