Horner-Wittig Synthesis of α, β-Unsaturated Sulfides and Sulfones. Part II

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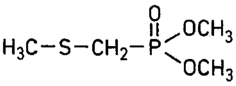
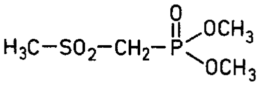
In a previous paper[1], we described the synthesis of dimethyl methylmercaptomethanephosphonate (**1**) and dimethyl methylsulfonomethanephosphonate (**2**) as reagents for the preparation of α,β-unsaturated sulfides and sulfones:



$\mathrm{H_3C{-}S{-}CH_2{-}P(O)(OCH_3)_2}$

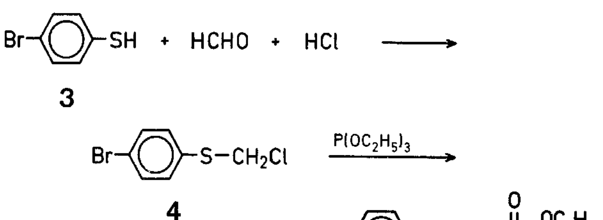
1



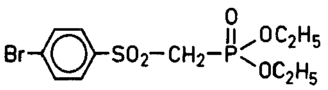
$\mathrm{H_3C{-}SO_2{-}CH_2{-}P(O)(OCH_3)_2}$

2

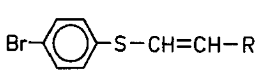
The corresponding arylmercaptomethanephosphonates which are synthetised without difficulty can be equally used for the preparation of α,β-unsaturated sulfides and sulfones. Diethyl (4-bromophenylmercapto)-methanephosphonate (**5**), for example, is prepared from 4-bromophenylmercaptan (**3**) by the following reaction:



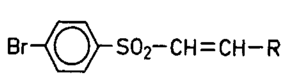
Compound **5** is readily oxidized by potassium permanganate in acid solution to give diethyl (4-bromophenylsulfono)-methanephosphonate (**6**). Both **5** and **6** react with aromatic aldehydes to give the corresponding unsaturated sulfides and sulfones (**7** and **8**):



6



7



8

The yields are usually very good, especially in the reaction of the sulfones. Neither **5** nor **6** react with ketones under a variety of conditions. The unsaturated sulfides and sulfones possess the *trans*-configuration, as indicated by the high coupling constants (14–16 cps) of the two vinylic protons in the NMR spectra.

Thus, the results are similar to those found for the corresponding unsaturated methyl-sulfides and -sulfones[1].

Chloromethyl 4-bromophenyl sulfide (4) was prepared according to Fancher[2] by the reaction of a solution of paraformaldehyde in hydrochloric acid with a solution of 4-bromophenyl mercaptan in benzene at 40° (in dichloromethane as solvent the yields were much lower); yield (83%); b.p. 113–116°/1 mm (Lit.[3], b.p. 150°/15 mm).

C_7H_6BrClS	calc.	C 35.5	H 2.5
	found	35.9	2.6

Diethyl (4-bromophenylmercapto)-methanephosphonate (5): A mixture of compound **4** (66 g, 0.25 mol) and triethyl phosphite (70 g, 0.42 mol) was refluxed for 4 hours. The resultant mixture was distilled under reduced pressure; yield: 83 g (98%); b.p. 180°/1 mm.

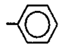
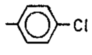
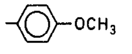
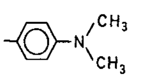
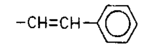
$C_{11}H_{16}BrO_3PS$	calc.	C 38.9	H 4.7
	found	38.7	4.9

NMR spectrum (in $CDCl_3$): 6H(t), $\delta = 1.3$ ppm (CH_3); 2H(d), $\delta = 3.16$ ppm, $J_{HP} = 13.5$ cps (CH_2); 4H(quin), $\delta = 4.16$ ppm, $J_{HP} = 7$ cps, $J_{HH} = 7$ cps; 4H(s), $\delta = 7.36$ ppm (aromatic protons).

When trimethyl phosphite was used instead of triethyl phosphite in the above reaction, only a small yield (about 5%) of the corresponding phosphonate was obtained, and **4** was recovered almost unchanged.

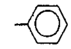
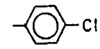
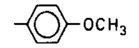
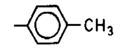
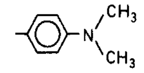
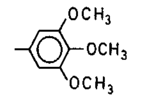
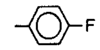
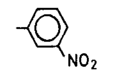
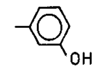
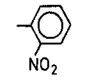
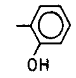
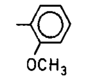
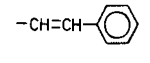
Diethyl(4-bromophenylsulfono)-methanephosphonate (6): To a solution of compound **5** (43 g, 0.13 mol) in benzene (250 ml), 25% sulphuric acid (250 ml) was added. Potassium permanganate was added in 10 g portions with shaking until the violet colour persisted for 20 min. The temperature was kept below 40°. The manganese dioxide which precipitated was dissolved by addition of solid sodium pyrosulphite ($Na_2S_2O_5$). The benzene layer was separated, washed with water and 5% sodium hydrogen carbonate solution, dried, and evaporated. On recrystallization from

Table 1. Preparation of (4-Bromophenylmercapto)-ethylenes (7)

R	Yield %	m. p.	Formula	Analysis			
	75	75°[a]	$C_{14}H_{11}BrS$	calc. found	C 57.8 57.9	H 3.8 3.8	Br 27.5 27.5
	80	114°[b]	$C_{14}H_{10}BrClS$	calc. found	C 51.6 51.4	H 3.1 3.1	S 9.8 10.3
	93	98°[b]	$C_{15}H_{13}BrSO$	calc. found	C 56.0 56.0	H 4.1 4.1	Br 24.9 25.1
	75	113°[b]	$C_{16}H_{16}BrNS$	calc. found	C 57.5 57.0	H 4.8 5.0	Br 24.0 24.1
	60	96°[c]	$C_{16}H_{13}BrS$	calc. found	60.6 60.3	4.1 4.2	26.1 25.2

[a] recrystallized from heptane
[b] recrystallized from cyclohexane
[c] recrystallized from methanol

Table 2. Preparation of (4-Bromophenylsulfono)-ethylenes (**8**)

R	m. p.	Formula	Analysis			
	$100^{\circ\,a}$	$C_{14}H_{11}BrO_2S$	calc. found	C 52.0 51.9	H 3.4 3.6	Br 24.8 25.2
	$184\text{–}185^{\circ\,b}$	$C_{14}H_{10}BrClO_2S$	calc. found	C 47.1 46.6	H 2.8 2.7	
	$149^{\circ\,b}$	$C_{15}H_{13}BrO_3S$	calc. found	C 51.0 51.2	H 3.7 3.6	Br 22.7 22.8
	$144^{\circ\,a}$	$C_{15}H_{13}BrO_2S$	calc. found	C 53.4 53.2	H 3.9 3.9	Br 23.8 23.9
	$176^{\circ\,b}$	$C_{16}H_{16}BrNO_2S$	calc. found	C 52.5 53.4	H 4.4 4.7	
	$116^{\circ\,c}$	$C_{17}H_{17}BrO_5S$	calc. found	C 49.4 49.5	H 4.1 3.8	Br 19.4 19.6
	$139\text{–}140^{\circ\,c}$	$C_{14}H_{10}BrFO_2S$	calc. found	C 49.3 49.4	H 2.9 3.1	Br 23.4 23.3
	$157^{\circ\,b}$	$C_{14}H_{10}BrNO_4S$	calc. found	C 45.6 45.4	H 2.7 2.6	Br 21.7 22.1
	$153^{\circ\,d,f}$	$C_{14}H_{11}BrO_3S$	calc. found	C 49.6 49.5	H 3.2 3.2	Br 23.6 24.1
	$180^{\circ\,e}$	$C_{14}H_{10}BrNO_4S$	calc. found	C 45.7 45.7	H 2.7 2.8	Br 21.7 22.0
	$180^{\circ\,f,g,h}$	$C_{14}H_{11}BrO_3S$	calc. found	C 49.6 50.1	H 3.2 3.5	Br 23.6 23.9
	$102\text{–}103^{\circ\,h}$	$C_{15}H_{13}BrO_3S$	calc. found	C 51.0 51.3	H 3.7 3.9	Br 22.7 22.8
	$175^{\circ\,b}$	$C_{16}H_{13}BrO_2S$	calc. found	C 55.0 54.9	H 3.4 3.6	Br 22.9 22.8
—COOH	$173^{\circ\,f,i}$	$C_9H_7BrO_4S$	calc. found	C 37.1 36.8	H 2.5 2.8	Br 27.5 26.9

[a] recrystallized from methanol
[b] recrystallized from benzene/methanol
[c] recrystallized from methanol (plus a little benzene)
[d] recrystallized from aqueous methanol
[e] recrystallized from chloroform/benzene
[f] prepared using 2 equivalents of $NaOCH_3$
[g] recrystallized from benzene
[h] moderate yield
[i] purified by dissolving the product in aqueous ammonia and precipitating with hydrochloric acid

benzene/heptane (1 + 1), the residue afforded colourless crystals; yield: 39.5 g (86%); m.p. 78–79°.

$C_{11}H_{16}BrO_5PS$	calc.	C 35.6	H 4.3	Br 21.6
	found	35.5	4.1	22.0

NMR spectrum (in CCl_4): 6H(t), $\delta = 1.34$ ppm (CH_3); 2H(d), $\delta = 3.80$ ppm, $J_{HP} = 17$ cps (CH_2); 4H(quin), $\delta = 4.28$ ppm, $J_{HP} = 7$ cps, $J_{HH} = 7$ cps (OCH_2); 4H(AB), $\delta = 7.84$ ppm, $J_{AB} = 9.5$ cps (aromatic protons).

Reaction of diethyl(4-bromophenylmercapto)-methanephosphonate (5) with aldehydes (Table 1): Sodium hydride (0.5 g, 53.5% suspension in paraffin oil, 0.01 mol) was washed three times by decantation with petroleum ether and re-suspended in dry benzene (50 ml). A solution of **5** (3.4 g, 0.01 mol) and the freshly distilled aldehyde (0.01 mol) in dry benzene (10 ml) was added in one portion. Hydrogen was evolved. After 5 min., the reaction mixture was refluxed for 30 min. and then allowed to cool. Methanol was added and the mixture was poured into cold water (100 ml). The benzene layer was separated, washed with water (20 ml), dried over magnesium sulfate, and evaporated. The residue was recrystallized from a suitable solvent.

Reaction of diethyl(4-bromophenylsulfono)-methanephosphonate (6) with aldehydes (Table 2): A 2 *N* solution of sodium methoxide in methanol (5 ml, 0.01 mol) was added to a solution of **6** (3.7 g, 0.01 mol) in methanol (15 ml). The product separated either immediately or after cooling and was filtered off, washed with cold methanol, and recrystallized. The yields were quantitative in nearly all cases.

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[1] I. Shahak, J. Almog, Synthesis **1969**, 170
[2] German Patent 1112735 (1958), L. W. Fancher (Stauffer Chemical Co.); C. A. **56**, 11499 (1962).
[3] F. G. Bordwell, B. M. Pitt, J. Amer. Chem. Soc. **77**, 572 (1955).