Synthesis of α,β-Unsaturated Sulphides, Sulphoxides, and Sulphones by the Horner-Wittig Reaction in Two-Phase System Catalysed by Quaternary Ammonium Salts and Crown Ethers*

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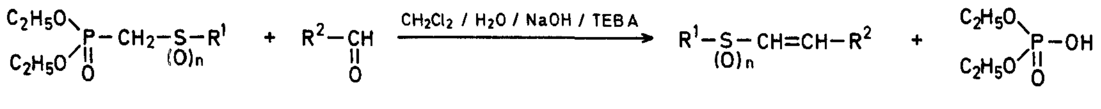
It has recently been recognized that α,β-unsaturated organosulphur compounds are valuable synthetic precursors. α,β-Unsaturated sulphides, for instance, may be easily converted into carbonyl compounds[1] and α,β-unsaturated sulphones afford olefins in a stereospecific manner after desulphurisation[2]. Therefore, the synthesis of α,β-unsaturated sulphides (**4**), sulphoxides (**5**), and sulphones (**6**) attracted considerable attention for the past few years.

The best synthetic approach to these compounds is based on the Horner-Wittig reaction of the corresponding α-phosphorylalkyl sulphides (**1**), sulphoxides (**2**), and sulphones (**3**)[3] since the sulphur moiety is able to stabilise effectively an adjacent phosphonate carbanion. However, the typical



1 n = 0
2 n = 1
3 n = 2

4 n = 0
5 n = 1
6 n = 2

experimental procedure for this type of olefination employing strong bases (sodium hydride, butyllithium) and anhydrous conditions makes the synthesis of **4**, **5**, **6** somewhat troublesome and expensive.

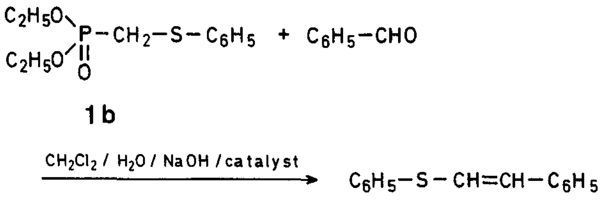
It was now found that the Horner-Wittig reaction of α-phosphoryl compounds **1**–**3** can be advantageously performed in the two-phase catalytic system developed and introduced to organic synthesis by Mąkosza[4,5,6].

An inspection of the data in Table 1 reveals that α-phosphoryl sulphides (**1**) and sulphones (**3**) give the corresponding unsaturated analogues **4** and **6** in more than 60% yield. The lower yield of sulphoxides **5** may be due to the good solubility of the starting α-phosphoryl sulphoxides (**2**) in the water phase.

The above reaction was found to be specific to aromatic aldehydes. Ketones and aldehydes capable of enolisation are unreactive. Thus, negative results have been obtained with benzophenone, acetophenone, cyclohexanone, acetone, acetaldehyde, and *n*-butyraldehyde.

It is interesting to note that the Horner-Wittig reaction carried out under the two-phase catalytic conditions was found to proceed with full stereoselectivity only with α-phosphoryl sulphones (**3**) affording the pure (*E*) isomers of **6**, whereas the mixtures of geometrical isomers were formed from α-phosphoryl sulphides (**1**) and sulphoxides (**2**).

In this connection, we have briefly examined the influence of various phase-transfer catalysts including also crown ethers[7] (dibenzo-18-crown 6, dicyclohexyl-18-crown 6) on the *E*/*Z* ratio of the sulphide **4b** produced by the reaction shown below. These results are summarised in the Table 2.

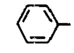
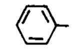
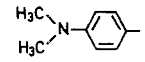
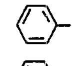
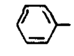
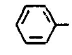
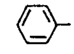
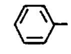
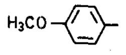
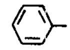
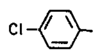
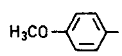


1b

4b (*E* + *Z*)

As can be seen from the Table 2 the use of quaternary ammonium chlorides as catalysts resulted in the formation of **4b** as a nearly 1:1 mixture of (*E*)- and (*Z*)-isomers. The preferential formation of the (*E*)-isomer was observed when the above reaction was catalysed by ammonium bromides and iodides. The same effect was found to be caused by crown ethers. As in the latter case the eventual isomerisation

Table 1. Synthesis of α,β-Unsaturated Sulphides (**4**), Sulphoxides (**5**), and Sulphones (**6**)

Product	R1	R2	Reaction conditions Temperature/time	(*E*):(*Z*) Ratio[a]	Yield (%)[b]	M.p. or B.p.	Elemental	Analyses			
4a	H3C–		reflux/1 h	87:13	59	46°/0.005 torr	$C_9H_{10}S$ (150.3)	calc. found	C 71.95 71.96	H 6.71 6.81	S 21.34 21.19
4b			reflux/1 h	48:52	81	102–103°/0.01 torr	$C_{14}H_{12}S$ (212.3)	calc. found	C 79.20 79.02	H 5.70 5.79	S 15.10 15.03
4c			reflux/2 h	80:20	40[d]	m.p. 72.5–73.5°[e]	$C_{16}H_{17}NS$ (255.4)	calc. found	C 75.25 75.35	H 6.71 6.69	S 12.56 12.35
5a	H3C–		r. t./2 h	70:30	51	m.p. 64–65°[e]	$C_9H_{10}OS$ (166.3)	calc. found	C 65.02 64.98	H 6.06 6.07	S 19.29 19.38
5b			r. t./0.5 h	83:17	54	m.p. 61.5–62°[e]	$C_{14}H_{12}OS$ (228.3)	calc. found	C 73.65 73.54	H 5.30 5.28	S 14.04 13.95
5c			r. t./4 h	—[c]	57	m.p. 94.5–95.5°[e]	$C_{14}H_{11}ClOS$ (262.8)	calc. found	C 63.99 63.95	H 4.22 4.20	S 12.20 12.07
5d			reflux/4 h	—[c]	48	m.p. 63–66°[e]	$C_{15}H_{14}O_2S$ (258.3)	calc. found	C 69.74 69.35	H 5.46 5.47	S 12.41 12,52
6a	H3C–		r. t./3 h	100:0	85	m.p. 80°	$C_9H_{10}O_2S$ (182.2)	calc. found	C 59.32 59.20	H 5.53 5.55	S 17.60 17.32
6b	H3C–		r. t./2 h	100:0	71	m.p. 128–129.5°	$C_9H_9ClO_2S$ (216.7)	calc. found	C 49.89 49.70	H 4.19 4.02	S 14.80 14.67
6c	H3C–		r. t./2 h	100:0	73	m.p. 143–144°	$C_{10}H_{12}O_3S$ (212.3)	calc. found	C 56.58 56.37	H 5.70 5.65	S 15.11 15.03

[a] The *E*/*Z* ratio was determined by ^{1}H-N.M.R. spectroscopy of the crude reaction products.

[b] Yield of analytically pure products.

[c] We were not able to estimate the *E*/*Z* ratio from the ^{1}H-N.M.R. spectrum of the crude product; its crystallisation afforded the pure *E* isomer.

[d] Yield after column chromatography.

[e] Melting point refers to the pure *E* isomer obtained after crystallisation.

around the double bond in **4b** or preferential decomposition of one of two isomers under the reaction conditions may be undoubtedly excluded, the present data indicate the dependence of stereochemical course of the Horner-Wittig reaction on the nature of the catalyst used. This observation may be utilized for practical purposes which is illustrated by the example shown below. The amounts of (*E*)- and (*Z*)-isomer were estimated by G.L.P.C. Further work in this field is in progress.

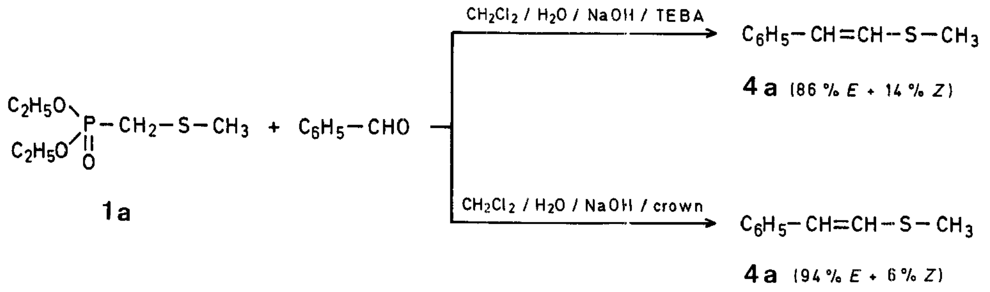


Table 2. Dependence of the *E*/*Z* Ratio in **4b** on the Structure of Phase-Transfer Catalyst

Catalyst	(*E*): (*Z*) ratio[a]
$(H_3C)_4N^{\oplus}Cl^{\ominus}$	59:41
$(n\text{-}C_4H_9)_4N^{\oplus}Cl^{\ominus}$	43:57
$(H_3C)_3C_6H_5CH_2N^{\oplus}Cl^{\ominus}$	47:53
$(C_2H_5)_3C_6H_5CH_2N^{\oplus}Cl^{\ominus}$	48:52
$(n\text{-}C_4H_9)_3C_6H_5CH_2N^{\oplus}Cl^{\ominus}$	44:56
$(H_3C)_4N^{\oplus}Br^{\ominus}$	77:23
$(C_2H_5)_3C_6H_5CH_2N^{\oplus}Br^{\ominus}$	50:50
$(n\text{-}C_4H_9)_4N^{\oplus}Br^{\ominus}$	81:19
$(H_3C)_4N^{\oplus}J^{\ominus}$	83:17
$(C_2H_5)_4N^{\oplus}J^{\ominus}$	72:28
$(n\text{-}C_4H_9)_4N^{\oplus}J^{\ominus}$	83:17
Dibenzo-18-crown 6	70:30
Dicyclohexyl-18-crown 6	70:30

[a] The *E*/*Z* isomer ratios (accuracy ±2.5%) were determined by integration of the two AB-systems in the crude product ($J_{AB} = 15.0$ and 10.6 Hz for the *E* and *Z* isomers, respectively).

General Procedure:

A solution of the α-phosphoryl compound (10 mmol) and aldehyde (10 mmol) in dichloromethane (5 ml) was added to the heterogeneous mixture of 50% aqueous sodium hydroxide (15 ml) containing 0.2 g triethylbenzylammonium chloride (TEBA) and dichloromethane (10 ml) and subsequent stirring the reaction mixture for a few hours at room temperature or under reflux. The dichloromethane extract afforded the α,β-unsaturated compounds **4**, **5**, and **6**. The results are shown in the Table 1. Further experimental details will be given in a full paper.

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