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Studies on the Wittig Reaction. XV. A Direct Preparation of ω-Unsaturated Bromides via Solid/Liquid Transferred Wittig Reactions of ω-Bromoalkyltriphenyl Phosphonium Salts with Aldehydes

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# STUDIES ON THE WITTIG REACTION(XV): A DIRECT PREPARATION OF ω-UNSATURATED BROMIDES VIA SOLID/LIQUID TRANSFERRED WITTIG REACTIONS OF ω-BROMOALKYLTRIPHENYL PHOSPHONIUM SALTS WITH ALDEHYDES

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Abstract: A new approach to the synthesis of  $\omega$ -unsaturated bromides was proposed using solid/liguid transferred Wittig reactions between  $\omega$ -bromoalkyltripheny phosphonium Salt and aldehydes.

The simplified Wittig reaction under the solid/liquid condition has been applied in organic synthesis as a useful method<sup>[1]</sup>. The implementation of this reaction can reach high yields in some cases whereas an anhydrous homogeneous medium condition leads to poor yields<sup>[2]</sup>. This can be due to its mild condition. Here we wish to report a new utilization of the solid/liquid transferred

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 Table 1. Wittig reaction of aldehydes diversely substituted with 4-bromobutyltriphenylphosphonium bromide

Alkene	R	Solvent	yield(%)*	Z-isomer(%)
2a	NO <sub>2</sub> -	CH <sub>2</sub> Cl <sub>2</sub>	75	54
		THF	78	85
2Ь	NO,	CH <sub>2</sub> Cl <sub>2</sub>	82	57
	· 2	THF	81	84
2c	CI-	CH <sub>2</sub> Cl <sub>2</sub>	85	47
	Cl	THF	83	88
2d	ci-	CH <sub>2</sub> Cl <sub>2</sub>	89	57
		THF	88	85
2e		THF	61	87
2f	$\bigcirc$	$CH_2Cl_2$	79	51
		THF	82	88
2g	Br	$CH_2Cl_2$	86	53
		THF	89	87

 $RCHO + Ph_{3}\overset{+}{P}(CH_{2})_{4}Br Br \xrightarrow{-N_{a}OH(s)} RCH = CH(CH_{2})_{3}Br + Ph_{3}PO$ 

\* isolated yield based on the starting material

process on the Wittig reaction of  $\omega$ -bromoalkyltriphenylphosphonium salts with aldehydes. It showed again the advantage of using a solid/liquid twophase medium for some Wittig reactions.

There are few reports on the direct Wittig reaction of  $\omega$ -bromoalkyltriphenyl phosphonium salt with aldehydes<sup>[3]</sup>. An early study on the reaction

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length	and $P-c$	chlorobenzalde	hyde	
$Ph_3 \overset{+}{P}(CH_2)_n Br Br^- + C$	$ \leq$	$-CHO \xrightarrow{NaOH(s)}_{THF}$	CI-CH =CH	I(CH <sub>2</sub> ) <sub>1-1</sub> Br+Ph <sub>3</sub> PO
	n	yiel <b>d</b> (%)	Z-isomer(%)	
	4	83	88	_
	6	81	87	
	8	78	89	
	10	72	91	
				<u> </u>

Table 2. Wittig reaction of phosphonium salt with different carbon chain length and P-chlorobenzaldehvde

using RONa as base resulted in a complexive mixture of the alkene<sup>[4]</sup>. These can be due to partial elimination of HBr or cyclization. The unstability of the bromides under the strong base condition limited the application of the direct Wittig reaction of  $\omega$ -bromo phosphonium salt in organic synthesis. However, When the Wittig reactions were carried out under the mild solid-liquid transferred conditions, We found the reaction took place smoothly and  $\omega$ -unsaturated bromides were obtained in high yields. No other by-products were found by GC-MS detection.

Ph<sub>3</sub><sup>+</sup>P(CH<sub>2</sub>)<sub>n</sub>Br Br<sup>-</sup>+RCHO 
$$\xrightarrow{\text{NaOH(s)}}$$
  
1. (n≥4)  
RCH=CH(CH<sub>2</sub>)<sub>n-1</sub>Br+Ph<sub>3</sub>PO  
2

This process proves to be efficient with different aldehydes and different carbon chain length on the phosphonium salts. The results are listed in Table 1 and Table 2. When THF was used as solvent, the reaction was Z—selectivity, however, when  $CH_2Cl_2$  was used, the E/Z of the alkene is approximately 1. The polarity of the solvent might played an imporant role in the different stereoselectivity.

The method we report here also supplies a facile synthesis of the otherwise not readily accessible  $\omega$  — unsaturated bromides, which have been showed to be important intermediates in the synthesis of some pharmaceutical compostions<sup>[5][6]</sup>. Compared with the other methods to the title compounds<sup>[7]</sup>, our approach affords a one pot and general high yield entry to a variety of  $\omega$  unsaturated bromides with variable substituents and carbon chain length.

### EXPERIMENTAL

Melting points were uncorrected. MS were measured on a HP 5988A spectrometer. IR were recorded on a shimadzu IR-408 infrared Spectrometer. NMR were taken on a Varian XL-200 spectrometer. Gas chromatographic analysis were performed on a HP 5988 GC-MS instrument employing a 12m capillary column and HP - 5 as liguid phase.  $\omega$  - bromoalkyl-triphenylphosphonium bromides were prepared from Ph<sub>3</sub>P and 1,  $\omega$  - dibromoalkane in 72-95% yields.

General procedure of the Wittig reactions:

A mixture of phosphonium salt (44mmol), aldehyde (40mmol), sodium hydroxide powder (2g,50mmol), several drops of water and an organic solvent (100ml) was stirred at reflux for 6-12 hours, filtered and seperated by a short column chromatography on silica gel. The E/Z of the alkene obtained was determinated by GC and HNMR

<sup>1</sup>HNMR, IR and MS for selected compounds 2:

- 2a: 'HNMR (CDCl<sub>3</sub>,200MHz) δ2. 0-2. 7(m,4H), 3. 46(t,2H, J=6. 6HZ), 5. 85(dt, 1H, J=11. 8, 6. 8Hz), 6. 48(d, 1H, J=11. 8Hz), 7. 3-8. 3(m, 4H); MS, m/z 269, 271 (M<sup>+</sup>, 1:1), 190(M-Br), 162, 116(100); IR (cm<sup>-1</sup>) 3030,1642, 1340, 970, 860, 742.
- 2d: 'HNMR (CDCl<sub>3</sub>,200MHz) δ1. 9-2. 5(m,4H),3. 38(t,2H, J=6. 6Hz), 5. 76 (dt, 1H, J=11. 4,7. 0Hz), 6. 49(d, 1H,J=11. 4Hz), 7. 1-7. 5(m, 3H); MS, m/z 292, 294, 296, 298 (M<sup>+</sup>, 9:15:7:1), 214(M<sup>+</sup>-Br), 185(100), 150, 115; IR(cm<sup>-1</sup>) 3030,1650, 968, 825, 870.

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