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A Facile Synthsis of ω-Bromo-Diene *Via* Solid/Liquid Transferred Wittig Reactions of ω-Bromobutyltriphenyl phosphonium Salts With α.β-Unsaturated Aldehydes

De Qing SHI, Ru Yu CHEN*

Research Institute of Elemento Organic Chemistry, NanKai University,Tianjin 300071

Abstract: A new approach to the synthesis of ω-bromo-dienes was carried out by using solid/liquid transferred Wittig reactions between ω-bromobutyltriphenylphosphonium salt and α.β-unsaturated aldehydes.
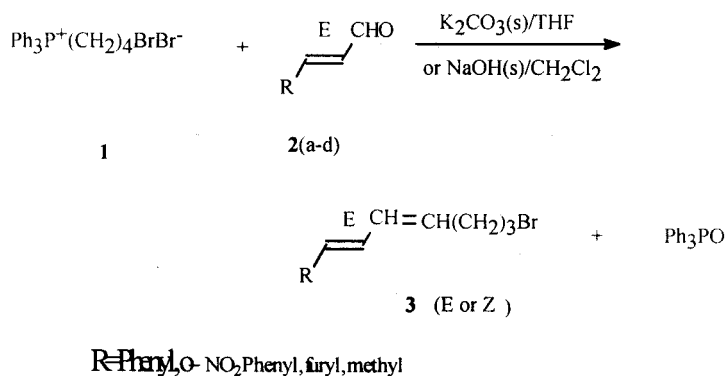
Keywords: Wittig reactions, ω-bromoalkyltriphenylphosphonium salts, synthesis, ω-bromo-dienes, stereoselectivity.

The simplified Wittg reaction under the solid/liquid conditions has been applied in organic synthesis as a useful method[1]. The implementation of this reaction can give high yields in some cases whereas in an anhydrous homogeneous medium leads to a poor yield[2]. There are few reports on the direct Wittig reaction of ω-bromoalkyltriphenylphosphonium salts with aldehydes[3]. An early study on the reaction using RONa as a base resulted a complex mixture of alkenes[4], because of the partial elimination of HBr or the cyclization reaction. The method of a direct preparation of ω-unsaturated bromide *via* solid/liquid Wittig reactions of ω-bromoalkyltriphenylphosphonium salts with aldehydes has been reported previously[5]. In this paper, we report the method of the Wittig reaction of ω-bromoalkyltriphenyl phosphonium salts with α.β-unsaturated aldehydes to synthesize ω-bromo-dienes, which are important intermediates of some pharmaceutical compounds[6,7] and insect sex hormones[8]. Our approach affords a one-pot reaction with mild conditions, good regioselectivity and high yields of ω-bromo-dienes.

Experimental

^{1}HNMR spectra were recorded with a BRUKER AC-P200 spetrometer . Mass spectra were recorded with a VG ZAB-HS spectrometer using the EI method. IR spectra were measured by a SHIMADZU-435 instrument. GC were recorded with a HEWLETT PACKARD G1800A GCD (Gas Chromatograph Electron Ionization Detector) system. Melting Points were determined with a Thomas-Hoover melting point apparatus and the thermometer was uncorrected. ω-

bromobutyltriphenylphosphonium salt 1 was prepared from Ph₃P and 1,4-dibromobutane in refluxing tulune in 96% yield[9]. α . β -unsaturated aldehydes 2 were purchased or prepared in the reported methods.

$$Ph_3P^+(CH_2)_4BrBr^- \quad + \quad \overset{E}{\underset{R}{\diagup}}\diagdown^{CHO} \quad \xrightarrow[\text{or NaOH(s)/CH}_2\text{Cl}_2]{K_2CO_3(s)/THF}$$

1   2(a-d)

$$\overset{E}{\underset{R}{\diagup}}\diagdown^{CH=CH(CH_2)_3Br} \quad + \quad Ph_3PO$$

3   (E or Z)

R=Phenyl,O- NO₂Phenyl,furyl,methyl

Table 1 The structures and reaction conditions of compounds 3

Compd.	R	Solvent/Base	State	Yield(%)	E,Z-isomer(%)*
3a	ph	THF/K₂CO₃(s)	light-yellow liq.	86	60.2
3a'	ph	CH₂Cl₂/NaOH(s)	light-yellow liq.	83	27.5
3b	o-NO₂ph	THF/K₂CO₃(s)	yellow liq.	81	86.8
3b'	o-NO₂ph	CH₂Cl₂/NaOH(s)	yellow liq.	89	66.1
3c	2-furyl	THF/K₂CO₃(s)	red-brown liq.	78	79.4
3c'	2-furyl	CH₂Cl₂/NaOH(s)	red-brown liq.	85	36.7
3d	CH₃	THF/K₂CO₃(s)	colorless liq.	63	79.5
3d'	CH₃	CH₂Cl₂/NaOH(s)	colorless liq.	58	77.9

*The contents of E,Z and E,E-isomers of the products were determinated by GC and ¹HNMR

General procedure for the synthesis of 3

A mixture of phosphonium salt 1 (24mmol), α . β -unsaturated aldehydes 2 (20mmol), sodium hydroxide powder (50mmol) and dichloromethane 45 ml or anhydrous potassium carbonate (80mmol) and Tetrahydrofuran 50 ml was stirred under reflux for 12-24 h (monitered by TLC), filtered and purified by column chromatography on silica gel using petroleum ether and ethyl ether as the eluent.

¹HNMR, IR and MS for selected compounds 3

3a: ¹HNMR(CDCl₃, 200MHz) δ 1.95-2.02 (m,2H), 2.31-2.47 (m,2H), 3.41-3.47 (t,2H), 5.39-5.52 (q,1H,J=7.3, 18.76Hz), 6.16-6.28 (t, 1H,J=10.44,11.46Hz), 6.50-6.58 (d,1H, J=15.64Hz), 7.02-7.15 (m,1H), 7.24-7.40 (m,5H); MS, m/z 250,252 (M⁺,1:1), 171 (M-Br), 143, 129 (100 %), 115, 91,77; IR(cm⁻¹)3137(m), 3012, 1592, 1488, 1458, 980(s), 727(s), 688(s), 562(m)

3b: ¹HNMR(CDCl₃, 200MHz) δ 1.95-2.02 (m,2H), 2.02-2.48

(m,2H), 3.41-3.47 (t,2H), 5.51-5.64 (q,1H), 6.23-6.33 (t,1H), 7.03-7.10 (m, 2H), 7.36-7.90 (m, 4H); MS, m/z 295, 297 (M$^+$,1:1), 216 (M-Br), 174, 146, 119 (100%), 92; IR (cm^{-1}) 3049 (m), 2919, 1630 (m), 1603 (m), 1516 (s), 1341(s), 980,728, 560

3c: ^{1}HNMR(CDCl$_3$, 200MHz) δ 1.94-2.00 (m, 2H), 2.25-2.44 (m,2H), 3.39-3.46 (t,2H), 5.37-5.50 (q,1H), 6.14-6.38 (m, 4H), 6.88-7.01 (q,1H), 7.35 (s,1H); MS, m/z 240, 242 (M$^+$,1:1), 161 (M-Br), 133 (100%), 119, 105

3d: ^{1}HNMR (CDCl$_3$, 200MHz) δ 1.75-1.78 (d, 3H, J=6.8Hz), 1.90-1.96 (m, 2H), 2.01-2.32 (m, 2H), 3.37-3.43 (t, 2H), 5.14-5.27 (q,1H), 5.63-5.74 (m,1H), 5.93-6.04 (t,1H), 6.26-6.39 (t,1H); MS, m/z 188,190 (M$^+$, 1:1), 109 (M-Br), 95, 81 (100%), 67

Results and Discussions

It was shown that the reaction of 1 and 2 led to very poor yields when anhydrous potassium carbonate was used as a base and CH$_2$Cl$_2$ as a solvent even after refluxing for 20 h; However, when NaOH/THF system was applied, elimination of HBr occurred; But when K$_2$CO$_3$/THF or NaOH/CH$_2$Cl$_2$ were used, the reaction took place smoothly and ω-bromodienes were obtained in high yields and no other by-products were found by GC-MS detection. The reaction of 3-bromopropyltriphenyl phosphonium salt with α.β-unsaturated aldehydes even in the presence of K$_2$CO$_3$ gave no ω-bromo-dienes but only more stable trienes (RCH = CHCH = CHCH=CH$_2$). The results of the stereoselectivity of the reaction are listed in Table 1. When THF was used as the solvent, the reaction showed Z-selectivity, however, when CH$_2$Cl$_2$ was used, the stereoselectivity of the reaction is irregular. The polarity of the solvent might play an important role in the stereoselectivity of the reaction.

Acknowledgment

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