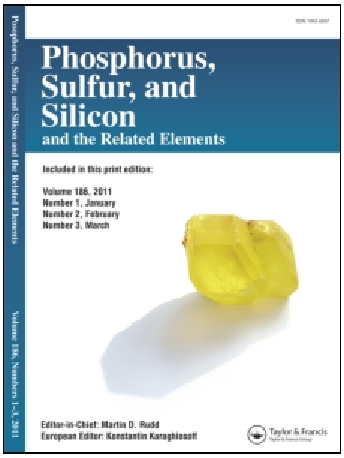


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

STUDIES ON THE WITTIG REACTION (XXV): THE STEREOCHEMISTRY OF BIS-WITTIG REACTION BETWEEN AROMATIC ALDEHYDES AND 1,2 AND 1,3 BIS-YLIDES

Wenjing Xiao[a]; Zilong Tang[a]; Mingwu Ding[a]; Wenfang Huang[a]; Tianjie Wu[b]
[a] Institute of Organic Synthesis, Central China Normal University, Wuhan, China [b] Center of Analysis and Testing, Central China Normal University, Wuhan, China

To cite this Article Xiao, Wenjing , Tang, Zilong , Ding, Mingwu , Huang, Wenfang and Wu, Tianjie(1996) 'STUDIES ON THE WITTIG REACTION (XXV): THE STEREOCHEMISTRY OF BIS-WITTIG REACTION BETWEEN AROMATIC ALDEHYDES AND 1,2 AND 1,3 BIS-YLIDES', Phosphorus, Sulfur, and Silicon and the Related Elements, 116: 1, 211 — 216

To link to this Article: DOI: 10.1080/10426509608040481

URL: http://dx.doi.org/10.1080/10426509608040481

Phosphorus, Sulfur, and Silicon, 1996, Vol. 116, pp. 211–216
Reprints available directly from the publisher
Photocopying permitted by license only

STUDIES ON THE WITTIG REACTION (XXV): THE STEREOCHEMISTRY OF BIS-WITTIG REACTION BETWEEN AROMATIC ALDEHYDES AND 1,2 AND 1,3 BIS-YLIDES

WENJING XIAO[a], ZILONG TANG[a], MINGWU DING[a], WENFANG HUANG[a,*] and TIANJIE WU[b]

[a]*Institute of Organic Synthesis, Central China Normal University, 430070, Wuhan China;* [b]*Center of Analysis and Testing, Central China Normal University, 430070, Wuhan China*

(Received 26 February; Revised 23 May 1996; In final form 23 May 1996)

1,2 and 1,3 bis-ylides derived from corresponding bis-phosphonium salts reacted with substituted benzaldehydes to give 19 dienes with E,E-selectivity.

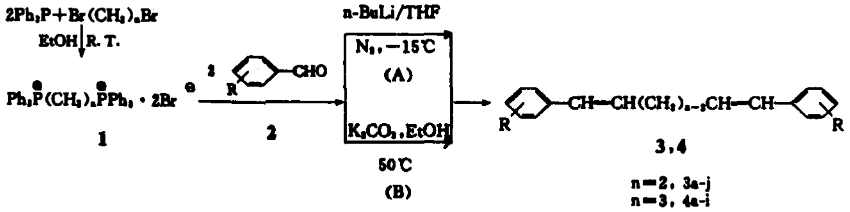
Keywords: bis-Wittig reaction; stereochemistry; bis-phosphonium ylide; diene synthesis

INTRODUCTION

Since the landmark papers presented by Wittig and co-workers in the early 1950s[1–3] were reported, a large number studies on the reaction of simple phosphonium ylides and carbonyl compounds have been carried out[4–6]. Because of its simplicity, convenience and stereoselectivity, the Wittig reaction has enjoyed wide spread prominence. Relatively few studies on the stereochemistry of the bis-Wittig reaction between bis-phosphonium ylides and carbonyl compounds are known. Among them, the synthesis of all trans squalene[7], β-carotene[8] and z,z dienic sex attractants[9] as well as the review made by Vollhardt[10] were very interesting. The stereochemistry of the bis-Wittig reaction between aromatic aldehydes and bis-ylides has not been systematically reported yet. One of our

---

*Corresponding author.



R: o-Cl, m-Cl, p-Cl, p-Me, p-OMe, p-NO_2, m-NO_2, 3,4-di-Cl, 2,4-di-Cl, H, o-Br.

interests has utilized the stereoselectivity of the Wittig reaction[11] to synthesize some bioactive compounds and also elucidate the reaction mechanism. In order to achieve the objectives, we have made use of phosphonium ylides to obtain insect sex pheromones[12] and fungicides[13]. In this work, we explore the stereochemistry of the bis-Wittig reaction between substituted benzaldehydes and bis-alkylidene triphenyl phosphoranes derived from the corresponding phosphonium salts. For simplification, we chose the 1,2 and 1,3-bis-phosphonium salt as the starting material. Thus, the isomer number of dienic products will not be more than three.

RESULTS AND DISCUSSION

1. Number of Isomer

It is interesting to note that the geometrical isomer number depends upon “n”. When n = 3, whether or not a substituent exists on the aldehyde benzene ring, three isomers are formed. When n = 2, there are two possibilities. If there is no substituent on the benzene ring, three isomers were obtained; if there is a substituent, only two isomers were detected. These results indicate that the structure of aldehydes play an important role in bis-Wittig reaction as mentioned above (Table I and Table II).

2. Stereochemistry

In the above bis-Wittig reactions, the E,E-isomer tends to dominate the mixture of dienes illustrated in Table I and Table II. The degree of stereoselectivity varies considerably with “n” and reaction conditions. For reactions of the same substituent R in the same condition, but different “n”, E,E% will be larger in the reaction with 1,2-bisylides i.e. 3c > 4c, 3d > 4f, 3i > 4h and 3j > 4a. Under typical Wittig reaction conditions (n-BuLi/THF, N_2) for the same substituent, i.e.

TABLE I Stereochemistry of the bis-Wittig reaction (n = 2)

No	*R*	*E,Z or Z,Z%*		*E,E%*	
3a	o-Cl	57.8		42.2	
3b	m-Cl	49		51	
3c	p-Cl	27	(11)	73	(89)
3d	p-Me	19	(17.3)	81	(82.7)
3e	p-OMe	11		89	
3f	p-NO_2		(19)		(81)
3g	m-NO_2		(21.5)		(78.5)
3h	3,4-di-Cl		(46.7)		(53.3)
3i	2,4-di-Cl		(23.3)		(76.7)
3j	H	10.2	11.8	78	

Data in brackets were obtained under phase transfer catalysis (PTC) conditions. E,Z% were determined by GC and ^{1}HNMR

chloro, E,E content increases in the following order: p- > m- > o- (n = 2) but under phase transfer catalysis conditions (K_2CO_3, EtOH) it is in the reverse order, i.e. p- < m- < o- (n = 3).

The explanation for the above results is not very clear. But according to these results, two pairs of oxaphosphetanes (cis and trans) may be exist simultaneously at a given time. The steric hindrance may be the main factor responsible for the E,E-selectivity. in spite of the puzzling mechanism, these bis-wittig reactions can serve as a method for the stereoselective α,ω-dienic synthesis.

TABLE II Stereochemistry of the bis-Wittig reaction (n = 3)

No	*R*	*Z,Z%*	*E,Z%*	*E,E%*
3j*	H	11.8	10.2	78
4a*	H	10.7	38.4	50.9
4b	o-Br	18.3	20.5	61.2
4c	p-Cl	49.3	9.9	40.8
4d	o-Cl	9.7	6.4	83.9
4e	m-Cl	6.1	12.5	81.4
4f	p-Me	29.4	8.5	62.1
4g	p-OMe	14.2	7.7	78.1
4h	2,4-di-Cl	10.8	14	75.2
4i	3,4-di-Cl	6.8	23.6	69.6

*Data obtained under typical Wittig conditions. E,Z% were determined by GC and ^{1}HNMR

EXPERIMENTAL

Melting points were uncorrected. MS were carried on a HP5988A spectrometer. IR were measured on a Perkin-Elmer-983 spectrometer. ^{1}HNMR were recorded on a Varian XL-200MHz spectrometer. GC analysis were performed on a HP5988 GC-MS instrument using a 25m × 0.2mm × 0.33μm capillary column and HP-5 or SE-30 as liquid phase. All solvents and materials are reagent grade and were purified as required.

Preparation of Bis-Phosphonium Salt 1[14]

A mixture of triphenyl phosphine (62.95g 0.24mol) and α,ω-dibromoalkane (0.1mol) dissolved in EtOH (100ml) was stirred at 100° for 24–28h. After cooling and condensation, Et_2O was added to give the crude product. It was then filtered, washed with Et_2O and dried by suction and then purified by recrystallization ($EtOH/Et_2O$). Yield: n = 2, 59.8g, 84% m.p. 287°C–290°C, n = 3, 58.8g, 69.01%, m.p. 320° (turned black, decomposed). ^{1}HNMR: n = 2, 7.60–7.90(m,18H,Ar-H) 7.9–8.15(m,12H,Ar-H) 4.10–4.46(d,4H,$2CH_2$); n = 3, 7.40–7.80 (m,18H,Ar-H), 7.80–8.00(m,12H,Ar-H), 4.50–4.80(m,4H,$2CH_2$), 1.80–2.00(m,2H,CH_2).

General Procedure for Pathway A. (Typical Wittig Reaction)

Under N_2, a suspension of bisphosphonium salt 1 (0.008mol), n-$BuLi/Et_2O$ (0.019mol) was dropped in at −15°C. The ruby red solution was stirred for 15min, then the corresponding aromatic aldehyde 2 (0.016mol) was slowly added. After 2h. stirring, 4 volumes petroleum ether (30–60°C) was added and then allowed to stand overnight to precipitate Ph_3PO out. On filtration, most solvent was evaporated under reduced pressure. Product 3 was isolated by TLC (petroleum ether/ether, 9:1) in yield of 50–65%.

General Procedure for Pathway B (PTC Wittig Reaction)

A mixture of bis-phosphonium salt 1 (0.01mol), aromatic aldehyde and solid potassium carbonate (0.05mol) in absolute EtOH was stirred at 50° for 15–18h. Cooled and filtered. The filtrate was treated with $NaHSO_3$. Extracted with petroleum ether. After work up, product 4, also some 3, was isolated by TLC (petroleum ether/ether, 9:1) in yield of 30–55%.

^{1}HNMR, IR and MS for some compounds 3 and 4

3c: Yield, 62%, ^{1}HNMR ($CDCl_3$, 200MH$_z$), δ 7.00–7.50(m,8H,2C_6H_4) 5.50–6.70(m,4H,-CH=CH-CH=CH); IR(cm^{-1}), 3000, 1650, 1440–1450, 960, 725; MS:275

3d: Yield, 54%, ^{1}HNMR ($CDCl_3$, 200MH$_z$), δ 7.10–7.50(m,8H,2C_6H_4) 6.10–7.00(m,4H,-CH=CH-CH=CH-), 1.86(s,3H,CH_3); IR (cm^{-1}), 3300, 1655, 1440–1450, 960, 725; MS:234

3e: Yield, 50%, ^{1}HNMR δ 6.80–7.40(m,8H,2C_6H_4) 6.10–6.70(m,4H,CH=CH-CH=CH), 3.8(s,3H,OCH_3); MS:265

3f: Yield, 50%, ^{1}HNMR δ 7.48–8.15(m,8H,2C_6H_4) 6.40–6.60(m,2H), 6.80–7.00(m,2H); MS:296

3j: Yield, 63%, ^{1}HNMR δ 7.10–7.60(m,10H,2C_6H_5) 6.40–6.60(m,2H), 6.70–6.90(m,2H); IR (cm^{-1}), 3300, 1650, 1440–1450, 960, 725; MS:207

4a: Yield, 55%, ^{1}HNMR δ 7.20–7.60(m,10H,2C_6H_5) 5.80–6.40(m,4H,2CH=CH), 3.30–3.60(m,2H,CH_2); IR (cm^{-1}), 3300, 1680–1700, 1440–1450, 960, 700; MS:220

4c: Yield, 40%, ^{1}HNMR δ 7.10–7.60(m,8H,2C_6H_4) 5.90–6.70(m,4H,2CH=CH), 33.31-3.60(m,2H,CH_2); IR (cm^{-1}), 3300, 1680–1700, 1650, 1440–1450, 965, 735; MS:290

4f: Yield, 35%, ^{1}HNMR δ 7.10–7.50(m,8H,2C_6H_4) 5.50–6.60(m,4H,2CH=CH), 3.31-3.60(m,2H,CH_2), 1.80(s,3H,CH_3); MS:248

4g: Yield, 30%, ^{1}HNMR δ 6.80–7.40(m,8H,2C_6H_4) 5.40–6.50(m,4H,CH=CH-CH=CH), 3.30–3.61(m,2H,CH_2), 3.80(s,3H,OCH_3); MS:280

Acknowledgment

We are grateful to the Dawn Plan of Science and Technology for Young Scientists of Wuhan City for financial support.

References

[1] G. Wittig and G. Geissler, *Annalen*, **580**, 44 (1953).
[2] G. Wittig and U. Schöllkopf, *Chem. Ber.*, **87**, 1318 (1954).
[3] G. Wittig and W. Hagg, *Chem. Ber.*, **88**, 1654 (1955).
[4] W. E. McEwen, B. D. Beaver and J. V. Cooney, *Phosphorus, Sulfur and Silicon*, **25**, 255 (1985).
[5] B. E. Maryanoff and A. B. Reitz, *Chem. Rev.*, **89**, 863 (1989).
[6] E. Vedejs and M. J. Peterson, *Top. Stereochem.*, **21**, 1 (1994).
[7] S. Trippett, *Chem. and Ind.*, 80 (1956).
[8] D. S. Joseph and O. Alfred, *J. Org. Chem.*, 1171 (1961).
[9] H. J. Bestmann, T. Zeibig and O. Vostrowsky, *Synthesis*, 1039 (1990).
[10] K. P. C. Vollhardt, *Synthesis*, 765 (1975).
[11] W. F. Huang, Ylide Chemistry Chap. 2. Central China Normal University Publishing House, Wuhan (1993).

[12] (a) W. F. Huang, W. J. Xiao and J. H. Wang, YOUJJ HUAXUE (Chinese Journal of Organic Chemistry), 377 (1986); (b) W. F. Huang, J. Zhu, W. J. Xiao and Y. N. Deng, *Phosphorus, Sulfur and Silicon*, **46**, 99 (1989).

[13] (a)W. M. Ding, D. Q. Shi, W. J. Xiao, W. F. Huang and T. J. Wu, *Chinese J. Applied Chem.*, **12**, 9 (1995); (b) ibid, *Phosphorus, Sulfur and Silicon*, **102**, 59.

[14] (a)E. E. Schweizer and R. D. Bach, *J. Org. Chem.*, **29**, 1746 (1964); (b) L. Horner, H. Hoffmann, W. Klink, H. Eritel and V. G. Toscano, *Chem. Ber.*, 581 (1962).