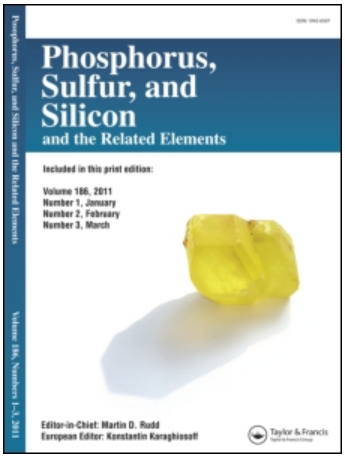


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

STUDIES ON THE WITTIG REACTION (XXII): A CONVENIENT SYNTHESIS OF ω-AZOLYLALKYLTRIPHENYL PHOSPHONIUM SALTS AND THEIR STEREOSELECTIVITY IN THE WITTIG REACTION

Ming Wu Ding[a]; De Qing Shi[a]; Wen Jing Xiao[a]; Wen Fang Huang[a]; Tian Jie 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 Ding, Ming Wu , Shi, De Qing , Xiao, Wen Jing , Huang, Wen Fang and Wu, Tian Jie(1995) 'STUDIES ON THE WITTIG REACTION (XXII): A CONVENIENT SYNTHESIS OF ω-AZOLYLALKYLTRIPHENYL PHOSPHONIUM SALTS AND THEIR STEREOSELECTIVITY IN THE WITTIG REACTION', Phosphorus, Sulfur, and Silicon and the Related Elements, 102: 1, 59 — 63
To link to this Article: DOI: 10.1080/10426509508042543
URL: http://dx.doi.org/10.1080/10426509508042543

Phosphorus, Sulfur, and Silicon, 1995, Vol. 102, pp. 59–63
Reprints available directly from the publisher
Photocopying permitted by license only

STUDIES ON THE WITTIG REACTION (XXII): A CONVENIENT SYNTHESIS OF ω-AZOLYLALKYLTRIPHENYL PHOSPHONIUM SALTS AND THEIR STEREOSELECTIVITY IN THE WITTIG REACTION

MING WU DING, DE QING SHI, WEN JING XIAO
and WEN FANG HUANG*

Institute of Organic Synthesis, Central China Normal University, 430070, Wuhan, China

and

TIAN JIE WU

Center of Analysis and Testing, Central China Normal University, 430070, Wuhan, China

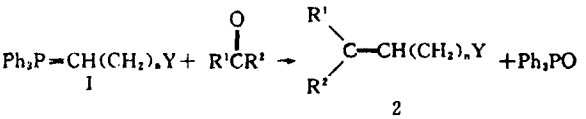
(Received October 16, 1994; in final form December 13, 1994)

ω-Azolylalkyltriphenylphosphonium bromides (**5**) were readily prepared from corresponding ω-bromo phosphonium salts (**4**) and azoles. The Wittig reactions of (**5**) with aromatic aldehydes were studied and 26 ω-azolyl alkenes were obtained. The reaction showed E-stereoselectivity.

Key words: Wittig reaction, azole, phosphonium, stereoselectivity, ω-azolyl alkene, synthesis.

INTRODUCTION

The Wittig reaction is one of the most widely used methods for the preparation of a variety of alkenes.[1] There were considerable studies on the Wittig reaction of ylide **1** with carbonyl compounds to give ω-functionalized alkenes **2**, where Y are



1 **2**

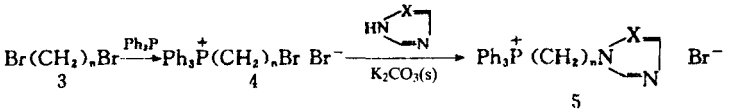
nucleophilic groups.[2–6] Most of the reactions have been utilized in the preparation of natural products, such as long-chain unsaturated fatty acids and pheromones.[7] They have also showed mechanistic interest with their anomalous E stereoselectivity.[1] In spite of the reports on the Wittig reaction of **1** when Y is a N-heterocycle containing group,[8,9] there are few reports of the Wittig reaction of azolyl-containing phosphonium salts which lead to fungicidal N-vinylazoles.[10–12] Many N-vinyl azoles are effective fungicides and plant growth regulators, such as diniconazole (S-3308L) and uniconazole (S-3307). In the present paper, we wish to report the synthesis of the ω-azolylalkyltriphenylphosphonium salts (**5**) as well as their unusual E-ste-

reoselectivity in the Wittig reaction. This will also provide an efficient synthesis of another fungicidal ω-azolyl alkene.

RESULTS AND DISCUSSION

Preparation of the ω-Azolylalkyltriphenylphosphonium Bromides (5)

The azolylalkyltriphenylphosphonium salts are precursors of the phosphonium ylides in preparation of some fungicidal N-vinylazoles.[10-12] They were usually prepared from Ph_3P with corresponding azolyl alkyl halides, however, some azolyl alkyl halides are prepared with difficulty or unstable.[13,14] Here we give a new and facile synthesis of ω-azolylalkyltriphenylphosphonium salts depicted as follows:



Dibromoalkane (3) reacted with Ph_3P in refluxing toluene to yield ω-bromoalkyltriphenylphosphonium bromide (4) in high yields. N-Alkylation of (4) with 1,2,4-triazole or imidiazole under solid/liquid transferred condition was found to be a practical method for the preparation of (5). When K_2CO_3(s) was used as the base, CH_3CN as solvent, ω-azolylalkyltriphenylphosphonium bromide (5) was obtained in moderate to good yields. See Table I.

Our experience may be summarized as follows:

1. The reaction temperature must be lower than 60°.
2. The stirring rate is a key factor for this reaction, a too rapid stirring rate must be avoided. Otherwise, a difficult crystalization of the phosphonium salt and low yields will result.
3. A better yield was obtained by using a catalytic amount of PEG and DMF.
4. Attempts to prepare 2-azolylethyltriphenyl phosphonium salt (n = 2) according to this method was unsuccessful.

Stereoselectivity of the Wittig Reaction of (5) *with Aromatic Aldehydes*

When 5 was treated with BuLi in THF, a red solution of the ylide (6) was formed, which was reacted subsequently with 1 molar equiv of aldehyde (7) to give

TABLE I

Preparation of ω-azolylalkyltriphenylphosphonium bromide (5)

phosphonium salt	n	X	reaction temperature(℃)	reaction time(hr)	yield * (%)
5a	3	N	60	6	76
5b	4	N	60	6	85
5c	3	CH	60	8	58
5d	4	CH	60	8	45

* isolated yield

TABLE II

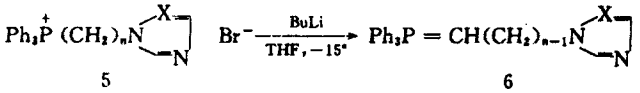
The yield and E/Z of the Wittig reaction of 5 with 7

Alkene(8)	X	n	R^1	R^2	yield(%)*	E/Z**
8a	N	3	H	H	79	71/29
8b			2-Cl	H	82	45/55
8c			3-Cl	H	83	64/36
8d			4-Cl	H	86	64/36
8e			2-Br	H	81	59/41
8f			4-F	H	91	72/28
8g			$4-CH_3$	H	81	70/30
8h			$4-OCH_3$	H	72	86/14
8i			$4-N(CH_3)_2$	H	74	88/12
8j			$4-NO_2$	H	76	49/51
8k	N	4	H	H	74	88/12
8l			2-Cl	H	75	55/45
8m			3-Cl	H	83	67/33
8n			4-Cl	H	85	81/19
8o			4-F	H	88	86/14
8p			$4-CH_3$	H	82	77/23
8q			$4-OCH_3$	H	70	88/12
8r			$4-N(CH_3)_2$	H	78	95/5
8s			3-Br	H	83	84/16
8t			2-Cl	4-Cl	81	57/43
8u			3-Cl	4-Cl	86	75/25
8v	CH	3	H	H	85	68/32
8w			$4-N(CH_3)_2$	H	75	97/3
8x			4-F	H	70	75/25
8y			$4-NO_2$	H	68	40/60
8z	CH	4	H	H	75	68/32

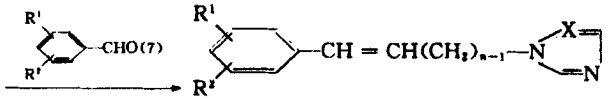
* isolated yield

* * E/Z was determinated by GC and ^{1}HNMR

ω-unsaturated azoles (**8**) in good yields. See Table II. This provides a facile synthesis of ω-unsaturated azoles which have been found to show fungicidal activities.[15]



5 6



8

It is noteworthy that these ylides are of a non-stabilized type, and were reacted with aromatic aldehydes under lithium salt. This factor should lead to poor stereoselectivity. However, the reactive ylides (**6**) showed E-stereoselectivity except in some cases under the above reaction condition. When R^1, R^2 are electrondonating substituents, the E-selectivity is good, whereas when R^1 is strong electron-withdrawing group (NO_2), the E/Z ratio is much lower. Ortho substitution also greatly decreases the selectivity.

The reason for the prodominance of the E alkene of this reaction is not clear yet, however, the presence of lithium salt and the azolyl group might be responsible. Further studies are needed.

EXPERIMENTAL

Melting points were uncorrected. MS were measured on a HP5988A 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 HP5988 GC-MS instrument employing a 12 m capillary column and HP-5 as liquid phase. ω-Bromoalkyltriphenylphosphonium bromides (**4**) were prepared from Ph_3P and dibromoalkane in refluxing toluene in 90–95% yields.

Preparation of **5**

A mixture of phosphonium salt **4** (0.1 mol), 1H-1,2,4-triazole (8.28 g, 0.12 mol) or imidiazole (8.16 g, 0.12 mol), solid potassium carbonate (33.2 g, 0.24 mol), a catalytic amount PEG600, DMF (5 ml) and CH_3CN (200 ml) was stirred at 60° for 6–8 hours. Filtered, the filtrate was condensed. After ether was added, a white precipitate formed was filtered, then washed with acetone and ether, dried to give **5**.

5a: yield 76%, mp 215–216°C, ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.6–8.6 (m, 17H), 4.98 (t, 2H), 3.88–4.10 (m, 2H), 2.22–2.46 (m, 2H); IR (cm^{-1}) 3045, 1450, 1110, 765, 763; MS, m/z 372 (2.03), 303 (3.19), 289 (100), 215 (39.26), 183 (41.93), 108 (13.51)
5b: yield 85%, mp 211–212°C, ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.6~8.6 (m, 17H), 4.54~4.62 (t, 2H), 3.85–4.10 (m, 2H), 2.18–2.40 (m, 2H), 1.68–1.42 (m, 2H); IR (cm^{-1}) 3100, 1440, 1112, 690, 740; MS, m/z 386 (M^+-Br, 2.83), 289 (70.14), 262 (97.05) 183 (100), 108 (57)
5c: yield 58%, mp 212–214°C, ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.1–8.1 (m, 18H), 4.95 (t, 2H), 3.80–3.98 (m, 2H), 2.26~2.48 (m, 2H); IR (cm^{-1}) 3100, 1440, 1180, 695, 760, 724; MS, m/z 371 (M^+-Br), 262, 148 (100), 183
5d: yield 45%, mp 206–208°C, ^{1}H NMR ($CDCl_3$, 200 MHz), δ 7.6–8.0 (m, 18H), 4.52 (t, 2H), 3.82–4.04 (m, 2H), 2.25–2.41 (m, 2H), 1.51–1.75 (m, 2H); IR (cm^{-1}), 3100, 1440, 1180, 695, 725; MS, m/z 385 (M^+-Br, 1.61), 289 (25.89), 262 (78.73), 183 (100), 108 (61.24)

General Procedure of the Wittig Reaction of (**5**) *with Aromatic Aldehyde*

A solution of BuLi (2.0 mmol) in ether was added dropwise to a suspension of dry phosphonium salt **5** (2.0 mmol) in anhydrous THF (20 ml) at −15°C under N_2. The mixture was stirred for 30 min to give a red solution. A solution of aromatic aldehyde **7** (2.0 mmol) in THF was added slowly. After 5 min, the reaction mixture was warmed slowly and stirred at room temperature for 12 hr. Then 2 volumes of petroleum ether were added to precipitate most of the phosphine oxide. Filtered, the solvent was removed and the residual was eluted with actone/ether (1:1) through a short silica gel column into a flask. The solvent was removed to give **8**. Its E/Z was determinated by GC and ^{1}H NMR.

^{1}H NMR, IR and MS for some compounds **8**:

8k: yield 74%, ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.07 (s, 1H), 7.97 (s, 1H), 7.1–7.4 (m, 5H), 5.5–6.6 (m, 2H), 4.0–4.3 (m, 2H), 2.1–2.4 (m, 2H), 1.9–2.1 (m, 2H); IR (cm^{-1}), 1650, 1500, 1274, 1140, 970, 770; MS, m/z 213 (M^+), 144, 129 (100)
8l: yield 75% ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.9–8.3 (s, 2H), 6.9–7.5 (m, 4H), 6.0–6.5 (m, 2H), 4.0–4.3 (m, 2H), 2.0–2.4 (m, 4H); IR (cm^{-1}), 1640, 1505, 1275, 1140, 965, 760, MS, m/z 249, 247 (M^+, 3:1), 178, 163, 143
8n: yield 85% ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.15 (s, 2H), 8.02 (s, 1H), 7.1–7.4 (m, 4H), 5.6–6.5 (m, 2H), 4.1–4.4 (m, 2H), 2.2–2.4 (m, 2H), 2.0–2.2 (m, 2H); IR (cm^{-1}), 1650, 1490, 1140, 1012, 960, 848, MS, m/z 247, 249 (M^+, 3:1), 178, 180, 143 (100)
8s: yield 83% ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.85–8.15 (s, 2H), 6.9–7.5 (m, 4H), 6.0–6.5 (m, 2H), 3.9–4.1 (m, 2H), 2.0–2.2 (m, 4H), IR (cm^{-1}), 1590, 1475, 1275, 1140, 965, 880, MS, m/z 293, 291 (M^+, 1:1), 222, 207, 143, 128
8t: yield 81% ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.11 (s, 1H), 7.98 (s, 1H), 7.0–7.5 (m, 3H), 5.7–6.7 (m, 2H), 4.23 (t, 2H, J = 7.4 Hz), 1.9–2.3 (m, 4H); IR (cm^{-1}), 1650, 1440, 1275, 1140, 960, 870; MS, m/z 281, 283, 285 (M^+, 9:6:1), 177, 179 (3:1)
8u: yield 86% ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.9–8.2 (s, 2H), 6.9–7.4 (m, 3H), 6.1–6.5 (m, 2H), 4.1–4.3 (m, 2H), 2.0–2.4 (m, 4H); IR (cm^{-1}), 1650, 1505, 1470, 1275, 965, 670, MS, m/z 281, 283, 285 (M^+, 9:6:1), 212, 177

ACKNOWLEDGEMENTS

We gratefully acknowledge financial support of this work by NSF of Hubei Province.

REFERENCES

1. B. E. Maryanoff and A. B. Reitz, *Chem. Rev.*, **89,** 863 (1989).
2. B. E. Maryanoff and A. B. Reitz, *Phosphorus Sulfur*, **27,** 167 (1986).
3. B. E. Maryanoff, A. B. Reitz and B. A. Duhl-Emswiler, *J. Am. Chem. Soc.*, **107,** 217 (1985).
4. A. Hercouet and M. Le Corre, *Tetrahedron*, **37,** 2861 (1981).
5. J. R. Tretter, US 3354155 (1967), CA69:10540q.
6. A. B. Astra Lakemedel, JP 7914976 (1979), CA 90: 203881u.
7. J. I. G. Cadogan, "Organophosphorus Reagents in Organic Synthesis," Academic Press, London, 1979, Chap. 2, 90–120.
8. R. J. Dubois, C. C. Lin and J. A. Beisler, *J. Med. Chem.*, **21,** 303 (1978).
9. R. J. Linderman and A. I. Meyers, *Heterocycles*, **20,** 1737 (1983).
10. W. Kunz, R. Nyfeler, A. Meyer, W. Frick, L. Maier and E. Sturm, EP 60223 (1982), CA 98:89361n.
11. L. Maier and W. Kunz, EP 63099 (1982), CA 98:126104d.
12. A. Meyer, W. Kunz, L. Maier and H. Rempfler, EP89920 (1983), CA 100: 103337c.
13. L. Maier, W. Kunz and G. Rist, *Phosphorus Sulfur*, **33,** 41 (1987).
14. L. Maier and W. Kunz, *Phosphorus Sulfur*, **30,** 201 (1987).
15. M. W. Ding, D. Q. Shi, W. J. Xiao, W. F. Huang and T. J. Wu, *Chinese J. Applied Chem.*, in press.