

Contents

1	Introduction to the Wittig Reaction and Discussion of the Mechanism	1
1.1	The Wittig Reaction: Introduction, Utility and Recent Developments.	1
1.2	Classification and Reactivity Trends of Phosphonium Ylides	4
1.3	Proposed Mechanisms: Description and Evaluation in the Light of Experimental Evidence.	6
1.3.1	The Betaine Mechanism	6
1.3.2	Bergelson's "C-P-O-C" Betaine Mechanism	10
1.3.3	Schweizer Mechanism	11
1.3.4	Olah's Single Electron Transfer Mechanism.	12
1.3.5	Bestmann's "P-O-C-C" Betaine Mechanism.	14
1.3.6	McEwen's Spin-Paired Diradical Mechanism	15
1.3.7	Schlosser Mechanism	16
1.3.8	Vedejs Cycloaddition Mechanism	17
1.4	Modern Mechanistic Interpretation of the Wittig Reaction	19
1.4.1	The Operation of Kinetic Control in the Wittig Reaction	19
1.4.2	The Nature of the First Formed Intermediate in the Wittig Reaction	31
1.4.3	Oxaphosphetane Structure and Pseudorotation	32
1.4.4	How Does the Observed Selectivity for <i>Z</i> or <i>E</i> Alkene Arise? An Explanation of the Currently Accepted Mechanism and Source of Stereoselectivity	35
1.5	Aldehydes Bearing Remote Heteroatoms: Influence of These Substituents on Selectivity in the Wittig Reaction	46
1.5.1	Wittig Reactions of Benzylidenetriphenylphosphoranes with <i>ortho</i> -Heteroatom Substituted Benzaldehydes	47
1.5.2	Wittig Reactions of Aliphatic Aldehydes Bearing a β -Heteroatom Substituent.	51
	References	53

2 Wittig Reactions of Aldehydes Bearing a β-Heteroatom Substituent	57
2.1 Fragility of Alkene Stereochemistry: The True <i>Z/E</i> Ratio	57
2.2 <i>Z/E</i> Ratios of Alkenes Produced in the Reactions of Benzylides with Benzaldehydes	60
2.2.1 Reactions of Benzyldenemethyldiphenylphosphoranes with Benzaldehydes	60
2.2.2 Reactions of Benzyldenetriphenylphosphoranes with Benzaldehydes	63
2.2.3 Discussion	64
2.3 <i>Z/E</i> Ratios of Alkenes Produced in the Reactions of Stabilised Ylides with Benzaldehydes	68
2.3.1 Reactions of (Alkoxy carbonylmethylidene) methyldiphenylphosphoranes (Ester-Stabilised Ylides)	68
2.3.2 Reactions of (2-oxoalkylidene) methyldiphenylphosphoranes (Keto-Stabilised Ylides)	70
2.3.3 Reactions of (2-oxoalkylidene)triphenylphosphoranes (Keto-Stabilised Ylides)	71
2.3.4 Discussion	72
2.4 Oxaphosphetane <i>cis/trans</i> Ratios in Reactions of Non-Stabilised Ylides with Benzaldehydes	76
2.4.1 The Determination of OPA <i>cis/trans</i> Ratios in Reactions of Non-stabilised Ylides	76
2.4.2 Determination of the Kinetic OPA <i>cis/trans</i> Ratio in Wittig Reactions of Non-stabilised Ylides by Low Temperature Acid Quenching	77
2.4.3 Determination of the Kinetic OPA <i>cis/trans</i> Ratio in Wittig Reactions of Non-stabilised Ylides by ^{31}P NMR	81
2.4.4 Investigation of the Operation of Stereochemical Drift in Reactions of Non-stabilised Ylides	84
2.4.5 NMR Observation of Oxaphosphetanes and β -Hydroxyphosphonium Salts Derived from Non-stabilised Ylides: Experimental Techniques and Further Information Acquired	86
2.4.6 Discussion	95
2.5 Reactions of an Aliphatic Aldehyde Showing Increased <i>Z</i> -Selectivity Due to a " β -Heteroatom Effect"	96
2.6 Conclusions	100
References	102

3	A Convenient Chromatography-Free Method for the Purification of Alkenes Produced in the Wittig Reaction	105
3.1	Introduction: Existing Methods for Phosphine Oxide Removal	105
3.2	Chromatography-Free Method for Phosphine Oxide Removal from Wittig Reaction Crude Products	108
	References	112
4	Experimental	113
4.1	General Experimental	113
4.2	Synthesis of Phosphonium Salts	115
4.2.1	Synthesis of Benzylmethyldiphenylphosphonium Salts	115
4.2.2	Synthesis of Benzyltriphenylphosphonium Salts	119
4.2.3	Synthesis of (Alkoxy carbonylmethyl) Methyldiphenylphosphonium Salts	123
4.2.4	Synthesis of Acetyl methyl diphenyl phosphonium Salts and Derived Ylides	125
4.2.5	Synthesis of Phosphonium Salt Precursors of Non-stabilised Ylides	128
4.3	General Procedures for Wittig Reactions and Assignment of <i>Z/E</i> Ratios	132
4.3.1	Procedure A: Ylide Generated Using NaHMDS Solution	132
4.3.2	Procedure B: Ylide Generated from “Instant Ylide Mix” Using Solid NaHMDS or KHMDS	132
4.3.3	Work-Up	133
4.3.4	Assignment of <i>Z/E</i> Ratios	133
4.4	Wittig Reactions of Semi-stabilised Ylides with Benzaldehydes	135
4.4.1	Work-Up Procedure and Stilbene Isomerisation Tests	135
4.4.2	Synthesis of Stilbenes from Benzylides	137
4.5	Wittig Reactions of Ester-Stabilised Ylides with Benzaldehydes	158
4.5.1	Work-Up Procedure	158
4.5.2	Synthesis of Alkyl Cinnamates from Ester-Stabilised Ylides	158
4.6	Wittig Reactions of Keto-Stabilised Ylides with Benzaldehydes	164
4.6.1	Synthesis of 4-arylbut-3-en-2-ones from Acetylidenetriphenylphosphoranes	164
4.6.2	Synthesis of 4-arylbut-3-en-2-ones from Acetylidenemethyldiphenylphosphoranes	167

4.7	Reactions of Non-stabilised Ylides	175
4.7.1	Synthesis of 1-Arylprop-1-enes	175
4.7.2	Synthesis of (1-aryl-1-hydroxyprop-2-yl) Phosphonium Salts	178
4.7.3	Low Temperature Acid Quenching of Wittig Reactions of <i>P</i> -Alyklidene- <i>P</i> -Phenyldibenzophospholanes to Give β -HPS and Subsequent Generation of OPA and Alkene.	189
4.7.4	Observation of Kinetic OPA <i>cis/trans</i> Ratio for Wittig Reactions of Non-stabilised Ylides	196
4.8	Reactions of Semi-Stabilised and Stabilised Ylides with 1,2-O-isopropylidene-3-O-methyl- α -D- xylopentodialdofuranose-(1,4)	204
4.8.1	General Procedure.	204
4.9	Phosphine Oxide Removal from Crude Product of Wittig Reaction.	213
4.9.1	Procedures for Wittig Reactions	214
4.9.2	Removal of Phosphine Oxide and Aldehyde from Crude Product by Oxalyl Chloride Treatment.	214
4.9.3	Characterisation of Purified Alkenes	215
	References	229