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Ramberg Bäcklund Type Reactions of Phosphonium Salts

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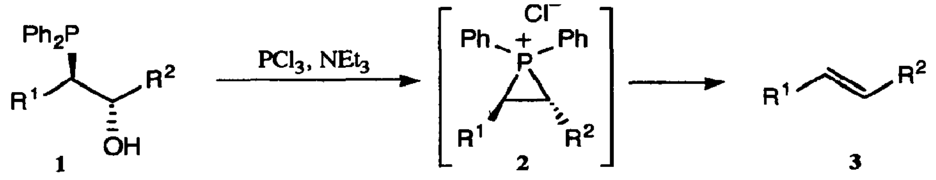
Abstract: Alkenes may be synthesised from (α-bromobenzyl)benzyldiphenylphosphonium salts by the action of amine bases. A series of stilbenes was synthesised by the action of *N*-bromosuccinimide and 2,2,6,6-tetramethylpiperidine directly upon dibenzyldiphenylphosphonium salts. The reaction, essentially a phosphonium analogue of the Ramberg Bäcklund displays a similar level of *cis* selectivity as that shown by the parent sulfone.

We recently reported a novel alkene synthesis via *anti* elimination of 1,2-phosphinyl alcohols in the sense **1** → **3**.[1] When the alcohol **1** is treated with phosphorus trichloride the alkene is obtained stereoselectively. We explain this selectivity by postulating that the reaction proceeds via the *epi*-phosphonium salt **2**, formed by intramolecular displacement of the oxyphosphorus group. In the course of showing whether this explanation is valid we have developed a new alkene synthesis that is essentially a phosphonium salt, Ramberg Bäcklund type,[2] reaction.



We argued that if the reaction is proceeding via **2**, then any other method of making *epi*-phosphonium salts would also be a potential route to alkenes. We chose to make the three-membered ring by construction of the carbon-carbon bond as the final step. This was achieved by the intramolecular displacement of a good leaving group, in this case a bromide ion, by the ylide formed at the α' carbon. The required α-bromophosphonium bromide **5**[3] was made by bromination of the ylide (from n-butyllithium) of dibenzyldiphenylphosphonium bromide **4**. When **5** is treated with triethylamine (see table 1) stilbene **6** is obtained in moderate to good yield with *cis* selectivity. Debromination of **5** by the amine is evidently a competing reaction since dibenzylphosphonium salt **4** may be isolated from the reaction. In an attempt to reduce this side-reaction we investigated the effect of the amine. The stereoselectivity is more or less independent of the base and for all amines small amounts of **4** were formed. The reaction is presumably proceeding via an *epi*-phosphonium salt of type **2** which readily decomposes to the alkene. Denney[4] has shown that a phosphirane containing a pentacoordinate phosphorus atom decomposes by a stereospecific concerted process to give an alkene. The decomposition of **2** may therefore require attack by a nucleophile (triethylamine or chloride ion), to produce a similar transient pentacoordinate phosphorus species.

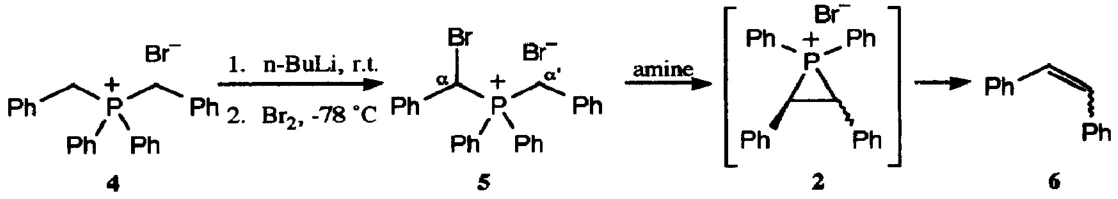


Table 1. Reaction of bromobenzylphosphonium salt **5** with amines

Amine	Yield **5** → **6** (%)	*E*:*Z*[a]	Recovered **4** (%)
Triethylamine	78	22:78	9
Diisopropylamine	65	25:75	31
2,2,6,6-Tetramethylpiperidine	61	20:80	~35[b]
Hexamethyldisilazane	44	22:78	~50[b]
N,*N*-Dimethylbenzylamine	38	33:67	—[d]
1,8-Diazabicyclo[5.4.0]undec-7-ene	40	20:80	~10[b,c]
Diisopropylethylamine	40	20:80	—[d]

a. As measured from the ^1H nmr spectrum of the crude reaction mixture and/or gas chromatography of the isolated product; b. As estimated from the ^1H nmr spectrum of the crude reaction mixture. c. In addition to **4** benzyldiphenylphosphine oxide (approx. 40%) is present; d. not measured.

Since both the bromination of **4** and the subsequent intramolecular bromide displacement occur via intermediate ylides we investigated whether both steps could be performed in the same pot — analogous to Meyers' carbon tetrachloride/KOH one-pot modification of the Ramberg Bäcklund reaction.[5] The ylide anion of **4** was prepared by addition of 2 equivalents of n-butyllithium, according to the method of Walker,[6] and treated with one equivalent of bromine. The reaction produced stilbene (*E*:*Z* 33:67) but in poor yield (42 %). The direct transformation of **4** into stilbene is more simply achieved by treatment with 2,2,6,6-tetramethylpiperidine and *N*-bromosuccinimide in chloroform at ambient temperature. To show that the reaction is general we synthesised a series of unsymmetrical dibenzylphosphonium salts **7** by our own method[7] of one-pot reduction [polymethylhydrosiloxane (PMHS)/Ti(O^{i}Pr)$_4$] and quaternisation of benzyldiphenylphosphine oxide. The symmetrical di(*o*–tolyl)diphenylphosphonium bromide was prepared simply by double alkylation of lithium diphenylphosphide according to the method of Cristau.[8] In all cases we isolated the stilbene **8** in good yield and with moderate (3-4:1) *Z*:*E* selectivity except when R^1 is *p*–methoxyphenyl (see table 2). The *trans*:*cis* ratio of the alkenes was determined from the crude reaction mixture by ^1H nmr spectroscopy. We prepared authentic samples of the *E*–stilbene **8** by Horner-Wadsworth-Emmons[9] reaction of diethyl benzylphosphonates **10** and

E/Z mixtures by standard Wittig reaction of benzyltriphenylphosphonium salts **9**. The selectivities we found in these reactions is essentially the same as that observed by others.[10]

The *cis* selectivity of this new reaction is intriguing and follows the same preference of the Ramberg-Bäcklund reaction for which no definitive explanation has been given.[2] The similarity is perhaps not too surprising since both the sulfone and diphenyl phosphorus groups are obviously tetrahedral. More work is clearly needed to elucidate the factors determining the stereoselectivity of the reaction. Our method joins several other Ramberg-Bäcklund like reactions in which the sulfone group is replaced by sulfide,[11] sulfoxide,[12] sulfoximine,[13] and more pertinently, phosphine oxide and phosphinate groups.[14]

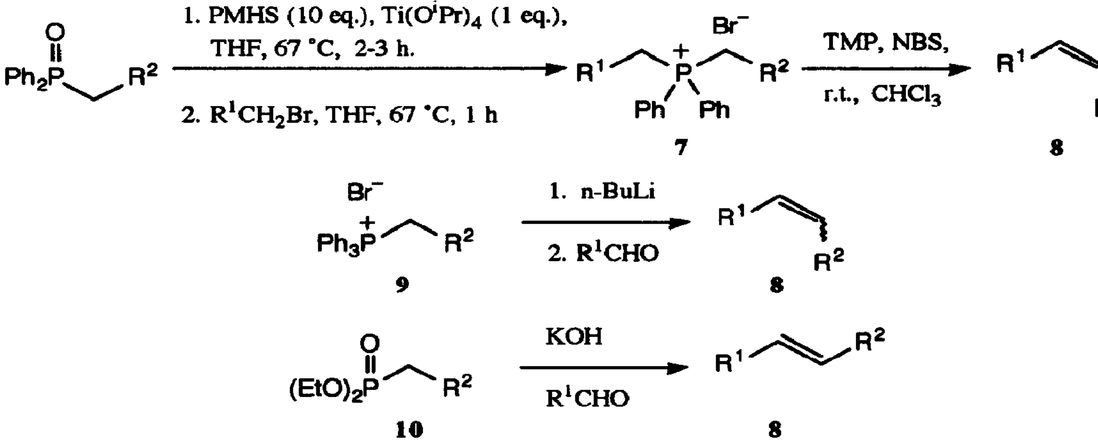


Table 2. Synthesis of stilbenes **8** from dibenzylphosphonium salts **7** and by standard Wittig methods

		Phosphonium Ramberg Bäcklund Reaction (**7** → **8**)		Wittig Reaction (**9** → **8**)		Horner Wadsworth Reaction (**10** → **8**)	
R^1	R^2	yield (%)	*E*:*Z*[a]	yield (%)	*E*:*Z*[a]	yield (%)	*E*:*Z*[a]
Ph	Ph	70	20:80	81	70:30	75	>98:2
o-Tolyl	Ph	79	20:80	76	46:54	97	96:4
p-Tolyl	Ph	94	30:70	98	35:65	71	>98:2
p-Nitrophenyl	Ph	85	50:50	75	76:24	76	>98:2
p-Methoxyphenyl	Ph	56	40:60	65	50:50	92	>98:2
o-Tolyl	*o*-Tolyl	77	26:74	72	36:64	78	>98:2

a. As measured from the ^{1}H nmr spectrum of the crude reaction mixture.

Standard procedure: To a stirred mixture of dibenzyldiphenylphosphonium salt **7** (1 mmol) and 2,2,6,6-tetramethylpiperidine (6 mmol) in dry dichloromethane (10 ml) was added *N*-bromosuccinimide (3 mmol) under nitrogen. The mixture was stirred at room temperature for 2.5 h. Water (50 ml) was added and the mixture extracted with dichloromethane (3 x 25 ml). The organic extracts were successively washed with dilute hydrochloric acid (50 ml), saturated sodium bicarbonate solution (50 ml) and dried (Na_2SO_4) and evaporated *in vacuo*. The residue was purified by chromatography (SiO_2, hexane).

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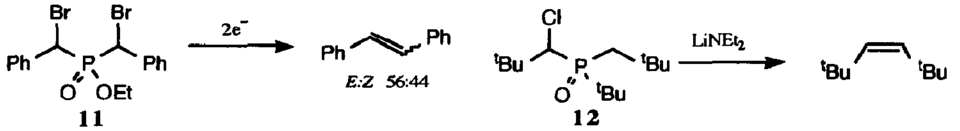

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