'trahedron Vol. 45, No. 11, pp. 3523 to 3534, 1989
inted in Great Britain.

0040-4020/89 $3.00+.00

THE WITTIG REACTION: COMMENTS ON THE MECHANISM AND APPLICATION AS A TOOL IN THE SYNTHESIS OF CONJUGATED DIENES

Rut Ideses and Arnon Shani*
Department of Chemistry, Ben-Gurion University of the Negev,
Beer Sheva, 84105, Israel

(*Received in UK* 27 *February* 1989)

Abstract. For construction, by the Wittig reaction, of conjugated dienes with specific ereochemistry (either Z or E) at the newly formed double bond, without isomerization of the existing ("old") ›uble bond, it is better to react a reactive (nonstabilized) saturated ylide with an α, β-unsaturated aldehyde. he opposite approach, namely, the reaction of a moderate (semi- stabilized) allylic ylide with a saturated dehyde produces a mixture of geometric isomers, as a result of increased production of the E-configuration at e new double bond, and significant isomerization of the existing double bond. The proposed betaine structure ›r the intermediate could account only for the two equivalents of Li reaction . In other reactions, the less able erythro-oxaphosphetane is probably the intermediate, produced by an early anti- or gauche C-C bond ›rmation from the ylide and the carbonyl, from which the Z-double bond is then formed.

INTRODUCTION

The Wittig reaction is used to construct an olefinic bond in a specific position in a molecule, but the ereochemistry of this new double bond depends on the conditions under which the reaction is conducted -6). Two distinct mechanisms have been proposed for the Wittig reaction. Schlosser (2) suggested that the action involves a betaine intermediate, stabilized by a Li^+ ion when available, which later collapses to form e end products. Bestmann (3) claimed that an oxaphosphetane is formed, in which the P-C bond is broken, us enabling the erythro-threo diastereomeric mixture to equilibrate and then disintegrate into the final products.

The conjugated diene system is common in natural products, including pheromones, and the Wittig action is used in the synthesis of these partial structures, aiming at specific stereochemistry. Two approaches e possible in constructing this diene system:

i) Reaction of a reactive (nonstabilized) saturated ylide with an α,β-unsaturated aldehyde:

$$\varphi_3\overset{+}{P}CH_2R^1\,\overset{-}{Br} + R^2CH{=}CHCHO \rightarrow R^1CH{=}CHCH{=}CHR^2$$

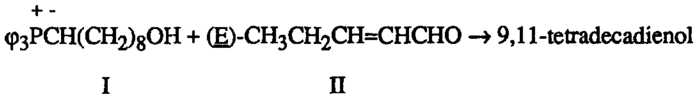
ii) Reaction of a moderate (semistabilized) allylic ylide with a saturated aldehyde:

$$\varphi_3\overset{+}{P}CH_2CH{=}CHR^3\overset{-}{Br} + R^4CHO \rightarrow R^3CH{=}CHCH{=}CHR^4$$

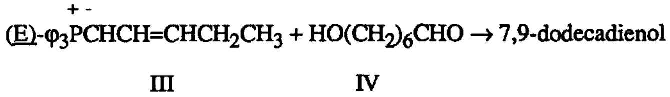
The stereochemistry of both the newly formed and the old (i.e. that already existing in one of the eactants) double bond depends on the reaction conditions, and a mixture of up to four geometric isomers can e formed. Several key factors can affect the final stereochemistry, among them are the base used to produce he ylide, the counter cation of the base, the solvent, and the temperature at which the reaction is conducted.

Examination of several previously published procedures for constructing the diene system shows that it is difficult to compare different reactions, as each involves a specific combination of base, solvent and temperature. When an (E)-α,β-unsaturated aldehyde is reacted with a saturated ylide the E/Z ratio of the new double bond ranges from 95:5 to 5:95, and there is very little change in the stereochemistry of the existing (E)-double bond(3, 7-15). On the other hand,when an allylic ylide is reacted with a saturated aldehyde, the E/Z ratio of the new bond is about 50-60 / 50-40,; and the "old" double bond also isomerizes to some extent to give an E / Z ratio of 80-90 : 20-10 when an (E)-allylic phosphonium salt is used as the starting material (3, 7, 13, 16).

In order to investigate the effect of each factor we designed a set of experiments, in which only one factor is changed at a time, thus enabling us to compare the different reactions, which are otherwise conducted under the same conditions. The chemicals selected for the study were the building unit of the tetradecadienol and dodecadienol pheromone skeleton:



$$\underset{\text{I}}{\varphi_3\overset{+}{P}\overset{-}{C}H(CH_2)_8OH} + \underset{\text{II}}{(E)\text{-}CH_3CH_2CH{=}CHCHO} \rightarrow \text{9,11-tetradecadienol} \qquad (1)$$



$$\underset{\text{III}}{(E)\text{-}\varphi_3\overset{+}{P}\overset{-}{C}HCH{=}CHCH_2CH_3} + \underset{\text{IV}}{HO(CH_2)_6CHO} \rightarrow \text{7,9-dodecadienol} \qquad (2)$$

In reaction 1 we studied the reaction of a reactive saturated ylide (I) with an α,β- unsaturated aldehyde [(E)-2-pentenal(II)] (17) to yield the 9,11-tetradecadienyl system. (9,11-C_{14}OR), which appears in the Egyptian cotton leafworm moth pheromone as the (Z, E- isomer (R = Ac) (18, 19). In reaction 2 we reacted the moderate allylic ylide (III), with a saturated aldehyde (7-hydroxyheptanal, IV) to yield the 7,9-dodecadienyl system. (7,9-C_{12}OR), which appears in the European grapevine moth pheromone as the (E, Z)-isomer (R = Ac) (20, 21). By studying these two reactions we can not only establish the optimal synthesis for two important diene systems, but also shed some light on the mechanism of the Wittig reaction.

PROCEDURE AND RESULTS

The reaction procedure involved three steps, after each of which a sample was withdrawn to determine the stereochemistry of the isomeric mixture. Each fraction was treated with absolute ethanol to quench any possible carbanion in the intermediate, and then acidified with acetic acid. The procedure may be summarized as follows:

Fraction I - One equivalent of base and reaction for 15 min
Fraction II - Two equivalents of base and reaction for 15 min
Fraction III - Two equivalents of base and overnight reaction.

This procedure might give an indication of any intermediate which could be formed through a betaine (Schlosser) mechanism.

The bases studied represent three alkali cations, Li^+, Na^+ and K^+. The polarity of solvents increases from the least polar toluene, to THF and DMF. The aldehydes were added at two different temperatures, 15-20°C (room temperature) and -30°C to investigate whether there was any effect on the stereoechemistry of the new and old (already existing) double bond.

Examination of the structure of the starting materials and the final products (Reactions 1 and 2) reveals how to measure the stereochemistry and ratio of Z/E isomers of the new and old double bonds [(no (Z, Z) isomer was detected, so its amount is less than 1 - 2%). Some workers have reported (Z, Z) in small amounts (0-5%)]. In the case of the (Z)-α,β-unsaturated aldehyde or of (Z)- allylic phosphonium salts, the content of (Z, Z)- isomer ranges from 26% to 85% (13, 14).The proportion in % was calculated as follows:

Z / E in the new double bond [(Z, E) / (E, Z) + (E, E)] x 100

Z / E in the old double bond [(E, Z) / (Z, E) + (E, E)] x 100

Reaction of the saturated ylide with an unsaturated aldehyde

Tables 1-3 summarize the results of the reaction of I and II in different solvents, using one of four bases (t-BuOK, $NaNH_2$, $LiNH_2$, BuLi). When the ylide is prepared, the hydrophylic and ionic character of the OH group in the phosphonium salt make it much less soluble in toluene and slow down the reaction. Thus, no reaction was detected in toluene at the low temperature or even at room temperature. Only after 24 h was some product observed (Fraction III in toluene, Tables 1 and 2).

Table 1. Distribution of isomers after the reaction of $Ph_3\overset{+}{P}(CH_2)_9OH\ \overset{-}{Br}$ and (E)-$CH_3CH_2CH=CHCHO$ in different solvents and temperatures, using t-BuOK as the base[a]

Solvent	Temp. of aldehyde Addition	Fract.	% composition				Z : E ratio in new bond	Z : E ratio in old bond
			(Z. E)	(E, Z)	(Z. Z)	(E, E)		
Toluene	RT	I		n. r. o.				
		II		n. r. o.				
		III	73	-	-	27	73 : 27	-
Toluene	-30°C	I,II,III		n. r. o.				
THF	RT	I	90	-	-	10	90 : 10	-
		II	88	-	-	12	88 : 12	-
		III	87	-	-	13	87 : 13	-
THF	-30°C	I		n. r. o.				
		II	89	-	-	11	89 : 11	-
		III	87	-	-	13	87 : 13	-
DMF	RT	I	82	5	-	13	82 : 18	5 : 95
		II	84	3	-	13	84 : 16	3 : 97
		III	84	4	-	12	84 : 16	4 : 96
DMF	-30°C	I	82	4	-	14	82 : 18	4 : 96
		II	84	4	-	12	84 : 16	4 : 96
		III	83	4	-	13	83 : 17	4 : 96

[a] Base was used in 2.1 equivalents because of OH group in (I), and after Fract I was withdrawn,1 more eq. was added.
RT = room temperature; n.r.o = no reaction observed.

The reactivity of the Li bases, BuLi and LiNH$_2$, toward DMF to form an aldehyde (22) obviated the use of this solvent from this part of the study. Thus, Table 3 includes only one solvent, but here we see the effect of the additional equivalent of base and that of the temperature (see Discussion). (In all the reactions of I, 2 equivalents of base were added at first to react with the OH group and to prepare the ylide).

Table 2. Distribution of isomers after the reaction of $Ph_3\overset{+}{P}(CH_2)_9OH\ \overset{-}{Br}$ and (E)-$CH_3CH_2CH{=}CHCHO$ in different solvents and temperatures, using $NaNH_2$ as the base[a]

Solvent	Temp. of aldehyde Addition	Fract.	% composition (Z, E)	(E, Z)	(Z, Z)	(E, E)	Z : E ratio in new bond	Z : E ratio in old bond
Toluene	RT	I	n. r. o.					
		II	n. r. o.					
		III	85	-	-	15	85 : 15	-
Toluene	-30°C	I,II,III	n. r. o.					
THF	RT	I	88	-	-	12	88 : 12	-
		II	91	-	-	9	91 : 9	-
		III	90	-	-	10	90 : 10	-
THF	-30°C	I	90	-	-	10	90 : 10	-
		II	92	-	-	8	92 : 8	-
		III	92	-	-	8	92 : 8	-
DMF	RT	I	91	-	-	9	91 : 9	-
		II	90	-	-	10	90 : 10	-
		III	90	-	-	10	90 : 10	-
DMF	-30°C	I	90	-	-	10	90 : 10	-
		II	91	-	-	9	91 : 9	-
		III	91	-	-	9	91 : 9	-

[a] For footnotes see Table 1.

Table 3. Distribution of isomers after the reaction of $Ph_3\overset{+}{P}(CH_2)OH\ \overset{-}{Br}$ and (E)-$CH_3CH_2CH{=}CHCHO$ in THF and different temperatures, using $LiNH_2$ and BuLi as bases[a]

Base	Temp. of aldehyde Addition	Fract.	% composition (Z, E)	(E, Z)	(Z, Z)	(E, E)	Z : E ratio in new bond	Z : E ratio in old bond
$LiNH_2$	RT	I	88	-	-	12	88 : 12	-
		II	75	-	-	25	75 : 25	-
		III	50	5	-	45	50 : 50	5 : 95
$LiNH_2$	-30°C	I	87	-	-	13	87 : 13	-
		II	64	-	-	36	64 : 36	-
		III	30	-	-	70	30 : 70	-
BuLi	-30°C	I	85	-	-	15	85 : 15	-
		II	60	-	-	40	60 : 40	-
		III	25	-	-	75	25 : 75	-

[a] For footnotes see Table 1.

Reactions of an allylic ylide with a saturated aldehyde.

Tables 4-6 summarize the results of the reaction of III and IV, which demonstrate different behavior as compared with the previous set of reactions (Tables 1-3). The hydrocarbon ylide III is soluble in all solvents, and we could thus get a broader coverage of solvent polarity and temperatures. In all fractions we detected significant isomerization of the existing double bond as well as a clear trend toward more E-isomer in the formation of the new double bond. The effect of the second equivalent of base, even with the Li^+ counter ion, was very slight.

Table 4. Distribution of isomers after the reaction of (E)-$CH_3CH_2CH{=}CHCH_2\overset{+}{P}Ph_3\overset{-}{Br}$ with $HO(CH_2)_6CHO$ in different solvents and temperatures, using t-BuOK as the base [a]

Solvent	Temp. of aldehyde Addition	Fract.	% composition				Z : E ratio in new bond	Z : E ratio in old bond
			(Z, E)	(E, Z)	(Z, Z)	(E, E)		
Toluene	RT	I	28	36	-	36	28 : 72	36 : 64
		II	27	35	-	38	27 : 73	35 : 65
		III	31	34	-	35	31 : 69	34 : 66
Toluene	-30°C	I	47	19	-	34	47 : 53	19 : 81
		II	45	17	-	38	45 : 55	17 : 83
		III	45	17	-	38	45 : 55	17 : 83
THF	RT	I	40	24	-	36	40 : 60	24 : 76
		II	38	25	-	37	38 : 62	25 : 75
		III	40	25	-	35	40 : 60	25 : 75
THF	-30°C	I	52	20	-	28	52 : 48	20 : 80
		II	52	18	-	30	52 : 48	18 : 82
		III	50	20	-	30	50 : 50	20 : 82
DMF	RT	I	40	25	-	35	40 : 60	25 : 75
		II	40	25	-	35	40 : 60	25 : 75
		III	42	24	-	34	42 : 58	24 : 76
DMF	-30°C	I	40	18	-	42	40 : 60	18 : 82
		II	38	20	-	42	38 : 62	20 : 80
		III	38	20	-	42	38 : 62	20 : 80

[a] For footnotes see Table 1.

DISCUSSION

With all solvents and temperatures studied the kinetic control of the reaction of the reactive (nonstabilized) ylide (I) is clear. The first equivalent of base reacts with the phosphonium salt to form the reactive ylide, which we assume, in the least crowded anti-or gauche approach, forms the C-C bond with the carbonyl carbon. Then, a rotation of 180° or 60° takes place around it to yield the less stable erythro-oxaphosphetane, which collapses immediately to the Z-isomer (Scheme 1). It seems that there is no equilibrium of the intermediate with other possible ionic species, as no effect of solvent polarity is observed. Thus, the formation of the Z-isomer is dictated by the first and least crowded short-lived intermediate, or transition-state Va or Vb (Scheme 1). The facts that no NMR signals were found for a betaine phosphorous at -78° and that calculations prefer the oxaphosphetane over a betaine structure, can still not exclude the anti- (Va) or gauche (Vb) betaine as first body formed in the reaction (4, 5).

Table 5. Distribution of isomers after the reaction of (E)-$CH_3CH_2CH{=}CHCH_2\overset{+}{P}Ph_3\ \overset{-}{Br}$ with $HO(CH_2)_6CHO$ in different solvents and temperatures, using $NaNH_2$ as the base [a]

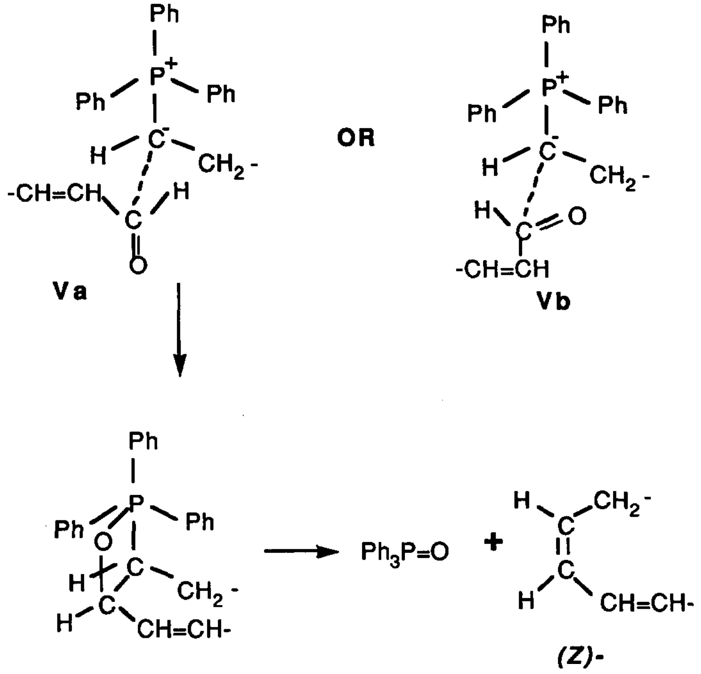
Solvent	Temp. of aldehyde Addition	Fract.	% composition				Z : E ratio in new bond	Z : E ratio in old bond
			(Z, E)	(E, Z)	(Z, Z)	(E, E)		
Toluene	RT	I	40	25	-	35	40 : 60	25 : 75
		II	42	26	-	32	42 : 58	26 : 74
		III	39	23	-	38	39 : 61	23 : 77
Toluene	-30°C	I	42	20	-	38	42 : 58	20 : 80
		II	45	17	-	38	45 : 55	17 : 83
		III	37	20	-	43	37 : 63	20 : 80
THF	RT	I	32	15	-	53	32 : 68	15 : 85
		II	35	15	-	50	35 : 65	15 : 85
		III	35	18	-	47	35 : 65	18 : 82
THF	-30°C	I	42	17	-	41	42 : 58	17 : 83
		II	40	17	-	43	40 : 60	17 : 83
		III	40	18	-	42	40 : 60	18 : 82
DMF	RT	I	45	22	-	33	45 : 55	22 : 78
		II	40	23	-	37	40 : 60	23 : 77
		III	39	22	-	39	39 : 61	22 : 78
DMF	-30°C	I	38	15	-	47	38 : 62	15 : 85
		II	40	18	-	42	40 : 60	18 : 82
		III	38	18	-	44	38 : 62	18 : 82

[a] For footnotes see Table 1.

Table 6. Distribution of isomers after the reaction of (E)-$CH_3CH_2CH{=}CHCH_2\overset{+}{P}Ph_3\ \overset{-}{Br}$ with $HO(CH_2)_6CHO$ in different solvents and temperatures, using $LiNH_2$ and BuLi as bases [a]

Base	Solvent	Temp. of aldehyde Addition	Fract.	% composition				Z : E ratio in new bond	Z : E ratio in old bond
				(Z, E)	(E, Z)	(Z, Z)	(E, E)		
$LiNH_2$	Toluene	RT	I	42	18	-	40	42 : 58	18 : 82
			II	34	21	-	45	34 : 66	21 : 79
			III	35	20	-	45	35 : 65	20 : 80
$LiNH_2$	Toluene	-30°C	I	42	20	-	38	42 : 58	20 : 80
			II	38	22	-	40	38 : 62	22 : 78
			III	29	20	-	51	29 : 71	20 : 80
$LiNH_2$	THF	RT	I	60	15	-	25	60 : 40	15 : 85
			II	58	18	-	24	58 : 42	18 : 82
			III	40	18	-	42	40 : 60	18 : 80
$LiNH_2$	THF	-30°C	I	45	16	-	39	45 : 55	16 : 84
			II	45	18	-	37	45 : 55	18 : 82
			III	47	15	-	83	47 : 53	15 : 85
BuLi	THF	-30°	I	50	18	-	32	50 : 50	18 : 82
			II	45	21	-	34	45 : 55	21 : 79
			III	45	17	-	38	45 : 55	17 : 83

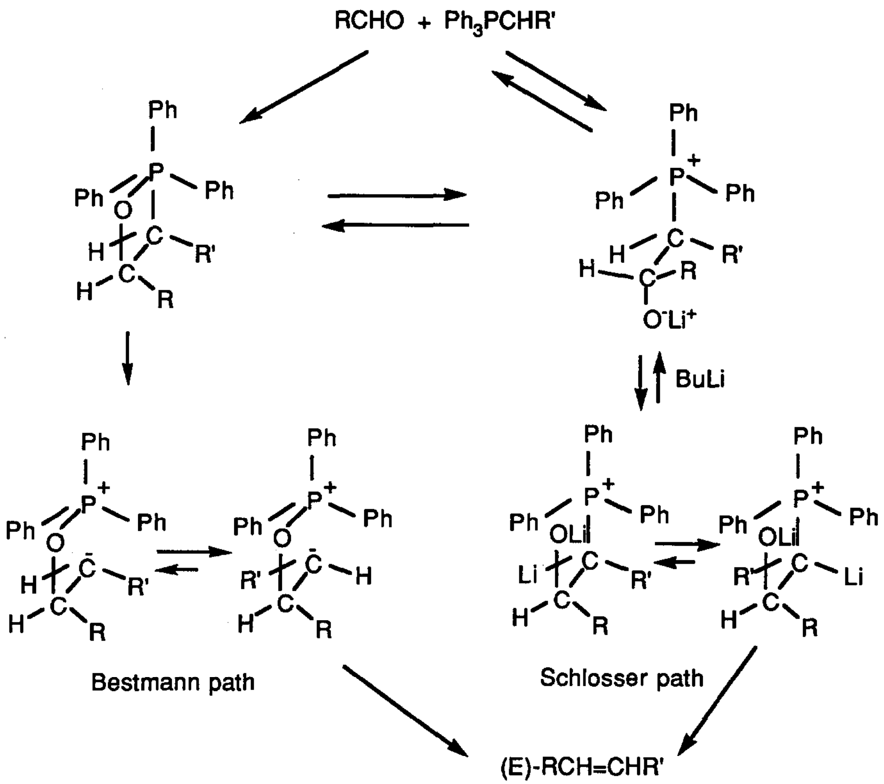
[a] For footnotes see Table 1.



Scheme 1

It is clear from Tables 1 and 2 that Na^+ and K^+ do not stabilize any betaine or complex with an ionic intermediate, as no effect of the second equivalent of base is found. [No difference between Fraction III and the first two fractions (I, II)]. This is in dramatic contrast to the behavior of a second equivalent of lithium base, which changes the stereochemistry of the new double bond to the E-isomer (Table 3) by deprotonation of the second hydrogen of the original ylide (2, 23). One can see the advancement of the isomerization as Fraction II in each of the three reactions already exhibits a transition composition. The results for Fraction I in all reactions in Table 3 show that the Li^+ ion does not behave differently from K^+ and Na^+ (Tables 1, 2) in equimolar (1 eq.) ratios. This fact may raise some doubts that a betaine is a real intermediate, as proposed by Schlosser, for the regular Wittig reaction. The betaine structure probably holds only for the second equivalent of base, as shown in Scheme 2. Under these conditions, thermodynamic control prevails, and the more stable E-isomer predominates (2, 23, 24).

The effect of temperature is also illustrative, since at room temperature there is less chance for thermodynamic control than at low temperature, because of the faster decomposition of the oxaphosphetane to the products at higher than at lower temperature. This is shown in Table 3 by comparing Fraction III of $LiNH_2$ at room temperature with $LiNH_2$ and BuLi at -30°C, as less E-double bond is formed at room temperature.

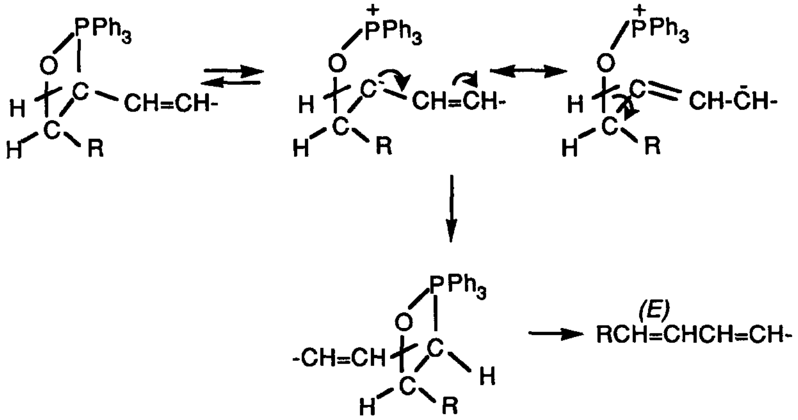


Scheme 2

It is interesting to observe the small amount of isomerization of the existing ("old") double bond during the reaction in DMF (Table 1). We assume that this process does not arise from the effect of intermediate formation on the old bond, but from independent isomerization of the unsaturated aldehyde in this solvent. It could also arise from the reverse reaction of the ylide and the aldehyde which could be enhanced by the polarity of the solvent. It is also possible that this effect depends on the base, as no such isomerization is observed in $NaNH_2$ reaction (Table 2).

The moderate or semistabilized allylic ylide behaves differently, as seen in Tables 4-6. In all solvents and all bases, both at low and at room temperatures, the same trend prevails: all systems are characterized by a slight or moderate shift toward the thermodynamic equilibrium of the isomeric mixture in the internal conjugated diene system, which we have already found to be: (E, E) 68-75%, (E, Z) 12-15%, (Z, E) 12-15% , (Z, Z) 1-3% (25).

Based on the above results we may suggest that the betaine (formed as described above) immediately closes to erythro-oxaphosphetane, or possibly this cyclic intermediate is formed at once. It is probably opened later on according to Bestmann's postulation by breaking the P-C bond. The bond energy of P-O is 95 kcal/mol and that of C-C is 63 kcal/mol, and there is also extra stabilization of the carbanion formed through resonance with the allylic system, and relief of the strain on the four-membered ring. This system can now rotate around the C-C bond to close to the more stable threo-oxaphosphetane, which disintegrates to the E-isomer at the new double-bond. Since this process is probably faster at higher temperatures, we expect that at room temperature the reaction is more likely to approach the equilibrium composition than at lower temperature. This was indeed found to be the case in toluene and THF with t-BuOK and $NaNH_2$ as bases (Tables 4 and 5). In the case of $LiNH_2$ or BuLi we see the increase of E-isomer with time (Table 6), as we found earlier (Table 3), but the effect is less dramatic, since it is only added to the more effective isomerization, which is demonstrated in Tables 4 and 5.



At the same time the existing E-double bond in III isomerizes to a significant degree to yield a mixture that also approaches the thermodynamic equilibrium of Z/E- isomers, which is 20-30: 80-70 (26). This process could take place at either or at both the stages of the reaction:

(i) isomerization during the formation of the ylide, before the reaction with the aldehyde; and/or

(ii) isomerization during breaking of the P-C bond of the oxaphosphetane.

Since no significant difference was found between the fractions in each reaction, we assume that the isomerization takes place at an early stage of the reaction, probably before the ylide reacts with the aldehyde. In some reactions (Tables 4,5) we see that the isomerization (yielding more of the Z-isomer) proceeds to a greater extent at room temperature than at -30°, which fits an early stage process.

The polarity of the solvent may also play a role, since toluene, the least polar solvent would better stabilize a less ionic structure, which can be established at the early stage (i), and not after the formation of the oxaphosphetane (ii). Indeed, the maximum isomerization of the existing double bond occurred in toluene (Tables 4, 5).

CONCLUSION

The results show clearly that for synthesis of a conjugated diene with a specific configuration it is better to react a reactive (saturated) ylide with unsaturated aldehyde in order to minimize the number of isomers, and to maximize only one of them. Under regular conditions with different bases and in several solvents the Z-isomers will predominate. If the E-isomer is needed,two equivalents of Li base are needed, and the system must be allowed to equilibrate for a longer time. If a mixture of all four isomers (or at least three) is required, the other system in which a moderate (E or Z) allylic ylide reacts with a saturated aldehyde, is recommended

The evidence for a betaine intermediate can be found only in the reactions with two equivalents of Li base. In all other cases, the anti- or gauche early C-C bond formation from the ylide and the carbonyl (on the way to a more crowded and probably less stable erythro-oxaphosphetane) to form a Z-double bond is the likely mechanism.

EXPERIMENTAL

Instrumentation. Gas-liquid chromatography (GLC) analyses were conducted on a Packard 417 instrument with a flame ionization detector. The column employed was a capillary fused silica SP 2340 (30 m x 0.25 mm). Proton NMR spectra were recorded on a Brucker WP 200 instrument with $CDCl_3$ as a solvent, and chemical shifts are given in δ units.

Solvents. Petroleum ether (60-80) was distilled. Pyridine was distilled and kept over CaH_2. THF was distilled over a dispersion of sodium and benzophenone (purple-blue color). DMF was dried by azeotropical distillation with toluene. Toluene was dried over sodium and distilled.

Preparation of 9-hydroxynonyltriphenylphosphonium bromide

A solution of 20 g (0.09 mol) of 9-bromononanol and 23.5g (0.09 mol) of triphenylphosphine in 200 ml of acetonitrile was refluxed for 48 h. The solvent was removed, and the product was crystallized from toluene. The yield was 37 g(85%). NMR 7.8 - 7.48 (15H, aromatic protons, m); 3.8 - 3.4 (4H, $C\underline{H}_2OH$ and $C\underline{H}_2P$, m); 1.7 - 1.2 (14H, - CH_2 -, m).

Preparation of 2-pentenyltriphenylphosphonium bromide

A solution of 7g (0.049 mol) of (E)-1-bromo-2-pentene and 13.1g (0.05 mol) of triphenylphosphine in 50 ml of toluene was stirred for three days. The product was filtered to yield 17g (85%) mp 198-200°C). NMR 8.1 - 7.5 (15H, aromatic protons, m); 6.1 - 5.08 (2H, olefinic protons, m); 4.8 - 4.48 (2H,$=CHC\underline{H}_2P^+$, dd, J = 15 cps, J = 7 cps); 2.2 - 1.92 (2H, $CH_3C\underline{H}_2CH=$, m); 0.95 (3H, $C\underline{H}_3CH_2$, t, J = 7 cps).

Preparation of 7-hydroxyheptanal

A three necked flask was charged with 16.8g (0.3 mol) of KOH and 360 ml of water. Ninety grams (0.3 mol) of 9,10,16-trihydroxyhexadecanoic acid were added, and the mixture was stirred vigorously. To the suspension , 300 ml of chloroform were added, followed by 31.18g (0.35 mol) of KIO_4 added portionwise at 35-40°C. After the addition had been completed, the mixture was cooled to 20°C and stirred for 15 min. The mixture was filtered, and the aqueous phase of the filtrate was washed with $CHCl_3$ (3 x 30 ml). The original phase and the extractions were stirred together with 108 ml of a saturated solution of

Na_2CO_3 and 144 ml of a saturated solution of $NaHCO_3$ for 90 min. The organic layer was dried over $MgSO_4$. After removal of the solvent it yielded 32 g of crude product (83%), as viscous liquid, which solidified when very pure. NMR 9.8 (1H, C$\underline{H}$O, broad singlet) ; 3.7 (2H, C$\underline{H}_2$OH, t, J = 7 cps); 2.5 (2H, C$\underline{H}_2$CO, t, J = 7 cps); 1.98 - 1.32(8H, CH_2, m).

Typical procedure for the Wittig reaction

A triple necked flask was charged with 0.05 mol of phosphonium salt and 60 ml of solvent (under an Ar atmosphere). Twenty milliliters of a solution of 0.1 M of base was added dropwise to the suspension. After the appearance of the orange color that characterized the ylide, the mixture was stirred for another hour. A solution of 0.05 mol of aldehyde in 60 ml of solvent was added dropwise to the reaction mixture. Fifteen minutes after the addition of the aldehyde had been completed, 45 ml (1/3) of the solution were transferred to another flask which contained 5 ml of absolute ethanol (Fraction I) and stirred under an Ar atmosphere. Thirty minutes after the addition of the solution to the ethanol, 2 ml of glacial acetic acid were added.

After withdrawing Fraction I, 0.04 mol of base was added to the original solution. Fifteen minutes later, another 45 ml were withdrawn (Fraction II) and treated as Fraction I.

The original solution was stirred for another 3 h after which time 10 ml of absolute ethanol were added, and the solution was then stirred overnight. On the next day 3 ml of glacial acetic acid were added (Fraction III).

The different fractions were acetylated in the following manner:

The solvent was removed, 5 ml of pyridine and 5 ml of acetic anhydride were added, and the mixture was stirred for 3 h. Then the mixture was poured into ice, extracted with petroleum ether, washed with 5% HCl, 10% $NaHCO_3$, 9:1 v/v DMSO: H_2O solution, H_2O, brine , and then dried over $MgSO_4$. Crude products were obtained after evaporation of the solvent.

The different fractions were purified by preparative TLC (two elutions with 2% ether in petroleum ether). Then, samples of the different fractions were subjected to GLC on a SP-2340 column, to check the composition of the diene that was obtained. Each sample was injected (1-2 μl) twice (± 1%).

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