

THE STEREOCHEMISTRY OF THE WITTIG REACTION WITH NON-STABILIZED AND SEMISTABILIZED YLIDS¹

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Abstract—The influence of a number of factors (solvent, inorganic halides, excess reactant, reaction time, etc.) on the reaction stereochemistry of the non-stabilized ylid I and the semistabilized ylid II with aldehydes has been investigated. In polar, aprotic solvents (DMF) the reaction is independent of the presence of salts. In such solvents ylid I gives predominantly *cis* olefins, while with ylid II the reaction is non-stereospecific. In non-polar solvents the stereochemistry of the reaction is salt-dependent. In the absence of salts, in non-polar media the non-stabilized ylid I yields selectively *cis* olefins and the semistabilized ylid II gives predominantly *trans* olefins. The results indicate that in benzene in the absence of salts the first reaction stage (formation of betaine intermediates) is rate determinant for both types of ylids and that the stereochemistry of the reaction is governed by kinetic factors. It has been found that in benzene LiI augments the yield of *cis* olefin in the case of semistabilized ylids and of *trans* olefins in the case of non-stabilized ylids. This effect of LiI on the stereochemistry of the reaction may be explained by its coordination with the intermediate betaine. In the case of semistabilized ylids the coordination promotes formation of erythro betaines, which (providing the first stage of the reaction is the rate-determining one) increase the yield of *cis* olefin. In the case of non-stabilized ylids coordination of LiI with the betaine so retards the second stage of the reaction (decomposition of the betaine into the end products) that this stage becomes rate-determinant. Consequently the stereochemistry of the reaction comes now under thermodynamic control with resultant increase in *trans* olefin. A number of recommendations are given for steric control of the Wittig reaction in the case of non-stabilized and semistabilized ylids.

SOME years ago we discovered the possibility of sterically controlling the Wittig reaction by appropriate selection of environmental and structural factors.¹⁻⁴ These findings were made use of for the stereospecific synthesis of various naturally occurring unsaturated acids of the oleic,^{5,6} linoleic⁷ and eleostearic^{8,9} series (see the Review¹⁰).

The object of the present work was to determine the areas wherein the Wittig reaction is amenable to steric control in the case of non-stabilized and semistabilized ylids. For this purpose the dependence of the reaction stereospecificity of these ylids

¹ For a preliminary communication see L. D. Bergelson, V. A. Vaver, L. I. Barsukov and M. M. Shemyakin, *Tetrahedron Letters* No. 38, 2669 (1964).

² L. D. Bergelson, V. A. Vaver, L. I. Barsukov and M. M. Shemyakin, *Dokl. Akad. Nauk SSSR* **143**, 111 (1962).

³ L. D. Bergelson and M. M. Shemyakin, *Tetrahedron* **19**, 149 (1963).

⁴ L. D. Bergelson and M. M. Shemyakin, *Pure and Appl. Chem.* **9**, 271 (1964).

⁵ L. D. Bergelson, V. A. Vaver, V. Yu. Kovtun, L. B. Senyavina and M. M. Shemyakin, *Zh. Obshch. Khim.* **32**, 1802 (1962).

⁶ L. D. Bergelson, V. A. Vaver, L. I. Barsukov and M. M. Shemyakin, *Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk* 1417 (1963).

⁷ L. D. Bergelson, V. A. Vaver and M. M. Shemyakin, *Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk* 1900 (1960).

⁸ L. D. Bergelson, V. D. Solodovnik and M. M. Shemyakin, *Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk* 1315 (1962).

⁹ L. D. Bergelson, E. V. Dyatlovitskaya and M. M. Shemyakin, *Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk* 388 (1963).

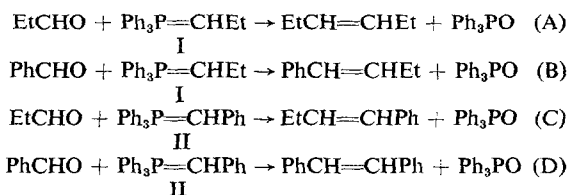
¹⁰ L. D. Bergelson, M. M. Shemyakin, *Angew. Chem.* **76**, 113 (1964).

upon a number of environmental factors, particularly the nature of the solvent and the halogen salts was investigated.

RESULTS

In order to correctly assess the effect of the halogen salts on the course of the Wittig reaction it must be carried out both in the presence and absence of the salts. As is well known, reaction with semistabilized or non-stabilized ylids heretofore always occurred in the presence of alkali metal salts formed alongside the ylid by the action of the alkali agents on the corresponding phosphonium salt. We found that benzene solutions of unstabilized ylids may be freed of lithium halide by their filtration in a dry, inert gas. With certain care this operation may be accomplished without significant loss of ylid. The resultant dark red filtrate contains no halide ions and may be used for olefinating aldehydes. Salt-free solutions of non-stabilized ylids in polar solvents can be prepared by evaporation of the benzene filtrate in vacuum and dissolving the residue in the desired polar solvent.

In the first stages of our work^{2,3} we investigated the effect of salts by adding a suspension of lithium halide in benzene to a benzene solution of the ylid (prepared by reaction of butyllithium with phosphonium chloride and thereby containing LiCl). The fine suspensions obtained by neutralizing benzene solutions of butyllithium with dry, gaseous hydrogen halides often exerted a marked influence on the stereochemistry of the Wittig reaction. The degree of this influence, however, was greatly dependent on the dispersity of the halides and the olefins were obtained in low yields and were accompanied by difficultly removable contaminants which sometimes produced variable results.* Therefore, in subsequent studies LiI or LiBr suspensions were not added to the ylid already containing LiCl, but butyllithium was reacted directly with the corresponding phosphonium chloride, bromide or iodide. In this way the experiments became reproducible and the results could be unambiguously interpreted, since each experiment was carried out in the presence of a single instead of two lithium salts. By this means, a comparative study of the stereochemistry of the following four reactions was carried out.



All reactions were carried out under standard conditions (Experimental). The total yield of olefins and the *cis:trans* isomer ratios were determined by GLC. The possibility of olefin isomerization under the reaction conditions, during treatment of the reaction mixture and during the chromatographic procedure was excluded and was continuously checked by special control experiments. The results obtained are summarized in Table 1.

I. Stereochemistry of the Wittig reaction in the absence of inorganic halides

The results obtained when reactions A–D were carried out in the absence of inorganic halides, show a high specificity of reaction A in both polar and non-polar

* This evidently was the reason for the divergence between some of our data and that of H. O. House *et al.*¹¹

¹¹ H. O. House, V. K. Jones, G. A. Frank, *J. Org. Chem.* **29**, 3327 (1964).

TABLE 1. EFFECT OF SOLVENT AND LITHIUM HALIDES ON THE STERIC COURSE OF REACTIONS A-D*

No. of run	Reaction	Solvent	<i>cis:trans</i> Olefin ratio			
			In the absence of salts	In the presence of		
				LiCl	LiBr	LiI
1	A	DMF	93:7	94:6	94:6	95:5
2	B	DMF	79:21	73:27	71:29	74:26
3	C	DMF	41:59	39:61	41:59	44:56
4	D	DMF	-	60:40	62:38	63:37
5	A	Benzene	92:8	89:11	90:10	77:23
6	B	Benzene	91:9	79:21	60:40	35:65
7	C	Benzene	18:82	21:79	27:73	41:59
8	D	Benzene	34:66	38:62	50:50	45:55
9	B	Hexane	89:11	83:17	79:21	61:39
10	C	Hexane	22:78	23:77	-	31:69
11	B	Ether	92:8	80:20	37:63	22:78
12	C	Ether	23:77	21:79	-	33:67

* The reactions were run at 20° for 1 hr with equimolar amounts of reactants.

medium (92–93% *cis* isomer; see Runs 1 and 5). The specifically *cis* course of the reactions of non-stabilized ylids of type I with aliphatic aldehydes had been observed several years ago, when carrying out the reaction in dimethylformamide,⁷ and has been repeatedly confirmed in our preparative studies on the synthesis of fatty acids with *cis* ethylenic bonds.^{8–10} If propionic aldehyde was replaced by benzaldehyde (reaction B), the *cis*-specificity of carbonyl olefination remained high in benzene, hexane and ether, but diminished somewhat in dimethylformamide (Runs 2, 6, 9 and 11; without LiX). With benzylidenetriphenylphosphorane (II), however, the same aldehydes give predominantly the *trans* isomers (Reactions C and D; Runs 3, 7, 8, 10 and 12; without LiX).

II. Stereochemistry of the Wittig reaction in the presence of inorganic halides

The data obtained do not confirm the viewpoint¹¹ that the effect of halides on the stereochemistry of the Wittig reaction is due only to the influence of the Lewis acid (coordination of the cation with carbonyl oxygen) and is independent of the nature of the Lewis base. The American authors base their conclusions primarily on the fact that the anion does not affect the stereochemistry of reaction C in dimethylformamide (see Run 3). However, we found that in this solvent the steric course of the reaction is also independent of the cation (see Table 2).

When the reactions A–D were carried out in non-polar solvents the stereochemical effect of lithium halide, contrary to House's¹¹ viewpoint, is definitely dependent on the nature of the halogen anion, i.e. of the Lewis base (Runs 5–12). At the same time the data of Table 1 show that the effect of the lithium halides in a non-polar medium depends also on the nature of the ylid. In the case of the non-stabilized ylid I the presence of LiI augments the yield of the *trans* isomer (Runs 5, 6, 9, 11), whereas in the case of the semistabilized ylid II the presence of the same salt leads to an increase in the *cis* isomer (Runs 7, 8, 10, 12).

III. Comparative study of reactions B and C

For a more detailed study of the stereochemical effect of the lithium halides reactions B and C were selected. These two reactions are convenient for comparative

TABLE 2. THE STERIC COURSE OF REACTION C
IN DIMETHYLFORMAMIDE IN THE PRESENCE OF
VARIOUS CATIONS*

No. of run	Cation present	<i>cis:trans</i> Olefin ratio
13	Li ⁺	39:61
14	Na ⁺	38:62
15	K ⁺	39:61

* The ylid II was prepared by reaction of BuLi, NaH or KH on triphenylbenzylphosphonium bromide. The reaction with aldehyde was carried out under the conditions indicated in the footnote to Table 1.

studies, because after formation of the betaines they differ little with respect to the steric factors, while differing greatly in the structure of the original ylids.

We found that in the absence of halides both reactions proceed at room temperature with high velocity in benzene for moderate concentrations of the reactants (0.1–0.2 mole/l). This can be seen from the yield of triphenylphosphine oxide, which according to IR data reaches a maximum value in 1 minute. When reaction B is carried out under similar conditions but in the presence of LiI it is strongly retarded at the betaine decomposition stage, the betaine being detectable as the hydroxyphosphonium bromide (III, R = Et, R' = Ph) formed by treating the reaction mixture with an ether solution of HBr¹² (see also Table 3, Run 17).



III

If reaction B is carried out in the absence of halides, after one minute only insignificant amounts of hydroxyphosphonium bromide can be detected (Run 16). The inhibiting effect of LiI on reaction B in benzene and hexane is also evident from the decrease in the over-all yield of olefin (see Table 4, Runs 20 and 22).

When reaction C is carried out in benzene (both with and without LiI) practically no hydroxyphosphonium bromide (III, R = Ph, R' = Et) can be detected after one minute since by that time the betaine is already decomposed into olefin and phosphine oxide (see Runs 18 and 19). The slight difference in the over-all yields of the

TABLE 3. RELATIVE AMOUNTS OF BETAINE AND OLEFIN AFTER
CARRYING OUT REACTIONS B AND C IN BENZENE FOR 1 MIN*

No. of run	Reaction	Salt present	Betaine:olefin ratio
16	B	—	<1:30
17	B	LiI	~1:2
18	C	—	<1:25
19	C	LiI	<1:35

* The reactions are carried out in benzene at 20° with equimolar amounts (0.5 mmoles) of reactants. One min after mixing of the reactants a ~0.6N ether soln of HBr was added to the reaction mixture which caused a ppt to form. The supernatant was decanted off, the ppt washed with ether and benzene and the wash liquids added to the main solution (soln 1). The ppt was treated with a benzene soln of BuLi, followed by water and the benzene soln was then separated (soln 2). The content of β -ethylstyrene in solns 1 and 2 was determined by gas chromatography.

¹² M. Schlosser, K. F. Christmann, *Angew. Chem.* 77, 682 (1965).

TABLE 4. THE EFFECT OF LITHIUM HALIDES ON THE YIELD OF β -ETHYLSTYRENE*

No. of run	Reaction	Solvent	% Yield of β -ethylstyrene			
			In the absence of salts	In the presence of		
				LiCl	LiBr	LiI
20	B	Benzene	80	62	70	33
21	C	Benzene	70	70	65	60
22	B	Hexane	71	52	46	11
23	C	Hexane	63	52	—	47

* The reactions were run for 1 hr at 20° with equimolar amounts of reactants.

olefins in Runs 21 and 23 (Table 4) indicates that the presence of lithium halides has little effect on the rate of reaction C.

We also investigated the effect of time, reactant ratio and twofold treatment of the reaction mixture with butyllithium on the steric course of reactions B and C (see Tables 5, 6 and 7).

As Table 5 indicates when reaction B is carried out in the absence of salts its steric course is independent of time, but the presence of lithium halides brings about a change in the proportion of stereoisomers with time (Runs 24–27). The stereospecificity of the reaction falls quite rapidly at first, and then becomes constant. This effect is more marked in the case of LiI than LiCl or LiBr. The steric course of reaction C is time-independent both in the presence and absence of lithium halides (Runs 28 and 29). The stereochemistry of the latter reaction is also independent of the reactant ratio (Table 6, Runs 39–46). A twofold excess of ylid or aldehyde likewise has no effect on the steric course of the reaction B in dimethylformamide (Runs 30–33). However in benzene in the presence of LiI an increase in the relative amounts of ylid or aldehyde sharply enhances the relative yield of the *cis* isomer (Runs 36–38).

Finally the *trans* effect discovered recently¹³ by treatment of betaines with butyllithium also can be observed only in the case of reaction B and then only in the presence of LiI (see Table 7, Runs 47–50). When butyllithium is added to the reaction mixture one minute after mixing together the reactants, a change in the steric course of the

TABLE 5. THE TIME DEPENDENCE OF THE STERIC COURSE OF REACTIONS OF B AND C*

No. of run	Reaction	Time	<i>cis:trans</i> β -Ethylstyrene ratio			
			In the absence of salts	In the presence of		
				LiCl	LiBr	LiI
24	B	1 min.	90:10	90:10	75:25	68:32
25	B	5 min.	—	85:15	68:32	46:54
26	B	1 hr	91:9	79:21	60:40	35:65
27	B	15 hrs	—	78:22	62:38	33:67
28	C	1 min.	19:81	22:78	26:74	43:57
29	C	1 hr	18:82	21:79	27:73	41:59

* The reactions were run in benzene at 20° with equimolar amounts of reactants.

¹³ M. Schlosser and K. F. Christmann, *Angew. Chem.* **77**, 736 (1965).

TABLE 6. EFFECT OF EXCESS REACTANTS ON THE STERIC COURSE OF REACTIONS B AND C*

No. of run	Reaction	Solvent	Salt present	Ylid:aldehyde ratio	<i>cis:trans</i> Olefin ratio
30	B	DMF	NaCl	1:1	75:25
31	B	DMF	NaCl	2:1	71:29
32	B	DMF	NaI	1:1	74:26
33	B	DMF	NaI	2:1	73:27
34	B	Benzene	LiCl	1:1	79:21
35	B	Benzene	LiCl	2:1	88:12
36	B	Benzene	LiI	1:1	35:65
37	B	Benzene	LiI	2:1	65:35
38	B	Benzene	LiI	1:2	59:41
39	C	DMF	NaCl	1:1	39:61
40	C	DMF	NaCl	2:1	38:62
41	C	DMF	NaI	1:1	44:56
42	C	DMF	NaI	2:1	48:52
43	C	Benzene	LiCl	1:1	21:79
44	C	Benzene	LiCl	2:1	20:80
45	C	Benzene	LiI	1:1	41:59
46	C	Benzene	LiI	2:1	44:56

* The reactions were run for 1 hr at 20°. When carried out in dimethylformamide the ylid was obtained by the action of NaH on the corresponding phosphonium salts; in benzene, by the action of BuLi on a benzene suspension of the salts.

reactions can be observed only in Run 48. Apparently only in this case does the mixture still hold sufficient undecomposed betaine at the time of adding BuLi.

IV. Relative reactivity of ylids and aldehydes

In order to evaluate the relative reactivity of the ylids and aldehydes, competitive experiments were performed in which the ylid II was simultaneously treated with propionic aldehyde and benzaldehyde, or one of these aldehydes was simultaneously reacted with ylids I and II. The reaction of the ylid II with *m*-chlorobenzaldehyde was also investigated to elucidate the dependence of the rate of olefination on the electrophilicity of the aldehyde.

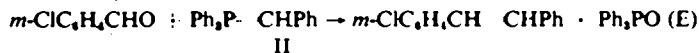


TABLE 7. EFFECT OF TREATMENT OF BETAINES WITH BUTYLLITHIUM ON THE STEREOCHEMISTRY OF REACTIONS B AND C*

No. of run	Reaction	Salt present	<i>cis:trans</i> β -Ethylstyrene ratio	
			Without BuLi treatment of the betaine ^b	With BuLi treatment of the betaine ^c
47	B	—	90:10	87:13
48	B	LiI	60:40	30:70
49	C	—	18:82	17:83
50	C	LiI	43:57	43:57

* The reactions were run at 20° in benzene with equimolar amounts of reactants.

^b One min after mixing together the reactants the reaction mixture is treated with water.

^c BuLi is added 1 min after mixing the reactants and another min later the reaction mixture is treated with water.

TABLE 8. RELATIVE REACTIVITY OF YLIDS AND ALDEHYDES*

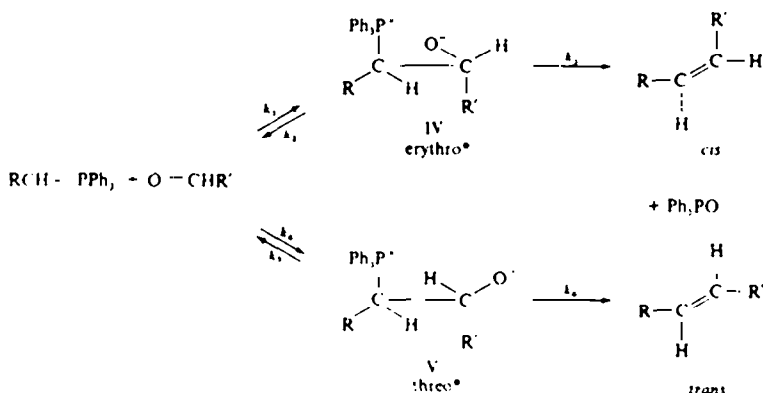
No. of run	Competitive reactions	Ylids	Aldehydes	Ratio of olefins	
51	A:C	I + II	EtCHO	Hex-3-ene:	β -ethylstyrene 4:4:1
52	C:D	II	EtCHO + PhCHO	β -Ethylstyrene:	stilbene = 1:4:6
53	B:D	I + II	PhCHO	β -Ethylstyrene:	stilbene = 5:1:1
54	D:E	II	PhCHO + <i>m</i> -ClC ₆ H ₄ CHO	Stilbene:	<i>m</i> -chlorostilbene = 1:6:7

* The reactions were run in benzene at 20° with equimolar amounts of reactants (0.5 mmoles each). After 1 min the mixture is treated with water.

The results obtained (Table 8) show that the non-stabilized ylid I reacts faster than the semistabilized ylid II. Propionic aldehyde reacts slower than benzaldehyde, whereas *m*-chlorobenzaldehyde reacts much faster than benzaldehyde.

DISCUSSION

The stereochemical results obtained may be interpreted in terms of the earlier concepts,⁴ according to which the steric course of carbonyl olefination depends on the effect of environmental and structural factors upon the rate of formation and decomposition of the betaines IV and V.



The high stereospecificity of reactions A and B in the absence of halides (see Runs 1, 2, 5, 6, 9 and 11) shows that the steric course of the reactions of the non-stabilized ylid I with aldehydes are controlled by kinetic factors. Evidently *cis* olefination can be realized only when the first stage of the reaction is the rate determining one and is nearly or completely irreversible, under the proviso of predominant formation of the erythro betaine ($k_1 > k_4$, $k_2 < k_3$ and $k_5 < k_6$). As for reactions C and D, there is as yet no unambiguous proof of the rate determining stage for reactions of the semistabilized ylids of type II with aldehydes. However, for the more stabilized carbonylcontaining ylids $\text{Ph}_3\text{P}=\text{CHCOR}$ (VI) it was found by kinetic measurements¹⁴⁻¹⁸ that the rate of decomposition of the corresponding

* On the terms threo and erythro as applied to betaines see.⁴

¹⁴ H. Goetz, F. Herdel and H. Michaelis, *Naturwissenschaften* **50**, 496 (1963).

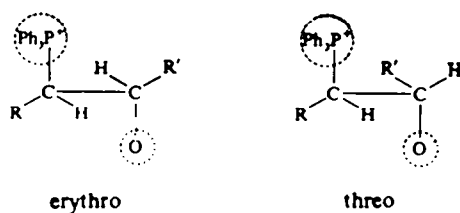
¹⁵ S. Fliszár, R. F. Hudson and G. Salvatori, *Helv. Chim. Acta* **46**, 1580 (1963).

¹⁶ A. J. Speziale and D. E. Bissing, *J. Am. Chem. Soc.* **85**, 1888 (1963).

¹⁷ A. J. Speziale and D. E. Bissing, *J. Am. Chem. Soc.* **85**, 3878 (1963).

¹⁸ D. E. Bissing and A. J. Speziale, *J. Am. Chem. Soc.* **87**, 2683 (1965).

betaines significantly exceeds the rate of their formation, the threo betaine V more readily decomposing into the end products and less readily into the starting compounds than the erythro betaine IV ($k_2/k_3 > k_6/k_4$). Since the ylids II occupy an intermediate position between ylids of the type I and VI, it is probable that the same relations are retained in reactions C and D. This assumption finds support in data from the reactions of various ylids and aldehydes under competitive conditions (Table 8). If the rate of the reaction of ylid II were determined by the rate of decomposition of the betaines into the end products, one should expect II to react more rapidly than I with propionic aldehyde, since in the first case betaine decomposition is facilitated by resonance in the transition state.⁴ Actually the reverse is true; namely the reactivity of the ylids falls with decrease in their nucleophilicity (see Runs 51 and 53). On the other hand *m*-chlorobenzaldehyde reacts with ylid II more rapidly than benzaldehyde whereas the latter reacts more rapidly than propionic aldehyde (see Runs 52 and 54), i.e. the reactivity of the aldehydes increases with increase in their electrophilicity, a fact that can be rationalized on the basis of the assumption that rate determining is the first stage of the reaction. Hence in the absence of salts both with the non-stabilized ylid I and the semistabilized ylid II it is formation of the betaine which is the rate determining stage. From this one may draw an assumption as to why the semistabilized ylid II gives predominantly the threo betaine (*trans* olefin), whereas under similar conditions reaction with the non-stabilized ylid I selectively yields the erythro betaine (*cis* olefin) (Table 1). It has already been pointed out⁴ that predominant formation of the erythro betaine IV is possible when there are factors favoring a decrease in electrostatic attraction between the phosphorus and oxygen and an increase in their sterical repulsion. In a polar solvent such a factor is solvation of the phosphorus and oxygen.



In non-polar solution the formation of erythro betaines might be promoted by association of the non-stabilized ylid I or by complex formation with the betaine.* The stabilized ylid II is less inclined towards association, because the electronic density on its methine carbon is lessened by resonance. The value of k_1/k_4 may therefore in this case be much lower than in the reactions of the ylid I, and when the first stage is rate determining this will lead to diminished stereospecificity (or predominant formation of the *trans* isomer).

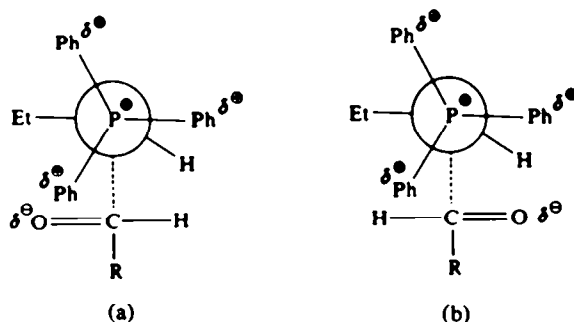
It is possible that the steric course of the reaction of ylids I and II is due to another cause. In compliance with the resonance and steric requirements, the preferred conformation of the ylid would be the one wherein the substituent on the ylid carbon (Et for ylid I and Ph for ylid II) is situated between the two phenyl groups of the

* Non-stabilized phosphoranes of type I should strongly associate in a non-polar medium, because, judging from their IR spectra, they exist almost wholly in the ylid form.¹⁰

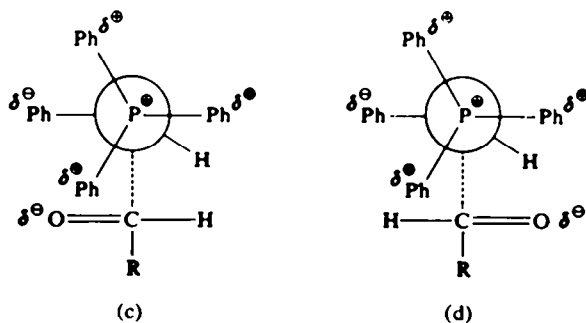
¹⁰ W. Lüttke and K. Wilhelm, *Angew. Chem.* 77, 867 (1965).

phosphorus atom and is transoidal to the third phenyl group. The stereoelectronic consequences of such an arrangement of the phenyl groups must be taken into account when comparing the transition states arising in the formation of the diastereomeric betaines.

In the case of ylid I the formation of an erythro betaine is facilitated by the attraction of one of the electron deficient phenyl groups of the ylid and the carbonyl oxygen of the aldehyde since in the corresponding transition state (a) these groups are much closer than in the transition state (b), leading to the threo betaine.



In the case of ylid II conjugation of the ylid carbon phenyl leads to an increase in the electron density in its *o*- and *p*-positions and this as was earlier suggested⁴ hampers formation of the erythro betaine [transition state (c)] because of the mutual repulsion of the negative groups of the ylid and aldehyde.



Since with the first stage of the reaction as rate determining the stereochemical result is determined mainly by the relative rates of formation of the diastereomeric betaines, the effect of the above-mentioned stereoelectronic factors leads to predominant formation of the *cis* olefin in the case of ylid I and to the *trans* isomer in the case of ylid II.

It can be seen from Table I that when reactions A-D are carried out in benzene, lithium halides always lower the stereospecificity, the effect being stronger with LiI than with LiCl. It may be assumed that this lowering of specificity by LiI and other halides is due to their complex formation with the betaine (on the complex formation of betaines with lithium halides see^{15,12,20}). In the case of the non-stabilized ylid I betaine halide interaction so retards the second stage of the reaction (k_3 and k_4) that

²⁰ M. Schlosser and K. F. Christmann, *Angew. Chem.* 76, 683 (1964).

it becomes the rate determining one. As a result the first stage of the reaction becomes more reversible, leading to an increase in probability of the initially formed erythro betaine IV to pass over into the threo form V. Hence retardation of the second stage of the reaction of ylid I by LiI causes its steric course to be governed by thermodynamic rather than kinetic factors. Therefore the reaction proceeds more and more via the threo betaine V, which in comparison with the erythro isomer IV more readily decomposes into the end products and less readily into the initial reactants. This mechanism of action of LiI is confirmed not only by isolation of the betaine as the hydroxyphosphonium bromide III, but also by the results of the investigation into the dependence of the stereochemistry of reaction B relative to time and to the reactant ratio (see Tables 5 and 6). It follows from the data of Table 5 (Runs 24-27) that equilibrium between the betaines is established relatively slowly in the presence of lithium halides. This shows that k_2 and k_3 are here much lower in value than k_1 and k_4 , which is explained by the high energy content of ylid I. In the initial period, when the amount of erythro betaine IV is still considerable, the reaction is more stereospecific and only with time is its stereospecificity lowered, the effect being more marked with LiI than with LiBr or LiCl (see Runs 24-27). On the other hand increase in yield of the *cis* isomer in reaction B with change in the reactant ratios (Runs 36-38, Table 6) is explained by the fact that in the excess of one of the reactants, the values of k_2 and k_3 fall thereby hindering still more the equilibration and transition of the initially formed erythro isomer IV into the threo form V.

At the same time these data serve as proof of the reversibility of betaine formation in reactions of the non-stabilized ylids of type I.

As for the effect of lithium halides on the reaction of the semistabilized ylid II in benzene, the data we have obtained lead to the conclusion that in this case lithium halides do not retard decomposition of the corresponding betaines into the end products to such an extent, that this stage becomes the rate determining one. Indeed: (1) The rate of reaction C depends little on the presence or absence of halides (Runs 21 and 23, Table 4); (2) The presence of betaine in the reaction mixture is practically undetectable one minute after start of the reaction (Runs 18, 19, Table 3 and Runs 49, 50, Table 7); (3) The stereoisomer ratio does not change with time either in the presence or in the absence of LiI (Runs 28 and 29, Table 5); (4) Finally the increase in yield of *cis* isomer under the action of lithium halides shows that the steric course of reactions C and D continues to remain under kinetic control (Runs 7 and 8, Table 1). The steric effect of lithium halides is here as in the case of non-stabilized ylid I due to their coordinating with the betaines. However, since in the case of ylid II the stage of betaine formation is still the rate determining one, betaine-halide coordination (promoting formation of the erythro betaine⁶) increases the yield of *cis* olefin. In this connection it should be mentioned that the *cis* effect of LiI is observable under certain conditions also in reactions of the CO-stabilized ylids VI.¹¹

The results of the present study have led to a refinement of earlier suggestions for the steric control of the Wittig reaction.¹⁰ The reaction in the absence of salts allows one to carry out *cis* olefination of aldehydes by non-stabilized ylids of type I. Using non-polar solvents, the same procedure permits the *trans* olefination of aliphatic aldehydes by semistabilized ylids of type II. When the reaction is carried out in the presence of halides, dimethylformamide should be used as solvent if one desires to increase the *cis* isomer yield. The use of LiI for the same purpose is feasible when olefination is carried out in a non-polar medium with ylids of type II. On the

other hand when it is necessary to carry out the reaction with non-stabilized ylids of type I in a non-polar medium in the presence of LiI, then, in order to increase the yield of the *cis* isomer, one should take an excess of ylid. However, it must also be remembered that in each concrete case the magnitudes of the steric effects of the solvent and inorganic salts may depend on the solubilities of the ylids, betaines and their complexes.

EXPERIMENTAL

All preparations and reactions of the ylids were carried out in argon. Solvents were purified by common methods and prior to use distilled over NaH. The phosphonium salts were recrystallized and dried *in vacuo* at 100° for several hr. Aldehydes were distilled and stored under argon and were made up into solns of known concentration immediately before use in the reaction with the ylids.

Analysis of stereoisomeric olefins formed in the reactions A-D

The *cis:trans* ratio of the olefinic products and their overall yields were determined by GLC with an internal standard using a Pye Argon Chromatograph (β -ethylstyrenes and stilbenes) or a Chrom-1 apparatus (hexenes). The detectors were calibrated with standard mixtures of known concentrations. The analysis of *cis* and *trans* β -ethylstyrenes was carried out at 90° on a 1200 \times 5 mm column with 10% polysiloxane SKTV-1 on chromosorb W (60-80 mesh); argon flow 40-50 ml/min. The same column was used at 170° for the analysis of *cis* and *trans* stilbenes. The *cis:trans* ratios and overall yields of hex-3-enes were determined on a 2000 \times 5 mm column with a sat AgNO₃ soln in triethylene glycol on chromosorb P (30-60 mesh) at 0°; N flow 50-60 ml/min. Retention times are given in Table 9.

TABLE 9. GAS CHROMATOGRAPHIC IDENTIFICATION OF *cis* AND *trans* OLEFINS FORMED IN REACTIONS A-D

Olefins	Internal standard	Relative retention times of		
		<i>cis</i> isomer	<i>trans</i> isomer	Internal standard
Hex-3-enes	n-Octane	0.46	0.27	1.00
β -Ethylstyrenes	n-Dodecane	0.52	0.71	1.00
Stilbenes	n-Octadecane	0.30	0.65	1.00

All runs were made in duplicate. The deviations between runs of the same type did not exceed 10% of the theoretical for the olefin yields and 2-3% for the *cis:trans* ratios (in experiments with ylid I in the presence of LiI the deviations sometimes reached 10%). Special experiments showed that no isomerization of olefins takes place under the reaction and the gas chromatography conditions (see ²¹). Individual *cis* and *trans* hex-3-enes were prepared by reduction of hex-3-yne²² and were 95% pure as shown by GLC.

Preparation of phosphonium salts

Benzyltriphenylphosphonium chloride, bromide and iodide were prepared by heating equimolar amounts of triphenylphosphine and benzylhalide in refluxing benzene. *n*-Propyltriphenylphosphonium bromide and iodide were obtained by refluxing a soln of triphenylphosphine in *n*-propylhalide. For preparation of *n*-propyltriphenylphosphonium chloride an acetonitrile soln of triphenylphosphine and *n*-propylchloride (50% excess) was heated at 140-150° in a sealed tube. For the reaction times, yields and m.p.s of prepared salts see Table 10.

²¹ L. D. Bergelson, V. A. Vaver, L. I. Barsukov and M. M. Shemyakin, *Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk* 1053 (1963).

²² K. N. Campbell, L. T. Eby, *J. Am. Chem. Soc.* 62, 216 (1941).

TABLE 10. REACTION TIMES, YIELDS AND MELTING POINTS OF PREPARED PHOSPHONIUM SALTS

Salt	Reaction time (hr)	% yield	M.p.
[Ph ₃ PCH ₂ Ph]Cl	6	60	298–300° (from MeOH–ether) ²²
[Ph ₃ PCH ₂ Ph]Br	0.5	68	283–285° (from EtOH) ²²
[Ph ₃ PCH ₂ Ph]I	0.5	77	257–260° (from EtOH) ²²
[Ph ₃ PCH ₂ Et]Cl	18	54	219–220° (from DMF)*
[Ph ₃ PCH ₂ Et]Br	5	45	230–231° (from MeOH–ether) ²²
[Ph ₃ PCH ₂ Et]I	0.5	62	205–206° (from EtOH) ²²

* (Found: C, 74.07; H, 6.72; Cl, 10.17; P, 9.04. Calc. for C₁₁H₁₃ClP: C, 74.00; H, 6.51; Cl, 10.40; P, 9.09%).

Standard Conditions of Reactions A–D (Table I).

1. In the presence of lithium halides

In benzene. A 1M benzene soln of n-butyllithium (0.5 ml) was added at 20° to a suspension of 0.5 mmoles of the appropriate phosphonium salt in 1 ml benzene. After stirring for 30 min, 1 ml of a benzene soln containing 0.5 mmoles of aldehyde and 0.5 mmoles of the internal standard was added and the stirring was continued for 1 hr. To the reaction mixture was added 3 ml water, the benzene layer was washed with water, dried over CaCl₂ and examined by GLC.

In dimethylformamide. To 0.5 mmoles of the phosphonium salt was added at 20° an equimolar amount of n-butyllithium (1M benzene soln) and the mixture was stirred for 30 min. The benzene was distilled off *in vacuo* and to the residue was added 1.5 ml DMF followed by a soln of 0.5 mmoles of the aldehyde in 1 ml DMF. The mixture was left to stand for 1 hr and then diluted with 5 ml water, after which 2.5 ml benzene containing 0.5 mmoles of the internal standard was added; the hydrocarbon layer was washed with water (2 × 2 ml), dried with CaCl₂ and examined by GLC.

In hexane and ether. The runs in hexane and ether were carried out exactly as in DMF except for the addition of benzene after ending the reaction. The internal standard was added together with the aldehyde.

2. In the absence of lithium halides

Ylids I or II were obtained by stirring of 5 ml of a 1M benzene soln of n-butyllithium with a suspension of 5 mmoles of the appropriate phosphonium salt in 7.5 ml of benzene for 30 min. The mixture was allowed to settle, filtered in dry argon and the resultant dark red soln of the ylid (solution A; 0.4 moles/l) was used for further experiments. The soln exhibits a negative Beilstein test.

In benzene. To 1 ml of soln A was added 1 ml of a benzene soln containing 0.4 mmoles of aldehyde and 0.4 mmoles of the internal standard. The mixture was stirred for 1 hr and treated as described above for the reactions in the presence of lithium halides.

In other solvents. An aliquot of solution A was evaporated to dryness *in vacuo*, the residue was dissolved in the appropriate solvent and further work carried out as described for the reactions in the presence of lithium halides.

Determination of the rates of reactions B and C

Aliquote volumes of 0.2M benzene solns of the ylid I and benzaldehyde or the ylid II and propionic aldehyde were mixed and the mixture was poured as quickly as possible into a 0.0117 cm NaCl cell. Estimation of the P=O (1203 cm⁻¹) bond intensity* shows that already within 1 min the yield of triphenylphosphine oxide amounts to 75–80%; it is not changed by increasing the reaction time or by treating the reaction mixture with water.

* The IR spectra were determined by Mrs. L. B. Senyavina on a Zeiss, model UR-10, recording spectrophotometer.

²² A. Michaelis and H. Soden, *Liebigs Ann.* **229**, 295 (1885).