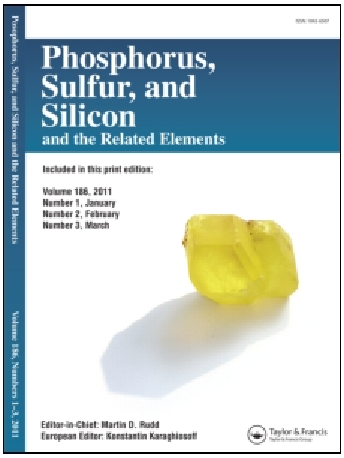

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TEMPERATURE AND SOLVENT EFFECTS IN WITTIG REACTIONS

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TEMPERATURE AND SOLVENT EFFECTS IN WITTIG REACTIONS

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The rates of the Wittig reactions between 4-nitrobenzaldehyde and five stabilized phosphoranes, $Ph_3P{=}CHC(O)R$, where R = OMe, OPh, NPh_2, Me, and Ph, are studied in benzene, dimethylformamid (DMF), and methanol, at 25, 35, and 45°C. The activation energies, E, when plotted as function of the corresponding activation entropies, ΔS^*, are found in two different regions in the E – ΔS^* diagram, approximately described by two parallel lines, one belonging to the reactions in benzene and DMF, the other to the reactions in methanol. The differences in the activation parameters in aprotic and protic solvents are most likely a consequence of strong H-bonding in protic solvents. Reaction mechanisms in aprotic and protic solvents are discussed.

Key words: Stabilized phosphoranes, 4-nitrobenzaldehyde, Wittig reaction, temperature and solvent effects.

In four previous papers[1–4] we have studied the influence of aprotic and protic solvents on the Wittig reaction of $Ph_3P{=}CHC(O)OPh$ and 4-nitrobenzaldehyde. It was found that the effect of the dielectric properties of the solvents on the rates correlated fairly well with the equation of Kirkwood[5]: Linear dependence between the logarithms of the rates, and the derived function of the dielectric constants, D – 1/D + 2, as long as the solvents belonged to related types, f.ex. hydrocarbons, chlorinated hydrocarbons, alcohols, and glycols.[4] The lack of a common dielectric relationship for all solvents, especially the discrepancy between the Wittig reactions in aprotic and protic solvents, pointed to important solvation differences, which might effect the rate of formation and decomposition of the betaine intermediate differently in aprotic and protic solvents.

Regarding the influence of temperature on Wittig reactions, it was observed that the activation parameters varied widely in aprotic and protic solvents, amounting to 5 to 8 kcal/M lower activation energy in the former, which, on the other hand, is counteracted by a very negative entropy (around −40 e.u.), resulting in rates which are lower in aprotic than in protic solvents.[1–3] However, within aprotic media of widely different dielectric properties, the activation parameters are often remarkably similar. Thus, the activation energies and entropies in benzene (D = 20), and acetonitrile (D = 55), are 10.6 and 10.5 kcal/M, and −37 and −35 e.u., respectively. For comparison, the activation energy and entropy in *n*-propylalcohol,[2] having exactly the same dielectric constant as benzene (D = 20), were 14.6 kcal/M and −21 e.u., respectively. Thus, existent data showed that the dielectric properties of the solvents correlated poorly with the activation parameters, especially when reactions in aprotic and protic media are compared.

In order to shed further light on the problem, the present paper reports solvent and temperature effects on Wittig reactions between five differently substituted phosphoranes and 4-nitrobenzaldehyde in two aprotic solvents, benzene and dimethylformamide (DMF), and one protic, methanol.

EXPERIMENTAL

Materials. Benzene (Merck Uvasol) and N,N-dimethylformamide (DMF, Fluka purris) were purified chromatographically by using aluminium oxide. The solvents were stored over molecular sieve, Type 4 Å, in desiccator. Methanol (Merck Uvasol) was used without further purification. 4-nitrobenzaldehyde (Fluka puriss) was purified by repeated recrystallization from ethanol, and dried in vacuum (m.p. 106.5°C). Triphenylphosphine oxide (Fluka puriss) was crystallized several times from benzene and petrol ether (b.p. 40–60°C) until constant m.p. 159°C. The five phosphoranes and the various alkenes formed during the Wittig reactions between the phosphoranes and 4-nitrobenzaldehyde (Table I), were synthesized according to descriptions in the literature,[5–9] except $Ph_2NC(O)CH{=}CHC_6H_4NO_2$, which was prepared in the following way: To 4-nitrocinnamoylchloride (1.5 g) in benzene (50 ml) was added pyridine (0.56 g) and diphenylamine (1.19 g) dissolved in benzene (50 ml). The reaction mixture was stirred and heated to 60°C for 6 hours. The pyridine chloride was filtered off and the filtrate evaporated to give the alkene, which after several recrystallizations from ethanol, gave a pure alkene, m.p. 168–69°C. (Found: C, 73.64; H, 5.03, N, 8.16; required C, 73.24; H, 4.68; N, 8.14%)

Kinetic procedure. The solutions were made up by weighing, and the molarity of each solution was calculated at various temperatures from the change in density with temperature of benzene, DMF, and methanol. Since the concentrations were very low, the densities of the solutions were supposed to be similar to the densities of the solvents. The reaction between the phosphorane and 4-nitrobenzaldehyde

TABLE I

The UV absorption maxima of the alkenes formed in the reactions of R-substituted phosphoranes, $Ph_3P{=}CHC(O)R$, and nitrobenzaldehyde in benzene, DMF, and methanol, together with the molar extinction coefficients of the alkenes, phosphoranes, and aldehyde at the same wavelength

Phosphorane R	Solvent	λmax Alkene	Molar extinction coefficient ε * ε_1 Alkene	ε_3 Aldehyde	ε_4 Phosphorane
-OMe	Benzene	307	18670	2704	3290
	DMF	308	19028	2819	2884
	Methanol	301	21637	2469	2453
-NPh 2	Benzene	320	19798	1663	7854
	DMF	323	20017	1485	7284
	Methanol	316	21999	850	7010
-OPh	Benzene	307	21246	2777	3906
	DMF	308	21241	2819	3965
	Methanol	303	25058	2093	3366
-Me	Benzene	308	19644	2631	4034
	DMF	312	19880	2580	3663
	Methanol	303	23654	2093	3908
-Ph	Benzene	317	22942	1753	7243
	DMF	321	24200	1540	8008
	Methanol	316	28825	850	11446

*The extinction coefficient, ε_2, of triphenylphosphine oxide was 0 in the three solvents.

TABLE II

Rate constants, k lM^{-1} s^{-1}, and activation parameters, E, kcal M^{-1}, and ΔS*, of the Wittig reactions between five R-substituted triphenylphosphine methylenes, $Ph_3P{=}CHR$, and 4-nitrobenzaldehyde in benzene (Bz), dimethyl formamide (DMF), and methanol (Met), together with the enthalpies, −ΔH, of the hydrogen bond associations of the same R-substituted triphenylphosphine methylenes and phenol (PhOH) in carbon disulphide

R	°C	Rate, k lM^{-1}s^{-1}			E, kcalM^{-1}			ΔS*, e.u.			ΔH [a]
		Bz	DMF	Met	Bz	DMF	Met	Bz	DMF	Met	PhOH
	25	0.14	0.082	0.57							
-C(O)OMe	35	0.20	0.11	1.02	5.4	4.5	10.2	-46	-50	-28	- 6.9
	45	0.25	0.13	1,70							
	25	0.016	0.013	0,35							
-C(O)OPh	35	0.023	0.018	0.70	7.0	6.2	12.8	-45	-49	-20	-6.6
	45	0.033	0.025	1.37							
	25	0.028	0.024	0.12							
-C(O)NPh$_2$	35	0.040	0.034	0.26	7.3	6.3	13.9	-43	-47	-18	-7.8
	45	0.060	0.048	0.51							
	25	0.0085	0.0062	0.0084							
-C(O)Me	35	0.015	0.0092	0.021	8.1	7.4	16.8	-43	-46	-14	-7.9
	45	0.020	0.014	0.051							
	25	0.0022	0.0019	0,0077							
-C(O)Ph	35	0.0038	0.0032	0.019	10.4	8.2	16.9	-38	-46	-14	-8.1
	45	0.0066	0.0046	0.046							

[a] Data from ref. 5.

was followed by measuring the UV absorption at the absorption peak of the alkene formed. Experimental details of the spectrophotometric procedure are described earlier.[2] The initial concentration range of the phosphorane and aldehyde was: $3.1–9.3 \cdot 10^{-4}$ M. The amount, $\underline{X}$, of the alkene formed at different time intervals were calculated applying the following equation:

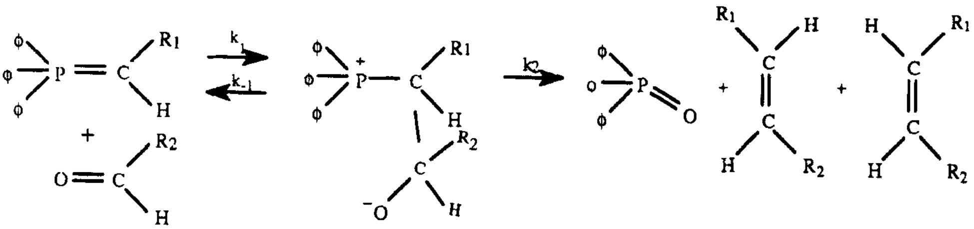
$$\underline{X} = \frac{\underline{A} - \underline{l}\underline{a}(\underline{\varepsilon}_3 + \underline{\varepsilon}_4)}{\underline{l}(\underline{\varepsilon}_1 + \underline{\varepsilon}_2 - \underline{\varepsilon}_3 - \underline{\varepsilon}_4)}$$

where $\underline{A}$ is the absorption of the reaction mixture at any time, $\underline{l}$ is the cell thickness (0.1 cm), $\underline{a}$ is the initial concentration of the phosphorane as well as aldehyde, and $\underline{\varepsilon}_1$, $\underline{\varepsilon}_2$, $\underline{\varepsilon}_3$, $\underline{\varepsilon}_4$, are the molar extinction coefficients of alkene, triphenylphosphine oxide, aldehyde, and phosphorane, respectively. The extinction coefficients of the five substituted phosphoranes, together with 4-nitrobenzaldehyde, and the alkenes formed in the respective Wittig reactions, were determined in benzene, DMF, and methanol (Table I).

The second order rate constants (Table II) at three different temperatures, are calculated from the following equation, using equimolecular concentrations of reactants: $kt = 1/(\underline{a} - \underline{x}) - 1/\underline{a}$. The reaction was followed at least to 40% completion. In methanol, where deviation from second order dependence was observed, only the linear part of the rate curve was used for calculation of the rate constants.

RESULTS AND DISCUSSION

Rate data, and activation parameters of the Wittig reactions of the five substituted phosphoranes with 4-nitrobenzaldehyde in benzene, DMF, and methanol are summarized in Table II. The data confirm earlier reported findings[4] of differences in the magnitude of the activation parameters in aprotic (benzene and DMF) and protic (methanol) solvents, amounting to 5 to 8 kcal/M lower activation energy in aprotic media, compensated by a much less negative entropy of activation in methanol. The compensating effect between the activation energy, E, and entropy, ΔS^*, is illustrated by the E $-$ ΔS^* plot in Figure 1. The activation parameters in aprotic and protic solvents are distributed approximately along two parallel lines. The line representing the reactions in aprotic solvents is displaced 7 kcal/M towards lower E-values, and 11 e.u. towards more negative entropy, than the line representing the same reactions in methanol. These differences are believed to be caused by different ratios between the rate constants k_1, k_{-1}, and k_2, of the Wittig reaction in aprotic and protic solvents:



Mathematically four distinct cases can arise from the above equation of the Wittig reaction[10]: a) rapid, irreversible betaine formation ($k_{-1} = 0$), and its rate determining decomposition to olefin and phosphine oxide; b) slow, irreversible, and rate determining formation of betaine ($k_{-1} = 0$), and its rapid decomposition to

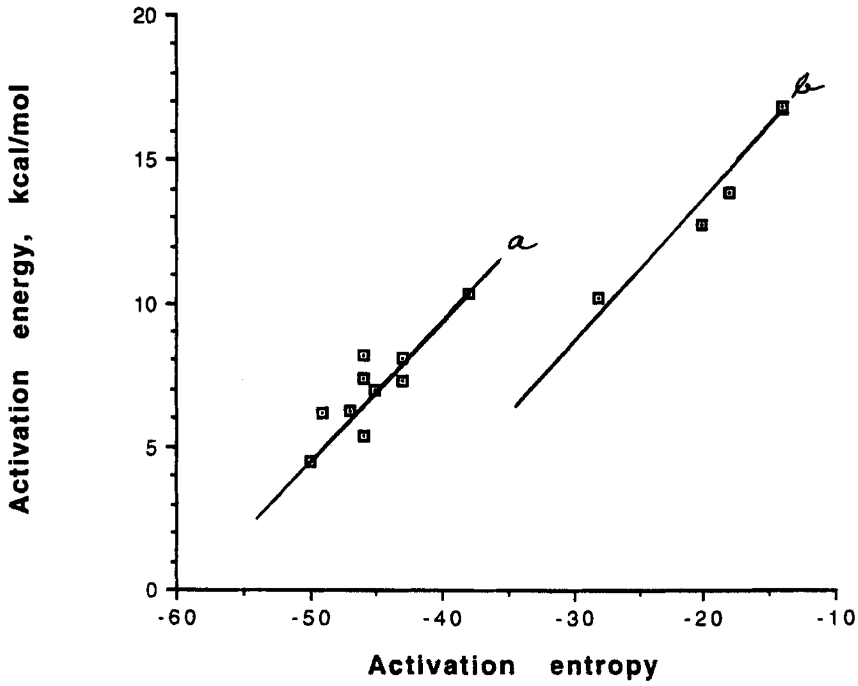


FIGURE 1 The plot of activation energy, E, against activation entropy, S*, of 5 Wittig reactions in a) benzene and DMF, b) methanol.

olefin and phosphine oxide; c) rapid, reversible, betaine formation ($k_{-1} \neq 0$), and its rate determining decomposition to products; d) slow, reversible, betaine formation ($k_{-1} \neq 0$), and its rapid decomposition to products.

Mechanisms a) and b) above can be ruled out, since betaine formed from epoxide and triphenylphosphine, in the presence of an aldehyde, yields an olefin derived from the aldehyde, in addition to the olefin formed from the original betaine.[10] This proves that the original betaine has decomposed to phosphorane, which thereafter has reacted with the aldehyde. Mechanism c), with $k_{-1} > k_2$ and k_1, in the above rate equation is, according to Speziale and Bissing,[10] poorly compatible with the effect of different substituents in phosphorane and aldehyde. These authors prefer mechanism d) where k_{-1} and k_2 are of same magnitude. Their judgement of the mechanism seems to be based only on Wittig reactions in aprotic solvents.

The Wittig reactions in alcohols show rate deviation from second order dependence on phosphorane and aldehyde. Already this information points to mutual changes of the rate constants k_1, k_{-1}, and k_2. Our earlier studies[2] of the reaction between $Ph_3P{=}CHC(O)OPh$ and 4-nitrobenzaldehyde in 15 different alcohols, including primary, secondary, and tertiary alcohols, showed that the deviation from second order rate dependence decreased with decreasing dielectric constant of the alcohol. This is in the same direction as the decreasing tendency of H-bond formation of the alcohols. The H-bond strengths between phenol and the 5 phosphoranes studied, amount to 6 to 8 kcal/M (Table II). Although the H-bond strengths are less in alcohols, the sum of the enthalpies of the H-bonds to the carbonyl groups of the phosphorane and aldehyde, should amount to several kcal/M, and therefore of same magnitude as the activation energy of the Wittig reaction in aprotic solvents.

The first step in the Wittig reaction (k_1), is bimolecular, the reverse step (k_{-1}), as well as the decomposition step (k_2), are both monomolecular. The kinetics, as well as the size of the rate constants, are accordingly expected to be differently influenced by the properites of the solvents. The deviation of the overall rate from second order dependence in alcohols, is most likely a consequence of the change in the rate ratio k_1/k_2. It is, however, important to stress the observation that the different polarities of the aprotic solvents have negligible effect on the kinetics of the Wittig reaction since the reaction remains second order, independent of the size of the dielectric constants of the aprotic solvents.[1] This points to internal saturation of the P^+ and O^- charges during formation of the betaine, a self-sufficient reaction little influenced by the surroundings.

A four-centered approach of the phosphorane and aldehyde, lays a strong restriction on the configuration on the collision complex. The small effect of the dielectric properties of the aprotic solvents, is in accordance with an internal, self-sufficient reaction which is relatively little dependent on the external surroundings. A restricted configuration during the approach of phosphorane and aldehyde accords with the high negative entropy in aprotic solvents (Table II).

In alcohols, on the other hand, the oxygen of the carbonyl group, which is H-bonded to alcohol, cannot obtain a simultaneously close contact with the phosphonium cation. Its developing negative charge will be less neutralized, resulting in higher activation energy. But the higher activation energy will be compensated by a more favourable entropy due to the less restriction laid upon the open conformation of the two-centered collision complex.

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