Detection of a Thiaphosphetane during the Reaction of the Ylide $Ph_3P{=}CH_2$ with Thiobenzophenone

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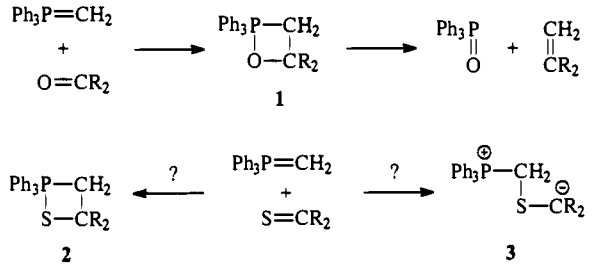
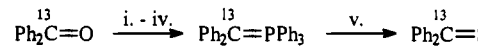
Oxaphosphetanes are the intermediates of the Wittig olefination reaction of ketones and aldehydes with phosphorus ylides under salt-free conditions. They have been detected by NMR spectroscopy at low temperature[1] and in special cases even isolated and characterized by X-ray diffraction.[2] Wittig oxaphosphetanes are formed without the involvement of betaines;[3] they decompose stereospecifically to yield olefin plus triphenylphosphine oxide, and thus, their formation determines the stereoselectivity of the Wittig olefination reaction.[4]

Thioketones and -aldehydes also react rapidly with phosphorus ylides. Sometimes the isolated products are analogous with those of the carbonyl Wittig olefination, namely olefin plus triphenylphosphine sulfide, but often episulfide formation is observed,[5] in at least one case stereoselectively.[6] It has been assumed that these reactions proceed via a thiaphosphetane intermediate, but such a species has, to our knowledge, not previously been observed directly in a thio-Wittig reaction under suitable reaction conditions. However, detecting the reactive intermediate in the reaction of the phosphorus ylide with the thioketone is important, since there is a possible alternative reaction pathway initiated by thiophilic addition[7] of the ylide carbon nucleophile to the $R_2C{=}S$ electrophile, leading to a betaine-type structure. Since both intermediates, the thiaphosphetane (**2**) and the betaine (**3**), are expected to eventually yield identical stable products in their consecutive reaction steps, direct detection of the intermediate is essentially required in order to decide between the possible reaction pathways taken in the thio analogue of the Wittig olefination reaction.

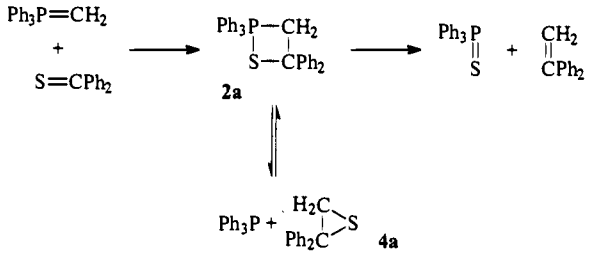


We have treated the ylide methylenetriphenylphosphorane with thiobenzophenone. When these reagents are mixed in [D_8]toluene solution at −50 °C, a rapid reaction ensues and a single reaction product is formed that is stable ($\tau_{1/2}$ > 1 h) up to −20 °C. The newly formed compound exhibits a single ^{31}P NMR resonance at δ −39 (relative to external H_3PO_4; for comparison, the oxaphosphetane **1a**, R = Ph, was prepared from $Ph_3P{=}CH_2$ and benzophenone under identical conditions, and it showed a ^{31}P NMR signal at δ −67)[4b] and a ^1H NMR methylene doublet at δ 4.7 ($^2J_{PH}$ = 17 Hz). For a clear identification of the essential ^{13}C NMR resonances, two experiments were carried out, each employing a singly ^{13}C-labeled reagent (i.e. $Ph_3P{=}{}^{13}CH_2$ + $S{=}CPh_2$ and $Ph_3P{=}CH_2$ + $S{=}{}^{13}CPh_2$; the synthesis of the ^{13}C-labeled thiobenzophenone was performed by means of a reaction sequence employing the Staudinger chalcogenation).[8] The product (**2a**, R = Ph) shows a methylene ^{13}C NMR resonance at δ 64.4 (**1a**, δ 65.9) and the CPh_2 signal at δ 50.4. A double labeling experiment employing both the ^{13}C-labeled ylide *and* thiobenzophenone has revealed the phosphorus−carbon−carbon connectivity which is as required of the thiaphosphetane **2** [$^{13}CH_2$ signal (^1H decoupled) of the product at δ 64.4, dd, $^1J_{PC}$ = 93 Hz, $^1J_{CC}$ = 37 Hz ($^1J_{CH}$ = 130 Hz); $^{13}CPh_2$ signal at δ 50.4, d, $^1J_{CC}$ = 37 Hz].



i. $LiAlH_4$, ether; ii. PBr_3; iii. PPh_3; iv. $NaNH_2$; v. S_8

Above −20 °C, the thiaphosphetane **2a** slowly decomposes to give triphenylphosphine (^{31}P NMR δ −6.6 at −40 °C) and 2,2-diphenylthiirane [(**4a**) ^1H NMR δ 2.61 (CH_2); ^{13}C NMR δ 34.6 ($^1J_{CH}$ = 170 Hz, $^1J_{CC}$ = 27 Hz, CH_2), 52.9 ($^1J_{CC}$ = 27 Hz, CPh_2)]. If the solution is warmed carefully under direct NMR observation, reaction conditions can be found where these two products are formed almost exclusively (>95%), i.e., without formation of the Wittig olefination products.[9] At higher temperatures (≥0 °C), the secondary reaction products PPh_3 and 2,2-diphenylthiirane (**4a**) disappear, and the final products triphenylphosphine sulfide and 1,1-diphenylethene are formed.



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(9) Experiments employing substituted ylides $Ph_3P{=}CHR$ (R = C_2H_5, C_6H_5, or p-$C_6H_4OCH_3$) and thiobenzophenone gave triphenylphosphine and the respective episulfides under closely related conditions. In these cases, we have not found the thiaphosphetanes as yet. We assume that the C-substituted analogues of **2** decompose at lower temperatures than **2a** and thus are more difficult to detect experimentally. We are planning to use thioketones and thioaldehydes, more reactive than $Ph_2C{=}S$, to extend the thiaphosphetane observation range to lower temperatures.

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For the thiaphosphetane (**2**) to episulfide (**4**) transformation, one can formulate two principally different mechanistic schemes: cleavage of both the P−S *and* the C−C bonds of **2** (pathway A) would lead to the formation of the starting materials $Ph_3P{=}CH_2$ and $Ph_2C{=}S$, which could then undergo thiophilic addition and proceed to the episulfide **4** via the betaine intermediate **3**; alternatively, only one of the bonds to the phosphorus of **2** might be broken. This would then lead to either the betaine $Ph_3P^+CH_2CPh_2S^-$ (by means of P−S bond cleavage, pathway B) or $Ph_3P^+SCPh_2CH_2^-$ (by P−C bond rupture, pathway C). Each of these dipolar intermediates could proceed to the thiirane product by intramolecular nucleophilic substitution of triphenylphosphine. Whether the thiirane formation (and its subsequent reaction to give 1,1-diphenylethene plus Ph_3PS) proceeds intra- or intermolecularly could easily be distinguished by the following experiment. The thiaphosphetane **2a** was generated from $Ph_2C{=}S$ in [D_8]toluene solution at 243 K with an excess of ~5−10% of the ylide $Ph_3P{=}CH_2$ remaining after the reaction had gone to completion. About 1 molar equiv of the ^{13}C-labeled $Ph_3P{=}{}^{13}CH_2$ reagent was then added at 223 K, and the solution was slowly warmed to 268 K. The reaction mixture was constantly monitored by ^{1}H and ^{13}C NMR spectroscopy; this revealed that no ^{13}C-labeled methylene became incorporated into the intact thiaphosphetane. At 268 K, compound **2a** decomposed with a half-life of ~20 min to the episulfide **4a**. Within the limits of ^{1}H NMR detection, no ^{13}C-labeled material had become incorporated into the thiirane formed in this experiment. Also, the eventually obtained 1,1-diphenylethene did not contain ^{13}C-enriched methylene groups. This makes it likely that the thiaphosphetane (**2a**) to thiirane (**4a**) transformation proceeds intramolecularly. Whether pathway B or C is involved cannot be deduced from our experiment. $Ph_3P^+CH_2CPh_2S^-$ betaine formation would be compatible with the reported stereochemistry of the literature example,[6] but complete confirmation of this pathway must await direct observation of the respective cis-disubstituted thiaphosphetane intermediate.

We conclude that thiophilic addition of $Ph_3P{=}CH_2$ to thiobenzophenone is not favored under the reaction conditions applied but that formation of the 1,2-thiaphosphetane is preferred. The ^{31}P NMR chemical shift difference between the thiaphosphetane **2a** and the oxaphosphetane **1a** (R = Ph) ($\Delta\delta \approx 28.5$ ppm) is about as expected (the ^{31}P NMR shift difference between Ph_3PS and Ph_3PO is of the same order, at $\Delta\delta \approx 18$ ppm). Therefore, the reactive intermediate **2** seems to contain a reasonably strong P−S bond and thus does not exhibit a measurable betaine character, even though the species **2** does probably react by means of subsequent P−S bond cleavage to form the episulfide (**4**). We are currently investigating whether substituent or solvent effects, or both, can be used to eventually detect a betaine (either of the $Ph_3P^+CH_2SCR_2^-$ or $Ph_3P^+CH_2CR_2S^-$ type) in the reaction of a phosphorus ylide with a chalcogenocarbonyl compound.

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