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A Novel Route to Phenyl-substituted Pyridines by the Reaction of N-(1-Phenylvinyl)iminophosphoranes with α,β-Unsaturated Ketones[1)]

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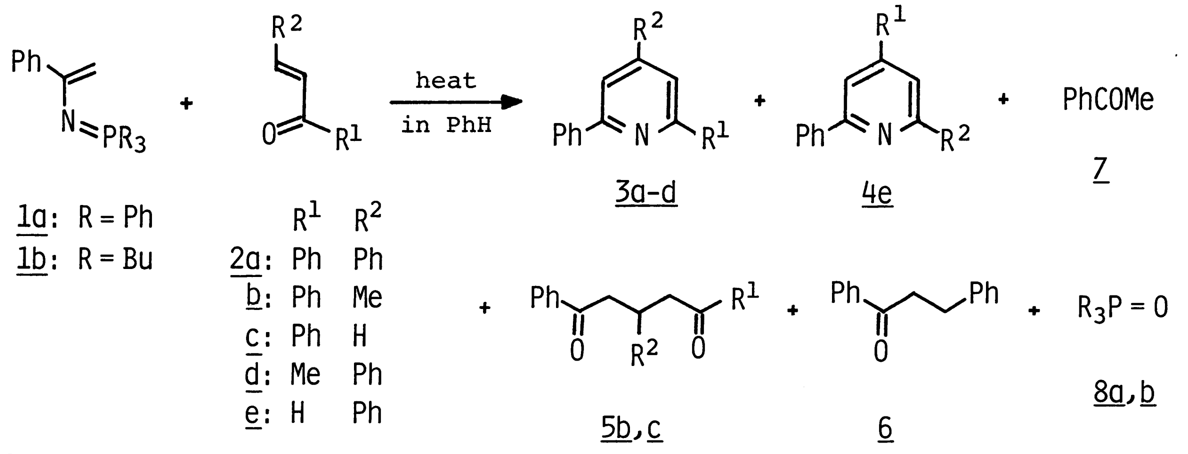
The N-(1-phenylvinyl)iminotriphenylphosphorane or N-(1-phenylvinyl)iminotributylphosphorane reacted with α,β-unsaturated ketones to undergo a novel C-C bond formation followed by aza-Wittig reaction to result in the formation of phenyl-substituted pyridines.

The reaction of tertiary phosphine with organic azide to produce an iminophosphorane after nitrogen evolution is known as the Staudinger reaction.[2)] Recent studies on the synthetic utilities of iminophosphoranes have been hydrolysis to amines,[3)] oxidation to nitro compounds,[4)] and intermolecular[5)] and intramolecular[6)] aza-Wittig reactions with carbonyl groups. Compared with that of methylenephosphoranes,[7)] however, the synthetic versatility of iminophosphoranes is still restricted. This fact would be ascribed in part to the poor variation of a substituent on the nitrogen atom of iminophosphoranes.[2)]

Previously, we have accomplished the preparation of N-(1-phenylvinyl)iminophosphoranes by the Staudinger reaction of α-azidostyrene with trimethyl phosphite, triphenylphosphine, or with tributylphosphine. These N-(1-phenylvinyl)iminophosphoranes were found to provide the convenient routes to phenyl-substituted 1,2-λ^5-azaphosphorine,[8)] 2-phenyl-1-azaazulenes,[9)] and phenyl-substituted pyrroles.[1)] We describe here a novel annulation reaction of either N-(1-phenylvinyl)iminotriphenylphosphorane (1a) or N-(1-phenylvinyl)iminotributylphosphorane (1b) with α,β-unsaturated ketones to result in the formation of the phenyl-substituted pyridines



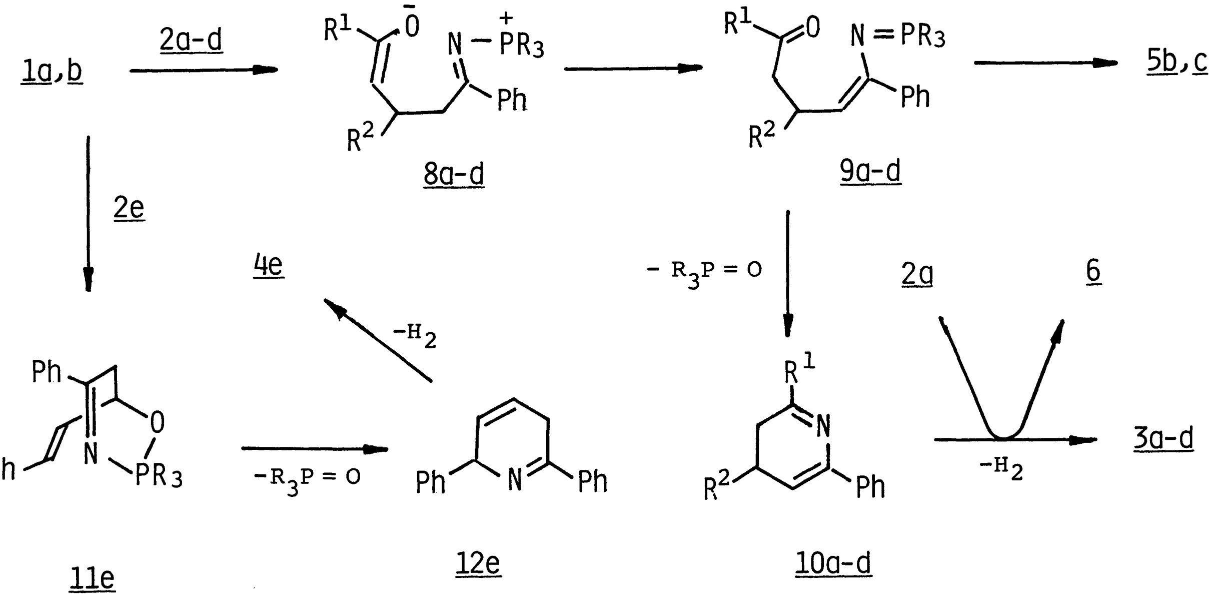
Scheme 1.

(3a-d, 4e), pentane-1,5-diones (5b,c), and 1,3-diphenylpropan-1-one (6), in addition to acetophenone (7) and triphenyl- or tributylphosphine oxide (8a or 8b) (Scheme 1).

The general procedure for the reaction was as follows: A solution of 1 (1 mmol) and α,β-unsaturated ketone 2 (1 mmol) in anhydrous benzene (10 cm^3) was heated under reflux for 24 h under a nitrogen atmosphere. The separation of the products was performed through TLC on silica gel, and the isolated yields are summarized in Table 1.

In the reaction of 1a,b with 2a, the pyridine 3a was obtained in addition to 7 and 8a,b (Entries 1 and 6 in Table 1). The compound 7 arose from the hydrolysis of the unreacted 1a,b on TLC plates. The low material balance for several reactions in Table 1 may be ascribed to the volatility of 7. In the cases of 1a,b with 2b or 2c, 1,5-diketones 5b,c were obtained (entries 2, 3, 7, and 8). The reaction of 1a with 2d afforded 3d in a very low yield (entry 4). Furthermore, the reactions of 2e with 1a or 1b afforded pyridine 4e instead of 3e (entries 5 and 10). The reaction of 2a also occurred in one case to give 6 (entry 6). The structures of pyridines, 3a,10) 3b,11) 3c,e,12) and 3d13) were determined by comparison of their physical data with those reported in the literature. The compounds 5b,c14) and 6 were easily confirmed.

In the present reactions, the Michael addition of the iminophosphoranes 1a,b to the β-carbon atom of the enones 2a-d occurs at γ-position first, followed by proton transfer to generate iminophosphoranes 9a-d which then undergo an intramolecular aza-Wittig reaction to produce dihydropyridines 10a-d (Scheme 2). This type of reaction sequences have been shown previously in the reaction of α,β-unsaturated ketones with allylidenephosphorane.15) The compounds 10a-d would be dehydrogenated to give 3a-d under the reaction conditions. The compound 2a seems to act as a hydride acceptor of 10a to result in the formation of 6.16) Although the steric or electronic factor does not seem to explain the prohibited aza-Wittig



Scheme 2.

Table 1. Reactions of N-(1-phenylvinyl)iminophosphoranes (1a,b) with α,β-unsaturated ketones (2a-e)a)

Entry	1	2	R^1	R^2	Product (Yield/%) 3	4	5	6	7	Unreacted 2 (%)
1	1a	2a	Ph	Ph	57	--	--	--	8	8
2	1a	2b	Ph	Me	25	--	26	--	56	10
3	1a	2c	Ph	H	16	--	65	--	5	--
4	1a	2d	Me	Ph	1	--	--	--	54	86
5	1a	2e	H	Ph	--	24	--	--	18	25
6	1b	2a			56	--	--	10	7	3
7	1b	2b			26	--	20	--	8	14
8	1b	2c			33	--	32	--	5	--
9	1b	2d			38	--	--	--	12	46
10	1b	2e			--	8	--	--	5	14

a) Reactions were carried out in anhydrous benzene solution under reflux for 24 h. In all cases, triphenylphosphine oxide (8a) or tributylphosphine oxide (8b) was obtained in good yields.

reaction of 9b,c, the formation of 5b,c, which derive from hydrolysis of 9b,c, seems to support the postulated Michael addition of 1 with 2.

On the other hand, the compound 2e does not undergo the Michael addition. In this case, the addition of γ-carbon atom of 1a,b to the carbonyl-carbon of 2e occurs, followed by a possible elimination of 8a,b and a concomitant cyclization to generate 12e. The compound 12e is dehydrogenated to give 4e under reaction conditions. The Michael addition is frontier orbital controlled and thus favored with 2a-d.17) However, 2e, which has no methyl or no phenyl group on the carbonyl-carbon atom, favors the charge-controlled reaction to generate 11e. Although, the yields of the products varied from the reaction of 1a to 1b, no definitive difference of the reactivity between 1a and 1b is clarified at this stage.

The present study clarified a reactivity of 1a,b toward α,β-unsaturated ketones. The present reaction might serve as a convenient route to the phenyl-substituted pyridines. Further studies concerning the preparations and synthetic applications of N-vinyliminophosphoranes are in progress.

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