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ON THE REACTION OF N-VINYLIMINOPHOSPHORANES 3.[1] A NOVEL ROUTE TO PHENYL-SUBSTITUTED PYRROLES BY THE REACTION OF N-(1-PHENYLVINYL)-IMINOPHOSPHORANES WITH α-BROMO KETONES

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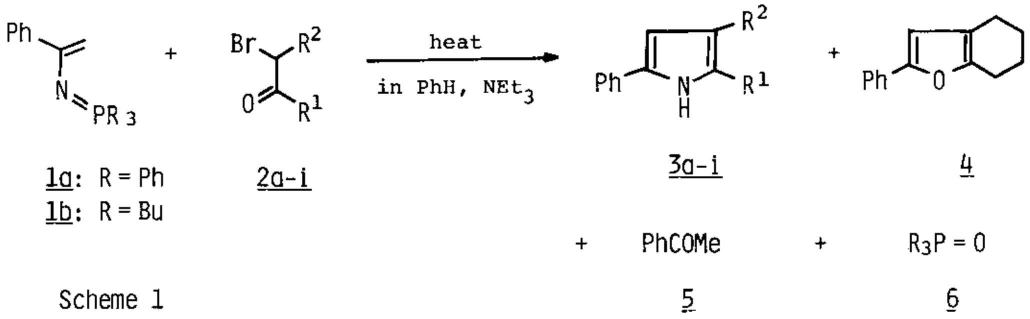
Abstract——N-(1-Phenylvinyl)iminotriphenylphosphorane or N-(1-phenylvinyl)iminotributylphosphorane reacted with α-bromo ketones to give phenyl-substituted pyrroles via a novel C-C bond formation followed by aza-Wittig reaction.

Recently, much attention has been focussed on the synthetic utilities of iminophosphoranes.[2] For example, a hydrolysis to amines or to ketones,[3] an oxidation to nitro compounds,[4] and the intermolecular[5] and intramolecular[6] aza-Wittig reactions with carbonyl groups have been reported. However, the synthetic versatility of iminophosphoranes is still not fully explored compared with that of methylenephosphoranes.[7] This fact can be ascribed in part to the poor variation of substituent on the nitrogen atom of iminophosphoranes. Although the preparation of substituted N-vinyliminotriphenylphosphorane derivatives has been known, their reactivity or synthetic utility is not clarified so far.[8]

Previously, we have accomplished the simple preparation of N-(1-phenylvinyl)iminophosphoranes by the reaction of α-azidostyrene with trimethyl phosphite, triphenylphosphine, or with tributylphosphine at room temperature. The N-(1-phenylvinyl)-



Scheme 1

iminophosphoranes were found to provide the convenient synthetic routes to phenyl-substituted 1,2-λ^5-azaphosphorines,[1a] 2-phenyl-1-azaazulene derivatives,[1b] and phenyl-substituted pyridines.[9] Recently, Motoki et al. have also reported the reaction of N-vinyliminophosphoranes with various isocyanates to give vinylcarbodiimides.[10] We describe here a novel annelation reaction of N-(1-phenylvinyl)iminotriphenylphosphorane (1a) or N-(1-phenylvinyl)iminotributylphosphorane (1b) with α-bromo ketones (2a-i) to give phenyl-substituted pyrrole derivatives or a furan derivative (Scheme 1).

General procedure for the reactions was as follows. A solution of 1 (1 mmol), α-bromo ketone (2) (1 mmol), and triethylamine (2 mmol) in anhydrous benzene (3 ml) was heated under reflux under a nitrogen atmosphere untill almost all of 2 disappeared. The separation of the products was performed through preparative TLC on silica gel. The reaction time and the isolated yields of the products are summarized in Table 1.

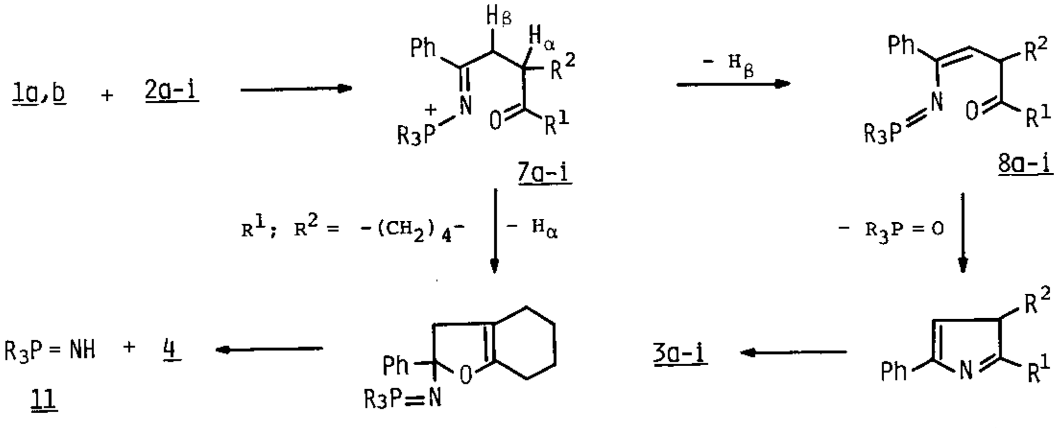
The reaction of 2a with 1a,b afforded 2,5-diphenylpyrrole (3a) along with acetophenone (5) (entry 1). The compounds 1a,b are labile under heating in the presence of water or on a TLC plate to give 5 and 6.[1a,b] Thus, 5 in Table 1 arises from the unreacted 1a,b. The low material balance for several reactions may be ascribed to the volatility of 5 under workup conditions. Since 3a was obtained albeit in low yield in the absence of triethylamine (entry 2), iminophosphorane 1a seems also act as a base instead of triethylamine. Similarly, 2b,e with 1a or with 1b gave unsymmetrically substituted pyrroles (3b-e) (entries 4-8). However, the α-bromo ketones (2f,g), both of which have a substituent on the α-carbon atom, reacted very slowly to give 3f,g in low yields even after prolonged heating (entries 9 and 10). Similarly, in the case of α-bromo ketones (2h,i), pyrroles (3h,i) were obtained in low yields (entries 11-14). A furan derivative (4) was obtained only in the case of 2h. The low yields of 3f-i are possibly ascribed to the steric factor at the stage of the C-C bond formation (vide infra). The compound 1a gives 3 in better yields, as compared with 1b (entries 3 and 8). The details are unclear at this stage. The structures of 3b-d were confirmed on the basis of the physical data,[11] and the compounds 3a,[12] 3e,[13] 3f,[14] 3g,[15] 3h,[14] 3i,[14] and 4[16] were determined by comparison of their spectral data with those reported in the literatures.

The present reactions are best explained by the mechanistic pathways shown in Scheme 2. The enamine alkylation process of 1 with 2 gives an intermediate (7), whose deprotonation (H_β) generates a new iminophosphorane (8). The intramolecular

Table 1. Reaction of N-(1-Phenylvinyl)iminophosphoranes (1a,b) with α-Bromo Ketones (2a-i)[a)]

Entry	(1)	(2)	R^1	R^2	Reaction time/h	Product (Yield/%) (3a-i)	(4)	(5)	(6)	Unreacted (2)
1	(1a)	(2a)	Ph	H	1	(3a) 66	--	28	71	--
2[b)]	(1a)	(2a)			24	(3a) 30	--	30	73	--
3	(1b)	(2a)			1	(3a) 34	--	13	73	--
4	(1a)	(2b)	4-MeC_6H_4	H	3	(3b) 56	--	25	81	--
5	(1a)	(2c)	4-ClC_6H_4	H	2	(3c) 62	--	20	70	--
6	(1a)	(2d)	4-BrC_6H_4	H	2	(3d) 66	--	23	76	--
7	(1a)	(2e)	Me	H	1	(3e) 61	--	7	80	--
8	(1b)	(2e)			1	(3e) 41	--	10	70	--
9	(1a)	(2f)	Ph	Me	24	(3f) 22	--	18	71	61
10	(1a)	(2g)	Ph	Ph	24	(3g) 25	--	18	87	45
11	(1a)	(2h)	$-(CH_2)_4-$		48	(3h) 20	12	25	78	--
12	(1b)	(2h)			24	(3h) 9	9	12	80	--
13	(1a)	(2i)	$-(CH_2)_5-$		24	(3i) 4	--	70	75	--
14	(1b)	(2i)			24	(3i) 8	--	13	70	--

a) Reactions were carried out in the presence of triethylamine. b) Reaction was carried out in the absence of triethylamine.



Scheme 2

aza-Wittig reaction of 8 results in the formation of 3 after hydrogen migration.[1b,6] On the other hand, the deprotonation of H_α of (7) followed by cyclization gives 10. The compound 10 undergoes an elimination of iminophosphorane (11) to give 4. In the intermediates (7a-g), only the deprotonation of H_β occurs to give 3a-g. Since the acidity of α-hydrogen of cyclohexanone is larger that that of acetophenone or acetone,[17] the deprotonation of H_α to give 4 could compete with that of H_β to give 3h in the case of 7h.

The present study clarified a reactivity of 1a,b toward α-bromo ketones. Although the several synthetic methods of pyrroles have been explored,[18] the present reaction might also serve as a route to the phenyl-substituted pyrrole derivatives. Further studies concerning the preparation and chemical behavior of several N-vinyliminophosphoranes are in progress.

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11 For (3b): mp 139-140 °C (from hexane – CCl_4/1:1); ^{1}H-NMR ($CDCl_3$) δ 2.30 (3H, s), 6.42 (2H, d, J=2.0 Hz), 7.05-7.70 (9H), 8.70-9.30 (1H, m); IR ($CHCl_3$) 3472, 1605, 1494, 1269 cm^{-1}. For (3c): mp 150-151 °C (from hexane-CCl_4/1:1); ^{1}H-NMR (acetone-d_6) δ 6.54 (2H, d, J=2.5 Hz), 7.10-7.80 (9H); IR ($CHCl_3$) 3460, 1606, 1483, 1263 cm^{-1}. For (3d): mp 156-157 °C (from hexane-CCl_4/1:1); ^{1}H-NMR (acetone-d_6) δ 6.60 (2H, d, J=2.7 Hz), 7.10-7.90 (9H); IR ($CHCl_3$) 3472, 1489, 1263 cm^{-1}.

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