A New and Safe Approach to (*N*-Vinylimino)phosphoranes

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1-[α-(Phosphoranylideneamino)alkyl]benzotriazoles, obtained by Staudinger phosphenimide-forming reaction of (azidoalkyl)benzotriazoles, possessing a proton in a β-position to nitrogen reacted with sodium hydride in THF to afford (*N*-vinylimino)phosphoranes in high yields. The latter were trapped with chalcone to give the corresponding 2,4-diphenylpyridines.

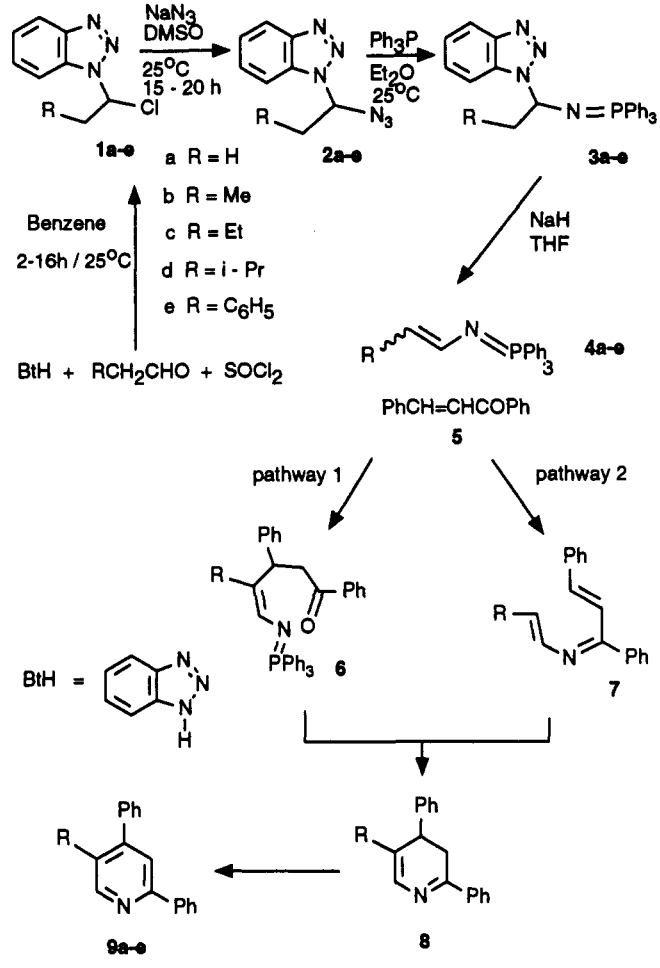
Introduction

(*N*-Vinylimino)phosphoranes are important synthetic intermediates. Their reactions with appropriate aza-Wittig substrates provide routes to a wide variety of azaheterocycles: pyrroles,[1] pyridines,[2] 1,5,6,7-tetrahydro-4*H*-indol-4-ones,[3] 1-azaazulenes,[4] 1,2-λ⁵-azaphosphorines,[5] pyridophanes,[6] 11*H*-cyclohept[*b*]indeno[2,1-*d*]pyrrole,[7] pyridotropones,[8] 8-azabicyclo[5.3.1]undeca-2,4,7,9-tetraenes,[9] 1-azamethanocyclpentacycloundecenes,[10] and *N*-vinylcarbodiimides.[11] However, the only hitherto known synthesis of (*N*-vinylimino)phosphoranes involves Staudinger phosphorylation of vinyl azides with trialkyl- or triarylphosphines. The explosive properties of vinyl azides have limited access to (*N*-vinylimino)phosphoranes and, hence, their application in organic synthesis.[12] We now report a new and safe preparation of (*N*-vinylimino)-phosphoranes using 1-[α-(phosphoranylideneamino)alkyl]-benzotriazoles.

Results and Discussion

BETMIP [1-[[(triphenylphosphoranylidene)amino]-methyl]benzotriazole] has been a valuable synthon for the synthesis of carbodiimides, imines, isothiocyanates, and aziridines[13] as well as primary[14] and secondary amines.[15] The BETMIP approach has now been used for a convenient synthesis of (*N*-vinylimino)phosphoranes. The starting (chloroalkyl)benzotriazoles **1** were prepared from benzotriazole, aldehydes, and thionyl chloride by a Mannich reaction. The previously reported method[16] was modified to optimize the yield for these specific (chloroalkyl)benzotriazoles. Compounds **1** were formed as oils

Scheme 1



in high yield and characterized, but for the present purpose they were used without any further purification and treated with sodium azide in DMSO during 15–20 h at room temperature to give the corresponding azides **2**. The azides, which displayed a remarkable stability, were purified by column chromatography using benzene as eluent of choice. The structures of the (chloroalkyl)-benzotriazoles **1** and the azides **2** were confirmed by analytical and spectral data (Tables 1 and 3; see also Table 2 in the supplementary material).

The azides **2** were subsequently treated with triphenylphosphine in a Staudinger phosphenimide-forming reaction to yield the 1-[α-(phosphoranylideneamino)alkyl]-benzotriazoles **3**. Compounds **3** possessing a proton in a

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Table 1. Preparation of 1-(α-Chloroalkyl)benzotriazoles 1 and 1-(α-Azidoalkyl)benzotriazoles 2

				molecular formula					
				calcd			found		
no.	R	yield (%)	time (h/rt)	C	H	N	C	H	N
1a	H	96	3	ref 16					
1b	Me	80	12	ref 16					
1c	Et	93	2	ref 16					
1d	i-Pr	91	12	59.06	6.31	18.78	59.34	6.45	18.43
1e	C_6H_5	92	16	a					
2a	H	82	15	51.04	4.28	44.66	51.42	4.27	44.39
2b	Me	77	16	53.46	4.98	41.56	53.14	5.00	41.85
2c	Et	77	20	55.54	5.59	38.86	55.50	5.53	38.79
2d	i-Pr	76	16	57.38	6.13	36.50	57.51	6.19	36.46
2e	C_6H_5	97	16	63.62	4.58	31.80	63.77	4.58	31.50

[a] No satisfactory microanalysis obtained: the compound (purity >95%) was satisfactory for further reactions.

β-position to nitrogen can now serve as convenient and safe precursors to (*N*-vinylimino)phosphoranes. The 1-[α-(phosphoranylideneamino)alkyl]benzotriazoles **3** were obtained as thick sticky oils which could not be purified due to their moisture sensitivity but which were quite satisfactory to use as such: they were refluxed in THF with sodium hydride in a 1:3 molar ratio to afford the (*N*-vinylimino)phosphoranes **4** in high yields (82–94% estimated from the ^{1}H NMR spectra). The β-substituted (*N*-vinylimino)phosphoranes **4b–4e** were all obtained as mixtures of *Z* and *E* isomers in which the *Z* isomer predominated. The *Z*:*E* ratio decreases with an increasing bulk of the β-substituent from 85:15 for R = Me (**4b**) to 57:43 for R = Ph (**4e**). The (*N*-vinylimino)phosphoranes thus prepared were admixed with 15–20% of sodium benzotriazolate: no further purification was performed due to their lability and the moisture sensitivity of the products, but the (*N*-vinylimino)phosphoranes were characterized by ^{1}H and ^{13}C NMR spectroscopy (Table 5; see also Table 4 in the supplementary material) and by further chemical transformations.

To demonstrate that (*N*-vinylimino)phosphoranes **4** could be used in further synthetic sequences, compounds **4** were reacted with chalcone **5** in the known route to substituted pyridines[2] (a similar approach was used to trap *N*,*N*-bis(silyl) enamines[17]). The crude iminophosphoranes **4** were refluxed in toluene with an excess of phenyl styryl ketone (chalcone),[2a] and the reaction was monitored by ^{1}H and ^{13}C NMR spectroscopy. The expected 2,4-diphenylpyridines **9a–e** were isolated in good yields by column chromatography and characterized as picrate salts[18] and by NMR spectroscopy (Tables 6 and 8; see also Table 7 in the supplementary material). Some 1,3-diphenyl-1-propanone (reduced chalcone) was isolated as well, which proved the role of the chalcone **5** in the dehydrogenation of the intermediate dihydropyridines **6** formed in the course of the reaction.[2b]

The formation of pyridines **9** may involve two pathways: (i) a Michael-type addition of **4** to an enone followed by proton transfer to generate an intermediate iminophosphorane **6** which then undergoes aza-Wittig reaction with the formation of dihydropyridine **8** and (ii) aza-Wittig reaction leading to an intermediate aza triene **7** which then undergoes a thermal 6π-electrocyclization. The first pathway seems to predominate for **4e** because, despite the disappearance of **4e** by NMR, the formation of only a little amount of triphenylphosphine oxide was observed during the first 2 days of the reaction. The second pathway seemed to prevail in the case of **4d** when triphenylphosphine oxide was readily formed at the beginning of the reaction and new signals temporarily appeared in the olefinic region of the ^{1}H NMR spectrum during the course of the reaction. This type of mechanism was previously described for the synthesis of fused pyridines.[19] The dihydropyridines **8** are evidently oxidized under the reaction conditions to form pyridines **9**.

The presently reported route enables a safe entry to (*N*-vinylimino)phosphoranes from readily available benzotriazole derivatives avoiding the use of the highly explosive *N*-vinylazides and allows the preparation of derivatives substituted in the β-position of the vinyl group. This provides an additional advantage to the known synthetic methods in which only the elaboration of the α-position was described.[2b,4b,11]

Experimental Section

General Remarks. THF, benzene, and toluene were distilled from sodium/benzophenone ketyl under a nitrogen atmosphere immediately before use. MP's were determined on a hot-stage microscope and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian VXR-300 (300 MHz) spectrometer using TMS as an internal standard. Elemental analyses were performed in this department under the supervision of Dr. D. Powell. Column chromatography was performed on Merck (230–400 mesh) silica gel.

Synthesis of 1-(α-Chloroalkyl)benzotriazoles 1a–e: General Procedure. Benzotriazole (21.5g, 0.18 mol), benzene (150 mL), and the appropriate aldehyde (0.15 mol) were stirred at room temperature for 0.5 h, and then $SOCl_2$ (12 mL, 0.165 mol) was added dropwise with stirring. The stirring was continued at room temperature for 2–16 h. The precipitate was filtered off, and the filtrate was evaporated at reduced pressure to give the products as oils. Compounds **1a–e** were used in further syntheses without additional purification. The analytical and spectroscopic data are summarized in Tables 1–3 (see Table 2 in the supplementary material). A satisfactory analysis was obtained for **1d** from the crude product.

Synthesis of 1-(α-Azidoalkyl)benzotriazoles 2a–e: General Procedure. Sodium azide (9.75 g, 0.15 mol) was added at room temperature to a vigorously stirred solution of the appropriate 1-(α-chloroalkyl)benzotriazole **1a–e** (0.1 mol) in DMSO (50 mL), and stirring was continued for 15–20 h. Water (100 mL) was added, followed by extraction with Et_2O (3 × 75 mL). The combined extracts were washed with water (75 mL) and 10% aqueous Na_2CO_3 (75 mL) and dried ($MgSO_4$). The solvent was evaporated under reduced pressure (30 Torr, 55–60 °C), and the crude azides **2a–e** were purified by silica gel column chromatography (Merck, 230–400 mesh; eluent benzene). The analytical and spectroscopic data are summarized in Tables 1–3 (see Table 2 in the supplementary material).

Generation of (*N*-Vinylimino)phosphoranes 4a–e and Their Conversion to 2,4-Diphenylpyridines 9a–e: General Procedure. Triphenylphosphine (1.31 g, 5 mmol) in THF (20 mL) was added dropwise with stirring to a solution of azide **2** (5 mmol) in THF (10 mL), and the reaction mixture was stirred at room temperature for 1.5 h. Sodium hydride (60% dispersion in mineral oil, 0.6 g, 15 mmol) was then added, and the reaction mixture was refluxed under nitrogen for 2 h with vigorous stirring. Benzene (30 mL) was added, and the precipitate of sodium benzotriazolate was filtered off under nitrogen and washed with benzene. The filtrate was evaporated under reduced pressure to give (*N*-vinylimino)phosphoranes contaminated with 15–20% of sodium benzotriazolate, which were examined by ^{1}H and ^{13}C

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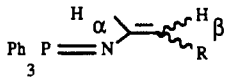
Table 3. ^{13}C-NMR Chemical Shifts (δ) of Compounds 1 and 2 ($CDCl_3$/TMS)

compd no.	benzotriazolyl ring 3a	4	5	6	7	7a	CHX[a]	CH_2	CH_3	$(CH_3)_2C$
1a[b]	146.6	120.4	124.7	128.3	110.4	131.5	66.7		24.5	
1b	146.3	120.3	124.8	128.2	110.5	131.4	72.4	31.3	10.7	
1c[b]	146.4	120.3	124.8	128.2	110.5	131.4	70.9	19.4, 39.6	13.0	
1d	146.7	120.5	124.7	128.2	110.5	131.4	69.9	46.2	21.8, 21.8	25.3
1e[c]	146.5	120.5	124.7	128.3	110.2	131.7	71.0	43.8		
2a	146.6	120.4	125.5	128.0	110.0	131.5	70.8		19.4	
2b	146.5	120.3	124.5	128.0	110.1	131.5	76.4	27.0	9.7	
2c	146.5	120.3	124.4	128.0	110.1	131.5	74.8	18.5, 35.3	13.1	
2d	146.6	120.4	124.5	128.0	110.1	131.5	73.7	41.8	22.0, 22.1	24.5
2e[d]	146.3	120.4	124.5	127.6[e]	109.9	131.8	75.7	40.0		

[a] X = Cl for 1 and N_3 for 2. [b] Agrees with literature.[16] [c] Phenyl carbons: 127.7, 128.7, 129.2, 134.6. [d] Phenyl carbons: 128.1,[e] 128.8, 129.2, 134.2. [e] Reversed assignment of the signals at 127.6 and 128.1 ppm also possible.

Table 5. ^{13}C-NMR Spectral Data of (*N*-Vinylimino)phosphoranes 4



compd no.	R	isomer	vinyl carbons, δ (ppm)/J_{C-P} (Hz) C_α	C_β	Ph_3P=N–, δ (ppm)/J_{C-P} (Hz) C_1	C_2	C_3	C_4	alkyl carbons δ (ppm) CH_3	CH_2	CH
4a	H		142.4/15.6	93.3/110	129.90/387	132.07/36.7	128.8/46.1	131.96/10.9			
4b	Me	*Z*	134.6/10.4	103.1/113	130.48/387	131.97/36.1	128.8./46.1	131 82/10.5	11.2		
4b	Me	*E*	136.3/15.8	103.5/115	130.43/386	*a*	*a*	d	15.3		
4c	Et	*Z*	133.3/11.4	111.8/110	130.48/387	131.98/36.3	128.8/45.6	131.82/10.0	15.0	18.6	
4c	Et	*E*	134.8/14.2	112.2/107	130.42/386	132.02/36.7	*a*	*a*	16.3	23.2	
4d	i-Pr	*Z*	133.0/15.8	118.0/109	130.51/387	131.96/36.3	128.73/46.1	131.79/10.5	23.6		24.39[b]
4d	i-Pr	*E*	*c*	118.6/104	130.45/386	132.02/37.6	128.69/45.6	*a*	24.49[b]		28.9
4e	Ph	*Z*[d]	138.1/13.3	107.9/102	128.98/390	132.16/37.6	129.05/46.7	*e*			
4e	Ph	*E*[d]	138.9/11.4	111.0/108	129.33/388	132.16/37.6	128.98/46.0	*e*			

[a] Not assigned; signal of the minor *E* isomer is hidden under the signal of the major *Z* isomer. [b] Reverse assignments of the signals at δ 24.39 and 24.49 are possible. [c] Not assigned. [d] Other signals of aromatic carbons: δ 122.88, 122.99, 126.9, 127.7, 128.2, 140.23 (d, J_{C-P} = 7.1 Hz), 140.34 (d, J_{C-P} = 7.1 Hz). [e] Only one signal of the C_4-carbon was observed at δ 132.34 (J_{C-P} = 10.0Hz); the assignment of this signal to a particular isomer is not possible.

Table 6. Preparation of 2,4-Diphenylpyridines 9

compd no.	R	reactn condns solvent	time (d)	yield[a] (%)	mp (°C)	previous ref or lit. mp (°C)	picrate mp (°C)	lit. mp (°C)
9a	H	benzene	2	59	oil	lit.[18]	185–186	187[18]
9b	Me	toluene	5	84	78.5–80	lit.[22]	195–196[b]	
9c	Et	toluene	4	76	oil[c]		198–199[d]	
9d	i-Pr	toluene	10	79	99–100	97.5–98.3[20]	231–233	225–228[20]
9e	Ph	toluene	6	68	109–111	108–109[21]	181–182	182–183[21]

[a] Based on azide. [b] Satisfactory microanalysis obtained. For $C_{24}H_{18}N_4O_7$ (474.43) Anal. Calcd: C 60.76; H, 3.82; N, 11.81. Found: C, 61.04; H, 3.83; N, 11.46. [c] Satisfactory microanalysis obtained. For $C_{19}H_{17}N$ (259.35) Anal. Calcd: C, 87.99; H, 6.64; N, 5.40. Found: C, 87.91; H, 6.62; N, 5.10. [d] Satisfactory microanalysis obtained. For $C_{25}H_{20}N_4O_7$ (488.46) Anal. Calcd: C, 61.47; H, 4.13; N, 1147. Found: C, 61.46; H, 4.09; N, 11.48.

Table 8. ^{13}C-NMR Spectral Shifts of Pyridines 9

compd no.	R	pyridine ring C-2	C-3	C-4	C-5	C-6	other aromatic carbons
9a	H	158.0	118.7	149.2	120.2	150.0	126.99, 127.03, 128.7, 128.98, 129.06, 138.47, 139.44
9b[a]	Me	155.2	120.9	149.9	129.1	151.1	126.7, 127.9, 128.4, 128.5, 128.62, 128.66, 139.27, 139.39
9c[b]	Et	154.9	121.2	149.7	135.3	150.3	126.7, 127.8, 128.40, 128.46, 128.66,[c] 139.24, 139.42
9d[d]	i-Pr	154.3	121.1	149.2	139.2	148.2	126.7, 127.8, 128.4, 128.59, 128.62, 128.66, 139.50, 139.74
9e	Ph	156.5	121.6	148.5	134.3	150.9	126.9, 127.2, 127.8, 128.26, 128.29, 128.8, 129.0, 129.3, 129.8, 137.6, 139.00, 139.01

[a] Alkyl carbon: 17.0 (CH_3). [b] Alkyl carbons: 15.5 (CH_3), 23.3 (CH_2). [c] Two overlapped unresolved signals. [d] Alkyl carbons: 23.9 (CH_3), 27.7 (CH).

NMR (Table 5; see Table 4 in supplementary material). The estimated overall yields of (*N*-vinylimino)phosphoranes (by ^{1}H NMR) were 82, 94, 92, 88, and 93% for R = H, Me, Et, i-Pr, and Ph, respectively, and the *Z*:*E* ratios were 85:15, 67:33, 66:34, and 57:43 for R = Me, Et, i-Pr, and Ph, respectively. Chalcone 5 (2.08 g, 10 mmol) was then added to a solution of the appropriate (*N*-vinylimino)phosphorane **4a–e** (5 mmol) in benzene or toluene (20 mL), and the mixture was refluxed with stirring under nitrogen for the time indicated in Table 6. A small amount of precipitate was then filtered off, the solvent was evaporated, and the pyridine derivative was isolated by silica gel column chromatography (eluent, benzene). The analytical and spectral data of pyridines **6a–e** are summarized in Tables 6–8 (see Table 7 in the supplementary material).

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Supplementary Material Available: Tables 2, 4, and 7 of ^{1}H NMR data (3 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.