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Studies on Organophosphorus Compounds 56† New Reaction of Dialkyl phosphites with 2-Nitrostyrene Derivatives—A Facile Route to N-Hydroxy-3-Indole Phosphonates and Indol-2-one Phosponates

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ABSTRACT

Reaction of a dialkyl phosphite with a 2-nitrostyrene in the presence of triethylamine, trimethylsilyl chloride, and hexamethyldisilazane provides a one-pot procedure for the synthesis of an N-hydroxy-indole-3-phosphonate and an indole-2-one-3-phosphonate besides the normal addition product, a 1-aryl-2-nitroalkylphosphonate. Such new indole derivatives are difficult to prepare by conventional methods. The ratios of reactant to silylating agent and base were found to have significant influence on the product composition. The mechanism of formation of these heterocyclic products is discussed.

INTRODUCTION

During the last 20 years, considerable effort has been devoted to the synthesis [1] and biological studies [2,3] of functionally substituted indole derivatives. Nevertheless, there are only a few papers describing the synthesis of indoles bearing a phosphoryl moiety [4,5]. We therefore wanted to develop a new method for the synthesis of indole phosphonates.

Nitroolefins, which may be regarded as the heteroatom analogues of α,β-unsaturated carbonyl compounds, are powerful synthetic intermediates in organic synthesis [6,7]. Michael-type additions of various kinds of nucleophiles to nitroolefins provide a versatile synthetic method for the preparation of many types of organic compounds [8]. Nitroolefins are also used for the synthesis of various heterocycles [9–13].

Investigations of the reactions of trivalent phosphorus compounds with nitroolefines showed that they have a very complex character involving addition, substitution, and deoxygenation reactions. These result from the various sites of attack of trivalent phosphorus on nitroolefins. [14,15] This reaction is therefore a useful method for the synthesis of a variety of organophosphorus compounds and of α,β-unsaturated phosphoryl compounds, in particular [14,16,17].

As a part of a program involving the synthesis of potentially bioactive organophosphorus compounds [18], we reinvestigated the reaction of various dialkyl phosphites **1a–e** with 2-nitrostyrene derivatives **2a–d** with the intention of developing this approach into a mild selective synthetic route to 2-nitroalkylphosphonates **3**. The nitro group of **3** can be converted into various other functionalities [6]. The preparation of **3** by the addition reactions of trimethylsilyl esters of trivalent phosphorous acids with **2** has been reported [19]. These

Dedicated to Professor Yao-Zeng Huang on the occasion of his eightieth birthday.

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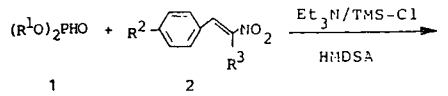
hydrolytically sensitive silylated phosphites **6** are isolated only in moderate yield.



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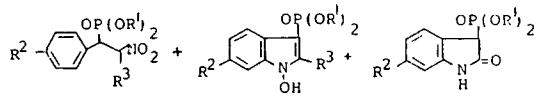


3 4 5

(1)

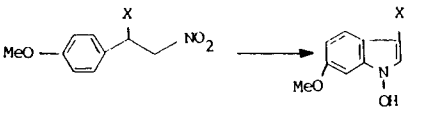
1a: R^1=Me
1b: R^1=Et
1c: R^1=Pr^n
1d: R^1=Pr^i
1e: R^1=Bu^n

2a: R^2=H, R^3=H
2b: R^2=Me, R^3=H
2c: R^2=MeO, R^3=H
2d: R^2=H, R^3=Me

3a: R^1=Me, R^2=H, R^3=H
4a: R^1=Et, R^2=H, R^3=H
5a: R^1=Et, R^2=H
3b: R^1=Et, R^2=H, R^3=H
4b: R^1=Et, R^2=MeO, R^3=H
5b: R^1=Et, R^2=MeO
3c: R^1=Et, R^2=H, R^3=H
4c: R^1=Pr^n, R^1=MeO, R^3=H
5c: R^1=Et, R^2=Me
3d: R^1=Et, R^2=MeO, R^3=H
4d: R^1=Pr^i, R^2=MeO, R^3=H
5d: R^1=Pr^i, R^2=H
3e: R^1=Pr^n, R^2=MeO, R^3=H
4e: R^1=Bu^n, R^2=MeO, R^3=H
3f: R^1=Pr^i, R^2=MeO, R^3=H
4f: R^1=Et, R^2=H, R^3=Me

We therefore prepared **6** in situ [20], which provides a more convenient and efficient route. As expected, the treatment of **1** and **2** with trimethylsilyl chloride (TMS-Cl) and Et_3N affords **3** in high yield [21]. When Et_3N is used alone, only poor yields of **3** are obtained [22].

Surprisingly, when the reaction was carried out with an excess of TMS-Cl and Et_3N in benzene at reflux temperature, two new types of compounds were obtained: N-hydroxyindole-3-phosphonates **4** [23] and indole-2-one-3-phosphonates **5**. (Equation 1). In contrast to Cadogan's reaction [15] which involves a nitrene intermediate, this cyclization seems to proceed via a different pathway. A tentative mechanism is proposed in Scheme 1. By control of the reaction conditions, each of the products **3**, **4** or **5** can be formed selectively (Table 1). Furthermore, X-ray crystallographic analysis of **3c** and **4e** have been reported by us [21,23]. The X-ray crystal structure of **5a** will be published elsewhere.



3d:, X=$(EtO)_2P$=O
17, X=H

4b(37%)
18(0%)

(2)

RESULTS AND DISCUSSION

Mechanism of Formation of Cyclic Products **4** *and* **5**

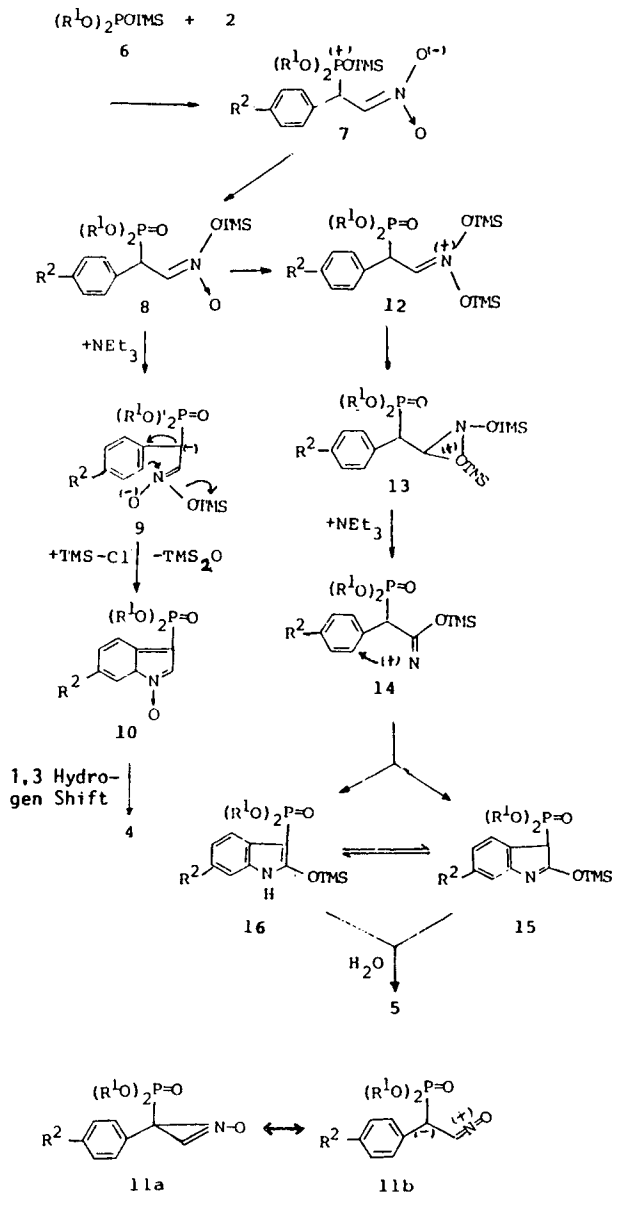
The formation of heterocyclic products **4** and **5** by a one-pot procedure involves the reaction of **1** and **2** in the presence of a silylating agent and base. This previously unknown reaction occurs by a Michael addition of **1** to **2**, followed by deoxygenation of the nitro group and subsequent formation of the indole ring. Based on the results of our studies and reactions of **2** with other nucleophiles [13], we can propose mechanistic pathways for the formation of **4** and **5** as outlined in Scheme 1.

The active nucleophile, a tricoordinate silylated phosphite **6**, is formed by reaction of phosphite **1** with TMS-Cl/Et_3N. This species attacks the β-carbon of the 2-nitrostyrene **2** to give a dipolar intermediate **7** which undergoes fast 1,6-silyl migration to form the intermediate **8**. α-Proton abstraction by Et_3N from **8** gives **9**. Nucleophilic attack of an ortho-carbanionic center of **9** on the nitrogen atom with loss of $TMSO^-$ followed by a 1,3-shift of hydrogen from carbon to oxygen yields **4**. An alternative pathway for the formation of **4** involves attack of the alpha carbanionic center of **9** on nitrogen with loss of $TMSO^-$ and formation of aziridine **11a** which receives a resonance contribution from **11b**. The formation of **5** is considered to proceed via a different mechanism. Intermediate **8** is converted to a disilylated cationic species **12**. A 1,2-bridging of one of trimethylsilyloxy group converts **12** into an oxonium intermediate **13** [13b]. Elimination of TMSOH in the presence of Et_3N affords **14** as a nitrenium species. Electrophilic attack of the nitrenium on the benzene ring establishes the indole skeleton **15**. A 1.3-proton shift gives **16** which can be hydrolyzed to **5**.

The proposed mechanism was supported by the following facts.

1. Stoichiometry has a substantial effect on product composition. More than 2 equiv of TMS-Cl and Et_3N are necessary for this cyclization reaction.

   The course of this reaction is determined by the nature of substituents either on the benzene ring or on the double bond of the nitroalkene as well as by the reaction con-



SCHEME 1

TABLE 1 Preparation of Compounds **3**, **4**, and **5**

	Molar Ratio					Yield	mp (°C)
	1	*2*	*TMS-Cl*	*HMDSA*	*Et_3N*	*(%)*	*(Literature mp)*
3a	1	1.1	1	1	0	71	106–108 (104–105) [21]
3b	1	1	1	1	0	84	67–69 (65–66) [21]
3c	1	1	1.5	1.5	0	76	126–127 (121–123) [21]
3d	1	1.1	1	1	0	92	54–57 (51–52) [21]
3e	1	1	1	1	0	86	53–56 (48–49) [21]
4a	1	1	3	1	1	57	94–96
4b	1.2	1	3	1	1.2	71	126–127
4c	1	1.2	3	1.4	1	51	103–105 (98–99) [23]
4d	1	1	3	1	1.5	65	132–136 (134–136) [23]
4e	1	1.2	3	1	1.2	58	105–107 (104–105) [23]
5a	1	1.2	3	2	2	48	137–139
5b	1	2	3	2	2.3	41	126–128
5c	1.1	1	3	2	3	37	131–133
5d	1	1.2	3	1.8	3	53	67–69

Reaction conditions are as follows: for **3**, reflux in CH_2Cl_2; for **4**, reflux in benzene for 4–8 hour; and for **5**, reflux in benzene for 18 hour.

ditions [21,23]. We have found that the reaction rate and selectivity can be increased by addition of hexmethyldisilazane (HMDSA). In most cases, compounds **3**, **4** and **5** are formed sequentially as shown by ^1H and ^{31}P NMR spectra. Compounds **1b** and **2a** were employed as model substrates, and the results are listed in Table 2.

Data in Tables 1 and 2 indicate that, under favorable reaction conditions, product **3**, **4** or **5** can be isolated as the major product. When the reaction was carried out at room temperature with a variety of ratios of **1** and **2** to TMS-Cl and Et_3N, the normal addition product **3** was formed predominately. In some cases, neither **4** nor **5** could be detected (entries 5, 7, and 11 in Table 2). When the reaction was carried out with heating and an excess of both TMS-Cl and Et_3N, the product ratio of **4** or **5** to **3** was increased. Excellent yield of **4** or **5** resulted when the ratio of TMS-Cl and Et_3N to **1** was at least 2 (entries 7, 8, 11, and 12 in Table 2).

2. The important role of both TMS-Cl and Et_3N in the cyclization process is well supported by the following experimental evidence. Reaction of **1b** and **2c** in the presence of N,O-bis(trimethylsilyl)acetamide (BSA) gave only addition product **3d** in quantitative yield, but addition of TMS-Cl and Et_3N to this reaction system provided the cyclization product **4b** in 41% yield together with 59% of **3d**. Analogously, reaction of diethyl trimethylsilylphosphite **6** with **2c** in benzene, even at reflux temperature, afforded **3d** quantitatively. However, with the aid of TMS-Cl and Et_3N, the cyclization process occurred forming **4b** (38%) and **3d** (62%). It is therefore reasonable to conclude that cyclization takes place only in the presence of TMS-Cl and Et_3N.
3. Compound **3d** can be converted to the cyclic product **4b** in the presence of TMS-Cl and

TABLE 2 The Composition of Products from Dialkylphosphite and 2-Nitrostyrenes[a]

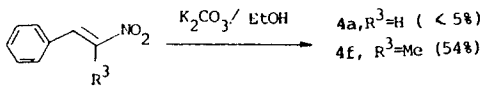
	Reaction Conditions						Yields (%)[b]			
	Molar Ratio									
	1b	**2a**	*TMSCl*	*HMDSA*	*Et_3N*	*Solvent*	**3b**	**4a**	**5a**	*by-product*
1	1	1	1	0	0	C_6H_6	No Reaction			
2	1	1	0	0	2	C_2H_5OH	Minor			
							—	—	—	
3	1	1	0	1.5	0	CH_2Cl_2	High mp Polymer			
4	1	1	1	0	1	C_6H_6	64	13	—	23
5	1	1	1	1	0	CH_2Cl_2 (RT)	100	—	—	—
6	1	1	1	1	1	CH_2Cl_2	51	15	15	
7a	1	1	2	1	1	CH_2Cl_2	20	48	12	20
7b	1	1	2	1	1	C_6H_6	10	54	15	21
7c	1	1	2	1	1	DMF (RT)	100	—	—	—
8	1.2	1	3	1	1.5	C_6H_6	7	72	18	—
9	1	1	3	1	1	CH_3CN	47	38	7	8
10	1	1	3	1	2	C_6H_6 (18 hours)	8	18	57	19
11a	1	1	2	1.5	2	CH_2Cl_2 (24 hours)	8	16	67	9
11b	1	1	2	1.5	2	CH_2Cl_2 (r.t.)	100	—	—	—
12	1.1	1	3	2	1.5	C_6H_6 (24 hours)	6	21	70	8

[a]The mixture of **1b**, TMSCl, HMDSA, or Et_3N as refluxed for 2 h, then **2a** was added. The reactions were carried out under reflux for 6 hours and worked up.
[b]The composition of reaction products was determined by ^1H and ^{31}P NMR.

Et_3N. However, the formation of 1-hydroxyindole (**18**) by the reaction of 1-(p-methoxyphenyl)-2-nitroethane (**17**) under similar reaction conditions is not observed (Equation 2). These data support our proposal that the presence of the electron-withdrawing phosphoryl moiety is critical to the formation of carbanion **9**. Unfortunately, replacement of the phosphoryl group by a cyano group in **3** resulted in the formation of a complex product mixture under analogous conditions.

As demonstrated by us, although **3** can be converted into **4** by use of TMS-Cl and Et_3N, it is impossible to transform **4** into **5** under similar conditions. However, use of excess TMS-Cl and Et_3N initially leads to an increase in the ratios of **5** to **4**. It seems likely that the formation of **5** proceeds via a similar mechanism to that proposed for the reaction of **2** with acetyl chloride under $FeCl_3$-catalysis [13b]. Our one-pot reaction probably proceeds in a stepwise manner, with the formation of **3**, **4**, and **5** controlled by the reaction conditions.

4. The catalytic effects of various bases, such as Et_3N, C_5H_5N, K_2CO_3, Na_2CO_3, NaH, and sodium alkoxides, on the reaction of **1** and **2** were reported by us earlier [21,23]. Based on our observations, Zhang [24] reported a similar method for the synthesis of **4**, but this is not applicable to unsubstituted 2-nitrostyrenes. For example, treatment of **2d** and **1b** in the presence of K_2CO_3 in ethanol at reflux temperature afforded **4f** in 54% yield. However, a polymeric substance was obtained as the major product when **2a** was used as starting material. The failure of this reaction is due to the different sensitivities of **2a** and **2b** in alkaline media (Equation 3).



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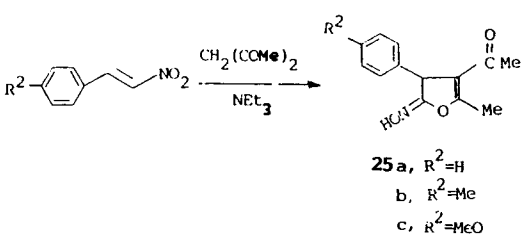
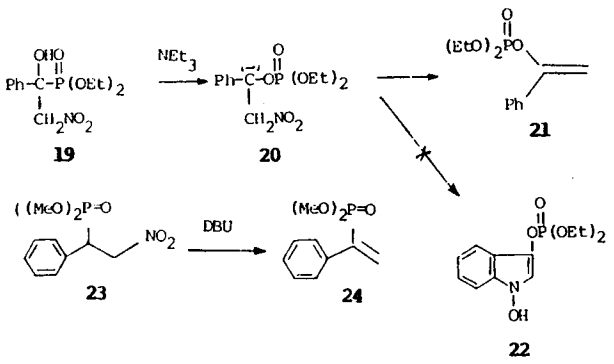


(4)

It should be emphasized that, in the absence of silylating agent, in addition to the polymerization of **2**, the β-elimination reaction of the nitro species in the intermediate stage of the reaction of trivalent phosphorus compounds with **2** will easily take place in alkaline media [14]. Treatment of 1-hydroxy-2-nitroalkylphosphonates **19** with Et_3N, for example, does not afford the cyclic



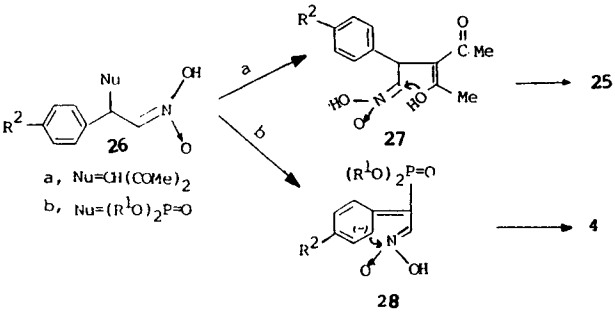
SCHEME 2

product **22**, although carbanion **20** [25] is involved. The vinyl phosphate **21** formed by β-elimination of the nitro group is obtained as the major product. The formation of vinylphosphonates **24** via β elimination of the nitro group of **23** serves as additional evidence (Scheme 2) [26].

On the other hand, reaction of acetylacetone with **2** in the presence of Et_3N at room temperature gave a new type of cyclic oxime **25**. Formation of both **4** and **25** proceeds via similar intermediates **26** derived from the initial Michael addition (Scheme 3). Compound **25** was formed by the nucleophilic attack of the hydroxyl group on the α-position of the acidic nitro group [27]. The ^{13}C NMR spectrum of **25b** is shown in Figure 1.

CONCLUSION

A one-pot procedure for the convenient synthesis of two new types of indole derivatives bearing the 3-phosphoryl moiety has been developed. The synthesis involves the reaction of substituted 2-nitrostyrenes with dialkyl phosphites in the presence of trimethylsilyl chloride, hexamethyldisilazane,



SCHEME 3

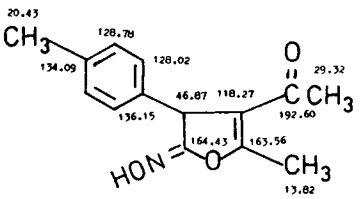


FIGURE 1 ^{13}C NMR data (FX-90MHz) of **25b**. Chemical shifts are given in parts per million relative reference to $CDCl_3$ (77.00).

and triethylamine. Various mechanisms can be proposed for the cyclization steps, all involving deoxygenation of the nitro group by trivalent phosphorus compounds. Trimethylsilyl chloride and triethylamine were found to be necessary for the cyclization process, and the ratio of these two reagents determined the composition of the reaction products. Meanwhile, the nature of the ring substituent has definite but smaller effects. Polymers are sometimes formed, particularly when starting materials or products are unstable in the basic medium.

EXPERIMENTAL

Melting points are uncorrected. ^1H, ^{31}P NMR, and ^{13}C spectra were recorded in $CDCl_3$ on a FX-90MHz spectrometer. TMS was used as an internal standard for ^1H NMR and 85% H_3PO_4 as an external standard for ^{31}P NMR. 1-(p-Methoxyphenyl)-2-nitroethane [28] and O,O-dialkyl O-trimethylsilyl phosphite (**6**) [29] were prepared by literature methods.

N-Hydroxy-Indole Phosphonates **4**; *Typical Procedure for the Synthesis of Compound* **4b**

Diethyl phosphite (0.5 g, 3.6 mmol) and TMS-Cl (1.1 g, 10 mmol) were added to a solution of HMDSA (0.8 g, 5 mmol), Et_3N (0.5 g, 5 mmol), and benzene (15 mL). The mixture was stirred and refluxed for 2 hours and 2-nitro-p-methoxy-styrene (0.7 g, 4 mmol) was added. The reaction mixture was stirred for 4–6 hours until no more starting material was detected by TLC. After removal of volatile substances under reduced pressure, the residue was extracted with ethyl acetate. The organic layer was washed with water, dried with $MgSO_4$, and concentrated to afford **4b** (0.86 g, 85%), mp 125–126°C (from ethyl acetate/petroleum). ν_{max} (KBr)/cm^{-1} 3400 (NOH), 1225 (P=O), 1020 (POC); λ_{max} (MeOH, logϵ)/nm 289.4 (0.321), 220.0 (1.469), 195.4 (0.814) δ_H 1.20 (6H, t, J 7.2), 3.80–4.20(4H, m), 3.90(3H, s), 6.70–7.60 (4H, m), 9.60 (1H, brs); δ_C 157.17 (C—6), 135.24 (J_{PC} 12, C—8), 131.49 (J_{PC3}, C—2), 120.78

(C—4), 117.75 (J_{PC} 10.9, C—9), 112.38 (C—5), 92.13 (C—7) 91.74 (J_{PC} 223.9, C—3), 62.24 (J_{PC} 5.5, C—11), 55.23 (C—10), 16.11 (J_{PC} 6.5, C—12); δ_P 19.38 ppm; *m/z* 299 (M^+, 39.07), 282 (9.87), 162 (23.88), 146 (100). Found: C, 51.82; H, 5.99; N, 4.84. Calc for $C_{13}H_{18}NO_5P$ (299.3); C, 52.17; H, 6.02; N, 4.86.

4a, 4c–e were obtained in a similar manner.

4a: ν_{max}/cm^{-1} 3100, 1650, 1500, 1225, 1020 δ_H 1.20 (3H, t), 3.80–4.20 (4H, m), 6.65–7.50 (4H, m), 9.80 (1H, b, NOH). δ_P 18.98 ppm. Found: C, 53.67, H, 5.94, N, 5.37. Calc for $C_{12}H_{16}NO_4P$ (269.2): C, 53.53; H, 5.94; N, 5.37. The spectral data of compounds of **4c–e** were consistent with the data reported previously by us [23].

Preparation of Compound **5**; *Typical Procedure for the Synthesis of* **5a**

Diethyl phosphite (2.0 g, 14 mmol) and TMS-Cl (2.2 g, 20 mmol) were added to a solution of HMDSA (3,3 g, 20 mmol), Et_3N (2.2 g, 20 mmol), and benzene (25 mL). The mixture was stirred and refluxed for 2 hours, then 2-nitrostyrene (1.5 g, 10 mmol) was added. The reaction was continued for 18 hours. After workup and purification by centrifugal thin-layer chromatography using ethyl acetate/petroleum ether (1:2) as eluent, **5a** was obtained in 48% yield. ν_{max} (KBr)/cm^{-1}) 3400 (NH), 1700 (C=O), 1220 (P=O), 1020 (POC); λ_{max} (MeOH, log ϵ)/nm 285.0 (0.403), 255.2 (0.807), 212.0(0.949); δ_H 1.15 (6H, t, J 7.0), 3.80–4.15 (4H, m), 6.02 (2H, b), 7.00–7.40 (4H, m); δ_c 167.16 (J_{PC} 4.4, C—2) 149.52 (J_{PC} 15.4, C—8), 126.42 (J_{PC} 9.9, C—9), 123.46 (C—4), 120.73 (C—6), 117.41 (C—5), 109, 26 (C—7), 72.15 (J_{PC} 223.3, C—3), 61.73 (J_{PC} 4.4, C—10), 16.34 (J_{PC} 6.6, C—11); δ_P 17.70 ppm; *m/z* 269 (M, 100), 52(12.26), 241(30.57), 213(37.12), 195(47.14), 133(81.08), 117(31.13). Found: C, 53.49; H, 5.97; N, 5.18. Calc for $C_{12}H_{16}NO_4P$ (269.2): C, 53.53; H, 5.94; N, 5.20.

5b: $\nu_{max}/^{-1}$ 3450, 1700, 1225, 1010; δ_H 1.20 (6H, t), 3.60–4.20 (4H, m), 5.60 (2H, b), 3.70 (3H, s), 6.60–7.40 (3H, m). Found: P, 10.71. Calc for $C_{13}H_{18}NO_4P$ (283.2): P, 10.91.

5c: ν_{max}/cm^{-1} 3400, 1700, 1220, 1020; δ_H 1.10 (6H, m), 2.30 (3H, s), 3.70–4.20 (4H, m), 5.70 (2H, b), 6.80–7.40 (3H, m). Found: P, 9.94. Calc for $C_{13}H_{18}NO_5P$ (299.2): P, 10.36.

5d: ν_{max}/cm^{-1} 3400, 1700, 1200, 995; δ_H 1.25 (12 H, dd), 4.40–4.60 (2H, m), 5.80 (2H, b), 7.00–7.40 (4H, m). Found: C, 56.57; H, 6.72; N, 4.70. Calc for $C_{14}H_{20}NO_3P$ (297.24): C, 56.31; H, 6.41; N, 4.76.

3a–e *were Synthesized by the following General Procedure*

The reaction was run by treatment of **1**, **2**, TMS-Cl and HMDSA (molar ratio 1:1:1:1) in CH_2Cl_2 under reflux until no more starting materal was detectable by TLC. Workup and purification by column chromatography on silica gel using ethyl acetate/petroleum ether (1:2) as eluents gave **3a–e** [21]. The spectra of compounds **3a–e** are consistent with the data reported by us previously [21].

Reaction of **1***-Nitro-***2***-(p-Methoxyphenyl)ethane with TMS-Cl and* Et_3N

TMS-Cl (20 mmol) and Et_3N (20 mmol) was added to a solution of **17** (1.8 g, 10 mmol) and benzene (10 mL). The mixture was stirred 12 hours under reflux. No reaction had taken place, as shown by TLC and ^1H NMR. After workup and purification, the starting materials were recovered.

*Reaction of O,O-Diethyl O-Trimethylsilyl Phosphite (***6***) with 2-Nitro-p-Methoxystyrene*

The reaction was carried out with the same reaction conditions used in the preparation of **4**. Both the use of large amounts of **6** and prolonged reaction time afforded the normal addition product **3d**. mp 67–68°C; Ref. [30] mp 65–66°C.

Reaction of **3d** *with TMS-Cl and* Et_3N

To a solution of **3d** (5 mmol) and benzene (10 mL) was added TMS-Cl (10 mmol) and Et_3N (10 mmol). The mixture was stirred for 8h under reflux. After workup and purification, **4b** was obtained in 37% yield. mp 125–127°C.

Reactions of **1b** *and* **2a** *with Various Amounts of TMS-Cl and* Et_3N *and HMDSA*

These reactions were carried out in a manner similar to the preparation of **4**. Reaction mixtures were analyzed by ^1H and ^{31}P NMR, and the results are listed in Table 2.

Cyclic Oximes **25**: *Typical Procedure for the Synthesis of* **25b**

Et_3N (3 mL) was added to a solution of **2c** (1 g, 6 mmol) and acetylacetone (2.0 g, 20 mmol) in methanol (10 mL). The resulting mixture was stirred for 4 hours at ambient temperature, and then water (20 mL) was added. The solid **25b** was isolated by filtration (1.4 g, 57%). mp 154–156°C (from CCl_4). ν_{max}/cm 3278, 1661, 1660; δ_H 2.0 (3H, s), 2.25 (3H, s), 2.40 (3H, s), 5.20 (1H, br), 7.50 (4H, s); ^{13}C NMR is shown in Figure 1. Found: C, 68.55; H, 6.18; N, 5.70. Calc for $C_{14}H_{15}NO_3$ (245.28): C, 68.57%; H, 6.12; N, 5.71.

25a: 47%, mp 152–154°C (from CCl_4); ν_{max}/cm^{-1} 3300, 1670, 1615; δ_H 2.83 (3H, s), 2.45 (3H, s), 5.05 (1H, m), 7.24 (5H, s); *m/z* 232 (M^+, 100), 214 (M—OH^+, 64.46), 200 (54.46), 188 (67.47), 172 (27.47), 158 (14.65), 144 (25.69), 125 (22.65), 115

(8.21). Found: C, 67.10; H, 5.94; N, 5.58. Calc for $C_{13}H_{13}NO_3$ (231.24): C, 67.50; H, 5.67; N, 6.06.

25c: 46%, mp 147–148°C (from ethyl acetate/hexane); ν_{max} (KBr)/cm^{-1} 3335, 1665, 1605; δ_H 1.80 (3H, s), 2.45 (3H, s), 3.80 (3H, s), 5.05–5.20 (1H, m), 6.80–7.40 (4H, m). Found: C, 64.47; H, 5.96; N, 5.12. Calc for $C_{14}H_{15}NO_4$ (261.28): C, 64.35; H, 5.74; N, 5.34.

*Reaction of Diethyl 1-Hydroxy-1-Phenyl-2-Nitroethyl Phosphonate (**19**) with Et_3N*

Et_3N (0.5 mL) was added to a solution of **23** (0.7 g, 2.3 mmol) in CH_2Cl_2 (5 mL). The resulting mixture was stirred for 4 hours at room temperature. Volatiles were removed under reduced pressure, and the residue was purified by chromatography to give **21** (65%). δ_H 1.30 (6H, t), 4.10 (4H, m), 5.20 (2H, d), 7.00–7.60 (5H, m); ν_{max}/cm^{-1} 1645, 1250, 1025; *m/z* 257 ($M + 1^+$, 100%); 155 (57.62), 130 (51.65), 105 (56.85). These data are consistent with the literature [26].

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REFERENCES

[1] P. Ulf, A. Reinhard, *J. Heterocyclic Chem., 25*, 1988, 1.
[2] U. Pindur, E. Akgun, *Chem. -Ztg., 103*, 1984, 371. (b) *Chem. -Ztg., 110*, 1986, 307.
[3] H.-P. Husson: in A. Brossi (ed): *The Alkaloids*, Academic Press, New York, 1985, Vol. 26, p. 1.
[4] J. P. Haelters, B. Corbel, G. Sturtz, *Phosphorus and Sulfur 37*, 1988, 41 and 65.
[5] D. Redmore, *Chem. Rev., 71*, 1971, 315.
[6] (a) A. G. M. Barrett, G. G. Graboski, *Chem. Rev., 86*, 1986, 751. (b) A. Yoshikoshi, M. Miyashita, *Acc. Chem. Res.*, 18, 1985, 284.
[7] A. Sera, H. Yamauchi, H. Yamada, K. Itoh, *Synth. Lett.*, 1990, 477.
[8] A. Kamimura, N. Ono, *Tetrahedron Lett.*, 1989, 731 and references cited therein.
[9] M. S. Akhtar, V. L. Sharma, A. P. Bhadur, *J. Hetrocycl. Chem., 24*, 1987, 23 and references cited therein
[10] M. A. Brimble, *J. Chem. Soc., Perkin. Trans. 1*, 1990, 311.
[11] E. J. Corey, H. Estreicher, *J. Am. Chem. Soc., 100*, 1978, 6294.
[12] S. E. Denmark, J. A. Sternberg, R. Lueoe, *J. Org. Chem., 53*, 1988, 1251.
[13] (a) A. Foucaud, *Bull. Soc. Chim. Belg., 99*, 1981, 545. (b) J. Guillaumel, P. Demerseman, J.-M. Clavel, R. Royger, *J. Heterocycl. Chem., 17*, 1980, 1531.
[14] R. D. Gareev, A. N. Pudovik, *Zh. Obsch., Khim., 56*, 1986, 241.
[15] (a) J. I. G. Cadogan, *Quart. Rev., 22*, 1968, 222. (b) M. M. Campell, N. Cosford, L. Zongli, M. Sainsbury, *Tetrahedron*, 1987, 1117. (c) G. A. Russell, C. F. Yao, H. I. Tashtonsh, J. E. Russell, and D. F. Dedolph, *J. Org. Chem., 56*, 1991, 663.
[16] H. Teichmann, W. Thierfelder, E. Schafer, A. Wejyt, *Tetrahedron Lett.*, 1977, 2899.
[17] W. E. Krueger, M. B. Mclean, A. Rizwaniuk, J. R. Maloney, G. L. Behelfer, *J. Org. Chem., 43*, 1978, 2877.
[18] C. Y. Yuan, G. H. Wang, *Synthesis*, 1990, 256 and 522; *Synthesis*, 1991, 490.
[19] (a) Ger (East) D. D. 130 354 (1978); C.A. 91 (1978) 20716w. (b) Ger (East) D. D. 156 861 (1982); C.A. 98 (1983) 198441j.
[20] J. K. Thottathil, C. A. Przybla, J. L. Moniot, *Tetrahedron Lett.*, 1984, 4374.
[21] (a) Y. G. Li, G. H. Wang, D. K. Chang, *Chemical J. Chinese Universities, 10*, 1989, 373. (b) Y. G. Li, Y. S. Liu, *Phosphorus, Sulfur and Silicon, 47*, 1990, 229.
[22] T. Y. Mastryukova, M. V. Lazarava, V. V. Perekalin, *Izv. Akad. Nauk. SSSR Ser Khim, 42*, 1972, 1164.
[23] Y. G. Li, G. H. Wang, D. K. Chang, et al.: Abstracts, *First International Conference on Heteroatom Chemistry*, Kobe, Japan, p. 46 (1987) *Scientia Sinica (B), 37*, 1988, 41.
[24] R. Zhang, X. Liao, Z. Gao, *Synthesis*, 1990, 801.
[25] F. Hammerschmidt, E. Zbiral, *Monatsh. Chem., 111*, 1980, 1015.
[26] M. Yamashita, Y. Tamada, A. Iida, T. Oshikawa, *Synthesis*, 1990, 420.
[27] (a) M. S. Akhtar, V. L. Sharma, A. P. Bhaduri, *J. Heterocycl. Chem., 24*, 1987, 23. (b) W. Huggenberg, M. Hesse, *Tetrahedron Lett.*, 1989, 5119. (c) I. W. Harvey, M. D. McFarlane, D. J. Moody, D. M. Smith, *J. Chem. Soc., Perkin. I*, 1988, 681.
[28] A. Bhattacharga, R. Mukhopadhyay, S. C. Pakrashi, *Synthesis*, 1985, 886.
[29] M. Sekine, K. Okimoto, K. Yamada, T. Hata, *J. Org. Chem., 46*, 1981, 2097.
[30] V. H. Teichmann, W. Thierfelder, A. Weigt, *J. Prakt. Chem., 329*, 1977, 207.