

The Reactions of Wittig–Horner Reagents with 1,3-Dioxo- $\Delta^{2,\alpha}$ -indanmalononitrile

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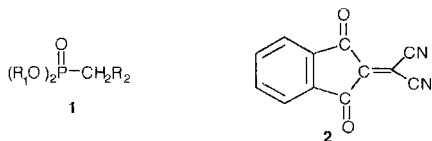
Received 10 October 1995; revised 8 November 1996

ABSTRACT

Wittig–Horner reagents (1a–e) react with 1,3-dioxo- $\Delta^{2,\alpha}$ -indanmalononitrile (2) to give the phosphonate adducts 3, 4, 5, 6, and 7, respectively. Structural reasoning for the new products was based on compatible analytical and spectral data (IR, ^1H , ^{31}P NMR, and MS). The mechanism that accounts for the formation of the new adducts is discussed. © 1997 John Wiley & Sons, Inc. *Heteroatom Chem* 8: 253–257, 1997.

INTRODUCTION

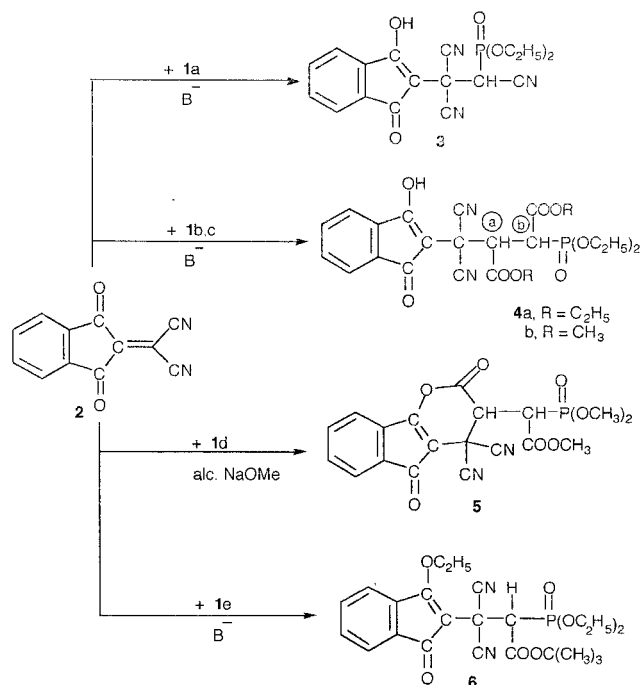
In continuation of our work on the behavior of Wittig–Horner reagents toward carbonyl functions [1–3], the action of the same reagents (1) on 1,3-dioxo- $\Delta^{2,\alpha}$ -indanmalononitrile (2) has now been investigated.



- a. $\text{R}_1 = \text{C}_2\text{H}_5$, $\text{R}_2 = \text{CN}$
- b. $\text{R}_1 = \text{C}_2\text{H}_5$, $\text{R}_2 = \text{COOC}_2\text{H}_5$
- c. $\text{R}_1 = \text{C}_2\text{H}_5$, $\text{R}_2 = \text{COOCH}_3$
- d. $\text{R}_1 = \text{CH}_3$, $\text{R}_2 = \text{COOCH}_3$
- e. $\text{R}_1 = \text{C}_2\text{H}_5$, $\text{R}_2 = \text{COOC}(\text{CH}_3)_3$

RESULTS AND DISCUSSION

We have found that the reaction of 1,3-dioxo- $\Delta^{2,\alpha}$ -indanmalononitrile (also known as 2-dicyanomethyleneindene-1,3-dione) (2) with 1 mol equivalent of diethyl (cyanomethyl)phosphonate (1a), in the presence of alcoholic sodium ethoxide solution, proceeds at room temperature to give a pure adduct formulated as 3 (Scheme 1). Structure elucidation of adduct 3 was based on the following evidence: (a) Cor-



SCHEME 1

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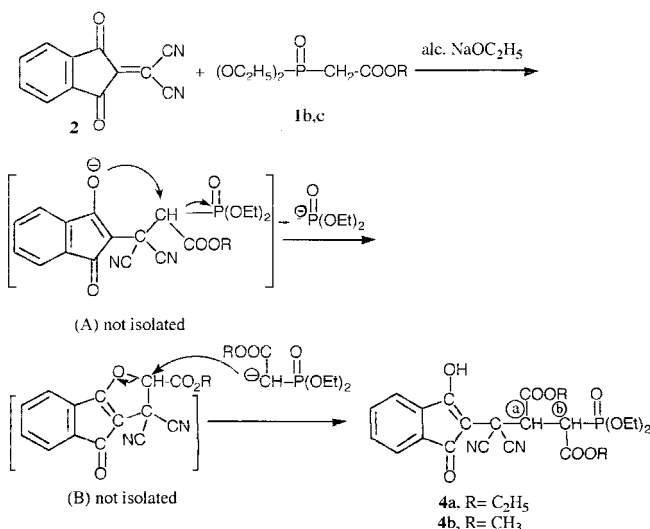
rect elemental analyses and a molecular-weight determination by mass spectroscopy (MS) were obtained, (b) Its IR spectrum in KBr exhibits strong absorption bands at 3524 cm^{-1} (OH), 1235 cm^{-1} (P=O, bonded) [4], 1047 cm^{-1} (P–O–C₂H₅), 2200 cm^{-1} (C≡N), and 1720 cm^{-1} (C=O, indene). (c) Adduct **3** possesses the phosphonate structure since it exhibits a positive shift in its ³¹P NMR spectrum ($\delta = +20.7$ vs. 85% H₃PO₄) and absorbs in the region characteristic for this class of compounds [5–7]. The ¹H NMR spectrum of compound **3** shows signals at $\delta = 1.14$ (6H, P–OCH₂CH₃, t), 4.05 (4H, P–OCH₂CH₃, m), 3.2 (1H, d, with $J_{\text{HP}} = 10$ Hz), and 8.32 (1H, exchangeable with D₂O, –OH proton, s). The spectrum also revealed a complex pattern due to the aromatic protons (4H, m) in the region δ 7.3–7.5. The mass spectrum of compound **3** yielded a prominent ion peak at m/z 385, which is in accord with structure **3**.

The reaction of **2** with triethyl phosphonoacetate (**1b**) was also investigated. When **2** was allowed to react with one equivalent of **1b** in the presence of alcoholic sodium ethoxide solution at room temperature for 6 hours, adduct **4a** and some unchanged indanmalononitrile **2** were isolated. Carrying out the reaction using 2 moles of Wittig–Horner reagent **1b** instead of 1 mole led to the formation of **4a** in good yield. Reasons for structure **4a** were as follows: (a) Elemental and mass spectral analyses for compound **4a** corresponds to an empirical formula C₂₄H₂₇N₂O₉P. (b) The ³¹P NMR spectrum shows a chemical shift, $\delta = +20.2$, that indicates a phosphonate structure. The IR (cm⁻¹) spectrum of **4a** revealed the presence of strong absorption bands at 1710 (C=O, indene), 3500 (OH), 2192 (C≡N), 1248 (P=O, bonded), and 1098 (P–OC₂H₅). The ¹H NMR spectrum of **4a** disclosed the presence of signals at $\delta = 0.85$ (6H, CH₃, m) and 4.2 (4H, CH₂, m), corresponding to the two carboxy groups. The two ethoxy groups attached to the phosphorus atom appeared as a triplet centered at 1.25 (6H, CH₃, t) and as a quintet centered at 4.25 (4H, CH₂, q). Moreover, the ¹H NMR spectrum of compound **4a** showed signals centered at 2.95 (dd with $J_{\text{HP}} = 10$ Hz, $J_{\text{HH}} = 7.5$ Hz) and at 3.05 (dd with $J_{\text{HP}} = 12$ Hz, $J_{\text{HH}} = 7.5$ Hz) corresponding to the two methine protons a and b, respectively [8] (Scheme 1). The exchangeable (D₂O) proton (OH) appears as singlet at δ 8.1. The mass spectrum of compound **4a** showed the molecular ion peak at m/z 518. Similarly, the reaction of methyl diethyl phosphonoacetate (**1c**) with **2** proceeds in alcoholic sodium ethoxide solution to give a pure adduct assigned structure **4b** (Scheme 1). The identity of compound **4b** was inferred from its correct analytical and mass spectroscopic analyses (cf. Experimental). Compounds **4a** and **4b** were obtained in essentially

the same yields irrespective of whether 1 or 2 mole equivalents of the phosphonate anions derived from **1b,e** were used. The mechanism proposed to account for the formation of adducts **4a** and **4b** is shown in (Scheme 2).

1,3-dioxo- $\Delta^{2,\alpha}$ -indanmalononitrile (**2**) reacts with 1 mole of each of the anions of alkyl phosphonoacetates **1b,c** to give the respective intermediates (A). Under the influence of the base present in the reaction medium, phosphonate (A) is converted to the expected intermediate (B) that could then be attacked by another molecule of each of the phosphonate anions **1b,c** to give, after a suitable proton transfer, the final products **4a,b** as depicted in Scheme 2. The dialkyl phosphite was detected in the water layer by the development of a violet color on addition of 3,5-dinitrobenzoic acid [9]. Such an observation has been made for the reaction of *p*-chloranil and N,N'-3,5-cyclohexadiene-1,2-diylidene bis(benzamide) with Wittig–Horner reagents [1,10].

We have also investigated the reaction of **2** with trimethyl phosphonoacetate (**1d**) using alcoholic sodium methoxide solution. Unexpectedly, the reaction was found to proceed in a different manner than that observed for the ethoxy analogues **1b,c**. This new reaction led to the formation of the cyclic product **5**. Compound **5** was isolated as yellowish brown crystals in 68% yield. The structure seemed possible for the reaction product since the IR data confirmed the absence of the –OH group. The ¹H NMR spectrum of **5** revealed the presence of singlet at δ 3.5 for the ester methoxy group. The two methoxy groups attached to the phosphorus atom appeared as a doublet centered at δ 3.6. Moreover, the ¹H NMR spectrum of **5** showed signals at δ 3.3 (dd with $J_{\text{HP}} = 10$



SCHEME 2

Hz, $J_{\text{HH}} = 7.5$ Hz) and 3.39 (dd with $J_{\text{HP}} = 12$ Hz, $J_{\text{HH}} = 7.5$ Hz) for the two methine protons attached at the α and β positions to the phosphorus atom. The mass spectrum of compound 5 gave a prominent ion peak at m/z 430 (M^+ , 10%) consistent with the suggested structure.

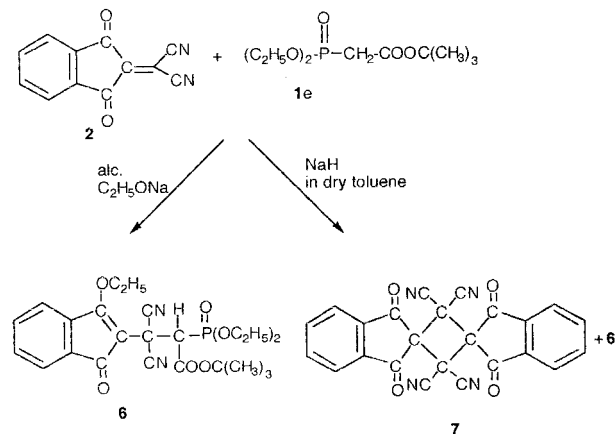
Compound 5, presumably, was formed via addition of 2 moles of trimethyl phosphonoacetate 1d to 2 followed by expulsion of methanol (Scheme 1).

Next, the reaction of 2 with tert-butyl diethyl phosphonoacetate 1e was performed in alcoholic sodium ethoxide solution in 1:2 molar ratio to give adduct 6. Compound 6 was obtained in chromatographically pure form and was found to possess a sharp melting point. Elemental and mass spectral analyses for compound 6 corresponded to an empirical formula of $C_{24}H_{29}N_2O_7P$. Its IR spectrum, in a KBr pellet, revealed the presence of strong absorption bands at 1715 cm^{-1} (C=O, indene), 1740 cm^{-1} (C=O, ester), 2200 cm^{-1} (C \equiv N), and 1246 cm^{-1} (P=O, bonded). Moreover, the IR spectrum of compound 6 indicated the absence of any absorption bands in the region 3000–3500 (–OH absorption band).

The ^1H NMR spectrum of compound 6 in CD_3OD showed signals at $\delta = 1.2$ (3H, OCH_2CH_3 , t) and 3.7 (2H, OCH_2CH_3 , q) corresponding to the OC_2H_5 group attached to the indene ring. The tert-butyl group appeared as a singlet at δ 1.9 (9H, $\text{C}(\text{CH}_3)_3$, s). Moreover, the ^1H NMR spectrum of compound 6 exhibits signals at $\delta = 1.8$ (6H, $\text{P}-\text{O}-\text{CH}_2\text{CH}_3$, t), 3.31 (4H, $\text{P}-\text{OCH}_2\text{CH}_3$, q) corresponding to the two ethoxy groups attached to the phosphorus atom. The methine proton resonance was centered at δ 3.5 (d, 1H with $^2J_{\text{HP}} = 10$ Hz). Actually, the mass spectrum of adduct 6 yielded a prominent ion peak M^+ at m/z 488 that also supports structure 6.

The reaction of 1,3-dioxo- $\Delta^{2,\alpha}$ -indanmalononitrile (2) with tert-butyl diethyl phosphonoacetate (1e) in different bases was also investigated. We have found that the reaction of 2-dicyanomethyleneindan-1,3-dione (2) with 1 mol equivalent of 1e, in the presence of sodium hydride, proceeds at room temperature to give two adducts formulated as compounds 6 and 7, respectively (Scheme 3). On the basis of comparative IR, ^1H NMR, MS, and elemental analyses, as described previously, the structure of compound 6 was deduced. The other isolated compound was established to be the dimeric product 7 from its analysis, IR, ^1H NMR, and mass spectroscopic data (cf. Experimental).

Formation of compound 6 can be explained in terms of initial addition of 1 mole of the Wittig–Horner reagent 1c to 2 followed by alkylation (Scheme 3). We suggest that the steric hindrance provided by

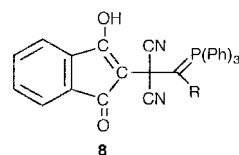


SCHEME 3

the t-butyl group inhibits the intramolecular displacement reaction (cyclization) and leads instead to the formation of 6. A similar alkylation was also observed in the reactions of Wittig–Horner reagents with pyrroles [11], quinoneimines [10], and nitrosonaphthols [12].

CONCLUSIONS

Although 1,3-dioxo- $\Delta^{2,\alpha}$ -indanmalononitrile (2) has been reported [13] to react with conventional Wittig reagents to give (1:1) adducts 8, a different behavior is observed in the reaction of Wittig–Horner reagents (1) with the same indanmalononitrile 2 (Scheme 1).



From the results of the present investigation, it can be concluded that the reaction of dioxoindanmalononitrile (2) with Wittig–Horner reagents (1) lead to different products, depending on the nature of the phosphonate anion used as well as on the stability of the addition products [14].

The significance of these findings is not only the discovery of a new pattern of the Wittig–Horner reaction but also the establishment of a novel method for the synthesis of different ring systems and phosphonate adducts.

EXPERIMENTAL

All melting points are uncorrected. Triethyl phosphonoacetate and diethyl (cyanomethyl)phosphonate were prepared by means of the Michaelis–Ar

buzov reaction [15–17]. The IR spectra were measured in KBr pellets with a Perkin Elmer infracord Spectrophotometer model 157, Grating. The ^1H NMR spectra were run on a Varian Spectrophotometer at 200 MHz, using TMS as an internal reference. The ^{31}P NMR spectra were recorded in CDCl_3 (vs. H_3PO_3 as external standard) with a JNM-PS-100Fa Spectrometer. The mass spectra were run at 70 eV with Kratos MS equipment and/or a Varian MAT 3M A Spectrometer.

Reaction of Diethyl (Cyanomethyl)phosphonate (1a) with Dicyanomethyleneindene-1,3-dione (2)

A solution of 2 mols of sodium ethoxide in absolute ethanol was treated with an equimolar amount of diethyl (cyanomethyl)phosphonate (1a), and then the dicyano compound (2) (1 mol) was added. The resulting reaction mixture was allowed to stir for 4 hours at room temperature. The color of the mixture changed from yellow to deep red. Then the reaction mixture was poured into a small amount of water, extracted with methylene chloride (3×20 mL), and the extract was dried over anhydrous sodium sulfate and evaporated under reduced pressure. The residual material was recrystallized from ethanol to give the new product 3 in 70% yield as red crystals, mp 120°C . Anal. calcd for $\text{C}_{18}\text{H}_{16}\text{N}_3\text{O}_5\text{P}$ (385.32): C, 56.11; H, 4.19; N, 10.91; P, 8.04%. Found: C, 55.84; H, 3.97; N, 10.59; P, 7.73%.

Reaction of Triethyl Phosphonoacetate (1b) with Dicyanomethyleneindene-1,3-dione (2)

The same method was used to react triethyl phosphonoacetate (1b) (0.002 mol) with the starting material (2) (0.001 mol). The reaction was monitored by thin-layer chromatography (TLC), which showed that it was completed after 6 hours. Then the reaction mixture was poured into water, extracted with chloroform (3×20 mL), and dried over anhydrous sodium sulfate. The solvent was evaporated under reduced pressure to give the crude compound (4a), which was recrystallized from benzene to give brown crystals in 75% yield, mp 127°C . Anal. calcd. for $\text{C}_{24}\text{H}_{27}\text{N}_2\text{O}_9\text{P}$ (518.466): C, 55.60; H, 5.25; N, 5.40; P, 5.97%. Found: C, 55.32; H, 4.92; N, 5.07; P, 5.65%.

Reaction of Methyl Diethyl Phosphonoacetate (1c) with Dicyanomethyleneindene-1,3-dione (2)

The reaction of methyl diethyl phosphonoacetate (1c) (0.002 mol) with dicyanomethyleneindene-1,3-dione (2) (0.001 mol) was carried out in the same

manner as previously described. The reaction was finished after 8 hours, and then the reaction mixture was poured into a small amount of water, extracted with ethyl acetate (3×20 mL), dried over anhydrous Na_2SO_4 , evaporated under reduced pressure to dryness, and the residue recrystallized from benzene to give brownish yellow crystals of 4b in 67% yield, mp 145°C . Anal. calcd for $\text{C}_{22}\text{H}_{23}\text{N}_2\text{O}_9\text{P}$ (490.416): C, 53.88; H, 4.73; N, 5.71; P, 6.32%. Found: C, 53.65; H, 4.35; N, 5.29; P, 5.91%. Mol. wt. (MS) = 490 (M^+ , 25%). IR: 3510 cm^{-1} (OH), 1753 cm^{-1} (C=O, ester), 1710 cm^{-1} (C=O, indene), 1230 cm^{-1} (P=O), 1049 cm^{-1} (P–O– C_2H_5). ^1H NMR: δ 1.01 [t, 3H, P(OCH₂CH₃)], 1.2 [t, 3H, P(OCH₂CH₃)], 4.05 [m, 4H, P(OCH₂CH₃)], 4.2 (d, 1H, CH–P with $J_{\text{HP}} = 10$ Hz, $J_{\text{HH}} = 7$ Hz), 4.3 (d, 1H, CH–CH–P) with $J_{\text{HP}} = 12$ Hz, $J_{\text{HH}} = 7$ Hz), 8.4 (s, 1H, OH), 3.5 (s, 3H, COOCH₃), 3.6 (s, 3H, COOCH₃). ^{31}P NMR: $\delta = +20.05$.

Reaction of Trimethyl Phosphonoacetate (1d) with Dicyanomethyleneindene-1,3-dione (2)

Two mols of sodium methoxide were added to a solution of an equimolar amount of trimethyl phosphonoacetate (1d) in methanol (20 mL), and then the starting material (2) was added. The reaction mixture was maintained overnight with stirring at room temperature. After workup to obtain the crude product 5, crystallization from dilute acetic acid was carried out to give yellowish brown crystals of 5 in 68% yield, mp $> 350^\circ\text{C}$. Anal. calcd for $\text{C}_{19}\text{H}_{15}\text{N}_2\text{O}_8\text{P}$ (430.304): C, 53.04; H, 3.51; N, 6.51; P, 7.20%. Found: C, 52.76; H, 3.19; N, 6.04; P, 6.79%.

Reaction of Tert-butyl Diethyl Phosphonoacetate (1e) with Dicyanomethyleneindene-1,3-dione (2)

The reaction of tert-butyl diethyl phosphonoacetate (1e) (0.002 mol) with the dicyano compound (2) (0.001 mol) was carried out in alcoholic sodium ethoxide solution (from reaction of 0.002 mol of Na in 20 mL $\text{C}_2\text{H}_5\text{OH}$). The mixture was maintained under stirring at room temperature overnight. The reaction mixture was poured into water and extracted with chloroform/*n*-butanol to provide compound 6, which was recrystallized from Ethanol/pet. ether to give pale brown crystals of 6 in 76% yield, mp 110°C . Anal. calcd for $\text{C}_{24}\text{H}_{29}\text{N}_2\text{O}_7\text{P}$ (mol. wt. 488.476): C, 59.01; H, 5.98; N, 5.73; P, 6.34%. Found: C, 58.62; H, 5.65; N, 5.34; P, 5.97%.

Use of Sodium Hydride Instead of Sodium Ethoxide

A 0.5 g amount of sodium hydride was suspended in dry toluene (25 mL), and then tert-butyl diethyl

phosphonoacetate (**1e**) (0.001 mol) and the starting material (**2**) were added. The reaction mixture was stirred at room temperature for 6 hours until the color of the mixture changed gradually to dark green. After that, the mixture was filtered to remove the excess of NaH, and then the solvent was evaporated from the filtrate. The residue was washed and extracted with ether to provide a green powder, which was recrystallized from toluene to give green crystals of **7** in 40% yield, mp 238–240°C. Anal. calcd for $C_{24}H_8N_4O_4$ (mol wt. 416.334); C, 69.23; H, 1.94; N, 13.46%. Found: C, 68.92; H, 1.75; N, 13.06%. IR: two indene C=O bands at 1700 and 1720 cm^{-1} . 1H NMR in DMSO, at 7.3–7.5 ppm (8H, aromatic protons). MS (by field ionization method) M^+ at 416.

Use of Weak Bases in Aqueous Medium

A 0.5 g amount of potassium carbonate or potassium bicarbonate was dissolved in 25 mL of water, and tert-butyl diethyl phosphonoacetate (**1e**) (0.001 mol) and the dicyano compound (**2**) (0.001 mol) were added to the aqueous solution. The reaction mixture was boiled on a hot plate for 24 hours. By TLC monitoring, we have found that the starting material (**2**) remained unchanged. The water solution was extracted with chloroform that was dried over anhydrous sodium sulfate and the solvent evaporated. The residue was recrystallized from acetonitrile to give the unchanged 2-dicyanomethyleneindene-1,3-dione (**2**), mp and mixed mp 280–285°C [18].

REFERENCES

- [1] L. S. Boulos, N. M. Abd El-Rahman, *Phosphorus, Sulfur and Silicon*, **62**, 1991, 163–167.
- [2] L. S. Boulos, N. M. Abd El-Rahman, *Phosphorus, Sulfur and Silicon*, **68**, 1992, 241–246.
- [3] L. S. Boulos, N. M. Abd El-Rahman, *Phosphorus, Sulfur and Silicon*, submitted for publication (1995).
- [4] I. J. Bellamy: *The Infra-red Spectra of Complex Molecules*, Wiley, New York, p. 311 (1964).
- [5] F. Ramirez, O. P. Madan, S. R. Heller, *J. Am. Chem. Soc.*, **87**, 1956, 731.
- [6] F. Ramirez, O. P. Madan, C. P. Smith, *Tetrahedron Lett.*, **3**, 1965, 201.
- [7] M. M. Crutchfield, C. H. Dungan, H. J. Letcher, V. Merk, J. R. Van Wazer: *Topics in Phosphorus Chemistry* **5**, Interscience Publishers, New York (1967).
- [8] R. N. Silverstein, G. C. Bassler: *Spectroscopic Identification of Organic Compounds*, 2nd ed., Wiley, New York, p. 145 (1967).
- [9] B. C. Saunders, B. P. Stark, *Tetrahedron*, **4**, 1964, 187.
- [10] L. S. Boulos, M. H. N. Arsanious, *Phosphorus, Sulfur and Silicon*, **89**, 1994, 185.
- [11] M. Mercey, P. Toube, *J. Chem. Res., Synop.*, **62**, 1987, 13; *C. A.* **107**, 1988, 236149x.
- [12] L. S. Boulos, M. H. N. Arsanious, N. K. Eldin, *Phosphorus, Sulfur and Silicon*, accepted for publication (1996).
- [13] F. M. Soliman, M. M. Said, *Phosphorus, Sulfur and Silicon*, **61**, 1991, 335–340.
- [14] L. S. Boulos, I. T. Hennawy, *Phosphorus, Sulfur and Silicon*, **84**, 1993, 173–179.
- [15] G. M. Kosalapoff: *Organophosphorus Compounds*, Wiley, New York, Chap. 7 (1950).
- [16] P. C. Crofts, *Quart Rev. Chem. Soc.*, **21**, 1958, 341.
- [17] H. J. Bestmann, *Angew Chem.*, **89**, 1977, 361.
- [18] S. Chatterjee, *J. Chem. Soc. B*, **6**, 1969, 725–729.