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Diels-Alder Reaction of (2,4,6-Trialkylphenyl)phospholes with *N*-Phenylmaleimide

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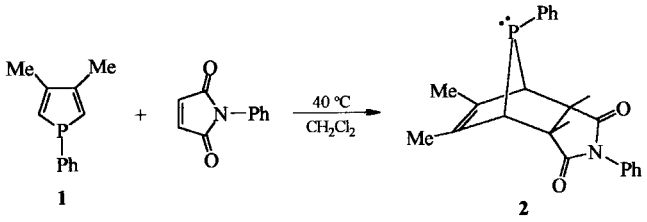
ABSTRACT: *2,4,6-Trialkylphenylphospholes* **3a** *(R = Me),* **3b** *(R = i–Pr) and* **3c** *(R = t–Bu), with increasing flattening at phosphorus and hence with increasing electron delocalisation, underwent the Diels-Alder reaction with N-phenylmaleimide to give predominantly cycloadducts* **4a–c** *with the trialkylphenyl substituents anti to the phosphanorbornene double bond. With increasing aromaticity, the cycloaddition was slower. The stereostructure of the products (***6** *and* **7***) obtained after oxidation was confirmed by stereospecific $^2J_{PC}$ NMR couplings and by an independent synthesis.* © 2000 John Wiley & Sons, Inc. Heteroatom Chem 11:271–275, 2000

INTRODUCTION

Diels-Alder reaction of phospholes with olefinic dienophiles has not been studied in detail [1]. Only the cycloaddition of 3,4-dimethyl-1-phenylphosphole (**1**) with *N*-phenylmaleimide (NPMI) and fumaronitrile has been described [2,3]. In the cycloadducts, for example, in **2** formed by reaction with NPMI (Scheme 1), the phenyl substituent is *anti* to the double bond. A different example of a Diels-Alder reaction, also leading to the *anti* isomer, is the dimerization of 1,3-dimethylphosphole [4]. Interestingly, the dimerization of phosphole oxides, or their cycloaddition with NPMI, gave the isomer with the P-substituent *syn* to the double-bond [5,6]. The Diels-Alder reactivity of common phospholes is in accord with the expectation; due to the pyramidal geometry of the phosphorus atom, they display only a slight extent of aromaticity [7].

Aiming at the synthesis of phospholes with aromatic character, we have recently elaborated the synthesis of (2,4,6-trialkylphenyl)phospholes [8–10].



SCHEME 1

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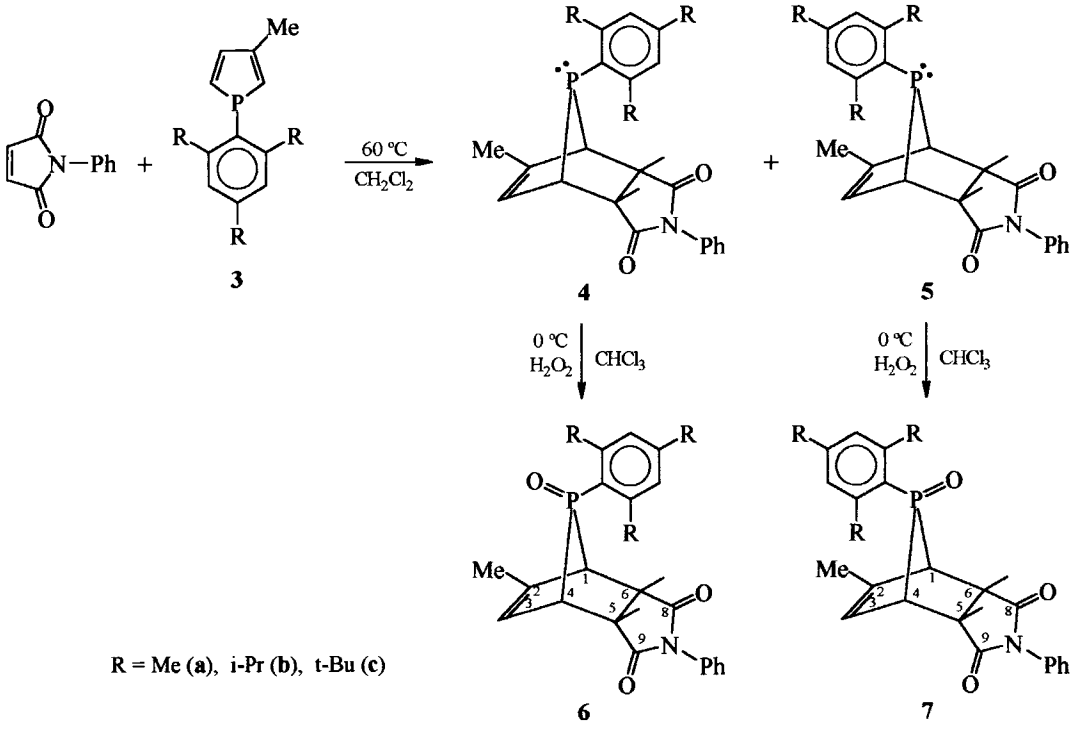
Due to the presence of the sterically demanding P-aryl substituent, the phosphorus pyramid of the phospholes under discussion was planarized to allow considerable electron delocalization. For the phospholes with triisopropylphenyl- and tri-*tert*-butylphenyl substituents on the phosphorus atom, a Bird-index (BI) of 40.4 and 56.5 was reported, respectively [8,9]. Hence, the tri-*tert*-butylphenylphosphole, displaying an aromaticity comparable with that of pyrrole (BI: 59) and thiophene (BI: 66), was found to undergo an aromatic electrophilic substitution [9]. In this article, we explore the behavior of the trialkylphenylphospholes with significant aromaticity in Diels-Alder reactions. The stereochemical outcome of the cycloadditions is also considered.

RESULTS AND DISCUSSION

The trialkylphenylphospholes **3** with methyl- (**a**), isopropyl- (**b**), and *tert*-butyl- (**c**) substituents in the phenyl ring participated in Diels-Alder reaction with NPMI at 60°C (Scheme 2), but with increasing planarization, completion of the cycloaddition required a prolonged reaction time (Table 1). The cycloadduct was formed in all three instances as a mixture of two isomers with **4a–c** predominating over **5a–c**. With the triisopropylphenyl substituent at the phosphorus atom, the proportion of the minor isomer (**5b**) was, however, somewhat higher than in the other instances (**5a,c**). To get air-stable products, the phosphines (**4a–c** and **5a–c**) were oxidized by hydrogen peroxide to the corresponding phosphine oxides (**6a–c** and **7a–c**, respectively) (Scheme 2). The structure of isomer **4**, or after oxidation isomer **6**, was assumed to be analogous with that of cycloadduct **2** formed in the reaction of phosphole **1** (Scheme 1) [2]. The formation of isomer **5** containing the aryl ring and the double-bond in the *syn* relationship is not favored as much as that of the other isomer (**4**). The isomeric compositions, ^{31}P NMR shifts, reaction times, and yields are listed in Table 1.

It can be seen that, proceeding from phosphole **3a** to **3c**, the reaction time increases and the yields obtained after chromatography decrease. In the reaction of **3c**, unidentified side reactions were observed. These observations obviously may be due to the increase in the electron delocalization resulting in a decreased Diels-Alder reactivity of the diene moiety. Of course, the steric hindrance may also contribute to the aforementioned phenomena.

Isomer **6b** could be separated from the other isomer (**7b**) by repeated column chromatography. The structures of isomers **6a–c** and **7b** were identified on the basis of stereospecific $^2J_{PC}$ couplings. It is known that the orientation of the P=*O* in 7-phosphanorbornenes has a significant impact on the $^2J_{PC}$ values; in the isomer having the P=*O anti* to the double-bond, the couplings are comparable on all *β*-carbon



SCHEME 2

TABLE 1 Preparation of Cycloadducts **6a–c** and **7a–c** by the Diels-Alder Reaction of Phospholes **3a–c** with NPMI[a] Followed by Oxidation[b]

	6		*7*			
R	*[%][c]*	δ_P[d]	*[%][c]*	δ_P[d]	t_r *[days]*	*yield of* **6** *[%]*
Me (**a**)	95	88.9	5	84.5	~1	57
i-Pr (**b**)	62	87.6	38	84.4	~1.5	58
t-Bu (**c**)	91	86.1	9	80.1	~3	31

[a]As a comparison, only isomer **2** was formed in the cycloaddition of phenylphosphole **1** with NPMI at 40°C. Reaction time: 4 hour. Yield 50% [2].
[b]See Experimental section for general procedure.
[c]On the basis of relative ^{31}P NMR intensities.
[d]In $CDCl_3$ solution.

atoms (10–13 Hz for *tert*-phosphine oxides), whereas in the other isomer exhibiting the P=*O syn* to the double-bond, the couplings become larger on C_5 and C_6, but will be smaller on C_2 and C_3 (16–21 Hz vs. 1–4 Hz for *tert*-phosphine oxides) [11,12]. Thus, the $^2J_{PH}$ couplings of 11.0–15.1 Hz observed on the four *β*-carbon atoms suggested structure **7**, and the 0–5.9 Hz couplings observed on C_2 and C_3, as well as the 19.1–22.9 Hz values detected on C_5 and C_6, confirmed the structure of isomer **6**. The ^{13}C NMR data for isomers **6a–c** and **7b** are collected in Table 2. The ^{13}C NMR assignments were confirmed by the Attached Proton Test Technique. Beside ^{31}P and ^{13}C NMR spectroscopy, products **6a–c** and **7b** were also characterized by their ^{1}H NMR and mass spectra. Elemental composition of compounds **6** and **7** was supported by HRMS.

The stereostructure of minor isomer **7b** was also confirmed by an independent synthesis. Diels-Alder reactions of phosphole oxides are known to afford a single isomer with the P-substituent *syn* to the double bond [5,6]. Thus, the reaction of NPMI with (triisopropylphenyl)phosphole oxide (**10**), obtained from the 2,5-dihydro-1H-phosphole oxide (**8**) in two steps according to Scheme 3, furnished a phosphanorbornene that was found to be identical with isomer **7b** according to the ^{31}P and ^{13}C NMR parameters.

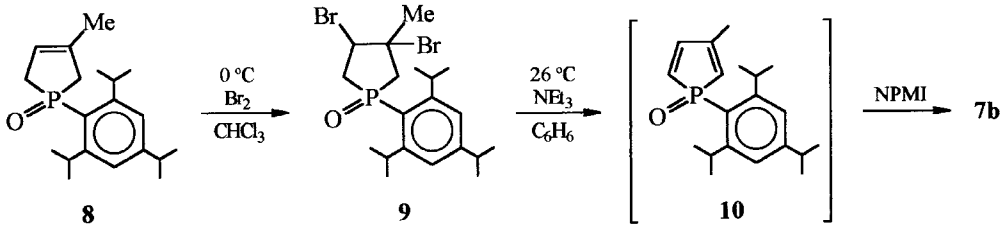
The Diels-Alder reaction of phosphole oxides with dienophiles is a good choice for the preparation of phosphanorbornenes with the P-substituent *syn* to the double-bond (for example, **7**). The phosphine oxides (e.g., **7**) can be easily deoxygenated to the corresponding phosphines (e.g., **5**). For the synthesis of phosphanorbornenes with the aryl group *anti* to the double bond (e.g., **4**), the procedure that is described in this article can be employed.

It can be concluded that, despite the electron de-

TABLE 2 ^{13}C NMR Spectral Parameters for Phosphanorbomenes **6a–c** and **7b** in $CDCl_3$ Solution

Comp.	C_1	C_2	C_3	C_4	C_5	C_6	C_8	C_9	C_2-*Me*	*CH*$_3$ *CH*(*CH*$_3$)$_2$ *C*(*CH*$_3$)$_3$	*CHMe*$_2$ *CMe*$_3$	C_α	C_β C_ω			C_γ C_ε	C_δ	$C_{\alpha'}$	$C_{\beta'}$	$C_{\gamma'}$	$C_{\delta'}$
6a	50.4	142.0	122.5	47.0	42.4	41.0	175.0[a]	175.4[a]	19.7	21.4	22.2		b	140.5	140.6	130.8	130.9	142.9	131.8	126.3[c]	129.6[c]	129.3
	(64.7)	(5.1)	(2.4)	(64.4)	(22.9)	(21.2)	(15.7)	(16.2)	(2.8)					(6.6)	(7.3)	(5.5)	(5.0)	(1.5)				
6b	51.2	141.7	122.2	47.7	42.5	41.1	174.6[d]	175.0[d]	19.4	23.1	23.2	23.6	32.4	32.4	34.2	124.1	152.0	152.0	122.8	122.9	153.7	131.6	126.3[a]	129.2[a]	129.1
	(64.6)	(5.4)		(64.7)	(22.5)	(20.8)	(14.9)	(15.7)	(2.3)	(5.0)			(7.2)			(80.8)	(9.5)	(9.5)	(10.8)	(11.3)				
7b	51.1	140.8	122.1	48.4	44.9	43.6	175.6[f]	175.9[f]	19.2	23.6	23.7	26.3	32.4	32.4	34.2	120.9	152.0	153.2	121.5	122.5	152.7	131.8	126.5[g]	129.3[g]	128.9
	(63.3)	(11.3)	(11.0)	(63.4)	(15.1)	(13.6)	(13.5)	(14.4)	(6.7)	(8.5)			(9.6)			(94.4)	(9.8)	(10.7)	(9.4)	(10.8)	(2.0)				
6c	53.0	142.8	123.2	49.6	42.0	40.8	175.2[h]	175.6[h]	19.8	31.2	33.6	33.6	34.9	40.0	40.1	121.2	156.9	157.0	124.8	124.9	153.9	131.6	126.4[f]	129.2[f]	128.9
	(67.7)	(5.9)	(3.8)	(67.8)	(20.7)	(19.1)	(14.0)	(14.5)	(2.3)		(8.2)	(8.2)	j			(80.2)	(8.5)	(9.1)	(11.7)	(11.5)	(3.0)				

[a,c–f]May be reversed.
[b]Not resolved.
[j]Broad signal.



SCHEME 3

localization in their hetero ring, the (2,4,6-trialkylphenyl)phospholes (**3a–c**) can take part in the Diels-Alder reaction with NPMI. With increasing flattening, the cycloaddition becomes less efficient (low yields and prolonged reaction times). The tri-*tert*-butylphenylphosphole (**3c**) clearly displays a dual reactivity; it can participate both in aromatic substitution and in Diels-Alder cycloaddition.

EXPERIMENTAL

The ^{31}P, ^{13}C, and ^{1}H NMR spectra were obtained on a Bruker DRX-500 spectrometer at 202.4, 125.7, and 500 MHz, respectively, with 85% phosphoric acid or TMS as the reference. The couplings are given in Hz. The mass spectra were recorded on a ZAB-2SEQ instrument at 70 eV.

The starting phospholes (**3a–c**) were prepared as described earlier [8,10].

General Procedure for the Preparation of Phosphanorbornenes **6a–c**

A solution of 1.33 mmol of phosphole **3a–c** and 0.28 g (1.60 mmol) of NPMI in 8 mL of dry dichloromethane was degassed by nitrogen and placed into a tube. After sealing the tube, the mixture was kept at 60°C for the time indicated in Table 1. Then, the solvent was evaporated [13], and the residue was taken up in 50 mL of chloroform. At 0°C, 0.23 mL of 30% hydrogen peroxide was added dropwise with intensive stirring. After 30 minutes at 0°C, the mixture was stirred for another 30 minutes at 26°C. The organic phase was extracted with 3 × 25 mL of water and dried over $MgSO_4$. The crude product obtained after filtration and evaporation was purified by repeated column chromatography (silica gel, 3% methanol in chloroform) to give a mixture of phosphine oxides **6a–c** and **7a–c** (Table 1).

Product **6a**: ^{31}P NMR, Table 1; ^{13}C NMR, Table 2; ^{1}H NMR ($CDCl_3$) δ 2.09 (s, C_2–Me), 2.31 (s, ArMe), 2.66 (s, ArMe), 2.67 (s, ArMe), 6.21–6.24 (m, C_3-H); MS, *m/z* (rel. int.) 405 (M^+, 54), 390 (M–Me, 2), 238 (M–ArPO–H, 40), 167 (ArPO + H, 36), 166 (ArPO, 36), 119 (Ar, 73), 92 (100); HRMS, M^+_{found} = 405.1481, $C_{24}H_{24}NO_3P$ requires 405.1494.

Product **6b**: ^{31}P NMR, Table 1; ^{13}C NMR, Table 2; MS, *m/z* (rel. int.) 489 (M^+, 28), 474 (M–Me, 3), 251 (250 + H, 56), 250 (ArPO, 100), 240 (M–ArPO + H, 50), 203 (Ar, 37), 92 (70); HRMS, M^+_{found} = 489.2439, $C_{30}H_{36}NO_3P$ requires 489.2433.

Product **6c**: ^{31}P NMR, Table 1; ^{13}C NMR, Table 2; ^{1}H NMR ($CDCl_3$) δ 1.35 (s, *p*-$C(CH_3)_3$), 1.58 (s, *o*-$C(CH_3)_3$), 1.59 (s, *o*-$C(CH_3)_3$), 2.02 (s, C_2–Me), 6.14–6.17 (m, C_3–H); FAB, 532 (M + H); HRFAB, $[M + H]^+_{found}$ = 532.2960, $C_{33}H_{43}NO_3P$ requires 532.2981.

Synthesis of Cycloadduct **7b**

To a solution of 1.5 g (3.14 mmol) of dibromotetrahydrophosphole oxide **9** [8] and 0.66 g (3.83 mmol) of NPMI in 40 mL of dry benzene was added 0.92 mL (6.59 mmol) of triethylamine at 26°C. The contents of the flask was allowed to stand for 7 days and then filtered. The amine salt was washed with 20 mL of benzene, and the liquids were combined. Volatile components were evaporated, and the residue so obtained was purified by column chromatography (as described previously) to give 1.07 g (70%) of product **7b**. ^{31}P NMR ($CDCl_3$) δ 84.5; ^{13}C NMR, Table 2; ^{1}H NMR ($CDCl_3$) δ 1.25 (d, J = 6.9, $CH(CH_3)_2$), 1.28 (d, J = 6.6, $CH(CH_3)_2$), 1.34 (d, J = 6.8) and 1.42 (d, J = 6.8) ($CH(CH_3)_2$), 1.68 (s, C_2–Me), 5.83–5.86 (m, C_3–H); MS, *m/z* (rel. int.) 489 (M+, 77), 474 (4), 251 (53), 250 (100), 240 (52), 203 (18), 92 (28); Anal. Found, C, 73.81, H, 7.55 $C_{30}H_{36}NO_3P$ requires C, 73.60, H, 7.41.

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[13] MS for **4a** and **5a**: 389 (M^+); MS for **4b** and **5b**: 473 (M^+); MS for **4c** and **5c**: 515 (M^+).