Pergamon

Tetrahedron 58 (2002) 1573–1579

TETRAHEDRON

Stereo- and regioselectivity in Diels–Alder reactions of 1,3-azaphospholo[5,1-*a*]isoquinoline and -[1,5-*a*]pyridine

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Received 3 September 2001; revised 27 November 2001; accepted 20 December 2001

Abstract—1,3-Bis(ethoxycarbonyl)-1,3-azaphospholo[5,1-*a*]isoquinoline and -[1,5-*a*]pyridine undergo stereoselective Diels–Alder reactions at the >C=P– functionality with 2,3-dimethylbutadiene and isoprene in the presence of sulfur or methyl iodide. The reaction with isoprene occurs regioselectively as well, as confirmed by an X-ray crystal structure determination of one cycloadduct. Semiempirical PM3 calculations also support the regioselectivity. © 2002 Elsevier Science Ltd. All rights reserved.

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1. Introduction

The Diels–Alder (DA) reaction is perhaps the most widely used synthetic methodology for the construction of a six-membered ring.[1] The reaction incorporates several interesting features such as regio- and stereochemical aspects which have been rationalised on the basis of the orbital symmetry.[2] In the last few years the scope of the DA reaction has been further extended to new classes of organophosphorus compounds bearing the >C=P– functionality, namely phosphaalkenes,[3–7] heterophospholes,[6,8–10] anellated azaphospholes[11–14] and phosphinines.[15] Several interesting [2+4]cycloadditions have been accomplished using many of these compounds as dienophiles,[8–10,15–18] but in some cases heterophospholes and λ^3-phosphinines can also act as the diene component.[15,19–21] 1*H*-1,3-Benzoxaphosphole was found to form a [2+4]cycloadduct with 2,3-dimethylbutadiene stereospecifically.[22] A similar observation was made in the reaction of cyclopentadiene with 2-acetyl-1,2,3-diazaphosphole.[23] The reaction of the latter with isoprene occurred regioselectively.[24]

We recently reported the syntheses of 1,3-bis(alkoxycarbonyl)-1,3-azaphospholo[1,5-*a*]pyridines[25,26] and 1,3-bis(alkoxycarbonyl)-1,3-azaphospholo[5,1-*a*]isoquinolines[27] via 1,5-electrocyclization. The >C=P– functionality in these systems acts as an electron-deficient dienophile and hence, in contrast to the inertness of 1-methyl-3-ethoxycarbonyl-1,3-azaphospholo[1,5-*a*]pyridine,[28] undergoes DA reaction with 2,3-dimethylbutadiene and isoprene in the presence of sulfur or methyl iodide. The reaction with isoprene occurs regioselectively, as has been confirmed by X-ray crystal structure determination of one cycloadduct. The observed regioselectivity is supported by semiempirical PM3 calculations. The results are described in this paper.

2. Results and discussion

1,3-Bis(ethoxycarbonyl)-1,3-azaphospholo[5,1-*a*]isoquinoline **1** reacts with 2,3-dimethylbutadiene in the presence of sulfur or methyl iodide in chloroform at room temperature to give [2+4]cycloadducts **3a** and **4a**, respectively. Likewise, the reaction of 1,3-bis(ethoxycarbonyl)-1,3-azaphospholo[1,5-*a*]pyridine **2** with 2,3-dimethylbutadiene and methyl iodide affords **4b**. The reaction of **1** with isoprene in the presence of sulfur proceeds regiospecifically to give **3b** only (Scheme 1), but the use of methyl iodide in place of sulfur leads to a mixture of two regioisomers, **4c** and **4c′** (Fig. 1).

The reaction of **1** with 2,3-dimethylbutadiene alone was very slow at room temperature and could be completed (δ $^{31}P=14.1$) only after refluxing in chloroform for 4 days. The role of the oxidizing agent, sulfur or methyl iodide, therefore appears to be to push a reversible reaction between 1,3-azaphosphole ring and diene in the forward direction by oxidizing the σ^3-P atom of the initially formed [2+4]cycloadduct.

The cycloadducts are obtained as pale to golden yellow

Keywords: stereoselectivity; regioselectivity; Diels–Alder reaction; X-ray crystal structure; 1,3-azaphosphospholes; semiempirical PM3 calculations.

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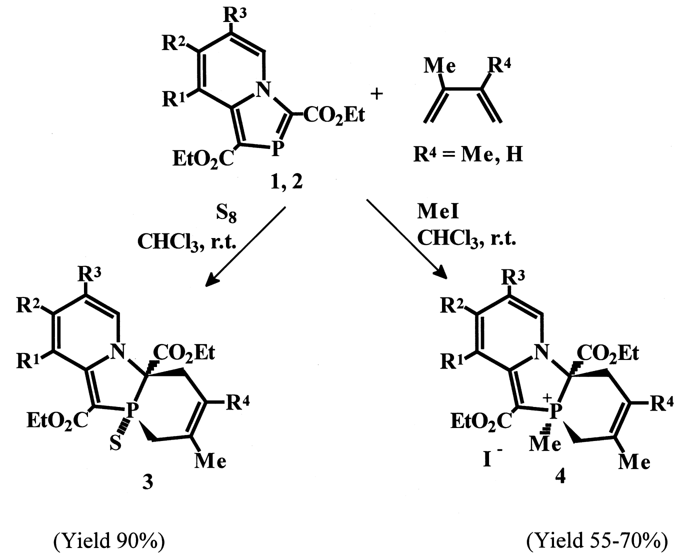
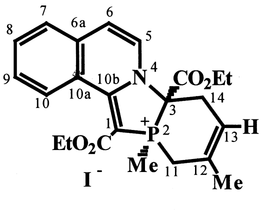
[†] X-Ray crystal structure determination.

PII: S0040-4020(02)00004-2

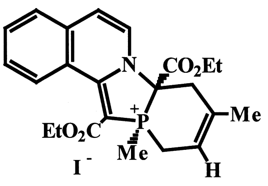


	1	2	3a	3b	4a	4b	4c
R^1		H				H	
R^2		H				H	
R^3	H	Et	H	H	H	Et	H
R^4	-	-	Me	H	Me	Me	H

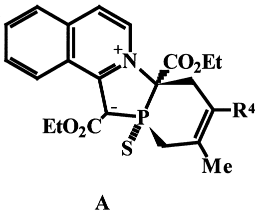
Scheme 1.



4c



4c′



A

Figure 1.

crystalline solids, soluble in polar solvents such as chloroform and acetonitrile.

^{31}P, ^{1}H and ^{13}C NMR data of the cycloadducts **3** and **4** are given in Section 4. The preliminary report of the cycloaddition of **1** with 2,3-dimethylbutadiene and sulfur has been published earlier.[27] The products **3a**,**b** and **4a**,**b** give each a ^{31}P NMR signal at δ 47.2–67.4, the range characteristic for four-coordinate phosphorus.[29] This shows the stereospecific as well as regiospecific nature of the cycloaddition reaction. The 12-Me group in **3b**, whose structure has also been determined by X-ray crystal studies (given later), gives a singlet at δ 1.72, slightly broadened due to coupling with phosphorus, which however could not be resolved. In other cycloadducts, this singlet appears at δ 1.75. Thus a somewhat upfield doublet at δ 1.61–1.64 ($^{5}J_{PH}$=3.8–5.1 Hz) observed in the cycloadducts obtained with 2,3-dimethylbutadiene can be assigned to 13-Me. The protons of 11-CH$_2$ and 14-CH$_2$ are diastereotopic and constitute an ABX spin system because of coupling with the geminal proton and with phosphorus. In **3b**, 14-H$_B$ also shows a three-bond coupling with the vinylic 13-H ($^{3}J_{HH}$=7.2 Hz). The P–Me group in **4** gives a doublet at δ 2.42–2.60 ($^{2}J_{PH}\approx$14.2 Hz). A characteristic feature of the ^{13}C NMR spectra of the cycloadducts **3** and **4** is found to be highly shielded C-1 (δ 65.7–82.6) and highly deshielded C-10b (δ 166.1–167.6) in contrast to **1**.[27] These unexpected chemical shifts are possibly due to the zwitterionic structure **A** (Fig. 1).

The reaction of **1** with isoprene in the presence of methyl iodide is regioselective, although the regioselectivity decreases to 62%, the other regioisomer **4c′** being formed in 38% amount. The product isolated gives two ^{31}P NMR signals at δ 49.4 and 56.3 corresponding to **4c** and **4c′** (Fig. 1). In the ^{1}H NMR spectrum, a singlet at δ 1.75 results due to 12-Me of **4c** while a doublet at δ 1.62 ($^{5}J_{PH}$=4.9 Hz) can be assigned to 13-Me of the isomer **4c′**. The ^{1}H NMR signals of H-6, H-8, H-9, H-12, H-13, 11-, 14-CH$_2$, 1-, 3-OCH$_2$, 1-, 3-OCH$_2$CH_3 of the two regiomers could not be resolved and give multiplets in the corresponding regions. Besides, the P–Me groups of the two isomers also could not be resolved and they give a doublet at δ 2.54 ($^{2}J_{PH}$=14.2 Hz).

The structure of the compound **3b** as determined by X-ray crystal investigation is shown in Fig. 2 and the relevant data

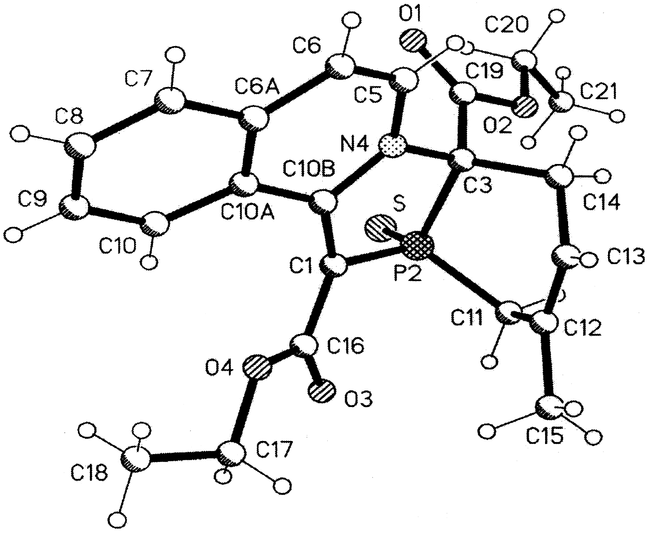


Figure 2. Crystal structure of **3b**.

are given in Table 1. It confirms many characteristic structural features of the reaction. It is obvious that the reaction leads to stereospecific *cis*-anellation of the diene at the >C=P– moiety, in accordance with the symmetry considerations[2] and has been observed earlier in the DA reactions of 1*H*-1,3-benzoxaphosphole,[22] 2-acetyl-1,2,3-diazaphosphole[23] and phosphaalkenes.[30] Furthermore, it also shows that the preferred regioisomer has the methyl group from the isoprene residue oriented *meta* to the phosphorus. A similar regio-orientation was observed in the reaction of 2-acetyl-1,2,3-diazaphosphole with isoprene[24] and can be explained on the basis of the symmetry rules.[2]

As a result of the change of hybridization of C3 (X-ray structure numbering) and P from sp^2 to sp^3 because of the cycloaddition at P=C bond, the planarity of the azaphosphole ring is lost with phosphorus atom moving 26 pm out of the plane of the other four atoms [cf. torsion angle P(2)–C(1)–C(10b)–N(4) −12.0°]. As expected, the significant increase in P(2)–C(3) bond length in **3b** by 17.6 pm as compared to that in **1**[31] is accompanied by small increase in C(1)–P(2) and C(3)–N(4) bond lengths, by 3.1 and 8.6 pm, respectively. The endocyclic angle at P increases by 2.3° only, because of the steric control imposed by the five-membered ring. A notable feature of the structure of **3b** is the conformation of the phosphacyclohexene ring, which is in boat form [C11 and C14 lie 70 and 58 pm out of the plane of the other four atoms, which have a mean deviation of only 2.9 pm; cf. torsion angles N(4)–C(3)–P(2)–C(11) 121.09° and C(1)–P(2)–C(3)–C(14) 108.75°]. Furthermore, this ring is folded towards the azaphosphole ring and away from the sulfur [torsion angles S–P(2)–C(11)–C(12) 175.87° and C(19)–C(3)–C(14)–C(13) −167.68°].

2.1. PM3 Calculations and regioselectivity

The regioselectivity in the DA reactions was correlated with the relative coefficient magnitudes on the terminal carbons of the addenda determined by computational calculations.[2,32,33] We have carried out semiempirical PM3 calculations[34] of **1** and isoprene to explain the observed regioselectivity. The frontier orbital energies of **1** and isoprene reveal that the cycloaddition is $\text{isoprene}_{\text{HOMO}}$–$\text{azaphosphole}_{\text{LUMO}}$ controlled and thus falls in the *Sustmann Type I* category.[35] Furthermore, it is found that the LUMO in **1** is centred on the –P=C< moiety. The coefficient magnitudes on the terminal atoms of the >C=P– in LUMO of **1** and HOMO of isoprene and their energies are shown in Fig. 3.

It is obvious that the overlap of the larger terminal coefficients in the transition state, resulting in greater stabilization, leads to the cycloadduct having methyl and COOEt substitutents in *para* position. Thus the favoured regioisomer as obtained experimentally has the methyl substituent of the isoprene residue *meta* to phosphorus. Similar regioselectivity has been observed in the reaction of 2-acetyl-2*H*-1,2,3-diazaphosphole[24] with isoprene. The

Table 1. Selected bond lengths and angles of **3b**

Bond lengths (pm)		Bond angles (°)		Torsion angle (°)	
P(2)–C(3)	189.1(2)	C(1)–P(2)–C(3)	91.93(9)	C(1)–P(2)–C(3)–N(4)	−9.97(13)
P(2)–C(1)	176.8(19)	C(1)–P(2)–S	118.37(7)	N(4)–C(3)–P(2)–C(11)	121.09(13)
P(2)–S	195.28(8)	C(1)–P(2)–C(11)	110.22(10)	C(10b)–C(1)–P(2)–C(11)	115.93(15)
P(2)–C(11)	182.0(2)	C(3)–P(2)–S	116.98(7)	C(14)–C(3)–N(4)–C(10b)	−113.34(19)
C(3)–C(14)	155.0(3)	C(11)–P(2)–S	114.48(7)	C(1)–P(2)–C(3)–C(14)	108.75(14)
C(3)–C(4)	147.7(2)	C(11)–P(2)–C(3)	101.71(10)	S–P(2)–C(3)–N(4)	113.44(11)
C(11)–C(12)	151.1(3)	C(14)–C(3)–P(2)	110.82(13)	S–P(2)–C(3)–N(14)	−127.84(12)
C(12)–C(13)	132.5(3)	N(4)–C(3)–C(14)	110.63(16)	P(2)–C(1)–C(10b)–N(4)	−12.0(2)
C(13)–C(14)	150.4(3)	N(4)–C(3)–P(2)	103.68(13)	S–P(2)–C(11)–C(12)	175.87(13)
C(10b)–C(1)	139.4(3)	C(5)–N(4)–C(3)	119.94(17)	C(19)–C(3)–C(14)–C(13)	−167.68(18)

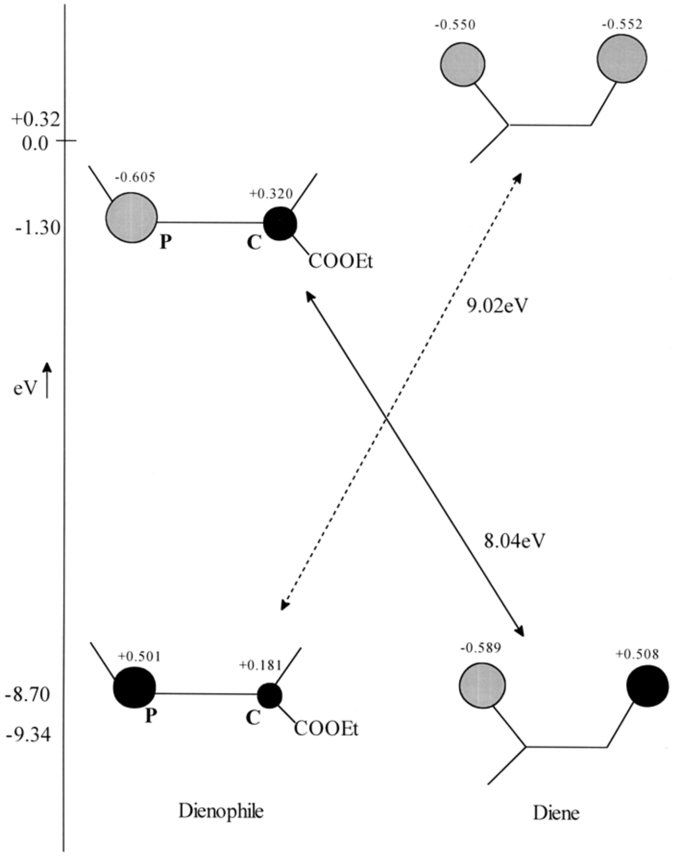


Figure 3.

reason for the difference in the regioselectivity observed in the presence of sulfur (100%) and methyl iodide (62%) is however not clear.

3. Conclusion

The >C=P– functionality in the anellated azaphospholes undergoes DA reaction only if 1,3-positions are substituted by electron-withdrawing groups. Furthermore, reaction occurs stereoselectively as well as regioselectively, the regioisomer having methyl group *meta* to phosphorous being preferred. The observed regioselectivity can be explained qualitatively on the basis of the semiempirical PM3 calculations.

4. Experimental

4.1. General

All reactions were performed under nitrogen atmosphere using Schlenk techniques. Solvents used were freshly dried and distilled. 1,3-Bis(ethoxycarbonyl)-6-ethyl-1,3-azaphospholo[1,5-*a*]pyridine[26] and 1,3-bis(ethoxycarbonyl)-1,3-azaphospholo[5,1-*a*]isoquinoline[27] were prepared by the methods already reported and commercially available dienes were used without further purification. Melting points were recorded by capillary method and are uncorrected. NMR spectra were recorded on Bruker ARX 300 (^{31}P NMR at 121.5 MHz, ^{1}H NMR at 300.1 MHz and ^{13}C NMR at 75.5 MHz). The chemical shifts refer to 85% H_3PO_4 (external) or tetramethylsilane (TMS) (internal) as standards. Mass spectra were recorded on Varian CH7 mass spectrometer. Elemental analyses were carried out using an elemental analyser LECO Model CHNS-932 under standard conditions (carbon combustion of compounds often incomplete giving consistently lower values). Eigenvalues (energy levels) and coefficients of frontier molecular orbitals were calculated by the PM3 procedure using MOPAC 6.0 package.[34]

4.1.1. Reaction of 1 with 2,3-dimethylbutadiene and sulfur (3a). To a clear solution of **1** (1.31 g, 4 mmol) in chloroform (20 mL) were added 1.2 equiv. of 2,3-dimethylbutadiene (0.54 mL, 4.8 mmol) and equimolar amount of sulfur (128 mg, 4 mmol). After stirring the mixture at ambient temperature for 12 days, the ^{31}P NMR spectrum indicated the completion of the reaction. The solvent was evaporated under reduced pressure and the sticky mass so obtained was macerated with hexane to afford yellow solid which on recrystalization from hot acetonitrile gave **3a** (1.94 g, 90%), mp 134–135°C (hot CH_3CN); (Found: C, 61.78; H, 5.99; N, 3.14. $C_{23}H_{26}NO_4PS$ (431.43) requires C, 61.95; H, 5.86; N, 3.15%); ^{31}P NMR ($CDCl_3$): δ 68.2; ^{1}H NMR ($CDCl_3$): δ 8.93 (1H, d, $^{3}J_{HH}$=8.3 Hz, H-5), 7.64 (1H, td, $^{3}J_{HH}$=7.3 Hz, $^{4}J_{HH}$=1.3 Hz, H-8), 7.49 (1H, td, $^{3}J_{HH}$=7.6 Hz, $^{4}J_{HH}$=1.4 Hz, H-9), 7.47 (1H, d, $^{3}J_{HH}$=7.6 Hz, H-6), 6.92 (1H, d, $^{3}J_{HH}$=7.3 Hz, H-10), 6.63 (1H, d, $^{3}J_{HH}$=8.3 Hz, H-7), 4.36–4.25 (4H, m, 1-, 3-OCH_2), 3.48 (1H, t, $^{2}J_{HAHB}$=15.5 Hz, $^{2}J_{PHA}$=15.5 Hz, H_A-11), 3.28 (1H, dd, $^{2}J_{HAHB}$=15.5 Hz, $^{2}J_{PHB}$=13.7 Hz, H_B-11), 2.98 (1H, dd,

$^2J_{HAHB}$=15.5 Hz, $^3J_{PHA}$=16.5 Hz, H$_A$-14), 2.82 (1H, dd, $^2J_{HAHB}$=15.5 Hz, $^3J_{PHB}$=23.0 Hz, H$_B$-14), 1.67 (3H, s, 12-CH$_3$), 1.53 (3H, d, $^5J_{PH}$=5.9 Hz, 13-CH$_3$), 1.41 (3H, t, $^3J_{HH}$=7.1 Hz, 1-OCH$_2$CH_3), 1.27 (3H, t, $^3J_{HH}$=7.1 Hz, 3-OCH$_2$CH_3); ^{13}C NMR (CDCl$_3$): δ 166.1 (C-10b), 164.4 (d, $^2J_{PC}$=9.8 Hz, 1-CO), 159.3 (d, $^2J_{PC}$=9.1 Hz, 3-CO), 134.5 (d, $^3J_{PC}$<1.0 Hz, C-5), 132.3 (C-10), 126.5 (d, $^4J_{PC}$=5.3 Hz, C-6a), 131.0, 125.8, 125.2 (C-7, C-8, C-9), 125.6 (C-10a), 125.0 (d, $^3J_{PC}$=12.8 Hz, C-13), 121.7 (d, $^2J_{PC}$=10.5 Hz, C-12), 109.7 (C-6), 81.6 (d, $^1J_{PC}$=83.3 Hz, C-1), 72.3 (d, $^1J_{PC}$=54.7 Hz, C-3), 62.1 (1-OCH$_2$), 59.2 (3-OCH$_2$), 39.4 (d, $^1J_{PC}$=51.3 Hz, C-11), 38.8 (C-14), 19.2 (d, $^3J_{PC}$=4.2 Hz, 12-CH$_3$), 19.1 (13-CH$_3$), 13.5, 13.3 (1-, 3-OCH$_2$$CH_3$).

4.1.2. Reaction of 1 with isoprene and sulfur (3b). To a solution of **1** (555 mg, 1.69 mmol) in chloroform (20 mL) were added 1.1 equiv. of isoprene (0.19 mL, 1.85 mmol) and 1 equiv. of sulfur (54 mg, 1.69 mmol). The reaction mixture was stirred at room temperature for 30 days. The solvent was evaporated in vacuum and the residue was extracted with diethyl ether (5×15 mL). On leaving the combined and concentrated ether extract in the refrigerator, **3b** (651 mg, 90%) was obtained as bright yellow crystalline solid, mp 138–140°C (C$_6$H$_6$); (Found: C, 59.85; H, 5.23; N, 3.09. C$_{22}$H$_{24}$NO$_4$PS (429.48) requires C, 61.47; H, 5.63; N, 3.26%); ^{31}P NMR (CDCl$_3$): δ 67.4; ^{1}H NMR (CDCl$_3$): δ 8.91 (1H, d, $^3J_{HH}$=8.8 Hz, H-5), 7.64 (1H, t, $^3J_{HH}$=7.9 Hz, H-8), 7.48 (1H, t, $^3J_{HH}$=7.3 Hz, H-9), 7.46 (1H, d, $^3J_{HH}$=8.8 Hz, H-6), 6.80 (1H, d, $^3J_{HH}$=7.3 Hz, H-10), 6.61 (1H, d, $^3J_{HH}$=7.3 Hz, H-7), 5.41 (1H, br unresolved m, H-13), 4.36–4.25 (4H, m, 1-, 3-OCH$_2$), 3.36 (1H, t, $^2J_{PHA}$=13.8 Hz, $^2J_{HAHB}$=13.8 Hz, H$_A$-11), 3.30 (1H, t, $^2J_{HAHB}$=15.9 Hz, $^3J_{PHA}$=15.9 Hz, H$_A$-14), 2.97 (1H, dd, $^2J_{PHB}$=17.4 Hz, $^2J_{HAHB}$=13.8 Hz, H$_B$-11), 2.94 (1H, ddd, $^2J_{HAHB}$=15.9 Hz, $^3J_{PHB}$=22.9 Hz, $^3J_{HBH\text{-}13}$=7.2 Hz, H$_B$-14), 1.72 (3H, s, 12-CH$_3$), 1.39 (3H, t, $^3J_{HH}$=7.1 Hz, 1-OCH$_2$CH_3), 1.28 (3H, t, $^3J_{HH}$=7.1 Hz, 3-OCH$_2$CH_3); ^{13}C NMR (CDCl$_3$): δ 167.3 (C-10b), 165.4 (d, $^2J_{PC}$=9.8 Hz, 1-CO), 160.2 (d, $^2J_{PC}$=9.0 Hz, 3-CO), 136.6 (d, $^3J_{PC}$=11.7 Hz, C-5), 135.7 (C-10), 131.9 (C-6a), 133.4, 126.8, 126.2 (C-7, C-8, C-9), 127.4 (d, $^3J_{PC}$=4.9 Hz, C-10a), 122.8 (d, $^3J_{PC}$=11.7 Hz, C-13), 118.8 (d, $^2J_{PC}$=13.1 Hz, C-12), 111.2 (C-6), 82.2 (d, $^1J_{P,C}$=83.5 Hz, C-1), 73.4 (d, $^1J_{P,C}$=54.6 Hz, C-3), 63.2 (1-OCH$_2$), 60.2 (3-OCH$_2$), 39.3 (d, $^1J_{PC}$=50.8 Hz, C-11), 32.9 (C-14), 24.0 (d, $^3J_{PC}$=5.6 Hz, 12-CH$_3$), 14.5, 14.3 (1-, 3-OCH$_2$CH_3).

4.1.3. Reaction of 1 with 2,3-dimethylbutadiene and methyl iodide (4a). To a clear yellow solution of **1** (850 mg, 2.58 mmol) in chloroform (20 mL), were added two folds of 2,3-dimethylbutadiene (0.58 mL, 5.16 mmol) and one fold of methyl iodide (0.16 mL, 2.58 mmol). After stirring at room temperature for 4 days, the ^{31}P NMR spectrum of the reaction mixture indicated completion of the reaction and formation of the cycloadduct **4a**. The solvent was removed under reduced pressure and the sticky mass so obtained on stirring with diethyl ether (5×15 mL), afforded golden yellow powder (971 mg, 68%), mp 150°C (dec.) (C$_6$H$_6$); (Found: C, 50.66; H, 5.65; N, 2.33. C$_{24}$H$_{29}$NO$_4$PI (553.37) requires C, 52.09; H, 5.28; N, 2.53%); ^{31}P NMR (CDCl$_3$): δ 49.7; ^{1}H NMR (CDCl$_3$): δ 9.41 (1H, d, $^3J_{HH}$=8.2 Hz, H-5), 7.84 (1H, t, $^3J_{HH}$=7.5 Hz, H-8), 7.67 (1H, d, $^3J_{HH}$=8.2 Hz, H-6), 7.66 (1H, t, $^3J_{HH}$=7.3 Hz, H-9), 7.54 (1H, d, $^3J_{HH}$=7.3 Hz, H-10), 7.05 (1H, d, $^3J_{HH}$=7.2 Hz, H-7), 4.53 (1H, dd, $^2J_{HAHB}$=15.6 Hz, $^2J_{PHA}$=14.2 Hz, H$_A$-11), 4.52 (2H, q, $^3J_{HH}$=7.1 Hz, 1-OCH$_2$), 4.39 (2H, q, $^3J_{HH}$=7.1 Hz, 3-OCH$_2$), 4.12 (1H, t, $^2J_{HAHB}$=15.6 Hz, $^2J_{PHB}$=15.6 Hz, H$_B$-11), 3.28 (1H, t, $^2J_{HAHB}$=15.8 Hz, $^3J_{PHA}$=15.8 Hz, H$_A$-14), 3.22 (1H, dd, $^2J_{HAHB}$=15.8 Hz, $^3J_{PHB}$=5.4 Hz, H$_B$-14), 2.60 (3H, d, $^3J_{PH}$=14.2 Hz, P–CH$_3$), 1.75 (3H, s, 12-CH$_3$), 1.61 (3H, d, $^5J_{PH}$=5.1 Hz, 13-CH$_3$), 1.46(3H, t, $^3J_{HH}$=7.1 Hz, 1-OCH$_2$CH_3), 1.43 (3H, t, $^3J_{HH}$=7.1 Hz, 3-OCH$_2$CH_3); ^{13}C NMR (CDCl$_3$): δ 163.9 (C-10b), 161.8 (d, $^2J_{PC}$=9.3 Hz, 1-CO), 160.7 (d, $^2J_{PC}$=10.6 Hz, 3-CO), 135.2 (C-5), 134.3 (C-10), 128.4 (d, $^3J_{PC}$=13.9Hz, C-6a), 130.9, 126.9, 126.3 (C-7, C-8, C-9), 127.5 (d, $^4J_{PC}$=5.7 Hz, C-10a), 121.9 (d, $^3J_{PC}$=11.7 Hz, C-13), 121.4 (d, $^2J_{PC}$=11.0 Hz, C-12), 113.9 (C-6), 68.6 (d, $^1J_{PC}$=67.5 Hz, C-1), 65.2 (d, $^1J_{PC}$=92.7 Hz, C-3), 64.5 (1-OCH$_2$), 60.6 (3-OCH$_2$), 38.6 (C-14), 28.9 (d, $^1J_{PC}$=47.2 Hz, C-11), 19.9 (d, $^3J_{PC}$=4.9 Hz, 12-CH$_3$), 19.6 (d, $^4J_{PC}$=3.1 Hz, 13-CH$_3$), 13.8, 13.5 (1-, 3-OCH$_2$CH_3), 10.2 (d, $^1J_{PC}$=51.7 Hz, P–CH$_3$); MS (EI, 70 eV): *m/z* (%)=428 (9) [M+1]$^+$, 427 (35) [M$^+$=C$_{24}$H$_{29}$NO$_4$P$^+$], 381 (8) (428−CH$_3$PH$_2$), 355 (11) (427−COOC$_2$H$_5$), 282 (7) (355−COOC$_2$H$_5$).

4.1.4. Reaction of 2 with 2,3-dimethylbutadiene and methyl iodide (4b). To a solution of **2** (770 mg, 2.5 mmol) in chloroform (20 mL), two equivalents of 2,3-dimethylbutadiene (0.56 mL, 5 mmol) and 1 equiv. of methyl iodide (0.16 mL, 2.5 mmol) were added. After stirring at room temperature for 30 days, the solvent was removed from the resulting brown solution under reduced pressure and residue extracted with diethyl ether (5×15 mL). Yellow brown solid deposited on cooling, was recrystallized from benzene (730 mg, 55%), mp 95–97°C (C$_6$H$_6$); (Found C, 49.69; H, 5.70; N, 2.49. C$_{22}$H$_{31}$NO$_4$PI (531.37) requires C, 49.72; H, 5.88; N, 2.63%); ^{31}P NMR (CDCl$_3$): δ 47.2; ^{1}H NMR (CDCl$_3$): δ 8.28 (1H, s, H-5), 7.97 (1H, t, $^3J_{HH}$=8.8 Hz, H-7 {corresponding to position 6a in Fig. 1}), 7.53 (1H, d, $^3J_{HH}$=8.8 Hz, H-8 {corresponding to position 10a in Fig. 1}), 4.53 (2H, q, $^3J_{HH}$=7.1 Hz, 1-OCH$_2$), 4.27 (2H, q, $^3J_{HH}$=7.1 Hz, 3-OCH$_2$), 3.99 (1H, dd, $^2J_{PHA}$=16.1 Hz, $^2J_{HAHB}$=15.3 Hz, H$_A$-11), 3.60 (1H, dd, $^2J_{PHB}$=24.1 Hz, $^2J_{HAHB}$=15.3 Hz, H$_B$-11), 3.49 (1H, dd, $^2J_{HAHB}$=13.8 Hz, $^3J_{PHA}$=6.9 Hz, H$_A$-14), 3.08 (1H, dd, $^2J_{HAHB}$=13.8 Hz, $^3J_{PHB}$=14.3 Hz, H$_B$-14), 2.66 (2H, q, $^3J_{HH}$=7.5 Hz, 6-CH_2CH$_3$), 2.42 (3H, d, $^3J_{PH}$=14.3 Hz, P–CH$_3$), 1.75 (3H, s, 12-CH$_3$), 1.64 (3H, t, $^5J_{PH}$=3.8 Hz, 13-CH$_3$), 1.45 (3H, t, $^3J_{HH}$=7.1 Hz, 1-OCH$_2$CH_3), 1.34 (3H, t, $^3J_{HH}$=7.1 Hz, 3-OCH$_2$CH_3), 1.24 (3H, t, $^3J_{HH}$=7.5 Hz, 6-CH$_2$CH_3).

4.1.5. Reaction of 1 with isoprene and methyl iodide (4c+4c′). **1** (736 mg, 2.23 mmol) was stirred with 2 equiv. of isoprene (0.45 mL, 4.46 mmol) and 1 equiv. of methyl iodide (0.14 mL, 2.23 mmol) in chloroform (20 mL) at room temperature for 10 days. The solvent was removed in vacuum and the sticky mass so obtained was recrystallized from benzene to afford a golden yellow solid which was found to be a mixture of **4c** and **4c′** (843 mg, 70%), mp 130°C (dec.) (C$_6$H$_6$); (Found C, 50.96; H, 5.28; N, 2.72. C$_{23}$H$_{27}$NO$_4$PI (539.34) requires C, 51.21; H, 5.04; N, 2.59%); MS (EI, 70 eV): *m/z* (%)=414 (48) [M+1]$^+$, 413

(100) [M^+=$C_{23}H_{27}NO_4P^+$], 367 (19) (414−CH_3PH_2), 340 (51) (413−$COOC_2H_5$), 269 (20) (340−$COOC_2H_5$).

Compound **4c**: ^{31}P NMR ($CDCl_3$): δ 49.7 (62%); ^{1}H NMR ($CDCl_3$): δ 9.42 (1H, d, $^3J_{HH}$=8.2 Hz, H-5), 7.84 (1H, t, $^3J_{HH}$=7.2 Hz, H-8), 7.69–7.62 (unresolved m, H-6, H-9), 7.50 (1H, d, $^3J_{HH}$=7.5 Hz, H-10), 7.08 (1H, d, $^3J_{HH}$=6.4 Hz, H-7), 5.34 (br unresolved m, H-13), 4.52–4.29 (unresolved m, 1-, 3-OCH_2), 4.10–2.80 (m, 11-, 14-CH_2), 2.54 (d, $^2J_{PH}$=14.2 Hz, P–CH_3), 1.75 (3H, s, 12-CH_3), 1.45–1.38 (m, 1-, 3-OCH_2CH_3); ^{13}C NMR ($CDCl_3$): δ 167.6 (C-10b), 164.7(d, $^2J_{PC}$=9.0 Hz, 1-CO), 161.6 (d, $^2J_{PC}$=9.5 Hz, 3-CO), 136.0 (C-5), 135.6 (C-10), 132.3 (C-6a), 132.3, 128.6, 126.7 (C-7, C-8, C-9), 127.0 (C-10a), 123.4 (d, $^3J_{PC}$=11.3 Hz, C-13), 118.1 ($^2J_{PC}$=14.3 Hz, C-12), 111.4 (C-6), 69.5 (d, $^1J_{PC}$=67.9 Hz, C-1), 67.5 (d, $^1J_{PC}$=92.3 Hz, C-3), 63.1 (1-OCH_2), 59.9 (3-OCH_2), 38.6, (C-14), 29.5 (C-11), 23.1 (d, $^1J_{PC}$=57.8 Hz, P–CH_3), 20.5 (12-CH_3), 13.9, 10.6 (1-, 3-OCH_2CH_3).

Compound **4c′**: ^{31}P NMR ($CDCl_3$): δ 56.3 (38%); ^{1}H NMR ($CDCl_3$): δ 9.08 (1H, d, $^3J_{HH}$=8.6 Hz, H-5), 7.69–7.62 (unresolved m, H-6, H-8), 7.52 (1H, t, $^3J_{HH}$=7.5 Hz, H-9), 6.95 (1H, d, $^3J_{HH}$=7.5 Hz, H-10), 6.71 (1H, d, $^3J_{HH}$=6.9 Hz, H-7), 5.34 (br unresolved m, H-12), 4.52–4.29 (unresolved m, 1-, 3-OCH_2), 4.10–2.80 (m, 11-, 14-CH_2), 2.54 (d,$^2J_{PH}$=14.2 Hz, P–CH_3), 1.62 (3H, d, $^5J_{PH}$=4.9 Hz, 13-CH_3), 1.45–1.38 (6H, m, 1-, 3-OCH_2CH_3); ^{13}C NMR ($CDCl_3$): δ 166.8 (C-10b), 165.1 (d, $^2J_{PC}$=9.0 Hz, 1-CO), 162.5 (d, $^2J_{PC}$=9.0 Hz, 3-CO), 135.4 (C-5), 135.3 (C-10), 133.3 (C-6a), 131.0, 128.2, 126.2 (C-7, C-8, C-9), 128.9 (C-10a), 124.5 (C-13), 122.3 (d, $^2J_{PC}$=12.0 Hz, C-12), 114.5 (C-6), 68.4 ($^1J_{PC}$=68.4 Hz, C-1), 65.7 ($^1J_{PC}$=90.0 Hz C-3), 65.3 (1-OCH_2), 61.4 (3-OCH_2), 32.5 (C-14), 28.8 (C-11), 23.1 (d, $^1J_{PC}$=57.8 Hz, P–CH_3), 14.6 (13-CH_3), 14.3, 10.8, (1-, 3-OCH_2CH_3).

4.1.6. X-Ray structure analysis of 3b. *Crystal data.* $C_{22}H_{24}NO_4PS$, triclinic, P(-1), a=739.36(8), b=1052.54(10), c=1402.20(14) pm, α=100.007(7), β=101.329(8), γ=97.361°, V=1.0387 nm^3, Z=2, μ=0.262 mm^{-1}, D_x=1.373 mg m^{-3}, λ(Mo K$_\alpha$)=71.073 pm, T=−100°C.

Data collection. An irregular yellow crystal ca. 0.4×0.3×0.2 mm^3 was mounted on a glass fibre and transferred to the cold gas stream of a Siemens P4 diffractometer. Data were recorded to 2θ(max) 50°.

Structure solution and refinement. The structure was solved by direct methods and refined anisotropically on F^2 using the program SHELXL-97 (G. M. Sheldrick, University of Göttingen, Germany). Hydrogen atoms were included using a riding model or rigid methyl groups. The final $wR2$ was 0.0893 for all 3643 unique reflections and 265 parameters, with conventional $R1$ 0.0356; S=1.04, max. $\Delta\rho$ 347 e nm^{-3}.

Complete crystallographic data (excluding structure factors) have been deposited at the Cambridge Crystallographic Data Centre under the reference numbers CCDC 168182. Copies of the data can be obtained free of charge on application to the following address: The Director, CCDC, 12 Union Road, GB-Cambridge CB2 1EZ (Telefax: Int. +1223/336-033; e-mail: deposit@ccdc.cam.ac.uk).

Acknowledgements

The financial assistance from Department of Atomic Energy, Government of India, Mumbai under a BRNS project (No.37/9/97-R and D-II) and of the Fonds der Chemischen Industrie (to P. G. J.) is gratefully acknowledged. We thank Dr M. K. Kindermann for recording some NMR spectra.

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