mixture was diluted with water and extracted with ether, which upon being washed with water, dried (anhydrous Na_2SO_4), and evaporated yielded 0.511 g of a gum that was flash chromatographed on SiO_2 with ether–*n*-hexane (1:1) to give 209 mg (55%) of a pale yellow thick oily residue that was identical with an authentic sample of xenognosin (1); same TLC mobility on SiO_2 identical ^1H NMR, IR, and mass spectra). The ^{13}C NMR spectrum ($CDCl_3$) is described in Table I.

Anal. Calcd for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29. Found: C, 74.71; H, 6.41.

Ethyl 3-(4-Hydroxy-2-methoxyphenyl)propanoate (9). Ether **5** (0.335 g) was dissolved in absolute ethanol (2.0 mL) and the solution stirred for 5 h under N_2 with 0.30 mL of concentrated HCl. Evaporation of the solution yielded an oily residue that was dissolved in $CHCl_3$ and chromatographed over SiO_2 to give 260 mg (93%) of **9** in the form of a colorless oil that crystallized from ether–*n*-hexane to give colorless prisms: mp 56–57 °C; IR ($CHCl_3$) 3584, 3360, 1715, 1612 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.50 (1 H, br s, exchangeable); ^{13}C NMR ($CDCl_3$), Table I; mass spectrum, *m/z* (relative intensity) 224 (M^+, 24), 137 (100).

Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 64.31; H, 7.33.

Acknowledgment. This research was supported in part by the Research Institute of Pharmaceutical Sciences, School of Pharmacy, University of Mississippi, and by a faculty research grant from the University of Mississippi. We thank Professor David G. Lynn of the Department of Chemistry, University of Virginia, for providing a sample of natural xenognosin (1).

Registry No. **1**, 76907-79-4; **2**, 93-35-6; **3**, 80754-21-8; **4**, 80754-22-9; **5**, 80754-23-0; **6**, 80754-24-1; **7**, 25458-45-1; **8**, 80754-25-2; **9**, 80754-26-3; **10**, 80754-27-4.

Isomeric 1,2-Oxaphospholene 2-Oxides from the Reaction of Diacetone Alcohol and Methyl- or Phenylphosphonous Dichloride

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Received June 22, 1981

The reaction of methyl- or phenylphosphonous dichloride with diacetone alcohol produces, in addition to the previously described 1,2-oxaphosphol-4-ene 2-oxide derivatives, isomers of the latter, corresponding 1,2-oxaphosphol-3-ene 2-oxides. Both pairs of isomers were characterized by ^1H, ^{31}P, and ^{13}C NMR, IR, and mass spectroscopy, and a mechanism is proposed for the formation of the two isomers on the basis of the isolation of 3-chloro-1,2-oxaphospholane 2-oxide as an intermediate.

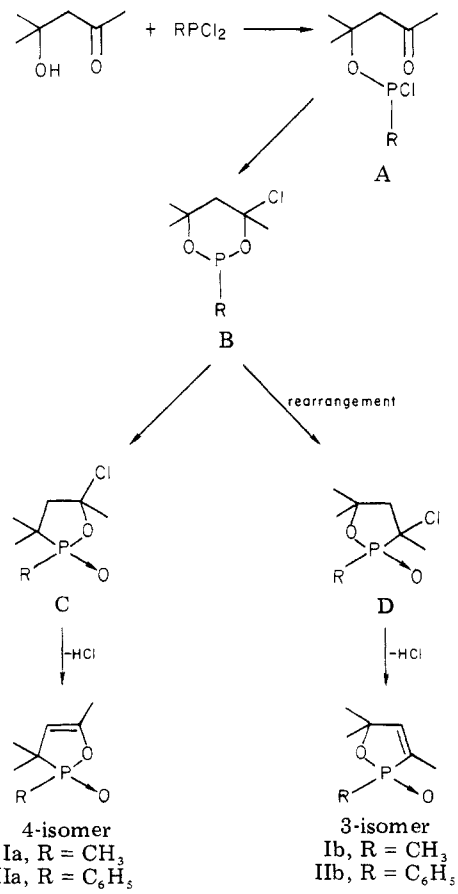
In the course of studies exploring various methods for the preparation of 1,2-oxaphospholene 2-oxides we were puzzled by the fact that in the cases of 2,3,3,5-tetramethyl-1,2-oxaphosphol-4-ene 2-oxide and the corresponding 2-phenyl drivative, prepared by the reaction of diacetone alcohol and methyl- or phenylphosphonous dichloride,[1] the ^{31}P NMR spectrum of distilled product samples showed an additional upfield resonance. This paper reports the isolation and characterization of the compounds corresponding to this upfield ^{31}P NMR resonance and their identification as isomeric 1,2-oxaphosphol-3-ene 2-oxides. The physical properties and characterization data of the two pairs of isomers are compared side by side, and a mechanism is presented rationalizing the formation of the pair of isomers on the basis of an isolated intermediate.

Results and Discussion

Earlier work[1] has shown that the reaction of phenylphosphonous dichloride with diacetone alcohol, which was reported to result in a 1,2-oxaphosphol-4-ene 2-oxide derivative as the final product, proceeds in several steps. The first step was assumed to be the alcoholysis of phenylphosphonous dichloride, with subsequent intermediates being phenylphosphinic acid, $C_6H_5P(O)(H)OH$, a β-keto phosphinic chloride, and a 5-chloro-1,2-oxaphospholane 2-oxide derivative, suggesting a five-step mechanism for this reaction.

We now report the unambiguous characterization of one of the key intermediates of the above-postulated sequence of reactions and on this basis suggest a mechanism for the formation of the observed two isomeric 1,2-oxaphospholene 2-oxides.

Scheme I



(1) B. A. Arbuzov, N. I. Rizpolozhenskii, A. O. Vizel', K. M. Ivanovskaya, F. S. Mukhametov, and E. I. Gol'dfarb, *Izv. Bull. Acad. Sci. USSR, Div. Chem. Sci. (Engl. Transl.)*, 1827 (1972).

0022-3263/82/1947-1530$01.25/0

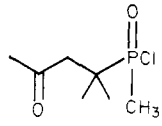
Table I. Data of 1,2-Oxaphospholene 2-Oxides and the Intermediate D

compd	bp, °C (mmHg)	analyses,[a] % C	H	Cl	^{31}P NMR,[c] δ
Ia	70 (0.4)	52.24 (52.50)	8.30 (8.18)		75.1
Ib	65 (0.1)	51.87 (52.50)	8.27 (8.18)		59.4
D	97[b]	42.45 (42.76)	7.22 (7.18)	18.38 (18.03)	65.7
IIa[d]	103 (0.2)	64.48 (64.86)	6.85 (6.80)		65.9
IIb	105 (0.1)	64.75 (64.86)	6.85 (6.80)		52.3

[a] Calculated values in parentheses. [b] Melting point. [c] Spectra were obtained in $CDCl_3$ at 40.3 MHz on a JOEL FX-100 FT NMR spectrometer and were proton decoupled; chemical shifts were measured vs. 85% H_3PO_4, with downfield shifts being positive. [d] This compound was prepared earlier by Bergesen.[3]

In agreement with the earlier data[1] it is reasonable to assume solvolysis as the first step of the reaction of methylphosphonous dichloride (R = CH_3) and diacetone alcohol (Scheme I). In analogy with the well-known[2] reaction of P^{III}–Cl compounds, acting as nucleophiles, with carbonyl compounds, the methylphosphonochloridous ester A in Scheme I cyclizes to form the intermediate B upon reaction with the intramolecular keto group. This intermediate may undergo Arbuzov rearrangement by two pathways, (1) via the intermediate C to form the 4-isomer of the 1,2-oxaphospholene 2-oxide, as observed earlier,[1] or (2) via the intermediate D to form a 3-isomer as observed for the first time in this study.

In the course of this work we were able to isolate for R = CH_3 a solid reaction intermediate of the reaction sequence of Scheme I. The molecular formula of this intermediate corresponded to either C, D, or a linear species of the structure of E.



E

Detailed spectroscopic characterization of this solid intermediate showed that its structure corresponds to D, which upon dehydrochlorination may produce the 3-isomer of the 1,2-oxaphospholene 2-oxide. However, when a sample of D was refluxed in Et_2O or toluene in the presence of excess of triethylamine, it did not dehydrochlorinate to form Ib which leads us to believe that B upon rearrangement forms an intermediary activated transition state which may either form D or directly form Ib. Thus, the conversion D → Ib in Scheme I seems to be a formal one only. Physical data of the intermediate D and the 1,2-oxaphospholene 2-oxides are summarized in Table I and spectroscopic data are discussed below.

It is noteworthy that other derivatives of the 3-isomer of 1,2-oxaphospholene 2-oxide were obtained previously[4] by the reaction of propargyl alcohol and phosphorus trihalides with the mechanism of this reaction and the resulting products having been studied in great detail. In another instance, 1,2-oxaphosphol-3-enes were obtained[5] by halogenation of (1,2-butadienyl)phosphonic dichlorides. A product claimed to have the 1,2-oxaphosphol-3-ene 2-oxide structure, on the basis of IR data, was reported[6] to have formed in the reaction of diacetone alcohol with $EtOPCl_2$ in the presence of triethylamine.

^{31}P NMR Spectra. The ^{31}P NMR chemical shift data of the 1,2-oxaphospholenes are presented in Table I. The phosphorus nucleus in the 4-isomers (Ia and IIa) is less shielded than that in the corresponding 3-isomers (Ib and IIb), resulting in downfield shifts of the 4-isomers vs. the corresponding 3-isomers. The chemical shift differences between the pair of isomers are 15.7 and 13.6 ppm, respectively, for the *P*-methyl and *P*-phenyl derivatives. On consideration of the pair of like isomers, the ^{31}P NMR chemical shifts of the *P*-methyl derivatives (Ia and Ib) are downfield of those of the *P*-phenyl isomers (IIa and IIb). As (cyclic) esters of phosphinic acids, the present 1,2-oxaphospholene 2-oxides display ^{31}P NMR chemical shifts which are at the low-field end of the range (ca. 18–58 ppm) normally found for this class of compounds[7] which is in agreement with shifts observed for other phospholene structures.[8]

Proton NMR Spectra. The assignments of chemical shifts and coupling constants in Table II initially were made on the basis of ^{31}P-coupled proton NMR spectra and supported by ^{31}P-decoupled spectra. The latter spectra were greatly simplified since the partially overlapping CH_3 doublets (coupling to ^{31}P) appearing within a range of less than 1 ppm collapsed to singlets.

In the 4-isomers (Ia and IIa) the olefinic proton is coupled to phosphorus ($^3J_{HP}$ = 25 Hz) and to methyl protons on the neighboring olefinic carbon atom[9] ($^4J_{HH}$ = 1.5 Hz), resulting in a doublet of quartets which only for Ia is well resolved. The two methyl groups on the carbon atom next to phosphorus are diastereotopic in view of the chirality on the neighboring phosphorus atom, with the two doublets exhibiting different chemical shifts and coupling constants. Assignments may be made in analogy to similar structures, e.g., in 2-methyl-1-phenylphosphol-3-ene 1-oxides[10] or 2,5-dimethyl-1-phenylphosphol-3-ene 1-oxides.[11] The shielding effect of the phenyl group in IIa readily permits the identification of the upfield resonance at 0.83 ppm to the methyl group in the position cis to the phenyl group. Only in this position will the effective shielding cone of the phenyl group be able to affect the shift of a methyl group on a neighboring carbon atom. The downfield resonance at 1.38 ppm, consequently, then represents the methyl group in the position trans to the phenyl group. In the corresponding *P*-methyl derivative (Ia), in agreement with the absence of shielding, only a small difference in chemical shift (0.05 ppm as opposed to 0.55 ppm) between the two methyl groups on C-1 is observed. However, the $^3J_{HP}$ coupling constants of the two methyl groups are

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(11) A. Bond, M. Green, and S. C. Pearson, *J. Chem. Soc. B*, 929 (1968).
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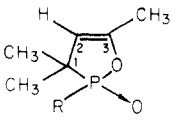
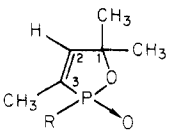
Table II. Proton NMR Spectral Data[a] of 1,2-Oxaphospholene 2-Oxides

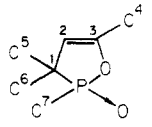


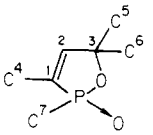


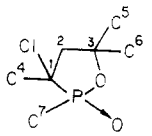
assignment	Ia (R = CH_3)[b]	IIa (R = C_6H_5)[b]	Ib (R = CH_3)	IIb (R = C_6H_5)
CH=	4.93 (dq, 25, 1.5)	4.88 (dm,[c] 25)	6.57 (dm,[c] 38)	6.53 (dm,[c] 38)
CH_3 on C-1	1.33 (d, 14)	1.38 (d, 15)	1.50 (s)	1.57 (s)
CH_3 on C-1	1.28 (d, 19)	0.83 (d, 19)	1.42 (s)	1.48 (s)
CH_3 on C-3	1.86 (d, 1.5)	1.95 (s)	1.97 (dd, 13, 1.7)	1.83 (dd, 13, 2)
R	1.63 (d, 13)	7.3-7.9 (m)	1.61 (d, 14)	7.2-7.9 (m)

[a] In $CDCl_3$ with chemical shifts in parts per million (δ) referenced vs. internal Me_4Si; multiplicities and coupling constants in hertz are listed in parentheses. Spectra were obtained at 60 MHz on a Varian T60 and at 100 MHz on a JEOL FX-100 FT NMR spectrometer, respectively. [b] Proton NMR data for these compounds were reported previously in a Russian reference,[12] the original of which was inaccessible to us. [c] Poorly resolved quartet.

Table III. ^{13}C NMR Chemical Shifts (ppm) and ^{13}C-^{31}P Spin-Spin Coupling Constants (in Parentheses in Hertz)[a]







carbon	Ia	IIa	Ib	IIb	D
C-1	38.78 (78.0)	39.40 (80.9)	129.31 (103.0)	b	64.34 (85.5)
C-2	112.08 (7.4)	112.35 (7.4)	148.46 (18.4)	148.80 (19.1)	51.65 (7.4)
C-3	149.95 (5.9)	150.29 (0.0)	87.20 (3.7)	87.71 (0.0)	85.13 (0.0)
C-4	21.96 (1.5)	22.44 (0.0)	14.71 (11.5)	11.66 (14.7)	29.15 (4.4)
C-5	16.03 (5.9)	16.00 (5.9)	28.77 (0.0)	29.06 (0.0)	31.93 (0.0)
C-6	23.94 (5.2)	25.34 (4.4)	27.71 (2.9)	27.54 (3.0)	25.55 (0.0)
C-7	10.74 (85.3)	c	15.84 (94.9)	c	10.69 (101.5)

[a] Spectra were obtained in $CDCl_3$ at 25.05 MHz on a JEOL FX-100 FT NMR spectrometer; peaks are referenced vs. Me_4Si, with downfield shifts being positive. [b] Only the upfield peak of the doublet for C-1 is seen at 127.38 ppm; the downfield peak overlaps with the aromatic carbons.[c] [c] Resonances for the aromatic carbon atoms not shown here.

significantly different in both compounds Ia and IIa. The protons of the methyl group on C-3 are coupled to the olefinic proton since on ^{31}P decoupling the doublet (resolved only for Ia) does not collapse into a singlet.

In the 3-isomers (Ib and IIb) the olefinic proton is coupled to phosphorus ($^3J_{HP}$ = 38 Hz) and to the protons of the methyl group on the olefinic carbon atom and appears as doublet of poorly resolved quartets. In comparison to that in the corresponding 4-isomers, the olefinic doublet in the 3-isomers is further downfield, and the coupling constants are considerably larger. The two methyl groups on C-1 again are diastereotopic by virtue of the chirality at phosphorus; however, they are not coupled to phosphorus and appear as singlets separated by 0.08 and 0.09 ppm, respectively. The protons of the methyl group on the olefinic carbon atom, due to coupling to phosphorus and the olefinic proton, appear as a doublet of doublets.

In the 1,2-oxaphospholane 2-oxide D the geminal methyl groups appear as two singlets at 1.55 and 1.53 ppm (only seen at 100 and 270 MHz), indicating diastereotopic arrangement relative to the chiral center on phosphorus. The two other methyl groups, on P and on C next to P, represent doublets at 1.86 (J_{HP} = 13 Hz) and 1.81 ppm (J = 14.9 Hz). Although the carbon atom in the ring next to phosphorus is a chiral center, there is no evidence in the proton NMR spectra for the presence of more than one isomer. Thus, one has to assume that D represents an isomerically pure species with Cl either in a cis or a trans position to P→O relative to the "plane" of the ring. The methylene protons give rise to an ABX pattern (X = P) with the following parameters determined from 270 MHz spectra: δ_A 2.54, δ_B 2.47, J_{AB} = 15.1 Hz, J_{AP} = 10.5 Hz, J_{BP} = 10.5 Hz.

^{13}C NMR Spectra. The ^{13}C NMR spectral parameters of the four 1,2-oxaphospholane 2-oxides and the intermediate D are summarized in Table III. Almost all ^{13}C resonances are doublets due to ^{13}C–^{31}P spin–spin coupling.

In the 4-isomers (Ia and IIa) the olefinic carbon atoms are easily identified by their downfield chemical shift, with the assignment to C-2 and C-3 based on off-resonance decoupling experiments, where the C-2 resonance was transformed into a doublet of doublets and the C-3 resonance remained a doublet. The carbon atoms C-5 and C-6, representing methyl groups attached to C-1 (next to phosphorus), show up as two distinct sets of doublets, indicating that C-5 and C-6 are diastereotopic in view of the chirally substituted phosphorus (cis or trans to the P→O bond relative to the "plane" of the five-membered ring). The coupling constants $^2J_{CCP}$ for C-5 and C-6 are of nearly the same value. This finding is in anology to data[13] obtained on stereoisomeric 2,5-dimethyl-1-phenylphosphol-3-ene 1-oxides where $^2J_{CCP}$ of the two methyl groups on the carbon atoms next to P also was independent of the stereochemistry. However, in the corresponding phosphines $^2J_{CCP}$ was strongly dependent on the stereochemistry. The carbon atoms C-1 and C-7, being next to phosphorus, are characterized by large ^{13}C–^{31}P coupling constants. Off-resonance decoupling allowed the assign-

(13) J. J. Breen, S. I. Featherman, L. D. Quin, and R. C. Stocks, J. Chem. Soc., Chem. Commun., 657 (1972).

ment of the doublet centered at 38.78 ppm to C-1 and that at 10.74 ppm to C-7.

Similar reasoning was applied to the interpretation of the ^{13}C NMR spectra of the 3-isomers (Ib and IIb). The olefinic carbon atoms C-1 and C-2 were assigned with no difficulty on the basis of chemical shifts and coupling constants. The carbon atoms C-5 and C-6, representing methyl groups on C-3, again are diastereotopic in view of the chirally substituted phosphorus, and this is manifested in differing chemical shifts. The remaining carbon atoms C-3, C-4, and C-7 were assigned on the basis of off-resonance decoupling experiments and ^{13}C–^{31}P coupling constants. The assignments in Table III for the 3-isomers are consistent with ^{13}C data obtained by others[14] in related 2-methoxy-5,5-dimethyl-1,2-oxaphosphol-3-ene 2-oxide, where the following assignments were made (in ppm): C-1 (114.5), C-2 (156.8), C-3 (85.3), and the diastereotopic methyl groups C-5 (27.4) and C-6 (26.6).

For the 1,2-oxaphospholane 2-oxide D, C-1 and C-7 were assigned on the basis of their large ^{13}C–^{31}P coupling constants, with C-1 remaining a doublet on off-resonance decoupling. The relatively low-field shift observed for C-1 is due to bonding to Cl and is consistent with literature data.[15] The carbon atoms C-2, C-3, and C-4 again were assigned on the basis of off-resonance decoupling, with the low-field shift observed for C-3 again consistent with bonding to oxygen. The observation of only one doublet for C-4 suggests that only one of the possible two stereoisomers had formed. The diastereotopic methyl groups again appear as two separate signals (C-5 and C-6).

IR Spectra. The olefinic double bond stretching vibration in IIa reported previously[3] has been assigned to a band at 1660 cm^{-1}, and the P=O stretching vibration, judging from the published spectrum, apparently is at 1205 cm^{-1}. This agrees very well with our data for IIa, where these two absorptions were assigned to bands at 1672 and 1205 cm^{-1}, respectively, and with another published spectrum.[1] For Ia these bands are at 1668 and 1205 cm^{-1}, respectively.

In the 3-isomers, these two vibrations were assigned to bands at 1640 and 1220 cm^{-1}, respectively, for Ib and at 1635 and 1220 cm^{-1}, respectively, for IIb.

The IR spectrum of D does not show a ν(C=O) absorption, thus excluding structure E for this compound on the basis of IR evidence alone. The P=O stretching vibration is assigned to the band at 1220.

Mass Spectra. The molecular ion is a prominent peak in the mass spectra of the 1,2-oxaphospholene 2-oxides, with the fragment $M^+ - CH_3$ in all four cases being the base peak. The latter originates from loss of a methyl group bonded to C rather than to P since this is the major transition for the CH_3–P as well as the C_6H_5–P derivatives. For both isomers Ia and Ib a set of fragmentation ions is produced which is identical but varies in intensity. Similar patterns are also seen for the pair IIa and IIb. For compound D the molecular ion is seen, with $M^+ - CH_3$ and $M^+ - Cl$ being prominent transitions. The base peak corresponds to $C_6H_{11}^+$ which is the six-carbon fragment left after loss of CH_3PO_2Cl.

Experimental Section

Materials and Instrumentation. Methylphosphonous dichloride was obtained from Ethyl Corp., phenylphosphonous dichloride from Aldrich Chemical Co., and diacetone alcohol from Fisher Scientific Co., and all were distilled prior to use. IR spectra were recorded on a Nicollet Fourier Transform Model 7199 IR spectrometer, and mass spectra were obtained on a Varian MAT CH-7 mass spectrometer at 70 eV with the source at 250 °C and the probe at 30 °C.

2,3,3,5-Tetramethyl-1,2-oxaphospholene 2-Oxides. A quantity of 101.7 g (0.87 mol) of methylphosphonous dichloride was added dropwise to 101.0 g (0.87 mol) of diacetone alcohol kept at 0 °C. In view of the exothermic reaction, efficient cooling is required to maintain the reaction temperature at 0 °C. The reaction product is then heated in vacuo on a water bath to drive off HCl during which operation the reaction product partially solidifies and upon further heating liquifies again completely to a viscous liquid. Distillation [bp 120–144 °C (0.2 mm)] yielded 86 g (61% yield) of product the ^{31}P NMR spectrum of which showed two signals at 77.0 (4-isomer) and 61.8 ppm (3-isomer), respectively, in the approximate intensity ratio 8:1. Slow spinning-band distillation (15 s/drop) resulted in 49.8 g (35.8% yield) of isomerically pure 4-isomer (Ia) and 15.4 g (10% yield) of 3-isomer (containing <5% 4-isomer), from which upon repeated distillation 1.5 g of an isomerically pure sample of the 3-isomer (Ib) was isolated. For analyses see Table I. The ^{31}P NMR chemical shifts of the pure isomers in Table I differ slightly from those measured in the mixture of isomers.

IR (film, NaCl). Compound Ia: 3060 (w), 2960 (s), 2920 (s), 2870 (s), 1715 (sh), 1668 (vs), 1656 (sh), 1465 (s), 1445 (s), 1415 (s), 1390 (s), 1370 (m), 1300 (s), 1270 (m), 1247 (s), 1205 (vs), 1115 (s), 1013 (s), 976 (m), 915 (s), 885 (s), 857 (s), 804 (s). Compound Ib: 3030 (w), 2978 (s), 2932 (s), 2920 (sh), 2868 (m), 1640 (m), 1462 (m), 1445 (m), 1415 (m), 1385 (m), 1367 (s), 1300 (vs), 1260 (sh), 1240 (sh), 1220 (vs), 1190 (sh), 1175 (vs), 1120 (s), 1040 (w), 1000 (m), 960 (vs), 935 (vs), 885 (s), 855 (s) cm^{-1}.

Mass Spectral Data. Compound Ia: *m/e* (relative intensity) 160 (52, M^+), 159 (14, $M^+ - H$), 145 (100, $M^+ - CH_3$), 127 (32, $M^+ - (CH_3, H_2O)$), 83 (17, $M^+ - (CH_3, CH_3PO)$), 82 (8, $M^+ - CH_3PO_2$), 81 (56, $M^+ - CH_3POOH$), 80 (9, $CH_3POOH_2^+$), 79 (35, CH_3POOH^+), 67 (64, $C_5H_7^+$), 55 (9, $C_4H_7^+$), 53 (11, $C_4H_5^+$), 47 (7, PO^+), 43 (24, $C_3H_7^+$). Compound Ib: *m/e* (relative intensity) 160 (26, M^+), 159 (3, $M^+ - H$), 145 (100, $M^+ - CH_3$), 127 (13, $M^+ - (CH_3, H_2O)$), 83 (10, $M^+ - (CH_3, CH_3PO)$), 81 (12, $M^+ - CH_3POOH$), 80 (8, $CH_3POOH_2^+$), 79 (14, CH_3POOH^+), 67 (69, $C_5H_7^+$), 47 (7, PO^+), 43 (25, $C_3H_7^+$).

3,3,5-Trimethyl-2-phenyl-1,2-oxaphospholene 2-Oxides. By use of the procedure for the corresponding 2-methyl derivative, 165.7 g (0.93 mol) of phenylphosphonous dichloride was reacted with 107.6 g (0.93 mol) of diacetone alcohol. Kugelrohr distillation [160 °C (0.1 mm)] of the reaction product yielded 163.3 g (80% yield) of product the ^{31}P NMR spectrum of which showed two signals at 65.9 (4-isomer) and 52.3 ppm (3-isomer), respectively, in the approximate intensity ratio of 8:1. Slow spinning-band distillation (15 s/drop) resulted in 130 g (58% yield) of isomerically pure 4-isomer (IIa) and 10.1 g (4.9% yield) of the corresponding isomerically pure 3-isomer (IIb). For analytical data see Table I.

IR (film, NaCl). Compound IIa: 3070 (sh), 3060 (m), 2970 (sh), 2960 (s), 2922 (s), 2900 (sh), 2864 (m), 1672 (vs), 1640 (sh), 1590 (m), 1485 (w), 1460 (s), 1440 (vs), 1380 (s), 1368 (w), 1315 (w), 1255 (sh), 1240 (vs), 1205 (vs), 1160 (w), 1120 (vs), 1070 (w), 1015 (s), 955 (m), 910 (vs), 870 (vs) cm^{-1}. These frequencies agree well with the partial IR spectrum of this compound reported[3] earlier. Compound IIb: 3077 (sh), 3058 (w), 3022 (w), 2978 (s), 2930 (m), 2920 (sh), 2864 (w), 1635 (m), 1592 (w), 1490 (w), 1462 (m), 1437 (s), 1383 (w), 1365 (m), 1295 (m), 1245 (s), 1220 (vs), 1190 (m), 1175 (s), 1120 (vs), 1070 (w), 1000 (m), 953 (vs), 935 (s), 855 (s) cm^{-1}.

Mass Spectral Data. Compound IIa: *m/e* (relative intensity) 222 (100, M^+), 221 (25, $M^+ - H$), 207 (100, $M^+ - CH_3$), 143 (23, $C_6H_5PH(OH)_2^+$), 141 (11, $C_6H_5POOH^+$), 125 (8, $C_6H_5POH^+$), 83 (21, $M^+ - (CH_3, C_6H_5PO)$), 82 (23, $M - C_6H_5PO_2$), 81 (13, $M^+ - C_6H_5PO_2H$), 77 (19, $C_6H_5^+$), 67 (74, $C_5H_7^+$), 55 (9, $C_4H_7^+$), 47 (18, PO^+), 43 (17, $C_3H_7^+$). Compound IIb: *m/e* (relative intensity) 222 (90, M^+), 221 (8, $M^+ - H$), 207 (100, $M^+ - CH_3$), 143 (23, $C_6H_5PH(OH)_2^+$), 141 (13, $C_6H_5POOH^+$), 125 (6, $C_6H_5POH^+$), 81 (8, $M^+ - (CH_3, C_6H_5PO)$), 77 (13, $C_6H_5^+$), 67 (21, $C_5H_7^+$), 47 (10, PO^+), 43 (14, $C_3H_7^+$).

3-Chloro-2,3,5,5-tetramethyl-1,2-oxaphospholane 2-Oxide. A quantity of 107 g (0.92 mol) of methylphosphonous dichloride

(14) G. A. Krudy and R. S. Macomber, *J. Org. Chem.*, **43**, 4656 (1978).
(15) F. W. Wehrli and T. Wirthlin, "Interpretation of Carbon-13 NMR Spectra", Heyden and Son, Ltd., London, 1976.

was added dropwise to a cooled (0 °C) solution of 106.2 g (0.92 mol) of diacetone alcohol and 202 g (2 mol) of dry (KOH) triethylamine in 1 L of diethyl ether. After completed addition, the white slurry was warmed to room temperature and filtered. The filtrate was refluxed for 24 h, generating additional amounts of precipitate which were filtered. The filtrate was concentrated on a rotary evaporator and the residue distilled on a Kugelrohr apparatus [Aldrich Chemical Co.; bp 130–190 °C (0.5 mm)] to give 50 g of a part crystalline, part liquid product: ^{31}P NMR δ 64.5 (D), 61.2 (Ib) (about equal intensity). The ^{31}P NMR chemical shifts as measured in the mixture differ slightly from those of the pure compounds. The crystalline material was separated to give 21.3 g of product which upon crystallization from toluene (in which solvent NEt_3·HCl present as an impurity is insoluble) gave 15 g (8.3%) of colorless crystals, mp 97 °C. For analyses see Table I: IR (KBr) 3000 (m), 2980 (s), 2930 (m), 2870 (w), 1445 (m), 1420 (m), 1380 (m), 1365 (m), 1300 (s), 1280 (m), 1222 (vs), 1163 (s), 1150 (s), 1100 (m), 1050 (m), 983 (m), 928 (vs), 880 (s), 842 (m), 785 (s), 735 (s) cm^{-1}; mass spectrum, m/e (relative intensity) 198 (3, M^+ (^{37}Cl)), 196 (9, M^+ (^{35}Cl)), 183 (3) and 181 (10) $M^+ - CH_3$, 161 (20, $M^+ - Cl$), 145 (7, $M^+ - (CH_3, HCl)$), 141 (3) and 139 (10) $M^+ - (CH_3, C_3H_6)$, 121 (12, $M^+ - (C_3H_4, Cl)$), 120 (13, $M^+ - (C_3H_5, Cl)$), 118 (35, $M^+ - (C_3H_7, Cl)$), 105 (10, $(CH_3)_2CPO_2^+$), 103 (22, $M^+ - (C_3H_7, Cl, CH_3)$), 83 (100, $M^+ - (CH_3PO_2, Cl)$), 67 (11, $C_5H_7^+$), 55 (12, $C_4H_7^+$), 43 (15, $C_3H_7^+$).

Acknowledgment. We thank Dr. J. J. Freeman for the FT IR spectra, Professor W. H. Urry, University of Chicago, for the 270-MHz proton NMR spectrum of D, and R. C. Scheibel for the mass spectra.

Registry No. Ia, 32503-56-3; Ib, 80754-28-5; IIa, 4529-76-4; IIb, 80754-29-6; D, 80754-30-9; methylphosphonous dichloride, 676-83-5; diacetonealcohol, 123-42-2; phenylphosphonous dichloride, 644-97-3.

Synthesis of the Cytochalasin D Isoindolone Unit: Solutions to the Problem of Regiochemistry in *N*-Benzoylpyrrolinone Diels–Alder Reactions

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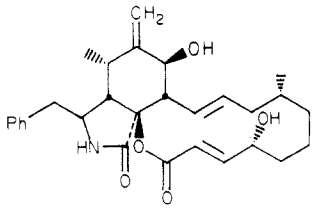
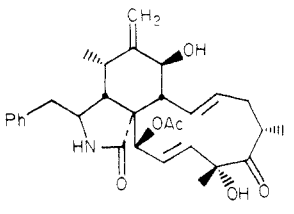
Received February 19, 1981

The bicyclic isoindolone portion of cytochalasin D with the correct relative stereochemistry has been prepared via a Diels–Alder sequence. Condensation of trienyl acetate **51** with doubly activated dienophile **4b** affords a single bicyclic adduct **52**. After oxidation to a sulfoxide, sulfenate–sulfoxide interconversion affords the key allylic alcohol **54a** with cytochalasin functionality. A related series of adducts has been prepared from monoactivated dienophile **4a** and various dienes or trienes. In all cases, the endo rule is obeyed although regioisomer mixtures are formed with unsymmetrical dienes. The (trimethylsilyl)methyl diene **37** reacts with much improved 3.5:1 regiochemistry due to the directive influence of silicon. Treatment of the major adduct **38** with MCPBA affords an allylic alcohol, **57**, having the cytochalasin D substitution pattern but the undesired hydroxyl stereochemistry. Oxidation appears to occur from the more congested face of **38**, apparently due to stereoelectronic factors involving silicon. An osmylation–deoxysilation approach affords the correct stereoisomer. A new Horner–Emmons reagent $Ph_2PO^-CHCH{=}CHCH_2O^-,2Li^+$ is described and is used for synthesis of trienol **24** from 2-[(trimethylsilyl)-methyl]acrolein **22**.

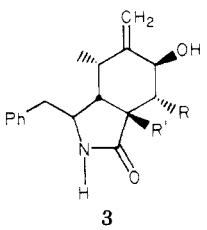
Derivatives of the "cytochalasan" nucleus have been isolated from a variety of molds and microorganisms[1] and include groups of structurally similar substances such as the cytochalasins,[2] chaetoglobosins,[2] and aspochalasins.[3] Cytochalasin B (phomin, 1, a 24-oxa[14]cytochalasan) was the first cytochalasin to be identified and remains the most important member of the series due to its fascinating biological properties. Cytochalasin D (2, an [11]cytochalasan) is also highly potent and like cytochalasin B has been used extensively as a tool to probe diverse aspects of cell metabolism.[1] The most highly active natural products have an exocyclic double bond in the isoindolone unit and an allylic alcohol function as in **1** and **2**. We will focus on the synthesis of structures **3** which duplicate the isoindolone substitution of **1** and **2** and allow for variation of groups R and R′ for eventual incorporation of the macrocycle.



1 (cytochalasin B)



2 (cytochalasin D)



3

As described in a preliminary paper,[4] our approach is based on the Diels–Alder reaction between an *N*-benzoylpyrrolinone, **4**, and a diene, **5**. Assuming the classical endo transition state with the diene approaching from the less hindered face of the dienophile, one would predict control of five assymetric centers in a single step. A conceptually similar approach was first described by Weinreb et al. using an enol lactone analogue of **4** in an intramolecular Diels–Alder process.[5] More recently, Weinreb et al. have shown that maleimide-derived Diels–Alder adducts can be selectively converted to structures similar to **6**[6] (eq 1). Other variations of the Diels–Alder

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(2) C. Tamm, ref 1, Chapter 2.
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(5) J. Auerbach and S. W. Weinreb, *J. Org. Chem.*, **40**, 3311 (1975).
(6) M. Y. Kim and S. M. Weinreb, *Tetrahedron Lett.*, 579 (1979).

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