(0.2 mL), and then water (20 mL) was added. The ether extract was dried and concentrated. Column chromatography of the residue on silica gel (8 g) using a 7:1 mixture of petroleum ether and ether gave pure ketone **12** (91 mg, 86% yield) as a colorless syrup. Recrystallization from hexane gave an analytical sample: mp 91–92 °C; $[\alpha]^{17.5}_D$ +35.2° (*c* 0.81, $CHCl_3$); IR ($CHCl_3$) 1740, 1700, 1640, 900 cm^{-1}. Anal. Calcd for $C_{31}H_{48}O_3$: C, 76.44; H, 10.32. Found: C, 79.28; H, 10.39.

Oxime 14. A solution of ketone **12** (180 mg, 0.38 mmol) and hydroxyamine hydrochloride (80 mg, 1.15 mmol) in a 1:1 mixture of pyridine and ethanol (3 mL) was refluxed for 2 h under an argon atmosphere. To the cooled mixture was added brine (20 mL), and following ethyl acetate extraction, the mixture afforded a crude product. Column chromatography on silica gel (15 g) using a 6:1 mixture of petroleum ether and ether gave oxime **14** (173 mg, 93% yield) as a colorless syrup: $[\alpha]^{16}_D$ −1.71° (*c* 1.46, $CHCl_3$); IR ($CHCl_3$) 3600, 3300, 1740, 1640, 890 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.80 (6 H, s), 1.05 (3 H, s), 1.17 (3 H, s), 1.76 (3 H, s), 1.78 (3 H, s), 3.64 (3 H, s), 4.58 (1 H, br s), 4.76 (2 H, m), 4.84 (1 H, br s), 5.29 (1 H, br); high-resolution mass spectrum calcd for $C_{31}H_{49}NO_3$ 483.3715, found 483.3720 (M^+).

Nitrile 15. To a solution of oxime **14** (75 mg, 0.16 mmol) in pyridine (2 mL) was added methanesulfonyl chloride (53 mg, 0.47 mmol) dropwise, and the mixture was stirred at 0 °C for 5 h. Evaporation of the volatile materials under reduced pressure and column chromatography on silica gel (15 g) using a 10:1 mixture of petroleum ether and ether afforded pure nitrile **15** (22 mg, 30% yield) as a colorless syrup; $[\alpha]^{16}_D$ +25.2° (*c* 1.06, $CHCl_3$); IR ($CHCl_3$) 3060, 2270, 1740, 1640, 900 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.74 (3 H, s), 0.83 (3 H, s), 1.73 (3 H, s), 1.78 (6 H, s), 3.68 (3 H, s), 4.61 (1 H, br), 4.70 (1 H, br), 4.80 (2 H, m), 4.90 (2 H, br), 5.38 (1 H, br); high-resolution mass spectrum calcd for $C_{31}H_{47}NO_2$ 465.3609, found 465.3580 (M^+).

Lansic Acid (5). The nitrile **15** (36 mg, 0.08 mmol) was dissolved in a 20% ethanol solution of potassium hydroxide (5 mL), and the mixture was refluxed for 3 h under an argon atmosphere. After addition of brine (15 mL), the mixture was acidified with 5% HCl. Ethyl acetate extraction and column chromatography on silica gel (10 g) using hexane and ethyl acetate (3:1) afforded lansic acid (**5**, 13 mg, 36% yield) as a crystalline solid. This product was identical with authentic material in all respects, including optical rotation.

Acknowledgment. We are indebted to Drs. N. Hamanaka and T. Miyamoto of Ono Pharmaceu. Co. Ltd. for the determinations of 200-MHz NMR, high-resolution mass spectra, and the biological examinations of lansiosides and to Professor Y. Tsuda of Kanazawa University for a helpful discussion. This work was supported by the research grants of The Naito Foundation (1980, 1981), The Toyota Foundation (1981), and the Suntory Institute for Bioorganic Research (1980) and the Grant-in-Aid for Special Project Research (No. 57218020, 1982) and the Grant-in-Aid for Scientific Research (No. 57470026, 1982) of the Ministry of Education, Japanese Government.

Registry No. **1**, 82537-86-8; **2**, 87453-34-7; **3**, 87453-35-8; **4**, 87453-36-9; **5**, 19954-99-5; **6**, 511-01-3; **7**, 87453-37-0; **8**, 87453-38-1; **9**, 87453-39-2; **10**, 87453-40-5; **12**, 87453-41-6; **13**, 6929-24-4; **14**, 87453-42-7; **15**, 87453-43-8; **16**, 2595-39-3; **17**, 2771-48-4; **18**, 604-70-6; **19**, 20880-54-0.

Insertion of Oxygen into C–P Bonds of Some Strained Phosphorus Heterocycles[1]

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Cyclic phosphine oxides with exceptionally contracted internal C–P–C angles have been found to undergo oxygen insertion into a C–P bond on treatment with peracids. The reaction is of synthetic value in creating 1,2-oxaphospha ring systems. It has been applied to two phosphetane oxides and the bridged compounds 5-isopropyl-2,6-dimethyl-6-phosphabicyclo[3.1.1]hept-2-ene 6-oxide and 4-methyl-4-phosphatetracyclo-[3.3.0.$0^{2,8}$.$0^{3,6}$]octane 4-oxide. Reaction with the former was regiospecific, insertion occurring at the least substituted carbon. The 7-phosphanorbornane moiety in the product of hydrogenation of a phosphole oxide dimer also underwent the ring expansion, providing a 1:1 mixture of the two possible insertion products. Some new insertion products from phosphole oxide dimers were also prepared. All new oxaphospha derivatives were characterized by ^1H, ^{31}P, and ^{13}C NMR spectroscopy.

The carbon–phosphorus bond in phosphoryl compounds is generally resistant to oxidizing agents, and many oxidation reactions of organic chemistry can be safely performed on carbon functional groups without involvement of the phosphorus function. Epoxidation of double bonds falls in this category, and conversions of unsaturated phosphonic or phosphinic acids or esters, and of phosphine oxides, into epoxy derivatives are known .[2] It was therefore of some significance when oxygen insertion into a C–P bond was noted[3] in the case of unsaturated phosphine oxides of the 7-phosphanorbornene[2] and the 8-phosphabicyclo[3.2.1]octene[4] systems. Kashman and Awerbouch observed[3] that a C–P bond of the 7-phosphanorbornene moiety of the phosphole oxide dimer structure **1** was attacked by *m*-chloroperbenzoic acid (MCPBA) in preference to the double bond. Of the two possible oxygen-insertion products, only **2** was obtained (75%); its structure was proposed from its ^1H NMR properties. Continued exposure of **2** to the peracid then provided the epoxy derivative **3**. The stability of the initial product **2** was poor, and it decomposed at 25 °C with a half-life of 3 h by retrocycloaddition to form a dihydrophosphindole **4** and a polymer of phenylmetaphosphonic acid. A similar insertion was noted for the phosphabicyclooctene system.[4]

Phosphole oxide dimers are unique in other regards, and a study of these compounds is presently in progress in this laboratory.[5] With several compounds on hand, we pro-

(1) Presented at the 184th National Meeting of the American Chemical Society, Kansas City, MO, Sept 15, 1982; ORGN 110.

(2) See, for example, Quin, L. D.; Symmes, C., Jr.; Middlemas, E. D.; Lawson, H. F. *J. Org. Chem.* **1980**, *45*, 9688.

(3) Kashman, Y.; Awerbouch, O. *Tetrahedron* **1975**, *31*, 53.

(4) Kashman, Y.; Awerbouch, O. *Tetrahedron* **1975**, *31*, 45.

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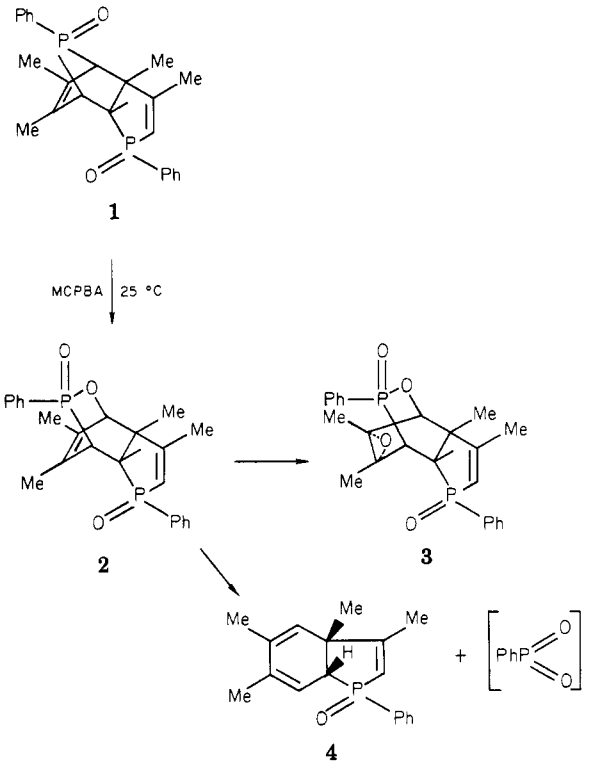
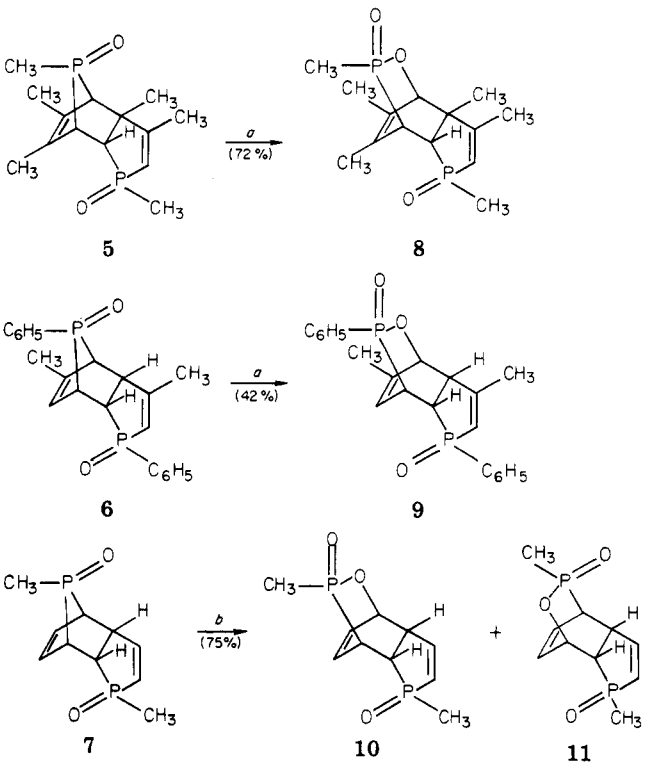


ceeded to show that the oxygen-insertion reaction is a general property of this family. The reaction was applied to three other dimers (**5**–**7**) with the results shown in Scheme I. In the first two cases, a single isomer was obtained; from **7**, however, both isomers resulted in roughly equal amounts. The instability noted by Kashman and Awerbouch was also present in these compounds; **9** was the most stable and could be stored at room temperature. Structures were confirmed by ^{13}C NMR spectroscopy; spectral features, in general, resembled those of the starting dimers[5c] but possessed additional signals at δ 72–84 for carbon attached to oxygen. Also, the one-bond ^{31}P–^{13}C coupling constant is greater for phosphinates than for phosphine oxides, and the signal attributed to the remaining C–P bond reflected this functional group change ($J \sim 72$–79 Hz; cf. to 60–65 Hz in the dimers[5c]). *P*-Methyl groups on the phosphinate P also had greatly increased $^1J_{PC}$ values (100–108 Hz). The magnitude of the ^{31}P–^{31}P coupling constant was useful in confirming the orientation of the oxygen insertion. A three-bond (as in **8**–**10**) or a four-bond (as in **11**) connection can result, but only the former should be of appreciable magnitude. In fact, $^3J_{PP}$ was in the range 39–44 Hz for **8**–**10** but was nil for **11**. Syn,anti isomerism at the bridging P is possible in these products, but the reaction provides a single isomer. In the absence of the other isomer, it has not been possible to employ spectral methods in the establishment of the steric structure at phosphorus. The products are shown as having resulted from retention of the syn structure of the starting phosphole oxide dimers, a result consistent with the proposed mechanism of the reaction (vide infra) but lacking experimental confirmation.

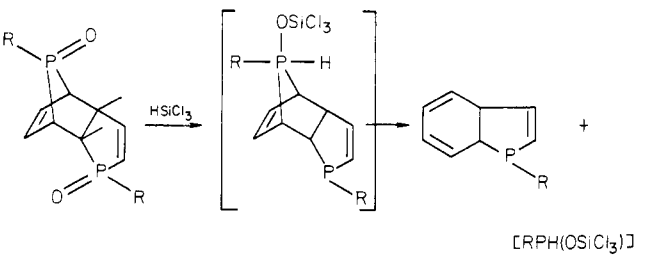
The oxygen insertion can be likened to the Baeyer–Villiger reaction of ketones, which has found special utility in the synthesis of lactones. The possibility was considered that the reaction could be of broader value in the synthesis

Scheme I



[a] Two molar equivalents of MCPBA at 25 °C for 1.5 h. [b] Two molar equivalents of MCPBA at 25 °C for 1.0 h.

of phosphorus heterocycles, and a definition of the structural requirements for its occurrence was therefore sought. The reaction is no doubt associated with the great strain involved in the internal C–P–C angle (83° has been determined[6] in the case of the *P*-methyl analogue of **6**). The allylic nature of the carbon attacked has also been suggested to be important.[4] We have encountered other reactions of the 7-phosphanorbornene system, however, that come about exclusively as a result of relief of strain in the C–P–C angle, suggesting that this may be a sufficient reason for the oxygen insertion. For example, trichlorosilane reduction of phosphine oxides appears in some cases to involve a pentacoordinate intermediate,[5b] as indicated from the fact that products of a retrocycloaddition process are found after the reaction. Trichlorosilane reductions in the absence of tertiary amines are generally considered[7] to proceed through a four-center transition state with retention of configuration. Also, phosphinates (R = OR′)



in this system are known to have much faster hydrolysis rates[8] than are found for less strained cyclic compounds. The tendency to form the P(V) structure (trigonal bipyramid) in these reactions, and also in the oxygen in-

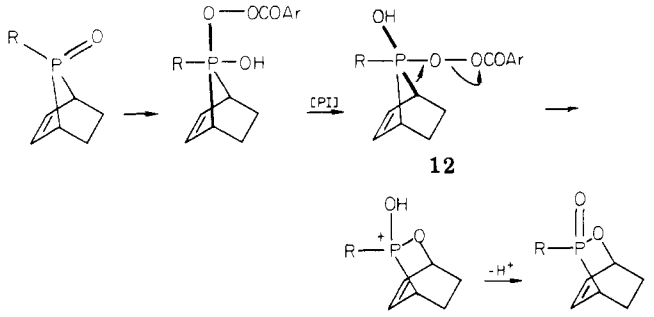
(5) (a) Quin, L. D.; Mesch, K. A. *Org. Magn. Reson.* **1979**, *12*, 442. (b) Quin, L. D.; Mesch, K. A. *J. Chem. Soc., Chem. Commun.* **1980**, 959. (c) Quin, L. D.; Mesch, K. A.; Bodalski, R.; Pietrusiewicz, K. M. *Org. Magn. Reson.* **1982**, *20*, 83.

(6) McPhail, A. T., unpublished results.

(7) (a) Horner, L.; Balzer, W. D. *Tetrahedron Lett.* **1965**, 1157. (b) Naumann, K.; Zon, G.; Mislow, K. *J. Am. Chem. Soc.* **1969**, *91*, 7012.

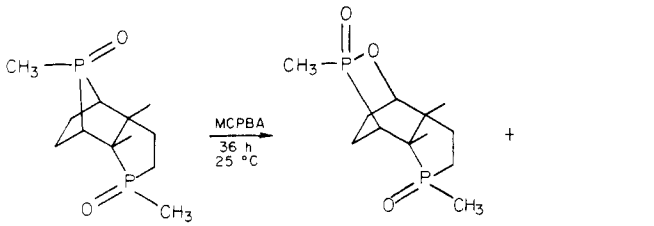
(8) Kluger, R.; Westheimer, F. H. *J. Am. Chem. Soc.* **1969**, *91*, 4143.

Scheme II

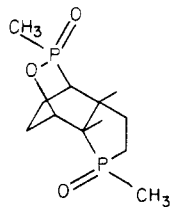


12

sertion, is great since a bond angle is offered at the apical-equatorial site (90°) that is more compatible with that forced on the 7-phosphanorbornene phosphorus than is present in the tetracoordinate condition with its close to tetrahedral bond angles. This carbon–oxygen bond formed in the insertion reaction can therefore be viewed (Scheme II) as arising from rearrangement of a P(V) intermediate (**12**) or transition state, possibly undergoing a permutational isomerization (PI) to place the involved atoms in favorable positions (presumably with apical carbon for departure, attacking an equatorial peroxy group). This view of the reaction predicts retention of configuration at phosphorus, but other PI to cause inversion could occur. This mechanism leaves no essential role for the allylic carbon, although it may expedite the process, and suggests that even saturated phosphorus compounds with severely contracted C–P–C bonds might in general be susceptible to oxygen insertion with peracids. Kashman and Awerbouch had attempted this reaction without success on the 8-phosphabicyclo[3.2.1]octane system, but we proceeded to test the idea with the more strained 7-phosphanorbornane system **13**[5c]. The reaction did indeed occur, and after 36 h at room temperature an 82% yield of a 1:1 mixture of the two isomers **14** and **15** was obtained. Here



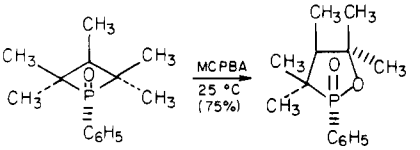
13 14



15

the products are quite stable thermally, since the possibility of decomposition by retrocycloaddition is eliminated. The ^{31}P–^{31}P coupling constants were again useful for assigning the isomer structure (**14**, $^3J_{PP}$ = 43.9 Hz; **15**, $^3J_{PP} \sim 0$). The ^{13}C NMR spectra contained the expected signals for carbon bearing oxygen (**14**, δ 74.1, $^2J_{PC}$ = 9.2 Hz; **15**, δ 72.5, $^2J_{POC}$ = 9.2, $^2J_{PCC}$ = 4.4 Hz).

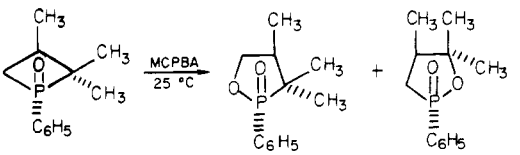
With this new view that a Baeyer–Villiger process may have some utility in the synthesis of special oxaphospha heterocycles, we have examined the family of phosphetane oxides as suitable reactants, since these compounds are known to have a severly contracted C–P–C angle not unlike that of the 7-phosphanorbornene system (e.g., 79.4° in 2,2,3-trimethyl-1-phenylphosphetane 1-oxide[9]). Furthermore, polymethylphosphetane oxides are especially readily synthesized from certain olefins, phosphorus(III) halides, and aluminum chloride[10] and could serve as practical precursors of new 1,2-oxaphospholanes (also known as phostones). This reaction was indeed realized as is seen in the conversion of **16** to **17**. After 122 h, the



16 17

^{31}P signal for **16** (+53.6) had vanished and a new one appeared at +62.4. In the ^{13}C NMR spectrum (Table I), the product contained a signal for carbon bearing oxygen (δ 87.37, J = 4.4 Hz) and the expected increase in $^1J_{PC}$ at the 3-position (**16**, 59.3 Hz; **17**, 82.4 Hz). As before, only one of the two possible diastereoisomers was formed, and the product is shown, but not established, to have retained the original configuration.

A similar result was obtained for phosphetane oxide **18**. Here the reaction can follow two pathways, but attack occurred primarily at the least substituted carbon to give a mixture consisting of about 90–95% **19** and 5–10% of **20**. The reaction was monitored by ^{31}P NMR and was



18 19 20

found to be substantially faster (complete in 39 h) than that with the more highly substituted **16**. After isolation, the yield was 56%. ^1H NMR spectroscopy was helpful here in confirming that the insertion had occurred at the least substituted carbon, since there was a signal at δ 4.2 for CH_2 attached to oxygen. The opposite orientation would normally be encountered in the Baeyer–Villiger reaction[11] of ketones. However, the special steric requirements at phosphorus appear to direct a different course for this and related rearrangement reactions of phosphetanes. It is known,[12] for example, that CH_2 migration occurs in preference to $C(CH_3)_2$ migration in the rearrangement of iodomethiodides with alkali to form phospholane oxides. The migrating carbon in such rearrangements departs from the apical position of a trigonal-bipyramidal intermediate; the CH_2 substituent is more electronegative than $C(CH_3)_2$ and is proposed[12] to occupy preferentially the apical position.

These results suggest that a simple new synthesis of the 1,2-oxaphospholane system has been discovered, limited only by the availability of the phosphetane oxides needed as starting materials. Obtaining samples of analytical

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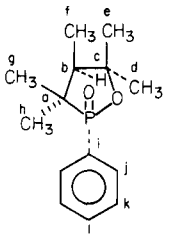
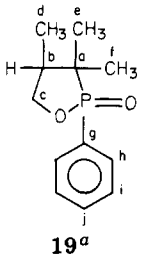
(12) Corfield, J. R.; Harger, M. J. P.; Shutt, J. R.; Trippett, S. *J. Chem. Soc. C* **1970**, 1855.

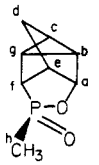
Table I. ^{13}C NMR Spectral Data for Oxygen-Insertion Products



17[a]



19[a]



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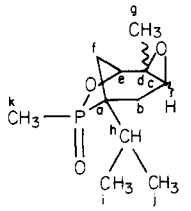
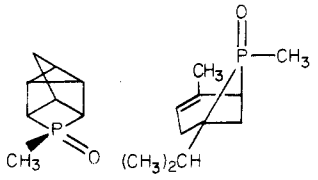


26[a,d]

C	17[a] δ	17[a] J_{PC}, Hz	19[a] δ	19[a] J_{PC}, Hz	23 δ	23 J_{PC}, Hz	26[a,d] δ	26[a,d] J_{PC}, Hz
a	38.15	82.4	36.32	84.1	85.37	1.8	42.57	76.3
b	52.80	6.6	41.56	9.8	14.13	3.1	22.43	4.3
c	87.37	4.4	72.82	2.9	19.07	12.2	58.10	
d	24.67		9.73	10.7	30.68	11.6	59.27	1.1
e	19.21	2.2	15.23	2.9	39.49	2.4	80.32	2.7
f	9.48	9.9	21.52	4.9	42.50	84.2	35.17	7.5
g	26.26	3.3	*b*		17.17	2.4	18.59	
h	29.72	7.7	132.19	9.8	13.48	94.6	30.58	4.8
i	*b*		128.44	12.7			18.79	1.6
j	132.33	8.8	132.25	2.9			17.37	12.9
k	128.30	12.1					12.61	87.6
l	132.86[c]	4.4						

[a] The spectra for 17, 19, and 26 are published as 859, 858, and 861, respectively, in Supplementary Volume G-12, "Selected ^{13}C Nuclear Magnetic Resonance Spectral Data"; Thermodynamics Research Center: Texas A&M University, College Station, TX. [b] Not observed. [c] Tentative assignment. [d] Assignment to secondary, tertiary, and quaternary carbons by INEPT program (Figure 1).

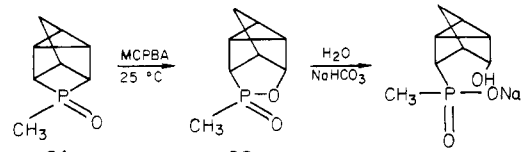
purity, however, is complicated by the strong tendency for the *m*-chlorobenzoic acid byproduct to associate with the product. Attention was then given to the application of the reaction to more complicated strained phosphorus heterocycles, and for this purpose the bridged systems prepared from reaction of methylphosphonous dichloride with norbornadiene[13] (product **21**) and with α-pinene[14] (product **22**) were chosen. The C–P–C angles in these



21 **22**

systems are quite small; for a phosphonium salt related to **21**, the angle was 74.8,[15] while 76.9° has been measured[14] for **22**.

The reaction of **21** with MCPBA was quite rapid and by ^{31}P NMR analysis was complete in 20 min. However, isolation of the product (**23**) was complicated by a difficulty not experienced with the monocyclic oxaphospholanes; the basic ($NaHCO_3$) medium needed for the removal of the *m*-chlorobenzoic acid from the product caused considerable hydrolysis of the strained oxaphospholane moiety, even at 0 °C, and gave the ring-opened phosphinate **24**. This

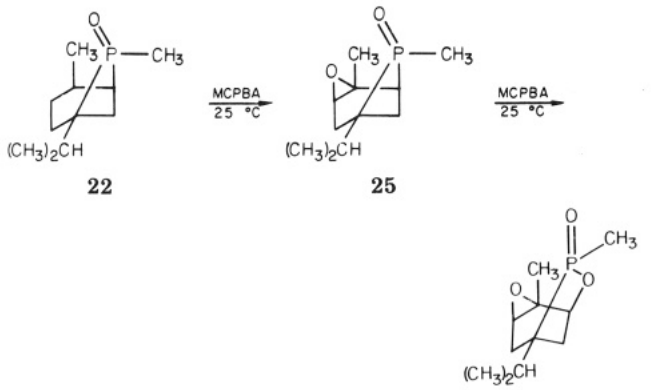


21 **23** **24**

(13) Green, M. *J. Chem. Soc.* **1965**, 541.
(14) Vilkas, E.; Vilkas, M.; Joniaux, D.; Pascard-Billy, C. *J. Chem. Soc., Chem. Commun.* **1978**, 125.
(15) Mazhar-ul-Haque; Rashid, M.; Cremer, S. E., *J. Chem. Soc., Perkin Trans. 2* **1978**, 1115.

was apparent from the change in ^{31}P NMR shift from δ +71.5 observed for the initial product to +23.6 after isolation. The phosphinate has not been adequately purified for conclusive identification, however. It proved possible to avoid this problem by using trifluoroperoxyacetic acid, since the low boiling point (72 °C) of the corresponding carboxylic acid allows its removal by vacuum stripping rather than by salt formation with base. The oxygen insertion with this peroxy acid was complete after 72 h, as determined by replacement of the ^{31}P signal of **21** with a signal at +64.8. The recovery of **23** (stereochemistry assumed) was only 28.5%, but the product was of good purity and had the identifying ^{13}C NMR (Table I, δ 84.37 for carbon on oxygen; $^1J_{PC}$ for CH_3, 94.6 Hz, and for C-3, 84.2 Hz) and ^1H NMR features expected for the oxaphospholane moiety. A few percent of an impurity detected in the product, with δ (^{31}P) +67.0, may be the isomer with the other (presumably endo) configuration at P. As noted, the occurrence of isomerism is not unexpected for a reaction where a trigonal-bipyramidal intermediate is involved but had not been detected in any of the other reaction products.

Oxygen insertion of MCPBA also occurred rapidly with **22**; here the product showed no tendency to undergo ring opening during the basic workup. However, the spectral properties of the product showed that the double bond had been epoxidized; no ^{13}C signals for sp^2 carbons were present, and there were three signals for carbon bearing oxygen (Table I). Structure **26** is assigned to the product, but neither the stereochemistry of the oxygen insertion nor that of the epoxidation are known. In the epoxidation, it seems reasonable that attack might occur from the least hindered (α) face of the double bond. That epoxidation occurred faster than oxygen insertion was shown by monitoring the reaction by ^{31}P NMR; the initially formed product had a shift (δ +52.7; cf. to the starting oxide, +35.3), implying no involvement of P in the reaction, but as the reaction proceeded, this signal diminished and was replaced with one of a considerably different chemical shift (+75.1) that is in the same range seen for the other 1,2-



22 25 26

oxaphospholane derivatives.

The ^{13}C NMR spectrum of **26** (Figure 1a) was difficult to interpret. Therefore, a series of spectra was prepared with use of the pulse sequences of the INEPT program (Insensitive Nucleus Enhancement through Polarization Transfer[16]), which can lead to ready recognition of secondary, tertiary, and quaternary carbons.[17] This recognition is more commonly done by restoration of partial or complete proton coupling, but with complex phosphorus compounds, where ^{31}P coupling is also present, signal overlap can be serious and inconclusive results are obtained. The INEPT program is vastly superior for typing the carbons, in that the basic coupling pattern is undisturbed and specific intensity changes are brought about for each type of carbon. Thus, CH_2 carbons are easily recognized when the pulse sequence employs a delay factor of $3/(4J_{CH})$ before final broad-band decoupling and data acquisition,[17] since these signals are specifically inverted on the spectrum (Figure 1c). With $2/(4J)$, CH carbons give greatly enhanced signals (Figure 1b), and with $1/(4J)$, quaternary carbon signals are eliminated from the spectrum (Figure 1d). Methyl carbons are then recognized from their lack of modification in these operations. The assignments made for **26** are given in the Experimental Section and are in complete accord with the structure. A similar series of INEPT spectra was obtained for the starting phosphine oxide **22** to assist in making the assignments; these spectra are recorded elsewhere.[18]

From the clear recognition of carbon types, it became obvious that the methyls of the isopropyl group in **26**, as well as in **22**, were nonequivalent and had very different values for $^3J_{PC}$. The presence of chiral centers in these molecules seemed to be a probable source of the nonequivalence, and this was confirmed when the spectrum of **22** was obtained at several temperatures up to 100 °C and found to remain unchanged. Nonequivalence due to restricted rotation would have led to changes in the high-temperature spectra. Nonequivalent methyls of isopropyls present in terpene molecules with chiral centers are, in fact, quite common,[19] but examples where ^{31}P coupling of different magnitudes to diastereotopic carbons such as these are quite rare. That the coupling constants should differ follows from the fact that $^3J_{CP}$ is controlled by dihedral angle relations,[20] which, for example, is the

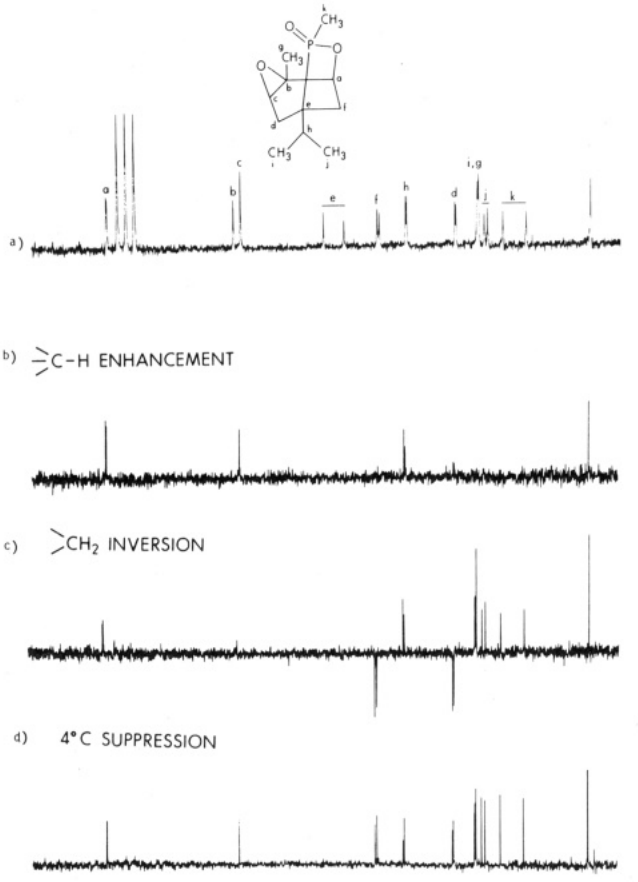
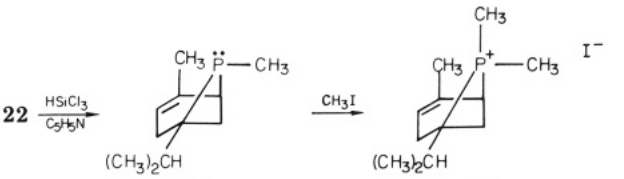


Figure 1. ^{13}C NMR spectra of compound **26** at 22.5 MHz: (a) normal conditions, (b) INEPT[17] with delay $2/(4J)$ before FID, (c) INEPT with $3/(4J)$, (d) INEPT with $1/(4J)$.

cause of different vicinal proton–proton coupling constants for diastereotopic protons in structural units such as RCH_2–CHXY.[21] We have also prepared the previously unknown phosphine **27** from oxide **22** and the methiodide **28** of the phosphine, and these derivatives also show the



27 28

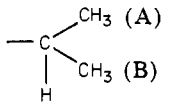
shift and coupling differences for the isopropyl methyls. In **28**, phosphorus is no longer unsymmetrically substituted, implying that other chiral centers in these molecules are sufficient causes of the nonequivalence. The ^{13}C data for the nonequivalent isopropyl methyls are summarized in Table II.

Experimental Section

General Procedures. Melting points were taken on a Mel-Temp apparatus and are corrected. The instruments used are as follows: for ^{13}C NMR JEOL FX-60 (15.0 MHz) or 90Q (22.5 MHz); for ^{31}P NMR, Bruker HFX-10 or JEOL 90-Q (36.43 MHz). All NMR measurements were run in the FT mode with proton decoupling. ^{13}C shifts are referenced to $(CH_3)_4Si$ as 0 ppm; ^{31}P shifts are referenced to 85% H_3PO_4, with downfield shifts positive.

(16) Morris, G. A.; Freeman, R. *J. Am. Chem. Soc.* **1979**, *101*, 760.
(17) Doddrell, D. M.; Pegg, D. T. *J. Am. Chem. Soc.* **1980**, *102*, 6388.
(18) Spectrum 848, "Selected ^{13}C Nuclear Magnetic Resonance Spectral Data"; Thermodynamics Research Center: Texas A&M University, College Station, TX, Supplementary Volume G-12.
(19) For example, see Spectrum No. 4013C for *p*-menthol in Sadtler Standard Carbon-13 NMR spectra.
(20) Quin, L. D.; Gallagher, J. J.; Cunkle, G. T.; Chesnut, D. B. *J. Am. Chem. Soc.* **1980**, *102*, 3136.
(21) Silverstein, R. M.; Bassler, G. C.; Morrill, T. C. "Spectrometric Identification of Organic Compounds", 4th ed.; Wiley: New York, 1981; pp 207–208.

Table II. ^{13}C NMR Data for Diastereotopic Methyls of Compounds 22 and 26-28



	22				
Me	54 °C	100 °C	26	27	28
A	15.95 (13.2)	15.76 (13.2)	17.37 (12.9)	14.18 (3.3)	15.43 (14.3)
B	18.27 (5.5)	17.93 (5.5)	18.79 (1.6)	16.18 (5.5)	18.67 (4.4)

Elemental analyses were run by MHW Laboratories, Phoenix, AZ. Mass spectra were run by Research Triangle Center for Mass Spectrometry, Research Triangle Park, NC.

3,5,6,9,10,11-Hexamethyl-3,9-diphospha-8-oxatricyclo-[5.2.2.0^{2,6}]undeca-4,10-diene 3,9-Dioxide (8). A mixture of 2.0 g (7.0 mmol) of **5**[5c] and 3.1 g (14.0 mmol) of *m*-chloroperbenzoic acid in 50 mL of chloroform was allowed to stand at room temperature for 1.5 h and then chromatographed on neutral alumina. Elution with $CHCl_3$ gave 1.5 g (72%) of **8** as the only product. This white solid was stored at −16 °C due to thermal instability and was not analyzed; ^1H NMR ($CDCl_3$) δ 1.40–2.00 (PCH_3 and CCH_3, 18 H), 2.55–3.12 (m, CH, 2 H), 4.60 (d, $^3J_{POCH}$ = 21 Hz, H_7), 5.94 (d, $^2J_{PH}$ = 24 Hz, CH=); ^{13}C NMR ($CDCl_3$) δ 13.7 (d of d, $^1J_{PC}$ = 108.0 Hz, $^4J_{PC}$ = 2.4 Hz, CH_3-P_9, 19.9 (d, $^1J_{PC}$ = 62.3 Hz, CH_3-P_3), 38.7 (d of d, $^1J_{P_3C}$ = 70.2 Hz, $^2J_{P_9C}$ = 6.8 Hz, C_2), 40.1 (d of d, $^1J_{P_9C}$ = 73.8 Hz, $^2J_{P_3C}$ = 1.8 Hz, C_1), 57.8 (d of d, $^3J_{P_9C}$ = 9.8 Hz, $^2J_{P_3C}$ = 9.8 Hz, C_6), 84.0 (d of d, $^2J_{P_9C}$ = 8.6 Hz, $^3J_{P_3C}$ = 2.4 Hz, C_7), 163.4 (d, $^2J_{P_3C}$ = 21.9 Hz, C_5); ^{31}P NMR ($CDCl_3$) +53.1 (P_9) and +65.7 (P_3), both d, $^3J_{PP}$ = 41.5 Hz.

3,9-Diphenyl-5,11-dimethyl-3,9-diphospha-8-oxatricyclo-[5.2.2.0^{2,6}]undeca-4,10-diene 3,9-Dioxide (9). A mixture of 2.5 g (6.6 mmol) of **6**[5c] and 2.5 g (13.2 mmol) of *m*-chloroperbenzoic acid in 30 mL of chloroform was allowed to stand at room temperature for 1.5 h and then chromatographed on neutral alumina. Elution with $CHCl_3$ gave 1.1 g (42%) of **9** as a white solid. This product was stored at −16 °C and was stable indefinitely at that temperature; ^1H NMR ($CDCl_3$) δ 1.88 (d, J_{PH} = 5 Hz, CCH_3), 2.10 (s, CCH_3), 3.40 (m, CH, 2 H), 4.04 (m, CH, 1 H), 5.18 (br d, $^3J_{POCH}$ = 20.0 Hz, CH, 1 H), 5.80–6.16 (m, CH=, 2 H), 7.25–7.80 (m, Ar H, 10 H); ^{13}C NMR ($CDCl_3$) δ 33.8 (d of d, $^1J_{P_3C}$ = 70.8 Hz, $^2J_{P_9C}$ = 7.4 Hz, C_2), 34.4 (d of d, $^1J_{P_9C}$ = 79.4 Hz, $^2J_{P_3C}$ = 2.4 Hz, C_1), 54.9 (d of d, $^3J_{P_9C}$ = 10.4 Hz, $^2J_{P_3C}$ = 10.4 Hz, C_6), 79.4 (d, $^2J_{P_9C}$ = 8.6 Hz, C_7), 160.8 (d, $^2J_{P_3C}$ = 23.3 Hz, C_5); ^{31}P NMR ($CDCl_3$) δ +36.2 (P_9) and +56.2 (P_3), both d, $^3J_{PP}$ = 43.9 Hz.

3,9-Dimethyl-3,9-diphospha-8-oxatricyclo[5.2.2.0^{2,6}]unde-ca-4,10-diene 3,9-Dioxide (10) and 3,8-Dimethyl-3,8-diphos-pha-9-oxatricyclo[5.2.2.0^{2,6}]undeca-4,10-diene 3,8-Dioxide (11). A mixture of 1.0 g (4.4 mmol) of **7**[5c], 1.9 g (8.8 mmol) of *m*-chloroperbenzoic acid, and 30 mL of chloroform was allowed to stand at room temperature for 1 h and then chromatographed on neutral alumina with $CHCl_3$ to give 0.8 g (75%) of a 1:1 mixture of **10** and **11** as a white solid. The sample was thermally unstable at 25 °C but was stable at −16 °C indefinitely; ^1H NMR ($CDCl_3$) 4.96–5.45 (m, POCH, 1 H); ^{13}C NMR ($CDCl_3$) δ 14.1 (d, $^1J_{PC}$ = 99.5 Hz, CH_3-P_8 of **11**), 14.2 (d of d, $^1J_{PC}$ = 100.1 Hz, $^4J_{PC}$ = 7.9 Hz, CH_3-P_9 of **10**), 18.6 (d, $^1J_{PC}$ = 69.5 Hz, CH_3-P_3 of **10** and **11**), 72.5 (d of d, $^2J_{POC}$ = 9.2 Hz, $^2J_{PCC}$ = 4.4 Hz, C_1 of **11**), 74.1 (d, $^2J_{POC}$ = 9.2 Hz, C_7 of **10**), 147.5 (d, $^2J_{PC}$ = 22.1 Hz, C_5 of **10**), 150.0 (d of d, $^2J_{PC}$ = 21.5 Hz, $^3J_{PC}$ = 13.4 Hz, C_5 of **11**); ^{31}P NMR ($CDCl_3$) δ +48.6 (s, P_8 of **11**), +64.4 (s, P_3 of **11**), +48.7 (P_9 of **10**) and +65.5 (P_3 of **10**), both d, $^3J_{PP}$ = 39.1 Hz.

3,9-Dimethyl-3,9-diphospha-8-oxatricyclo[5.2.2.0^{2,6}]unde-cane 3,9-Dioxide (14) and 3,8-Dimethyl-3,8-diphospha-9-ox-atricyclo[5.2.2.0^{2,6}]undecane 3,8-Dioxide (15). A mixture of 736 mg (3.2 mmol) of **13**[5c] and 1.1 g (6.4 mmol) of *m*-chloroper-benzoic acid in 10 mL of dichloromethane was allowed to stand at room temperature for 36 h. The mixture was then poured into 5% K_2CO_3 (15 mL) and extracted with $CHCl_3$ (5 × 25 mL). The organic layer was dried over $MgSO_4$ and concentrated to give 650 mg (82%) of 1:1 mixture of **14** and **15** as a yellow oil; ^1H NMR ($CDCl_3$) δ 4.40 (d, $^3J_{PH}$ = 17 Hz, POCH), 4.74 (d, $^3J_{PH}$ = 17 Hz, POCH); ^{13}C NMR ($CDCl_3$) δ 74.7 (d of d, $^2J_{P_8C}$ = 6.8 Hz, $^2J_{P_3C}$ = 3.0 Hz, C_1 of **15**), 78.0 (d of d, $^2J_{P_8C}$ = 6.8 Hz, $^3J_{P_3C}$ = 1.8 Hz, C_7 of **14**); ^{31}P NMR ($CDCl_3$) δ +52.9 (P_9 of **14**), +70.1 (P_3 of **14**), both d, $^3J_{PP}$ = 43.9 Hz, +55.2 (s, P_8 of **15**), +66.4 (s, P_3 of **15**).

3,3,4,5,5-Pentamethyl-2-phenyl-1,2-oxaphospholane 2-Oxide (17). A mixture of *trans*-2,2,3,4,4-pentamethyl-1-phenylphosphetane 1-oxide[22] (**16**; 1.0 g, 4.2 mmol) and *m*-chloroperbenzoic acid (2.92 g, 16.9 mmol) in 20 mL of CH_2Cl_2 was allowed to stand for 122 h at 25 °C in the absence of light. During this time *m*-chlorobenzoic acid precipitated. The mixture was filtered and the filtrate washed with three 25-mL portions of cold 5% NaOH. The solution was dried (Na_2SO_4) and concentrated under reduced pressure, yielding **17** as a white solid (0.8 g, 75%). The solid was Kugelrohr distilled at 80–87 °C (0.01 mm); mp 109.5–112.5 °C; ^{31}P NMR ($CDCl_3$) δ +62.4; ^{13}C NMR ($CDCl_3$), Table I. Anal. Calcd for $C_{14}H_{21}O_2P$: C, 66.65; H, 8.39; P, 12.27. Found: C, 66.73; H, 8.52; P, 12.20.

3,3,4-Trimethyl-2-phenyl-1,2-oxaphospholane 2-Oxide (19). A mixture of *trans*-2,2,3-trimethyl-1-phenylphosphetane 1-oxide[22] (**18**; 1.0 g, 4.8 mmol) and *m*-chloroperbenzoic acid (3.36 g, 19.2 mmol) in 20 mL of CH_2Cl_2 was allowed to stand for 39 h at 25 °C in the absence of light. Precipitated *m*-chlorobenzoic acid was removed by filtration and the filtrate was washed with ten 10-mL portions of cold 5% NaOH to remove most of the *m*-chlorobenzoic acid. The solution was dried (Na_2SO_4) and concentrated under reduced pressure to yield 0.6 g (56%) of **19**, containing 5–10% of isomer **20**. The colorless oil was Kugelrohr distilled at 75–87 °C (0.01 mm); ^{31}P NMR ($CDCl_3$) δ +66.6; ^{13}C NMR ($CDCl_3$), Table I. The distillation was repeated five times to obtain a sample free of final traces of *m*-chlorobenzoic acid and giving the correct analysis. Anal. Calcd for $C_{12}H_{17}O_2P$: C, 64.28; H, 7.64; P, 13.81. Found: C, 64.11; H, 7.45; P, 14.01.

5-Methyl-4-oxa-5-phosphatetracyclo[4.2.0.0^{2,9}.0^{3,7}]octane 5-Oxide (23). To 4.9 mL of trifluoroacetic anhydride in 5 mL of methylene chloride in an ice bath was added very slowly 0.676 mL (8.6 mmol) of 30% hydrogen peroxide in 5 mL of methylene chloride. To this clear solution was added 0.495 g (2.7 mmol) of phosphine oxide **21**[13] in 5 mL of methylene chloride. The solution was stirred for 72 h at room temperature in the absence of light. ^{31}P NMR then showed only a broad singlet at +79 ppm. The organic layer was washed twice with 20 mL of water and was dried over sodium sulfate. The solvent and residual trifluoroacetic acid were removed by rotary evaporation and then by a high vacuum, yielding 0.15 g (28.5%) of **23**, which crystallized. The crystals were recrystallized from cyclohexane but were very hygroscopic and a melting point could not be obtained; ^{31}P NMR ($CDCl_3$) δ +64.82; ^{13}C NMR ($CDCl_3$), Table I; MS, *m/e* 170.0496 (M^+, $C_8H_{11}O_2P$; calcd 170.0496).

1-Isopropyl-3,4-epoxy-4,7-dimethyl-6-oxa-7-phosphabicy-clo[3.2.1]octane 7-Oxide (26). A mixture of 0.5 g (2.5 mmol) of 5-isopropyl-2,6-dimethyl-6-phosphabicyclo[3.1.1]hept-2-ene 6-oxide[14] (**22**) and *m*-chloroperbenzoic acid (1.76 g, 10.0 mmol) in 10 mL of CH_2Cl_2 was allowed to stand for 16 h at 25 °C in the absence of light. The mixture was filtered and the filtrate washed with cold 5% NaOH. The solution was dried (Na_2SO_4) and concentrated under reduced pressure, yielding 0.3 g (52%) of **26** as a white solid. The solid was Kugelrohr distilled at 80–85 °C (0.01 mm) and then recrystallized from cyclohexane–benzene; mp 110–113 °C; ^{31}P NMR ($CDCl_3$) δ +75.1; ^{13}C NMR ($CDCl_3$), Table I. Anal. Calcd for $C_{11}H_{19}O_3P$: C, 57.38; H, 8.32; P, 13.45. Found: C, 57.38; H, 8.06; P, 13.28.

5-Isopropyl-2,6-dimethyl-6-phosphabicyclo[3.1.1]hept-2-ene (27) and Methiodide 28. To 3.0 mL (30 mmol) of freshly distilled trichlorosilane in 20 mL of dry benzene was added 10 mL (0.125

(22) Cremer, S. E.; Chorvat, R. J. *J. Org. Chem.* **1967**, *32*, 4066.

mol) of dry pyridine in 10 mL of dry benzene. To this solution was added 1.0 g (5 mmol) of the phosphine oxide **22**. The mixture was refluxed for 1.5 h and allowed to stir for 2 h at room temperature. It was cooled in an ice bath and then treated slowly with 50 mL of 30% sodium hydroxide. The organic layer was separated and dried ($MgSO_4$). The solvent was removed, leaving 0.55 g (60%) of **28** as a clear oil; ^{31}P NMR ($CDCl_3$) δ +25.5; ^{13}C NMR ($CDCl_3$)[23] δ 7.38 (k, 35.2 Hz), 14.18 (i or j, 3.3 Hz), 16.18 (i or j, 5.5 Hz), 21.81 (g), 30.29, 31.46, 32.20 (b, f, or h), 40.29 (e, 4.4 Hz), 43.44 (a, 3.3 Hz), 118.13 (c, 12.1 Hz), 144.36 (d, 5.5 Hz).

(23) Carbon designations are those used for **22** in Table I; values in parentheses are $^{13}C^{31}P$ coupling constants (hertz).

The phosphine was dissolved in hexane and excess methyl iodide was added to form the phosphonium salt **28**. The salt was isolated as a white solid; mp 204-206 °C dec; ^{31}P NMR ($CDCl_3$) + 41.1. Anal. Calcd for $C_{12}H_{22}IP$: C, 44.46; H, 6.84; P, 9.55. Found: C, 44.25; H, 6.85; P, 9.99.

Registry No. **5**, 73376-41-7; **6**, 76549-55-8; **7**, 76505-31-2; **8**, 87432-88-0; **9**, 87432-89-1; **10**, 87432-90-4; **11**, 87432-91-5; **13**, 87450-35-9; **14**, 87432-92-6; **15**, 87432-93-7; **16**, 16083-91-3; **17**, 87432-94-8; **18**, 34136-10-2; **19**, 87432-95-9; **20**, 87432-96-0; **21**, 57377-76-1; **22**, 87507-29-7; **23**, 87432-97-1; **26**, 87432-98-2; **27**, 87432-99-3; **28**, 87433-00-9; *m*-chloroperbenzoic acid, 937-14-4; trifluoroperoxyacetic acid, 359-48-8.

Sterols of Marine Invertebrates. 44.[1a] Isolation, Structure Elucidation, Partial Synthesis, and Determination of Absolute Configuration of Pulchrasterol. The First Example of Double Bioalkylation of the Sterol Side Chain at Position 26

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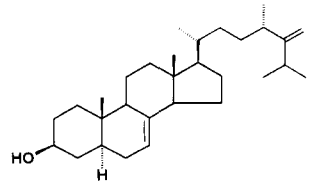
A new C_{30} marine sterol, (24*S*)-24,26,26-trimethylcholesta-7,25(27)-dien-3β-ol (pulchrasterol), has been isolated as the major component from the sterol fraction of the New Zealand deep sea sponge *Aciculites pulchra*. Its general structure was deduced from spectral data (360-MHz ^1H NMR and MS) and partial synthesis of its Δ^5 analogue, while its stereochemistry was determined by correlating spectral data (300-MHz ^1H NMR and CD) from synthetic steroids of similar structure and known configuration. The side chain of pulchrasterol is doubly biomethylated at position 26, which is discussed with respect to its possible biosynthetic origin and its unexpected 24*S* absolute configuration.

Introduction

It frequently occurs that the *trace* sterol components of a marine invertebrate possess unique hydrocarbon side chains unlike any found in terrestrial plants or animals.[2,3] The biosynthetic pathways that produce these novel side chains are currently under intense investigation.[2,3] When a *major* sterol component is discovered to possess a previously unknown side chain, then, aside from its biosynthetic novelty, the question of its biological function as an active membrane constituent becomes relevant. Herein, we report the isolation, structure elucidation, partial synthesis, and determination of absolute configuration of pulchrasterol (1), the major sterol component of *Aciculites pulchra*, which constitutes the first example of double biomethylation of the sterol side chain at position 26 and which probably serves as a membrane constituent.



1

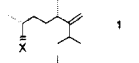
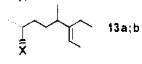
Pulchrasterol

(1) (a) For Part 43 in this series, see: Popov, S.; Carlson, R. M. K.; Djerassi, C. *Steroids*, submitted for publication. (b) Visiting investigator at Stanford University from the Shenyang College of Pharmacy and Liaoning Institute of Materia Medica, China. (c) Department of Zoology, University of Auckland, Auckland, New Zealand.

(2) (a) Djerassi, C. *Pure Appl. Chem.* **1981**, *53*, 873-890. (b) Djerassi, C.; Theobald, N.; Kokke, W. C. M. C.; Pak, C. S.; Carlson, R. M. K. *Ibid.* **1979**, *51*, 1815-1828.

(3) Catalan, C. A. N.; Thompson, J. E.; Kokke, W. C. M. C.; Djerassi, C. *Tetrahedron*, submitted for publication.

Table I. Sterols of *Aciculites pulchra*

structure	rel retent times[a] HPLC RRT	rel retent times[a] GC RRT	M^+ *m/z*	% of total sterol fraction
	1.00	1.00	386	10.6
 1	1.07	2.24	426	73.7
 13a;b	1.07	2.53	426	15.7

[a] Cholesterol was used as the standard (1.00) for both HPLC RRT and GC RRT. The conditions for HPLC were 100% methanol on a Whatman ODS-2 column at ambient temperatures. The conditions for GC were 260 °C on a 3% OV-17 column. (See Experimental Section for further details.)

Isolation and Structure Elucidation

The 4-demethyl sterol fraction (15 mg) of the New Zealand deep sea sponge *Aciculites pulchra* was isolated by column chromatography, checked by GC for composition (three components, see Table I), and subjected to HPLC. Analysis by GC/MS revealed cholesterol (M^+ = 386) as one of the minor components and two other sterols both having M^+ = 426 daltons, which indicated an empirical formula of $C_{30}H_{50}O$ and two degrees of unsaturation in the nucleus and/or the side chain. The 246-dalton peak corresponding to loss of side chain and part of ring D of each of the unidentified sterols was used to assign a Δ^7 unsaturation,[4] which was confirmed by ^1H NMR analysis[5]

(4) Patridge, L. G.; Midgley, I.; Djerassi, C. *J. Am. Chem. Soc.* **1977**, *99*, 7686-7692.

0022-3263/83/1948-4472$01.50/0