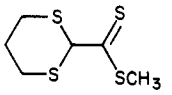
Alkylation of the monoanion 1 can be achieved if the reaction with alkylating agent is rapid enough to avoid disproportionation of 2. For example, addition of CS_2 to lithio-1,3-dithiane followed immediately by CH_3I produces the methyl ester of 1,3-dithiane-2-dithiocarboxylic acid (6).



6

All compounds were identified by NMR and elemental analyses.

Experimental Section

All reactions were carried out with standard Schlenk techniques employing anhydrous Ar. THF was freshly distilled from Na/benzophenone just prior to use. Dithiane was either prepared by the standard procedure[7] or obtained from Aldrich Chemical Co. and was sublimed prior to use. *n*-BuLi was used as a 1.6 M solution in hexane.

NMR spectra were obtained in $CDCl_3$, employing a Varian HA-100 spectrometer. Elemental analyses were obtained from Atlantic Microlabs, Atlanta, GA.

Dilithio-1,3-dithiane-2-carbodithioate (2). *n*-BuLi (10.4 mL, 1.6 M in hexane) was added to a solution of 2 g of dithiane in 100 mL of THF at −28 °C over a 5-min period. This solution was stirred for 1.5 h after which CS_2 (0.95 mL) was added to yield a red solution. Immediately an additional 10.4 mL of *n*-BuLi solution was added all at once. In 5–10 min, a white solid (2) precipitated. This solid was isolated by filtration in a standard Schlenk filter which was jacketed with dry ice. The solid was dried under vacuum while maintaining the low temperature. Once dry, 2 was stored under Ar in a freezer. The yield was essentially quantitative.

Alkylation of 2. 2-(1,3-Dithiolan-2-ylidene)-1,3-dithiane (4). 2 was prepared as above and kept as a slurry in THF at −28 °C. To this was added 1 equiv of anhydrous ethylene bromide. The reaction mixture immediately became a homogeneous solution. After the mixture was stirred for 1 h, the dry ice bath was removed, and the solvent was removed by vacuum. Ethanol (50 mL) was added to give a light yellow solid. (From this point anhydrous conditions were no longer necessary.) The solid was recrystallized from ethanol and chloroform to yield yellow crystals: yield 45–50%; mp 104–105 °C; NMR ($CDCl_3$) δ 2.17 (2 H, m), 2.82 (4 H, singlet), 3.4 (4 H, m). Anal. Calcd for $C_7H_{10}S_4$: C, 37.80; H, 4.53; S, 57.66. Found: C, 37.85; H, 4.52; S, 57.59.

2-[Bis(methylthio)methylene]-1,3-dithiane (5). 2 was prepared as above and kept as a slurry at −28 °C. To this was added 2 equiv of methyl iodide. The reaction mixture became a homogeneous solution. After the mixture was stirred for 1 h, the dry ice both was removed and solvent was removed by vacuum. Ethanol (50 mL) was added to give a yellow solid. Crystallization from ethanol/chloroform gave 5: yield ~50%; mp 110–112 °C; NMR ($CDCl_3$) δ 2.0 (2 H, m), 2.35 (6 H, s), 2.98 (4 H, m).

Alkylation of 1. Methyl 1,3-Dithiane-2-dithiocarboxylate (6). Dithiane was treated with 1 equiv of *n*-BuLi at −28 °C. After 1.5 h, CS_2 was added all at once followed immediately by 1 equiv of CH_3I. The red solution turned yellow upon addition of the CH_3I. The solution was warmed and solvent was removed by vacuum. Addition of ethanol produced a yellow solid which was recrystallized from ethanol and chloroform: yield 85%; mp 125–126 °C; NMR ($CDCl_3$) δ 2.0 (2 H, m), 2.27 (3 H, s), 2.53 (2 H, m), 5.27 (1 H, s). Anal. Calcd for $C_7H_{12}S_4$: C, 34.25; H, 4.80; S, 60.96. Found: C, 34.22; H, 4.82; S, 60.89.

Acknowledgment. Support from the Department of Chemistry, North Carolina State University, is acknowledged. Robert D. Bereman acknowledges the Camille and Henry Dreyfus Foundation for a Teacher-Scholar Grant (1974–1979). Comments of Dr. Fred Wudl, Bell Laboratories, are greatly appreciated.

Registry No. 2, 75812-75-8; 4, 75812-76-9; 5, 75812-77-0; 6, 75812-78-1; dithiane, 505-23-7; CS_2, 75-15-0; ethylene bromide, 106-93-4.

(7) Corey, E. J.; Seebach, D. *J. Org. Chem.* **1970**, *35*, 72–4.

Cyclic Phosphonium Ylides. A Short Synthesis of Gossyplure[1]

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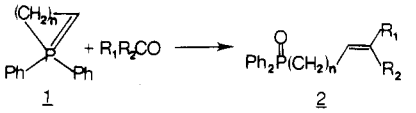
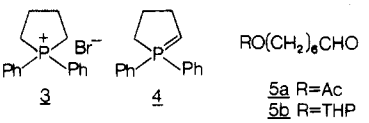
The use of triarylphosphonium ylides in organic chemistry, particularly in the Wittig olefination reaction, has become a cornerstone of synthetic methodology. In contrast to the extensive knowledge in this area, the corresponding cyclic phosphonium ylides have been investigated only sporadically and have never been exploited in a synthetic manner.[2] In principle, such ylides of the general structure 1 possess considerable synthetic potential because, for example, a Wittig reaction therewith generates an olefinic phosphine oxide 2, upon which subsequent chemical transformations can be effected. This note re-



1 2

ports the first synthetic utilization of a cyclic phosphonium ylide by describing the incorporation of the five-membered ylide 4 into a short synthesis of the sex pheromone of the female pink bollworm moth gossyplure, the 1:1 mixture of (7*Z*,11*Z*)- and (7*Z*,11*E*)-7,11-hexadecadien-1-yl acetates **9b** and **10b**.[3]

The introduction of the 7*Z* olefin was accomplished in a straightforward manner via a Wittig reaction. The salt 1,1-diphenylphospholanium bromide (3), prepared in



3 4 5a R=Ac 5b R=THP

quantity by variation of a recent procedure,[4] was converted to ylide 4 upon treatment with potassium *tert*-butoxide in THF at room temperature. Addition of either 7-acetoxyheptanal (**5a**)[5] or 7-(2-tetrahydropyranyloxy)heptanal (**5b**)[6] to the ylide gave the corresponding diphenylphosphine oxide *Z* olefin **6** or **6b** in high yield. The *Z*

(1) Contribution no. 555 from the Syntex Research Institute of Organic Chemistry.

(2) Johnson, A. W. "Ylide Chemistry"; Academic Press: New York, 1966. Savage, M. P.; Tripett, S. *J. Chem. Soc. C.* **1968**, 591. Lednicer, D. *J. Org. Chem.* **1970**, *35*, 2307.

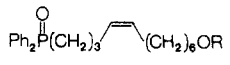
(3) For previous syntheses of the pheromone mixture and the components thereof, see: Henrick, C. A. *Tetrahedron* **1977**, *33*, 1845; Hammoud, A.; Descoins, C. *Bull. Soc. Chim. Fr.* **1978**, *2*, 299.

(4) Purdum, W. R.; Berlin, K. D. *J. Org. Chem.* **1975**, *40*, 2801.

(5) Isolated as a minor solvolysis product previously: Paquette, L. A.; Begland, R. W.; Storm, P. C. *J. Am. Chem. Soc.* **1970**, *92*, 1971.

(6) Burton, T. S.; Caton, M. P. L.; Coffee, E. C. J.; Parker, T.; Stuttle, K. A. J.; Watkins, G. L. *J. Chem. Soc., Perkin Trans. 1* **1976**, 2550.

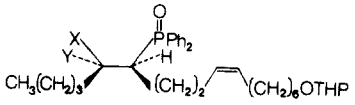
0022-3263/81/1946-0459$01.00/0



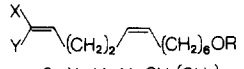
6a R=Ac
6b R=THP

configuration of the newly introduced double bond was supported by comparison of the ^{13}C NMR chemical shifts of the allylic carbon atoms (between 27.2 and 28.6 ppm) with those observed for the analogous *cis*-4-octene (29.4 ppm) and *trans*-4-octene (35.7 ppm). The *Z* isomer was the sole product; the *E* isomer, 5% of which would have been easily detectable in the ^{13}C NMR spectrum, was not observed.

The newly generated phosphine oxide moiety of **6b** was then exploited in a Horner reaction to introduce the second double bond of the 1,4-diene system of gossyplure. (Acetate **6a**, purified by distillation but unstable to the next transformation, could be converted into the required THP ether **6b** by saponification followed by reprotection in quantitative yield.) Formation of the anion of phosphine oxide **6b** with *n*-butyllithium followed by reaction with *n*-valeraldehyde gave the diastereomeric alcoholates **7a** and **8a**. Decomposition of the alcoholates to the diene



7 X=OR Y=H
8 X=H Y=OR
a R=Li b R=H



9 X=H Y=$CH_3(CH_2)_3$
10 X=$CH_3(CH_2)_3$ Y=H
a R=THP b R=Ac

THP ethers **9a** and **10a** could be accomplished by either addition of HMPA followed by heating to 60 °C or by isolation of the alcohols **7b** and **8b** followed by treatment with NaH in DMF at room temperature. Conversion to acetates **9b** and **10b**, the components of gossyplure, was carried out by brief treatment of the THP ethers with acetyl chloride in acetic acid. The overall yield of the acetates **9b** and **10b** from phosphine oxide **6b** was consistently 60–70%.

As expected from literature precedent,[2,7] the stereochemical course of the Horner reaction was strongly affected by the conditions of the condensation reaction. In all cases, the *Z,Z*/*Z,E* ratio of the gossyplure acetates **9b** and **10b**, as determined by GLC vs. authentic pure components, was found to depend solely on the solvent composition used in the reaction and not on the method of decomposition to olefin product. A representative number of cases are presented in Table I. As can be seen, the 1:1 gossyplure mixture **9b** and **10b** could be obtained within ±5% by carrying out the condensation in a 1:1 mixture of THF and ether.

The results detailed above strongly suggest that, unlike in the Wittig reaction, thermodynamic equilibration of the initial diastereomeric adducts **7a** and **8a** is not occurring under the reaction conditions of the Horner condensation or the subsequent decomposition to olefin. Since stereospecific decomposition must occur, i.e., *erythro*-**7** to *Z* olefin **9** and *threo*-**8** to *E* olefin **10**, only control of the initial condensation will lead to stereospecific olefin formation. Both the range of factors affecting this aspect of the Horner reaction and the further transformation of phosphine oxide olefins represented by **2** to allow variable functionalization at the newly generated terminus are under investigation.

Table I. Gossyplure *Z,Z*/*Z,E* Ratio[a]

solvent[b]	method of decomposition	% *Z,Z* (9b)	% *Z,E* (10b)
Et_2O	NaH/DMF	38.6	61.4
Et_2O	HMPA/heat	31.6	68.4
THF	NaH/DMF	58.3	41.7
THF	HMPA/heat	62.8	37.2
hexane/Et_2O (9:1)	HMPA/heat	44.2	55.8
THF/Et_2O (1:1)	HMPA/heat	45.6	54.4
HMPA[c]	HMPA/heat	66.4	33.6

[a] Analyzed on a 12 in. × 3 mm glass column packed with 10% PDEAS on Chromosorb WAW (100–120 mesh) at a column temperature of 180 °C and a helium flow rate of 60 mL/min. [b] Both addition of *n*-BuLi and aldehyde were carried out at −78 °C. [c] Additions at 0 °C.

Experimental Section

Melting points were determined on a Fisher-Jones hot stage and are uncorrected. ^1H NMR spectra were determined in $CDCl_3$ on a Varian EM-360 spectrometer. Chemical shifts are expressed as parts per million downfield from tetramethylsilane. IR spectra were recorded on a Perkin-Elmer 710B and are reported in reciprocal centimeters. Gas chromatography was carried out on F and M 402 gas chromatograph.

1,1-Diphenylphospholanium bromide (3) was prepared by a modification of the method of Purdum and Berlin.[4] To toluene (1.5 L) saturated with hydrogen bromide at room temperature was added a solution of (4-hydroxybutyl)diphenylphosphine[4] (103 g, 0.4 mol) in toluene (150 mL) with stirring. The resulting milky suspension was brought to reflux with azeotropic removal of water via a Dean–Stark trap. After 1 h, the mixture was cooled to 80 °C and resaturated with hydrogen bromide. The suspension was again brought to reflux and maintained for 1 h, after which the mixture was again saturated with hydrogen bromide. The reaction was maintained at reflux overnight, and then allowed to cool to room temperature. The supernatant toluene was decanted away from the residual oil and was replaced with water (1.5 L) containing Na_2CO_3 and $NaHCO_3$ (80 g each). The resulting mixture was stirred for 72 h at room temperature. The aqueous solution was then saturated with sodium bromide and extracted with chloroform (6 × 300 mL). The combined organic layers were dried over Na_2SO_4, filtered, and evaporated to yield 94.1 g (293 mmol, 71%) of **1** on trituration with acetone: mp 163–164 °C (lit.[8] mp 162 °C); NMR 7.45–8.40 (m, 10 H), 3.00–3.55 (m, 4 H), 2.00–2.85 (m, 4 H); IR (KBr) 2990, 2910, 1575, 1430, 1390, 1120.

7-Acetoxyheptanal (5a).[5] To a suspension of 7-hydroxyheptanal[6] (26.0 g, 200 mmol) in dry pyridine (80 mL) was added 4-(dimethylamino)pyridine (0.20 g) and acetic anhydride (80 mL). After 1.5 h at room temperature, TLC of an aliquot showed disappearance of starting material. The solution was diluted with ether, extracted with 1 M HCl and saturated brine, dried over Na_2SO_4, filtered, and evaporated to give a crude oil, which was Kugelrohr distilled (90 °C, 0.5 mm) to yield 19.0 g (110 mmol, 55%) as a clear colorless oil: NMR 9.72 (t, J = 1.5 Hz, 1 H), 4.0 (t, J = 6 Hz, 2 H), 2.40 (t of d, J = 7, 1.5 Hz, 2 H), 2.0 (s, 3 H), 1.2–1.8 (m, 8 H); IR 2940, 2860, 2725, 1720, 1460, 1390, 1365, 1240, 1040.

7-(2-Tetrahydropyranyloxy)heptanal (5b) was prepared by the method of Burton and co-workers,[6] bp 110 °C (0.1 mm, Kugelrohr) [lit.[6] bp 78–106 °C (0.1 mm)].

Phosphine Oxides (6). To solids phospholanium bromide **3** (24.1 g, 75 mmol) and potassium *tert*-butoxide (8.42 g, 75 mmol) under a blanket of nitrogen was added dry THF (100 mL) via syringe. The resulting orange solution was allowed to stir for 1 h at room temperature. Aldehyde **5** (50 mmol) was added via syringe over 30 min, resulting in a noticeable rise in temperature.

(7) Davidson, A. H.; Warren, S. *J. Chem. Soc., Perkin Trans. 1* **1976**, 639 (footnote 5).

(8) Isslieb, K.; Krech, K.; Gruber, K. *Chem. Ber.* **1963**, *96*, 2186.

The reaction was allowed to stir overnight at room temperature and then was quenched with water (50 mL). The mixture was partitioned between diethyl ether and water (200 mL), and the resulting organic layer was washed with additional water (3 × 100 mL) and with brine (3 × 100 mL). The organic extract was dried and evaporated to yield the crude diphenylphosphine oxide *Z* olefin **6**.

Acetate **6a** was purified by Kugelrohr distillation, bp 230 °C (1.0 mm), to yield 18.5 g (45 mmol, 90%) as a yellow oil: NMR 7.30–8.10 (m, 10 H), 5.20–5.50 (m, 2 H), 4.10 (t, 2 H, J = 7 Hz), 2.10 (s, 3 H), 1.0–2.5 (m, 16 H); IR (film) 2925, 1730, 1435, 1360, 1240, 1180, 1120, 1030, 720; ^{13}C NMR 131.825, 131.695, 131.370, 131.110, 130.687, 128.997, 128.477, 128.347, 64.628, 30.851 and 27.665 (J_1PC), 29.518, 28.900, 28.575, 27.893 (allylic carbons), 27.210, 25.844, 21.618 and 21.456 (J_2PC), 21.001; mass spectrum, m/e 412 (M^+), 369, 353, 298, 277, 255, 229, 215, 202, 201, 183, 180, 152, 125, 107, 77, 61, 43, 32; exact mass (high-resolution mass spectrum) calcd for $C_{25}H_{33}O_3P$ 412.2167, found 412.2166.

THP ether **6b** was purified by filtration through silica gel with 3:1 EtOAc–CH_2Cl_2 to yield 22.30 g (49.1 mmol, 98%) as an oil: NMR 7.10–8.20 (m, 10 H), 5.25–5.65 (m, 2 H), 4.60 (m, 1 H), 3.30–4.25 (m, 6 H), 1.0–2.60 (m, 20 H); IR (film) 2950, 2870, 1440, 1350, 1200, 1120, 1040; ^{13}C NMR 131.793, 131.663, 131.553, 131.110, 130.687, 128.964, 128.447, 128.184, 98.958, 67.684, 62.418, 30.818, 29.746, 29.616, 29.290 and 27.633 (J_1PC), 29.160, 28.510, 27.860, 27.242 (allylic carbons), 26.170, 25.519, 21.586 and 21.423 (J_2PC), 19.733; mass spectrum, m/e 454 (M^+), 370, 369, 353, 340, 298, 277, 255, 229, 215, 202, 201, 183, 155, 152, 125, 104, 85, 77, 67, 55, 47; exact mass (high-resolution mass spectrum) calcd for $C_{28}H_{39}O_3P$ 454.2637, found 454.2642.

Conversion of Acetate 6a to THP Ether 6b. A solution of acetate **6a** (16.5 g, 40 mmol) and KOH (34 g, 60 mmol) in methanol (100 mL) and water (50 mL) was stirred at room temperature until TLC showed complete disappearance of starting material. The methanol was evaporated, and the resulting aqueous layer was extracted with ether (5 × 50 mL). The combined organic extracts were dried with Na_2SO_4, filtered, and evaporated to give an oil. The oil was dissolved in CH_2Cl_2 (100 mL), and to it was added dihydropyran (4.6 mL, 50 mmol) and *p*-toluenesulfonic acid (0.4 g). The reaction mixture was stirred at room temperature until TLC showed complete disappearance of the intermediate alcohol, approximately 2 h. The organic layer was extracted with saturated $NaHCO_3$ and brine, dried over Na_2SO_4, filtered, and evaporated to yield 17.7 g (39 mmol, 97%) as a thick yellow syrup, identical with THP ether **6b** produced by the alternate method in all respects.

Gossyplure (9b and 10b). To a cooled solution of phosphine oxide **6b** (0.45 g, 1 mmol) in dry solvent (10 mL) was added *n*-butyllithium (0.75 mL, 1.6 M in hexane, 1.2 mmol) dropwise via syringe. After 15 min, *n*-valeraldehyde (0.132 mL, 1.3 mmol) was added via syringe, and the resulting solution was stirred for 30 min and then allowed to warm to room temperature. Alcoholates **7a** and **8a** could then be decomposed by either of two methods, both monitored by TLC.

(a) Via heating in HMPA. Addition of HMPA (5 mL) followed by warming for 2 h at 70 °C effected decomposition to dienes **9a** and **10a**.

(b) Via NaH in DMF. Isolation of alcohols **7b** and **8b** by aqueous extraction, followed by dissolution in DMF (5 mL) and addition of sodium hydride (0.120 g, 5 mmol) effected decomposition to dienes **9a** and **10a** in approximately 30 min.

In both cases, the reaction mixture was partitioned between ether and water, filtered, and evaporated to give crude THP dienes **9a** and **10a**.

Crude THP dienes **9a** and **10a** were dissolved in glacial acetic acid (2 mL) and to the solution was added acetyl chloride (1 mL). The reaction mixture was stirred at room temperature for 30 min, at which time TLC showed complete conversion to diene acetates **9b** and **10b**. The mixture was partitioned between ether and water, and the acetic acid carefully quenched by cautious portionwise addition of solid $NaHCO_3$. The organic layer was washed with saturated aqueous bicarbonate and brine, dried (Na_2SO_4), filtered, and evaporated to give an amber oil, which was chromatographed on silica gel in CH_2Cl_2 to yield gossyplure mixture **9b** and **10b**, 180 mg (0.64 mmol, 64%), as a clear colorless oil. The ratio was determined by gas chromatography (see Table I). On a preparative scale, the mixture **9b** and **10b** can be isolated by distillation: bp 150 °C (0.5 mm, Kugelrohr) [lit.[3] bp 80 °C (0.025 mm)]; NMR 5.45 (m, 4 H), 4.05 (t, J = 6 Hz, 2 H), 2.0 (m, 11 H), 1.33 (m, 12 H), 0.90 (t, J = 6 Hz, 3 H); IR 2930, 2850, 1730, 1450, 1355, 1230, 1030, 960, 720; mass spectrum, m/s 280 (M^+), 220, 96, 81, 67, 61, 55, 43.

Acknowledgment. We are very grateful to Drs. C. A. Henrick and R. J. Anderson, Zoecon Corp., Palo Alto, for providing us with generous amounts of the pure gossyplure components. The ^{13}C NMR spectral and GLC measurements were made by Dr. M. Maddox and Mr. J. Nelson of this Institute, whose valuable assistance in this regard is gratefully acknowledged.

Registry No. 3, 43017-36-3; **5a**, 29425-54-5; **5b**, 34335-17-6; **6a**, 75812-59-8; **6b**, 75812-60-1; **9a**, 53155-17-2; **9b**, 52207-99-5; **10b**, 53155-14-9; **10b**, 53042-79-8; (4-hydroxybutyl)diphenylphosphine, 7526-70-7; 7-hydroxyheptanal, 22054-13-3; 4-(dimethylamino)-pyridine, 1122-58-3; *n*-valeraldehyde, 110-62-3.

Synthesis of Hexahydrophosphindole Oxides with Oxygen Functions at C-6[1]

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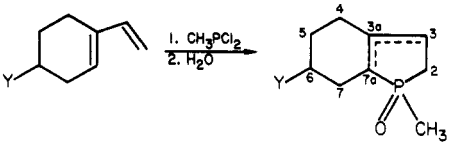
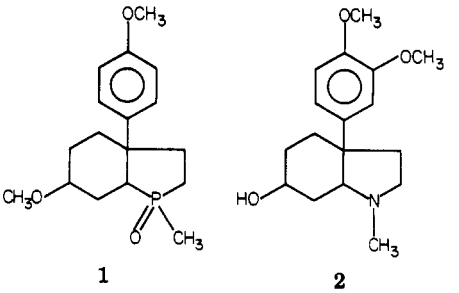
Received August 13, 1980

Hexahydrophosphindole 1-oxides are readily obtained by the McCormack cycloaddition of 1-vinylcyclohexene with phosphorus(III) halides.[2] We have now extended the scope of this reaction to include the use of 1-vinylcyclohexenes bearing ketal or ether functionality at the 4-position. The resulting hexahydrophosphindole products in



Y = OCH_2CH_2O, $OCH_2C_6H_5$, OCH_3

turn serve as precursors of 6-keto and 6-hydroxy derivatives of this ring system. The former may prove useful as substrates for annelations to produce multicyclic structures. Both functionalities are frequently found in alkaloids bearing reduced indole moieties. In another report,[3] we show that the 6-methoxy derivative can be converted to perhydrophosphindoles such as **1**, which bear resemblance to the mesembrine family of alkaloids from *Sceletium* (e.g., mesembranol, **2**).



1 **2**

(1) Taken from the Ph.D. Dissertation of J. E. MacDiarmid, Duke University, Durham, NC, 1980.
(2) Symmes, C., Jr.; Quin, L. D. *J. Org. Chem.* **1976**, *41*, 238.
(3) MacDiarmid, J. E.; Quin, L. D. *J. Org. Chem.*, submitted for publication.

0022-3263/81/1946-0461$01.00/0