recrystallization from Et_2O gave **12** (1.66 g, 97%) as colorless needles: mp 93–94 °C (Et_2O); IR (CH_2Cl_2) 3600, 2920, 2870, 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.76 (d, 3 H, J = 1.0 Hz, 4a-CH_3), 1.36–2.60 (m, 13 H), 3.48 (dd, 1 H, $J_{4,3}$ = 11.2 Hz, $J_{4,3'}$ = 4.5 Hz, 4-H), 3.70 (s, 3 H, CO_2CH_3); MS, M^+ 240.1364, calcd for $C_{13}H_{20}O_4$ 240.1361. Anal. Calcd for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39. Found: C, 64.79; H, 8.38.

Methyl (1β,4β,4aβ,8aα)-4a-Methyl-6-oxo-4-[(p-tolylsulfonyl)oxy]-1,2,3,4,4a,5,6,7,8,8a-decahydro-1-naphthoate (3). To a stirred solution of **12** (500 mg, 2.08 mmol) in dry CH_2Cl_2 (15 mL) at 0 °C under N_2 was added anhydrous pyridine (0.33 mL, 4.1 mmol) followed by *p*-toluenesulfinyl chloride[23] (0.38 mL, 4.1 mmol). The mixture was stirred for 3 h at 0 °C, then poured into 1 N HCl, and extracted with CH_2Cl_2. The combined extracts were washed with 5% $NaHCO_3$ solution, water, and brine and dried over $MgSO_4$. Evaporation of the solvent in vacuo gave a mixture of diastereomeric sulfinate esters (786 mg) as a colorless oil: IR (CH_2Cl_2) 2870, 1705, 1130, 1115, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.76 and 0.78 (2 s, 3 H, 4a-CH_3), 1.28–2.40 (m, 11 H), 2.42 (s, 3 H, $ArCH_3$), 2.54–2.68 (m, 1 H, 1-H), 3.67 and 3.70 (2 s, 3 H, CO_2CH_3), 4.09 and 4.20 (2 dd, 1 H, J = 4.40, 12.2 Hz, 4-H), 7.38 and 7.65 (2 d, 2 H each, J = 8.0 Hz, Ar). To a stirred solution of the crude sulfinate ester (786 mg, 2 mmol) in dry CH_2Cl_2 (15 mL) at 0 °C under N_2 was added *m*-chloroperbenzoic acid (500 mg, 2.9 mmol). After having been stirred for 3 h at 0 °C, the mixture was poured into saturated $NaHCO_3$ solution, washed with water and brine, and dried over $MgSO_4$. Evaporation of the solvent in vacuo and purification of the residue by flash chromatography (PhH–Et_2O–petroleum ether, 1:2:2) gave the tosylate **3** (656 mg, 80%) as colorless crystals: mp 153–154 °C (Et_2O); IR (CH_2Cl_2) 2850, 1725, 1355, 1180, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.78 (s, 3 H, 4a-CH_3), 1.54–2.40 (m, 11 H), 2.46 (s, 3 H, $ArCH_3$), 2.54–2.64 (m, Hz, H, 1-H), 3.68 (s, 3 H, CO_2CH_3), 4.45 (dd, 1 H, J = 4.40, 12.18 Hz, 4-H), 7.40 and 7.84 (two d, 2 H each, Ar); MS, m/e (relative intensity) 394 (7, M^+), 239 (12), 223 (base), 222 (30), 207 (44). Anal. Calcd for $C_{20}H_{28}O_6S$: C, 60.89; H, 6.64; S, 8.13. Found: C, 60.70; H, 6.61; S, 8.05.

Methyl (1β,4β,4aβ,8aα)-4a-Methyl-6-oxo-7-[2-hydroxy-3-[(tetrahydropyranyl)oxy]propanyl]-1,2,3,4,4a,5,6,7,8,8a-decahydro-1-naphthoate (13). To a stirred solution of LDA (0.97 mmol) in dry THF (2 mL) at −78 °C under N_2 was added dropwise a solution of **3** (175 mg, 0.44 mmol) in dry THF (4 mL). After 0.5 h, anhydrous zinc chloride (137 mg, 1.01 mmol) in dry THF (2 mL) was added. After another 5 min, 1-[(tetrahydropyranyl)oxy]-2-propanone[7] (153 mg, 0.97 mmol) in dry THF (1 mL) was added, and the stirring was continued at −78 °C for 0.5 h and then at −20 °C for 1 h. Aqueous NH_4Cl solution was added, and the product was extracted with Et_2O. The combined extracts were washed with water and brine and dried over $MgSO_4$. Evaporation of the solvent in vacuo followed by flash chromatography (PhH–Et_2O–CH_2Cl_2, 2:2:1) of the residue gave unreacted **3** (17 mg, 10%), the THP adduct **13** (121 mg, 52%), and the dialkylated adduct **14** (109 mg, 35%), both as colorless oils. THP adduct **13**: IR (CH_2Cl_2) 3500, 2940, 2870, 1705, 1695, 1360, 1180, 840, 820 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.73, 0.76, 0.86, 0.89 (4 s, CH_3), 1.22 and 1.27 (2 s, R′(CH_3)CHOHR″), 1.56–2.30 (m, 18 H), 2.47 and 2.48 (2 s, $ArCH_3$), 3.34–3.94 (s overlapping m, 7 H, CO_2CH_3 and THP), 4.41 (dd, 1 H, J = 4.38, 12.20 Hz, 4-H), 4.54–4.72 (m, 2 H, R′(Me)CHOHR″ and THP), 7.38 and 7.82 (2 d, 2 H each, J = 8.0 Hz, Ar); MS, m/e (relative intensity) 506 (0.1, M − CH_3), 190 (3), 172 (62), 155 (7), 108 (25), 107 (33), 91 (base). Dialkylated adduct **14**: IR (CH_2Cl_2) 3500, 2930, 2860, 1725, 1360, 1180, 840, 820 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.82–0.96 (m, CH_3), 1.08–1.40 (m, 6 H, two CH_3), 1.44–2.40 (m, 24 H), 2.47 and 2.56 (2 s, $ArCH_3$), 3.30–3.93 (s overlapping m, 11 H, CO_2CH_3 and THP), 4.40–4.72 (m, 5 H, R′(Me)CHOHR″, THP, and 4-H), 7.34–7.50 (m, 2 H, Ar), 7.70–7.94 (m, 2 H, Ar).

(4aα,5β,8β,8aβ)-5-(Methoxycarbonyl)-3,8a-dimethyl-8-[(p-tolylsulfonyl)oxy]-4,4a,5,6,7,8,8a,9-octahydronaphtho[2,3-b]furan (2). A stirred solution of **13** (40 mg, 0.08 mmol) in THF–H_2O (2:1, 1.5 mL) containing a catalytic amount of *p*-toluenesulfonic acid (1 mg) was heated at 60 °C for 0.5 h. The solution was cooled and poured into aqueous $NaHCO_3$ solution, and the product was extracted with Et_2O. The combined ethereal extracts were washed with water and brine and dried over $MgSO_4$. Evaporation of the solvent in vacuo, followed by immediate flash chromatography (CH_2Cl_2), gave the furan **2** (6 mg, 18%) as a colorless oil which is unstable and decomposes slowly on standing at room temperature: IR ($CHCl_3$) 2933, 2845, 1729, 1597, 1175, 1019, 940 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.87 (s, 3 H, 8a-CH_3), 1.91 (d, 3 H, J = 1.16 Hz, C3-CH_3), 1.55–2.66 (m, 10 H), 2.46 (s, 3 H, $ArCH_3$), 3.69 (s, 3 H, CO_2CH_3), 4.44 (dd, 1 H, J = 4.41, 12.16 Hz, 8-H), 7.01 (br s, 1 H, 2-H), 7.40 and 7.86 (2 d, 2 H each, J = 8.0 Hz, Ar); MS, m/e (relative intensity) 432 (11, M^+), 261 (2), 260 (6), 155 (31), 108 (57), 91 (base).

Sericenine (1). To the furan **2** (12 mg, 0.03 mmol) in dry THF (1 mL) was added potassium bis(trimethylsilyl)amide in THF (0.06 mL, 0.06 mmol). After stirring for 1 h at 25 °C under N_2, the reaction had gone to completion by TLC. The mixture was poured into water and extracted with Et_2O. The ethereal extracts were washed with water and brine and dried over $MgSO_4$. Evaporation of the solvent in vacuo followed by flash chromatography (CH_2Cl_2–petroleum ether, 3:7) of the residue gave **1** as white needles (3 mg, 43%): mp 111–114 °C (lit.[4] mp 115 °C); IR ($CHCl_3$) 3040, 1706, 1640, 1550 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.36 (br s, 3 H, 14-CH_3), 1.97 (d, 3 H, J = 1.16 Hz, 13-CH_3), 2.2–2.64 (m, 4 H), 2.78–2.94 (m, 1 H, 7-βH), 3.15 and 3.54 (2 d, 1 H each, J = 14.7 Hz, 10β, 10α-H), 3.52–3.66 (br d, 1 H, 7α-H), 3.73 (s, 3 H, CO_2CH_3), 5.50 (t, 1 H, J = 7.5 Hz, 2-H), 6.63 (br d, 1 H, 6-H), 7.06 (br s, 1 H, 12-H); MS, m/e (relative intensity) 260 (45, M^+), 245 (11), 229 (6), 201 (19), 108 (base), m/e calcd for $C_{16}H_{20}O_3$ 260.1412, found 260.1422. Comparison of the IR, ^1H NMR, and MS with the corresponding spectra of natural sericenine[4] was identical.

Acknowledgment. We thank Professor N. Hayashi and Dr. I. Horibe for providing us with the IR, ^1H NMR, and MS of natural sericenine.

(23) Kurzer, F. "Organic Synthesis", John Wiley and Sons: New York, 1963; Collect. Vol. 4, p 937.

Ultrasound in Phosphine Preparation. Simple Preparations of Some Bis(alkylphenylphosphino)alkanes

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Diphosphines of the class $RPhP(CH_2)_nPPhR$ (n = 2–6) have been prepared from the reactions of the corresponding $Ph_2P(CH_2)_nPPh_2$ with alkali metal followed by alkylation. Ultrasound irradiation should be applied in the reductive cleavage stage so as to assure the purity of the final products.

Diphosphines of the general type $PhRP(CH_2)_nPRPh$ are important chelating reagents for the preparation and mechanistic study of various transition-metal complexes and catalysts. The conventional method preparation in-

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volves the deprotonation and subsequent alkylation of a secondary diphosphine $HPhP(CH_2)_nPPhH$, prepared from PhP^{2-} or $HPhP^-$ and a α,ω-dihaloalkane.[2] These preparations are expensive and multistep and require the manipulation of extremely air-sensitive intermediates such as secondary phosphines. Obviously, simpler approaches toward the preparation of this class of compounds are desired.

It is well established that the P–Ph bond of triphenylphosphine[3] and an alkyldiphenylphosphine[4] can be cleaved by an alkali metal to the corresponding phenyl phosphide anion and then can be alkylated with electrophiles to give the substituted tertiary phosphines. However, the double reductive cleavage of the P–Ph bonds at the two ends of a bis(diphenylphosphino)alkane (diphos) has not been achieved although this appears the most convenient source of $^-PhP(CH_2)_nPPh^-$, the requisite precursor to the diphosphine $RPhP(CH_2)_nPPhR$. We therefore investigated the possibility of the double reductive cleavage of the P–Ph bond of diphos 1 (n = 2–6) with alkali metals.

The reaction of a slight excess of K with the diphos **1a** (n = 2) was completed in 20 min at 0 °C, giving a dark red solution, indicating the formation of certain type of phosphide anion. After destroying the phenyl anion with t-BuCl, 2 equiv of MeI were added, yielding a complex mixture in which **2a** was the major component (eq 1). By

$$Ph_2P(CH_2)_nPPh_2 \xrightarrow{i} [^-PhP(CH_2)_nPPh^-] + [Ph^-] \xrightarrow{ii,iii}$$

1a, n = 2; **b**, n = 3; **c**, n = 4; **d**, n = 5; **e**, n = 6

$$PhMeP(CH_2)_nPMePh + MePPh_2 + \text{impurities} \quad (1)$$

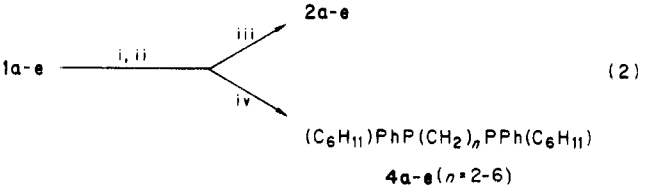
2a, n = 2; **b**, n = 3; **c**, n = 4; **d**, n = 5; **e**, n = 6 — **3**

(i) K, 0 °C; (ii) t-BuCl; (iii) MeI.

TLC and temperature-programmed mass spectral analyses, $MePPh_2$ (**3**) was found as a side product. The product mixture could not be purified by chromatography or fractional distillation. Lowering the reaction temperature down to −78 °C resulted in the product being less contaminated, but the reaction proceeded at a much slower rate. For example, 100 mg of **2a** required 12 h for complete reaction. Similar difficulties were encountered for the reaction of K with **1b–e**. Therefore, the attempt of using K for the double reductive cleavage was abandoned.

The use of Li instead of K with **1a–e** in this reaction sequence at 0 °C gave similar, but slightly cleaner, products **2a–e** at a very slow rate. Attempts to accelerate the reaction rate by using a large excess of Li or by raising the reaction temperature all caused the formation of the side product **3** and other unseparable impurities. If the reaction was carried out at higher temperature or by prolonged stirring, the ether linkage of the solvent THF was cleaved by the nucleophilic attack of the phosphide anion[5] causing additional side products.

Since the reductive cleavage of the P–Ph bond of triphenylphosphine by metal Li can be accelerated by ultrasound irradiation,[6] it was anticipated that a similar rate enhancement should be observed on the reactions of diphosphines. Indeed, when a diphos **1a–e** and a slight excess of Li were irradiated with ultrasound at 0 °C,[7] the reaction took place immediately and was complete within minutes. After the addition of 2 equiv of t-BuCl, the alkyl halide (MeI or bromocyclohexane) was added to yield the disubstituted product **2a–e** or **4a–e** (eq 2). The result was

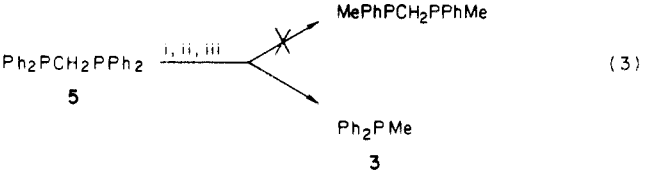


(2)

(i) Li, ultrasound irradiation; (ii) t-BuCl; (iii) MeI; (iv) $C_6H_{11}Br$.

excellent not only because the rate was enhanced but also because the product contained only one component. Further purification by rapid column chromatography or simple distillation gave the product in high yield (Table I). It was noted that once the addition of t-BuCl was completed, the alkyl halide should be added immediately. Otherwise, a major side product containing the P–t-Bu bond[8] would form in significant quantity.[8] The later the alkyl halide was added, the more this side product formed. Also, if alkyl halide was added without the addition of t-BuCl, the product mixture was even more complex. This agreed with the report that the phenyl anion would induce side reactions.[9]

The reductive cleavage reaction and alkylation reactions were successful for the diphosphines **1a–e**. However, for bis(diphenylphosphino)methane (dppm) (**5**), the reductive cleavage proceeded via a completely different route. The reaction of **5** with either K or Li by usual stirring or ultrasound irradiation all failed to give the diphosphide dianion. Instead, the CH_2–P bond was cleaved as evidenced by the fact that $MePPh_2$ (**3**) was produced when the reaction was worked up by MeI (eq 3).



(3)

(i) Li, ultrasound irradiation; (ii) t-BuCl; (iii) MeI.

Tests were also made to control the amount of Li or K to about 2 equiv during the reduction with the diphosphines **1a–e** in the expectation that only one P–Ph bond would be cleaved to yield the species $Ph_2P(CH_2)_nPPh^-$ and, after alkylation, the unsymmetrical diphosphine $Ph_2P(CH_2)_nPRPh$ (**6**). However, after the Li was completely consumed and MeI added, only the disubstituted product **2a–e** and the unreacted starting material **1a–e** were detected in about a 1:1 ratio, while the desired monosubstituted product was barely detected by temperature-programmed mass spectral analysis. The inability to produce the monophosphide anion by this method might have been attributed to the heterogeneous

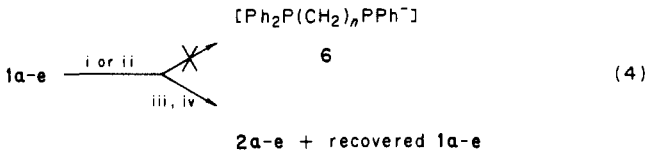
(1) Graduate student of Chinese Culture University, Taipei, Taiwan.
(2) Issleib, K.; Krech, F. *Chem. Ber.* **1961**, *94*, 2656.
(3) Bianco, V. D.; Doronzo, S. *Inorg. Synth.* **1976**, *16*, 155.
(4) Grim, S. O.; Molenda, R. P.; Keiter, R. L. *Chem. Ind. (London)* **1970**, 1378.
(5) Mallion, K. B.; Mann, F. G. *J. Chem. Soc.* **1964**, 6121.
(6) Chou, T. S.; Yuan, J. J.; Tsao, C. H. *J. Chem. Research Synop.* **1985**, 18.
(7) An ordinary laboratory ultrasound cleaner was used. (Bransonic 220, Branson Cleaning Equipment Co. Shelton, CT).
(8) We were unable to isolate this type of side products in pure states. However, in each case for **1a–e**, the ^1H NMR spectrum showed a doublet around δ 0.95 (J = 12 Hz), indicating that the existence of $P–C(CH_3)_3$ was highly possible. The mass spectrum showed a distinct peak at the mass number of $PhHP(CH_2)_nPPhBu$. The side products were thus speculated to be $PhHP(CH_2)_nPPh(t\text{-Bu})$, which are reasonable side products of the reactions of the diphosphine dianions with isobutene which came from t-BuCl.
(9) Aguiar, A. M.; Beisler, J.; Mills, A. *J. Org. Chem.* **1962**, *27*, 1001.

Table I. Preparation of Bis(alkylphenylphosphino)alkane

diphos	alkyl halide	reacn time, h	prod.	yield, %	NMR, δ	IR, cm^{-1}	MS, *m/e*	elemental analyses: calcd	elemental analyses: found	physical data
1a	MeI	1	2a	84	1.25 (d, 6 H, *J* = 2 Hz), 1.6-1.8 (m, 4 H), 7.5 (br s, 10 H)	3080, 2950, 1840, 1500, 1060	274 (M^+), 259 (base), 246, 227, 123, 121, 91	C, 70.1; H, 7.3	C, 70.1; H, 7.4	$bp_{1.0}$ 180-182 °C (lit. bp 250-260 °C[a])
1b	MeI	1	2b	86	1.25 (d, 6 H, *J* = 2 Hz), 1.4-1.75 (m, 6 H), 7.5 (br s, 10 H)	3080, 2950, 1840, 1500, 1060	288 (M^+), 273 (base), 165, 123, 121, 109, 91	C, 70.8; H, 7.6	C, 71.0; H, 7.5	$bp_{1.0}$ 195-200 °C (lit. $bp_{0.4}$ 199-201 °C[b])
1c	MeI	1	2c	91	1.3 (d, 6 H, *J* = 2 Hz), 1.35-1.65 (m, 8 H), 7.5 (br s, 10 H)	3080, 2950, 1840, 1500, 1060	302 (M^+), 287 (base), 179, 123, 121, 109, 91	C, 71.5; H, 7.9	C, 71.8; H, 7.9	mp 42 °C, disulfide mp 135-139 °C (lit. disulfide mp 138-141 °C[b])
1d	MeI	1	2d	91	1.25 (d, 6 H, *J* = 2 Hz), 1.25-1.75 (m, 10 H), 7.5 (br s, 10 H)	3080, 2950, 1840, 1500, 1060	316 (M^+), 301 (base), 193, 123, 109, 91	C, 72.1; H, 8.2	C, 72.2; H, 8.2	$bp_{1.0}$ 255-262 °C (lit. $bp_{0.6}$ 257-258 °C[b])
1e	MeI	1	2e	94	1.25 (d, 6 H, *J* = 2 Hz), 1.0-1.7 (m, 12 H), 7.5 (br s, 10 H)	3080, 2950, 1840, 1500, 1060	330 (M^+), 315 (base), 208, 207, 193, 138, 123, 121, 109, 91	C, 72.7; H, 8.5	C, 72.9; H, 8.4	mp 47-48 °C, disulfide mp 135-140 °C (lit. mp 45 °C, disulfide mp 130-150 °C[b])
1a	$C_6H_{11}Br$	2	4a	80	1.0-2.4 (m, 26 H), 7.5 (br s, 10 H)	3080, 2950, 1840, 1500, 1060	410 (M^+), 327 (base), 219, 217, 191, 109, 108	C, 76.1; H, 8.8	C, 76.0; H, 8.6	disulfide mp 252-256 °C
1b	$C_6H_{11}Br$	2	4b	85	1.0-2.2 (m, 28 H), 7.5 (br s, 10 H)	3080, 2950, 1840, 1500, 1060	424 (M^+), 341 (base), 233, 191, 109, 108	C, 76.4; H, 9.0	C, 76.1; H, 8.9	disulfide mp 198-203 °C
1c	$C_6H_{11}Br$	2	4c	88	1.0-2.0 (m, 30 H), 7.5 (br s, 10 H)	3080, 2950, 1840, 1500, 1060	438 (M^+), 355 (base), 247, 191, 178, 109, 108	C, 76.7; H, 9.1	C, 76.8; H, 8.9	mp 102-104 °C. disulfide mp 242-245 °C (lit. mp 104-105 °C, disulfide mp 248-250 °C[c])
1d	$C_6H_{11}Br$	2	4d	90	0.9-1.9 (m, 32 H), 75. (br s, 10 H)	3080, 2950, 1840, 1500, 1060	452 (M^+), 369 (base), 261, 191, 178, 109, 108	C, 77.0; H, 9.3	C, 76.8; H, 9.3	disulfide mp 182-185 °C (lit. disulfide mp 184-185 °C[c])
1e	$C_6H_{11}Br$	2	4e	87	0.9-1.8 (m, 34 H), 7.5 (br s, 10 H)	3080, 2950, 1840, 1500, 1060	466 (M^+), 383 (base), 275, 191, 109, 108	C, 77.2; H, 9.4	C, 77.1; H, 9.5	disulfide mp 210-214 °C (lit. disulfide mp 211-214 °C[c])

[a] Issleib, K.; Standtke, K. *Chem. Ber.* **1963**, *96*, 279. [b] Issleib, K.; Krech, F.; Gruber, K. *Chem. Ber.* **1963**, *96*, 2186. [c] Issleib, K.; Krech, F. *Chem. Ber.* **1961**, *94*, 2656.

nature of this type of reactions. Because of the heterogeneity, once the monophosphide anion was formed, it became the species that was closest to the Li metal. Therefore, the second P–Ph bond on the same molecule would be cleaved faster than that of another molecule. Therefore, the diphosphines **1a–e** were either doubly cleaved or unreacted (eq 4).



(4)

(i) 2 equiv of Li, ultrasound irradiation; (ii) 2 equiv of K, -78 °C; (iii) *t*-BuCl; (iv) MeI.

In conclusion, the double reductive cleavage of the P–Ph bond of a diphosphine can normally be achieved under mild conditions such as with K at −78 °C or with the less reactive Li at 0 °C at extremely slow rate. Subsequent alkylation gives the disubstituted diphosphine with contamination. Attempted rate enhancement by increasing the reaction temperature is unsatisfactory while ultrasonic irradiation not only accelerates the reaction but also eliminates the formation of side products. The reason why ultrasonic irradiation selectively increases only the rate of the main reaction and not that of the side reactions is still unclear. It is suspected, however, that the main product is derived from a heterogeneous reaction on whose rate the ultrasound irradiation normally has significant influence[10] and that the side reactions may be derived from some type of homogeneous reactions on whose rate the ultrasound has little or no influence.

(10) Suslick, K. S.; Johnson, R. E. *J. Am. Chem. Soc.* **1984**, *106*, 6856 and references cited therein.

Experimental Section

All reactions and workup procedures were manipulated under anhydrous nitrogen atmosphere. All solvents were dried and deoxygenated before use. NMR spectra were recorded on a JEOL C-60-HL NMR spectrophotometer. IR spectra were recorded on a Perkin-Elmer 297 infrared spectrophotometer. MS spectra were taken on a HP 5990B gas chromatograph/mass spectrometer. Elemental analyses were taken at National Taiwan University.

Preparations of the Diphosphines 2a–e and 4a–e. Since the procedures are similar, **2b** is used here as a typical example. To a vial containing finely chopped metal Li (50 mg, 7.2 mmol) in THF (3 mL) cooled at −10 °C was added dropwise bis(diphenylphosphino)propane (dppp) (**1b**) (300 mg, 1.2 mmol) in THF (2 mL). The colorless reaction mixture was put into an ultrasound cleaner kept at 0 °C and irradiated. The reaction was followed by TLC (alumina, hexane/EtOAc) until the starting material was consumed (less than 10 min). The dark red solution was separated from the excess of Li metal, and *t*-BuCl (220 mg, 2.4 mmol) in THF (1 mL) was added immediately at room temperature. No color change was observed at this stage. The resulting solution was again cooled to 0 °C, and as MeI (340 mg, 2.4 mmol) was added, the color faded instantaneously. After the mixture was stirred for another 60 min, water (8 mL) was added, and the layers were separated. The aqueous layer was extracted with benzene (4 × 10 mL). The combined organic layers were dried (Na_2CO_3), concentrated under reduced pressure and purified by flash column chromatography (alumina, benzene), giving the diphosphine **2b**.

Acknowledgment. We thank the National Science Council of the Republic of China for financial support (NSC73-0201-M001C-04).

Registry No. **1a**, 1663-45-2; **1b**, 6737-42-4; **1c**, 7688-25-7; **1d**, 27721-02-4; **1e**, 19845-69-3; **2a**, 23808-01-7; **2b**, 98170-68-4; **2c**, 98170-69-5; **2d**, 98170-70-8; **2e**, 98170-71-9; **4a**, 98170-72-0; **4b**, 98170-73-1; **4c**, 72144-83-3; **4d**, 90116-42-0; **4e**, 98170-74-2; MeI, 74-88-4; $C_6H_{11}Br$, 108-85-0.

Conversion of Thiosulfinate Derivatives of Cystine to Unsymmetrical Cystines and Lanthionines by Reaction with Tris(dialkylamino)phosphines

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Synthetic routes to the unsymmetrical lanthionines **2** and **3** have been developed. Reaction of a thiosulfinate, derived by oxidation of the corresponding symmetrical cystine with *m*-chloroperbenzoic acid, with a protected cysteine in the presence of a tris(dialkylamino)phosphine, hexaethylphosphorus triamide, yielded an unsymmetrical or mixed cystine. Contraction of the disulfide linkage in the appropriate mixed cystine by reaction with hexaethylphosphorus triamide provided the unsymmetrical lanthionines **2** and **3**. A second route to unsymmetrical lanthionines was investigated that involved the attempted displacement of sulfonate leaving groups from di- or tripeptides containing a serylvaline residue. The sulfonate ester function was observed to be very unreactive toward displacement by mercaptide anion in these peptides, a fact that may be due to steric or conformational effects originating from the adjacent valine residue.

The quinomycin antibiotics[1] are a structurally unique group of cyclic depsipeptides that contain a novel β-methylthiolanthionine as a constituent of the peptide. Echinomycin (**1**), the most prominent of the quinomycins, is known to bind to deoxyribonucleic acids by bifunctional intercalation and to thereby function as a potent inhibitor of RNA synthesis.[2] The antibiotics are known to possess

(1) Dell, A.; Williams, D. H.; Morris, H. R.; Smith, G. A.; Feeney, J.; Roberts, G. C. K. *J. Am. Chem. Soc.* **1975**, *97*, 2497. Martin, D. G.; Mizsak, S. A.; Biles, C.; Stewart, J. L.; Baczynskyj, L.; Meulman, P. A. *J. Antibiot.* **1975**, *28*, 332.

(2) Waring, M. J. In "Antibiotics V Part 2: Mechanism of Action of Antileukaryotic and Antiviral Compounds"; Hahn, F. E., Ed.; Springer-Verlag: Heidelberg, 1979; pp 173–194.

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