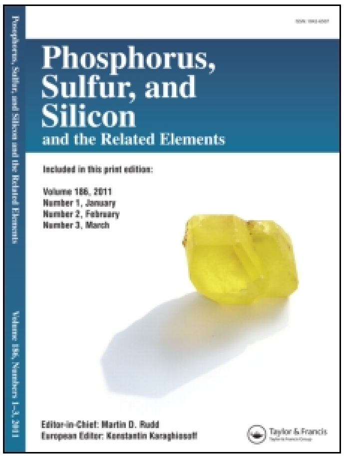

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

SYNTHESIS OF 2-S-(2-TETRAHYDROPYRANYL)THIOETHYLPHOSPHINES RADICAL ADDITION OF PHOSPHINES TO AND 2-MERCAPTOETHYLPHOSPHINES BY FREE 2-(VINYLTHIO)TETRAHYDROPYRAN

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To cite this Article Dilworth, J. R. , Griffiths, D. V. , Hughes, J. M. and Morton, S.(1992) 'SYNTHESIS OF 2-S-(2-TETRAHYDROPYRANYL)THIOETHYLPHOSPHINES RADICAL ADDITION OF PHOSPHINES TO AND 2-MERCAPTOETHYLPHOSPHINES BY FREE 2-(VINYLTHIO)TETRAHYDROPYRAN', Phosphorus, Sulfur, and Silicon and the Related Elements, 71: 1, 249 — 251

To link to this Article: DOI: 10.1080/10426509208034518

URL: http://dx.doi.org/10.1080/10426509208034518

Phosphorus, Sulfur, and Silicon, 1992, Vol. 71, pp. 249–251
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Communication

SYNTHESIS OF 2-S-(2-TETRAHYDROPYRANYL)THIOETHYLPHOSPHINES AND 2-MERCAPTOETHYLPHOSPHINES BY FREE RADICAL ADDITION OF PHOSPHINES TO 2-(VINYLTHIO)TETRAHYDROPYRAN

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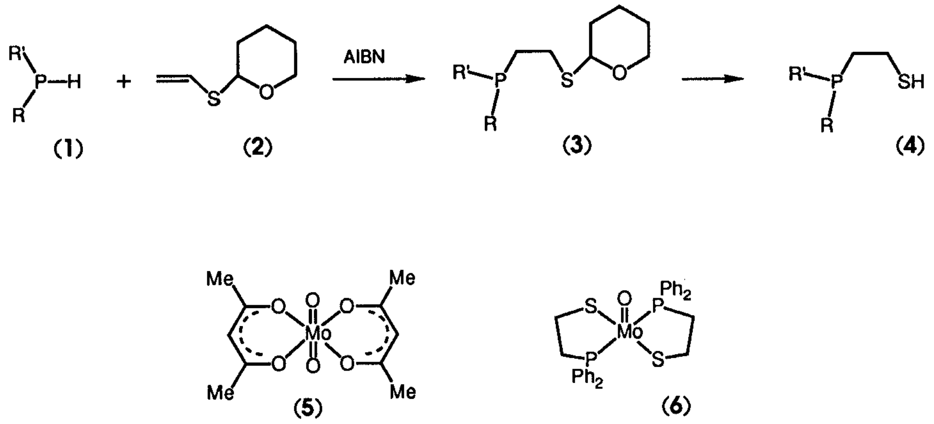
(Received May 29, 1992)

The synthesis of 2-(2-tetrahydropyranylthioethyl)phosphines has been achieved in high yield by the free radical addition of primary and secondary phosphines to 2-(vinylthio)tetrahydropyran. Hydrolysis of the S-tetrahydropyranylhemithioacetal group results in the formation of 2-mercaptoethylphosphines.

Key words: Synthesis; ligand; phosphine; thiol; radical addition.

INTRODUCTION

The synthesis of metal complexes of phosphine-thiol ligands with potential biomedical applications is an area which has attracted considerable interest in recent times. 2-Phosphinoethylthiols (**4**) are usually prepared by the base catalysed addition of primary and secondary phosphines to thiirane, (ethylene sulphide). Thus, for example, 2-diphenylphosphinoethylthiol (**4**; R=R′=Ph)[1] has been prepared by add-



SCHEME

ing thiirane to a solution of diphenylphosphide in tetrahydrofuran, the phosphide being generated by the action of methyl lithium in diethyl ether on diphenylphosphine at room temperature. Similarly, 3-phenyl-3-phosphapentane-1,5-dithiol (**4**; R=Ph, R'=$HSCH_2CH_2$—) has been prepared in a 'one pot' two step procedure[2] by adding thirane first to phenylphosphide, and then to the phosphide anion of the 2-phenylphosphinoethylthiol (**4**; R=H, R'=Ph) resulting from this reaction. In both steps of this sequence the phosphides were generated by the action of sodium in liquid ammonia on the phosphine at −60°C. However, not only are these procedures often inconvenient, they frequently result in the formation of an impure product due to subsequent reaction of the initially formed 2-phosphinoethylthiolate anion with further thiirane. Such byproducts are not easy to remove from the desired ligand.

RESULTS AND DISCUSSION

During our work on phosphine ligands synthesis we have developed a convenient route for the preparation of tetrahydropyranyl protected 2-phosphinoethylthiols (**3**) in high yield. This involves the addition of primary or secondary phosphines to 2-(vinylthio)tetrahydropyran (**2**)[3] in the presence of a free radical catalyst, such as azoisobutyronitrile. As examples we give below details of the preparation of both diphenyl(2-S-(2-tetrahydropyranyl)thioethyl)phosphine (**3**; R=R'=Ph) and phenyl-bis-(2-S-(2-tetrahydropyranyl)thioethyl)phosphine (**3**; R=Ph, R'=$ThpSCH_2CH_2$—). These S-protected ligand systems can be deprotected to liberate the free thiols (**4**) using a mixture of hydrobromic acid in trifluoroacetic acid if required,[4] but in many cases we have found that the S-protected ligands will undergo deprotection under the conditions used for complex formation avoiding the need for prior generation of the free thiol. Thus, for example, bis[2-(diphenylphosphino)-ethane-1-thiolato]oxomolybdenum (IV) (**6**) was prepared by the reaction of diphenyl[2-S-(2-tetrahydropyranyl)thioethyl]phosphine (**3**; R=R'=Ph) with dioxobis(pentane-2,4-dionato)molybdenum (VI) (**5**) under the same conditions as reported for its formation from the free thiol ligand (**4**; R=R'=Ph).[1]

In conclusion, our procedure for the preparation of tetrahydropyranyl-protected 2-mercaptoethylphosphines has many advantages over routes involving thiirane. The procedure is simple and gives high yields of product in a sufficiently high state of purity to avoid the need for further purification. It is particularly convenient when dealing with phosphines which are very air sensitive.

The complexing behaviour of these, and related ligands, is currently being investigated using molybdenum, technetium, ruthenium, rhenium, the platinum group of metals, silver and gold. The results of these studies will be reported elsewhere.

EXPERIMENTAL

N.m.r. spectra were obtained on a JEOL EX270 spectrometer.

Diphenyl(2-S-(2-tetrahydropyranyl)thioethyl)phosphine (**3**; R=R'=Ph): The following reaction and subsequent work up procedure was carried out in a glove box containing nitrogen as the inert atmosphere. To diphenylphosphine (2.5 g, 13.4 mmol) in dry 1,4-dioxan (20 cm^3) was added 2-(vinylthio)tetrahydropyran[3] (2.12 g, 14.7 mmol) together with a small quantity of azoisobutyronitrile (10 mg).

The reaction mixture was then heated under reflux and the reaction monitored by ^{31}P n.m.r. spectroscopy. After about 1 h the reaction was complete. The reaction mixture was filtered through a glass frit (porosity 4) and the solvent and other volatile components removed under reduced pressure (80°C at 0.01 mmHg) to give the product (**3**; R=R′=Ph) as a translucent viscous oil in essentially quantitative yield. $\delta p(CDCl_3)$ – 16.7; $\delta_H(270$ MHz, $CDCl_3)$ 1.45–1.90 (6H, complex envelope of overlapping resonance), 2.39 (2H, t, J_{HH} 8 Hz, α-CH_2), 2.68 (2H, m, β-CH_2), 3.41 (1H, m, H-6), 4.00 (1H, m, H-6), 4.83 (1H, dd, J_{HH} 3 and 6 Hz, H-1), 7.2–7.3 (6H, m, H-2,4,6), 7.35–7.45 (4H, m, H-3, 5); $\delta_C(CDCl_3)$ 21.28 (s, CH_2), 25.12 (s, CH_2), 26.50 (d, J_{PC} 22 Hz, β-C), 28.70 (d, J_{PC} 15 Hz, α-C), 30.76 (s, CH_2), 64.01 (s, CH_2), 81.79 (s, CH), 128.02 (×4)(d, J_{PC} 6 Hz, C-3,5), 128.2 (×2)(s, C-4), 132.20 (×2)(d, J_{PC} 19 Hz, C-2,6), 132.22 (×2)(d, J_{PC} 19 Hz, C-2,6), 137.52 (d, J_{PC} 14 Hz, C-1), 137.56 (d, J_{PC} 14 Hz, C-1).

Phenyl-bis[2-S-(2-tetrahydropyranyl)thioethyl]phosphine (**3**; R=Ph, R′=$ThpSCH_2CH_2$—): This material was prepared by heating a solution of phenylphosphine (1 g, 9.1 mmol) in dry 1,4-dioxan (20 cm^3) with 2-(vinylthio)tetrahydropyran[3] (2.8 g, 20 mmol) together with a small quantity of azoisobutyronitrile (10 mg) using the method previously described for the preparation of (**3**; R=R′=Ph). The product (**3**; R=Ph, R′=$ThpSCH_2CH_2$—) was isolated, as a mixture of 4 diastereoisomers, as a translucent viscous oil in essentially quantitative yield. $\delta_p(CDCl_3)$ −25.04, −25.10, and −25.15 (ratio *ca* 1:2:1); $\delta_H(270$ MHz, $CDCl_3)$ 1.48–1.95 (12H, complex envelope of overlapping resonance), 2.05 (4H, m, α-CH_2), 2.48–2.79 (4H, m, β-CH_2), 3.45 (2H, m, H-6), 4.03 (2H, m, H-6), 4.82 (2H, m, H-1), 7.3–7.4 (3H, m, H-3,4,5), 7.48–7.58 (2H, m, H-2,6); $\delta_C(CDCl_3)$ 21.51 (×4)(s, CH_2), 25.30 (×4)(s, CH_2), 26.54 (×2)(d, J_{PC} 19 Hz, β-C), 26.72 (d, J_{PC} 19 Hz, β-C), 26.73 (d, J_{PC} 19 Hz, β-C), 28.48 (d, J_{PC} 11 Hz, α-C), 28.55 (d, J_{PC} 11 Hz, α-C), 28.61 (d, J_{PC} 11 Hz, α-C), 28.68 (d, J_{PC} 11 Hz, α-C), 30.98 (×4)(s, CH_2), 64.33 (×2)(s, CH_2), 64.40 (×2)(s, CH_2), 81.92 (×2)(s, CH), 82.15 (×2)(s, CH), 128.26 (×8)(d, J_{PC} 7 Hz, C-3,5), 128.82 (×4)(s, C-4), 132.07 (×2)(d, J_{PC} 20 Hz, C-2,6), 132.12 (×4)(d, J_{PC} 20 Hz, C-2,6), 132.14 (×2)(d, J_{PC} 20 Hz, C-2,6), 136.62 (×4)(d, J_{PC} 16 Hz, C-1).

Bis[2-(diphenylphosphino)ethane-1-thiolato]oxomolybdenum (IV) (**6**): This material was prepared in 65% yield from diphenyl[2-S-(2-tetrahydropyranyl)thioethyl]-phosphine (**3**; R=R′=Ph) and dioxobis(pentane-2,4-dionato)molybdenum (VI) (**5**) using the procedure previously described for the preparation of this material from the free thiol ligand (**4**; R=R′=Ph).[1] The spectroscopic properties of the product were the same as those previously reported.

ACKNOWLEDGEMENT

We wish to thank Amersham International p.l.c. and the S.E.R.C. for financial support.

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