Novel diphenylphosphine derivatives of 2,2′-bithiophene, 2,2′:5′,2″-terthiophene, 2-(2′-thienyl)pyridine and 2,6-di-2′-thienylpyridine. Crystal structures of 5,5′-bis(diphenylphosphino)-2,2′-bithiophene, diphenyl{5-[6′-(diphenylphosphino)-2′-pyridyl]-2-thienyl}phosphine and 2,6-bis[5′-(diphenylphosphino)-2′-thienyl]pyridine

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We report the synthesis and characterisation of eight molecules that have in common a diphenylphosphino group bonded to an α-carbon atom of a thienyl or pyridyl ring: 5,5′-bis(diphenylphosphino)-2,2′-bithiophene **1**; diphenyl(2,2′-bithienyl-5-yl)phosphine **2**; 5,5″-bis(diphenylphosphino)-2,2′:5′,2″-terthiophene **3**; diphenyl-(2,2′:5′,2″-terthienyl-5-yl)phosphine **4**; diphenyl[5-(2′-pyridyl)-2-thienyl]phosphine **5**; diphenyl[6-(2′-thienyl)-2-pyridyl]phosphine **6**; diphenyl{5-[6′-(diphenylphosphino)-2′-pyridyl]-2-thienyl}phosphine **7**; and 2,6-bis[5′-(diphenylphosphino)-2′-thienyl]pyridine **8**. Methods used for their synthesis range from lithiation of the parent heterocycle and subsequent reaction with PPh_2Cl to the use of coupling reactions catalysed by metal complexes to assemble the molecule from its subunits. The crystal and molecular structures of **1**, **7** and **8** have been determined and show that the 2,2′-bithienyl moiety in **1** adopts an s-*trans*-conformation, while the 2-(2′-thienyl)pyridyl moieties in **7** and **8** adopt s-*cis*-conformations in the solid state. These compounds represent a new series of ligands that are expected to bond to metals through the phosphorus and/or nitrogen atoms rather than a sulfur atom, in view of the poor donor ability of a thiophene sulfur towards metals.

Introduction

Diphenylphosphine derivatives of various pyridines and polypyridines are of current interest, especially with respect to their use as ligands for the synthesis of transition metal complexes that function as catalysts.[1] We have synthesised a range of ligands of this type and, in particular, have reported the synthesis of 6-diphenylphosphino-2,2′-bipyridine and shown this to be a useful tridentate bridging ligand, in particular with regard to stabilising dinuclear complexes to fragmentation.[2] We wished to extend this work to the synthesis of diphenylphosphine derivatives of 2,2′-bithiophene and 2,2′:5′,2″-terthiophene for several reasons. Thiophene compounds, in particular α-linked bithiophenes and terthiophenes, have been found to possess antiviral and cytotoxic properties[3] and, as such, are good candidates as ligands in transition metal complexes for which biological activity is a desired property. However, the thiophene sulfur atom is a very poor donor towards metals.[4] On the other hand, the diphenylphosphino group readily bonds to a wide range of transition metals and thus by functionalising the thiophene with this group the incorporation of thiophene units into a transition metal complex is facilitated. During the course of the work it was found that diphenylphosphine derivatives of 2,2′-bithiophene and 2,2′:5′,2″-terthiophene tend to be insoluble in most polar solvents, the most important of these from the biological testing point of view being water. It was therefore decided to modify the thienylphosphines by replacing the 2,2′-bithienyl and 2,2′:5′,2″-terthienyl moieties with the 2-(2′-thienyl)pyridyl and 2,6-di-2′-thienylpyridyl moieties respectively; our hope was that since the pyridyl-containing moieties are more polar the corresponding diphenylphosphine derivatives would show improved solubility in polar solvents. Altogether eight new ligands have been synthesised and fully characterised: 5,5′-bis(diphenylphosphino)-2,2′-bithiophene **1**; diphenyl(2,2′-bithienyl-5-yl)phosphine **2**; 5,5″-bis(diphenylphosphino)-2,2′:5′,2″-terthiophene **3**; diphenyl(2,2′:5′,2″-terthienyl-5-yl)phosphine **4**; diphenyl[5-(2′-pyridyl)-2-thienyl]phosphine **5**, diphenyl[6-(2′-thienyl)-2-pyridyl]phosphine **6**, diphenyl{5-[6′-(diphenylphosphino)-2′-pyridyl]-2-thienyl}phosphine **7** and 2,6-bis[5′-(diphenylphosphino)-2′-thienyl]pyridine **8** (Fig. 1). The crystal and molecular structures of **1**, **7** and **8** are also reported.

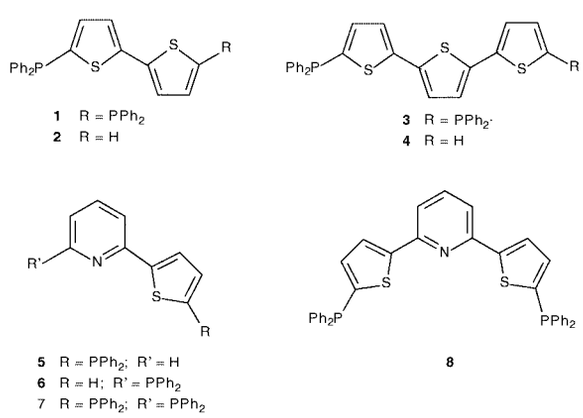

Fig. 1 Phosphines synthesised in this work.

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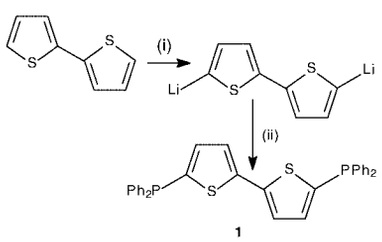
Results and discussion

A logical departure point for the synthesis of compounds **1**–**8** is to selectively lithiate the parent heterocycle for subsequent reaction with PPh_2Cl. A similar approach involves the synthesis of the appropriate halogenated derivative of the parent heterocycle that can then be reacted directly with $LiPPh_2$, or converted to the Grignard reagent for subsequent reaction with PPh_2Cl. However, though these approaches worked for the syntheses of **1**, **2** (in part), **3**, **4** and **5** it was necessary to assemble the remaining compounds by preparing Grignard derivatives of the appropriate subunits and coupling these in the presence of a metal complex catalyst. The latter approach is based on the methods developed by Kumada and other workers for the coupling of various heterocycles.[5,6] We note that the Suzuki coupling reaction has been successfully used for the synthesis of thienylpyridines in high yields;[7] however, no attempt was made to couple the thienyl and pyridyl units in compounds **5** to **8** using this method.

Derivatives of 2,2′-bithiophene (1 and 2)

Scheme 1 gives the reaction sequence used for the synthesis of **1**.



Scheme 1 *Reagents*: (i) 2.2 equiv. *n*-BuLi, Et_2O; (ii) 2 PPh_2Cl, Et_2O.

The amount of *n*-BuLi used for the dimetallation of 2,2′-bithiophene was optimised in this study. Use of exactly two equivalents of the reagent results in incomplete formation of 5,5′-dilithio-2,2′-bithiophene. Addition of 2.5 or more equivalents results not only in metallation at the 5-positions of the bithiophene, but at other positions as well, as indicated by ^{31}P NMR spectroscopy of the product mixture obtained after addition of excess PPh_2Cl. It was finally established that addition of 2.2 equivalents of *n*-BuLi gives complete lithiation of 2,2′-bithiophene at positions 5 and 5′, without noticeable contamination by polymetallated species. After quenching the reaction mixture with PPh_2Cl, pure **1** was obtained as a pale yellow, crystalline solid in 61% yield. Compound **1** is stable in air, soluble in chlorinated solvents and benzene, but insoluble in alcohols, acetone and saturated hydrocarbons. The $^{31}P\{^1H\}$ NMR spectrum of **1** recorded in $CDCl_3$ exhibits a singlet at δ −18.75, a chemical shift typical of diphenylphosphines with 2-thienyl substituents.[8]

Single crystals of **1** were grown by slow evaporation of a chloroform solution of the compound and the crystal structure determined by means of X-ray diffraction techniques. Fig. 2

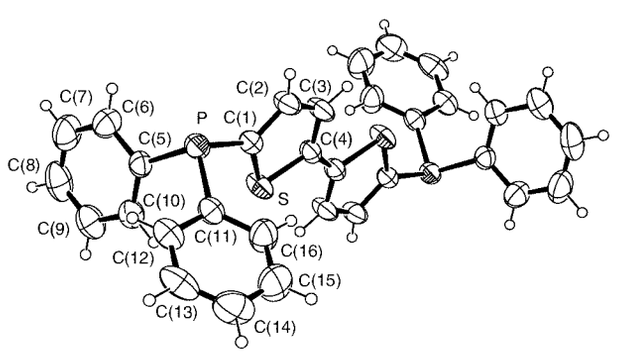


Fig. 2 ORTEP drawing of **1** with 40% thermal probability ellipsoids for the non-hydrogen atoms. The molecule has a crystallographically imposed centre of inversion at the centre of the interannular bond.

Table 1 Selected interatomic distances (Å) and angles (°)

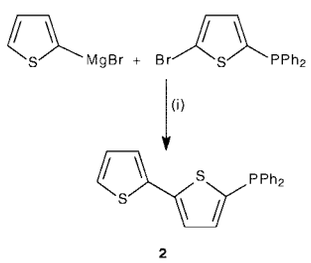
1			
P–C(1)	1.800(3)	P–C(5)	1.828(3)
P–C(11)	1.815(3)	S–C(1)	1.723(3)
S–C(4)	1.719(3)	C(4)–C(4′)	1.448(6)
C(1)–P(1)–C(5)	101.6(2)	C(1)–P(1)–C(11)	103.5(2)
C(5)–P(1)–C(11)	102.8(2)	C(1)–S(1)–C(4)	92.8(2)
7			
P(1)–C(1)	1.808(6)	P(1)–C(10)	1.816(6)
P(1)–C(16)	1.836(6)	P(2)–C(9)	1.835(5)
P(2)–C(22)	1.821(6)	P(2)–C(28)	1.832(5)
S–C(1)	1.715(5)	S–C(4)	1.719(5)
N–C(5)	1.343(6)	N–C(9)	1.336(6)
C(4)–C(5)	1.458(7)		
C(1)–P(1)–C(10)	103.1(3)	C(1)–P(1)–C(16)	102.4(3)
C(10)–P(1)–C(16)	102.0(3)	C(9)–P(2)–C(22)	101.2(3)
C(9)–P(2)–C(28)	105.2(2)	C(22)–P(2)–C(28)	102.6(3)
C(1)–S–C(4)	93.0(3)	C(5)–N–C(9)	118.1(5)
8			
P(1)–C(1)	1.805(3)	P(1)–C(26)	1.823(3)
P(1)–C(32)	1.827(3)	P(2)–C(13)	1.811(3)
P(2)–C(14)	1.834(3)	P(2)–C(20)	1.825(3)
S(1)–C(1)	1.725(3)	S(1)–C(4)	1.714(3)
S(2)–C(10)	1.718(3)	(2)–C(13)	1.725(3)
N–C(5)	1.342(3)	N–C(9)	1.339(3)
C(4)–C(5)	1.467(4)	C(9)–C(10)	1.462(4)
C(1)–P(1)–C(26)	102.0(2)	C(1)–P(1)–C(32)	101.3(2)
C(26)–P(1)–C(32)	104.1(2)	C(13)–P(2)–C(14)	101.8(2)
C(13)–P(2)–C(20)	104.7(2)	C(14)–P(2)–C(20)	100.9(2)
C(1)–S(1)–C(4)	92.3(2)	C(10)–S(2)–C(13)	92.3(2)
C(5)–N–C(9)	118.4(2)		

gives a perspective view of the ligand and also shows the atomic labeling scheme. Selected interatomic distances and angles are given in Table 1. The molecule is situated on a crystallographic centre of inversion at the centre of the interannular bond. As a consequence, the bithiophene moiety adopts a planar s-*trans* arrangement as was observed for 2,2′-bithiophene in the solid state.[9] Interestingly, both the *cis*- and *trans*-conformers have been shown to co-exist in solutions of 2,2′-bithiophene and its 5,5′-disubstituted derivatives, with the latter being more stable and thus predominant.[10] It appears that packing effects are important in determining the conformation of 2,2′-bithiophene and **1** in the solid state. Also of interest is that the lone pairs on the phosphorus atoms are directed away from the adjacent sulfur atom, as reflected by S(1)–C(1)–P(1)–C(5) and S(1)–C(1)–P(1)–C(11) torsion angles of 63.9 and −42.5° respectively, which are significantly less than 90°. A similar observation is made for the molecular structures of **7** and **8** and is discussed further below.

Initial attempts to synthesise **2** by first preparing 5-lithio-2,2′-bithiophene and subsequently reacting the intermediate with PPh_2Cl were unsuccessful as the selective monolithiation of 2,2′-bithiophene proved impossible, despite the use of a wide range of stoichiometries and reaction conditions. The Grignard route was then considered with 5-iodo-2,2′-bithiophene as the preferred precursor. The iodo derivative has been previously synthesised, either by iodination of 2,2′-bithienyl-5-ylmercury chloride in chloroform[11] or according to the Curtis method,[12] in which 2,2′-bithiophene-5-carboxylic acid methyl ester is treated with iodine followed by NaOH and finally $Hg(OAc)_2$ in acetic acid. Both methods give pure product but are time consuming with relatively low yields, and thus an improved synthesis of 5-iodo-2,2′-bithiophene was attempted. The method chosen

makes use of a mixture of iodine and iodic acid in a two-phase solution of glacial acetic acid and chloroform to selectively iodinate 2,2′-bithiophene; addition of a small amount of concentrated sulfuric acid speeds up the reaction. The yield of 56% and the time taken for the synthesis (one day) are significant improvements on the previously reported procedures.[11,12] Since the method is new full details are given in the Experimental section. Treatment of a solution of 5-iodo-2,2′-bithiophene in THF with magnesium followed by addition of PPh_2Cl afforded a mixture containing both the desired product **2** and 2,2′-bithiophene. Fortunately, it proved possible to separate **2** by gradient elution on a silica column. An oil is obtained that when left to stand under methanol at 0 °C for 3 months solidifies to afford a pure product in a 24% yield.

The low final yield of 24% prompted a third approach for the synthesis of **2** that is summarised in Scheme 2. An advantage of

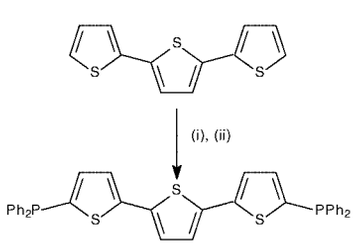


Scheme 2 *Reagents*: (i) $[NiCl_2(dppp)]$, Et_2O.

the method is that diphenyl(5-bromo-2-thienyl)phosphine can be prepared directly *via* the Grignard route from commercially available 2,5-dibromothiophene and PPh_2Cl, making the overall synthesis of **2** a two-step one. Since the preparation of diphenyl(5-bromo-2-thienyl)phosphine has not been previously reported, full details of its synthesis and characterisation are given in the Experimental section. The product mixture contained mainly **2**, but also small amounts of **1** and 2,2′-bithiophene. Separation on a silica column allowed the isolation of **2**, but in a low yield of only 25%. Thus, the only advantage of this method is that it involves two steps, whereas the previous method requires three steps since 2,2′-bithiophene must first be prepared from commercially available 2-bromothiophene. Pure **2** is colourless, stable in air and, unlike **1**, dissolves in a wide range of organic solvents. The $^{31}P\{^1H\}$ NMR spectrum of **2** recorded in $CDCl_3$ exhibits a peak at δ −18.83. This is a very similar chemical shift to that recorded for **1**, indicating that the introduction of a second diphenylphosphino group in the 5′-position of the bithiophene moiety has no influence on the chemical shift of the phosphorus atom in the first diphenylphosphino group.

Derivatives of 2,2′:5′,2″-terthiophene (3 and 4)

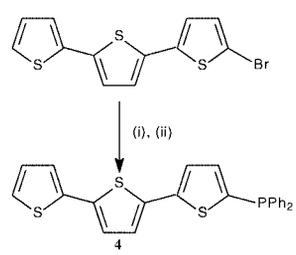
Dimetallation of 2,2′:5′,2″-terthiophene with a slight stoichiometric excess (2.2 equiv.) of *n*-BuLi in dry ether at 0 °C, followed by addition of the corresponding amount of PPh_2Cl afforded **3** in a 66% yield. Scheme 3 summarises the reaction sequence.



Scheme 3 *Reagents*: (i) 2.2 equiv. *n*-BuLi, Et_2O; (ii) 2 PPh_2Cl, Et_2O.

Few by-products are formed in this reaction and the target diphosphine is easily separated from the impurities by a combination of precipitation and chromatographic methods. Pure **3** is a bright-yellow crystalline solid, soluble in THF and chlorinated solvents. The solid material is indefinitely stable in contact with air, but decomposes on exposure to light with the formation of unidentifiable by-products. The $^{31}P\{^1H\}$ NMR spectrum of **3** measured in $CDCl_3$ exhibits a peak at δ −18.71, a chemical shift very similar to those recorded for **1** and **2**, indicating that the presence of a third thiophene ring has little effect on the local magnetic field at the phosphorus atom attached to the first thiophene ring.

Initial attempts to synthesise **4** by the first preparing 5-lithio-2,2′:5′,2″-terthiophene and subsequently reacting the intermediate with PPh_2Cl were unsuccessful as the selective monolithiation of 2,2′:5′,2″-terthiophene proved impossible, despite the use of a wide range of stoichiometries and reaction conditions. Accordingly, further efforts focussed on the Grignard route. First 5-bromo-2,2′:5′,2″-terthiophene was synthesised using a slight modification of the method of selective bromination developed by Effenberger and co-workers that involves addition of *N*-bromosuccinimide (NBS) to 2,2′:5′,2″-terthiophene in DMF at low temperatures.[13] The next step *i.e.*, the preparation of the Grignard reagent by reaction of 5-bromo-2,2′:5′,2″-terthiophene with magnesium in THF required special conditions. It was found that the reaction only took place in the presence of an entrainer (1,2-dibromoethane) with continuous ultrasonic activation and at a temperature of no less than 20 °C. Once formation of the Grignard reagent is complete, the mixture is quenched with PPh_2Cl, producing the desired phosphine. Scheme 4 summarises the reaction sequence.

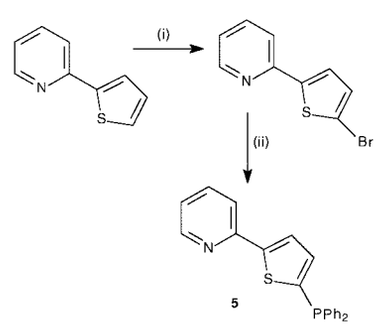


Scheme 4 *Reagents*: (i) Mg, THF, 1,2-$C_2H_4Br_2$; (ii) PPh_2Cl.

The overall yield of **4**, based on 2,2′:5′,2″-terthiophene is 30%. The compound is isolated as a yellow solid that is stable in air, but which decomposes in light to form unidentifiable products. As expected, the ^{31}P chemical shift of δ −18.71, measured in $CDCl_3$, shows no significant difference from those obtained for **1**, **2**, and **3**.

Derivatives of 2-(2′-thienyl)pyridine (5, 6 and 7)

Scheme 5 outlines the route employed for the synthesis of **5**.

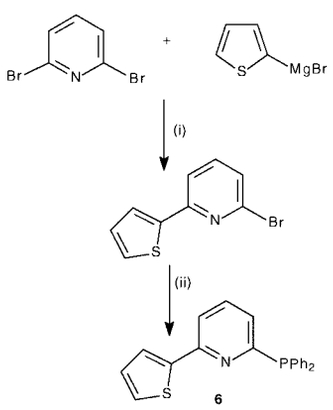


Scheme 5 *Reagents*: (i) Br_2, CH_3COOH; (ii) $LiPPh_2$, THF.

Selective bromination of 2-(2′-thienyl)pyridine in the 2-position of the thiophene ring proceeded routinely using bromine in glacial acetic acid to afford 2-bromo-5-(2′-pyridyl)thiophene.[14] Reaction of the latter with $LiPPh_2$ (prepared *in situ*

from the reaction of PPh_2Cl with lithium in THF) afforded a dark-coloured mixture that contained, in addition to the desired product, small amounts tetraphenyldiphosphine, as evidenced by a peak in the $^{31}P\{^1H\}$ NMR spectrum at *ca.* δ −14. Acid extraction of the reaction mixture, followed by basification of the extracts and a final extraction with diethyl ether enabled the separation of crude **5** from the less polar impurities. Final purification was achieved by means of column chromatography on silica with hexane–diethyl ether as eluent. Compound **5** is a colourless, microcrystalline, air-stable solid that is more soluble in polar solvents than the bithienyl analogue, **2**. The $^{31}P\{^1H\}$ NMR spectrum of **5** recorded in $CDCl_3$ exhibits a singlet at δ −18.35 that is slightly downfield of that observed at δ −18.83 for **2**.

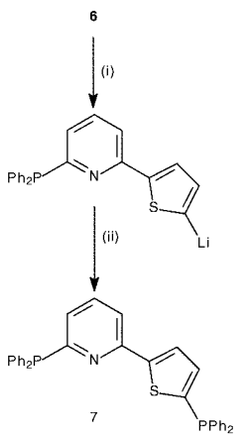
The method employed for the synthesis of **6** required in the first instance the preparation of 2-bromo-6-(2′-thienyl)pyridine, selected as the preferred precursor in view of its expected ease of reaction with $LiPPh_2$ to give the desired product. The procedure followed was based on that developed by Kumada and co-workers for the preparation of the chloro analogue,[15] and is shown as the first step in Scheme 6.



Scheme 6 *Reagents*: (i) $[PdCl_2(dppb)]$, Et_2O; (ii) $LiPPh_2$, THF.

The success of the reaction depends on the selective coupling of 2,6-dibromopyridine with only one equivalent of 2-thienylmagnesium bromide in the presence of the catalyst, $[PdCl_2(dppb)]$ [dppb = 1,4-bis(diphenylphosphino)butane]. However, despite repeated attempts to achieve the stoichiometry required, an oily product mixture was obtained that inevitably included unreacted 2,6-dibromopyridine, as well as 2,6-di-2′-thienylpyridine formed as a result of the reaction of two equivalents of the Grignard reagent with one equivalent of 2,6-dibromopyridine. Removal of the 2,6-dibromopyridine was achieved by cooling the oily residue to 10 °C which induced its separation as a solid; further cooling forced the precipitation of both 2,6-di-2′-thienylpyridine and the desired product. Other separation techniques such as distillation and chromatography also failed to afford pure 2-bromo-6-(2′-thienyl)pyridine. Eventually it was decided to proceed with the next step despite the contamination of the starting material with about 5% of 2,6-di-2′-thienylpyridine. Fortunately, the reaction of impure 2-bromo-6-(2′-thienyl)pyridine with $LiPPh_2$ proceeded smoothly to afford, after work-up, pure **6** in a 42% yield (Scheme 6). The compound is a colourless crystalline material that is oxygen-sensitive, especially in solution. It is more soluble in polar solvents such as methanol, acetonitrile and acetone than **2**. The $^{31}P\{^1H\}$ NMR spectrum recorded for **6** in $CDCl_3$ exhibits a single peak at δ −3.64, a chemical shift characteristic of a phosphorus atom of a diphenylphosphino group bonded to the 2-position of a pyridine ring. For comparison purposes the ^{31}P chemical shifts recorded in CD_2Cl_2 and also measured relative to 85% H_3PO_4 are δ −3.7 for 6-diphenylphosphino-2,2′-bipyridine[2a] and δ −3.7 for 2,6-bis(diphenylphosphino)pyridine.[16] Significantly, there is a downfield shift of about 15 ppm compared to the ^{31}P resonances typically observed at *ca.* δ −19 when the diphenylphosphino group is linked to the 2-position of a thiophene ring as in compounds **1**–**5** and diphenyl(2-thienyl)phosphine.[8]

We first investigated the use of 6-bromo-2-(5-bromo-2-thienyl)pyridine as the starting material for the synthesis of **7**, with the expectation that it would react smoothly with two equivalents of $LiPPh_2$ to give the desired product. However, preliminary attempts to synthesise the dibromo derivative indicated that it would be difficult to obtain in pure form and it was therefore decided to employ compound **6** as the starting material for the synthesis of **7**. The procedure is outlined in Scheme 7. The choice of solvent (THF) is critical to the success of the reaction. As shown by Queguiner and Ribereau,[17] lithiation of 2-(2′-thienyl)pyridine with *n*-BuLi only occurs selectively at the 5-position of the thienyl ring provided that the solvent coordinates strongly to the lithium atom. If poorly coordinating solvents such as diethyl ether are used, lithiation occurs at the 3-position of the thiophene ring as well and a complex mixture of products is obtained. Compound **7** was initially isolated from the product mixture as a yellow oil that eventually separated as a solid when left to stand under cold methanol for a period of *ca.* 3 weeks. Final purification was by means of chromatography on silica to afford a colourless, air-sensitive and crystalline material in 38% yield. Unfortunately, there is no significant improvement in the solubility of **7** in polar solvents compared to that for the bithienyl analogue, **1**.



Scheme 7 *Reagents*: (i) *n*-BuLi, THF; (ii) PPh_2Cl, THF.

The $^{31}P\{^1H\}$ NMR spectrum of **7** is interesting since it allows an internal comparison of the chemical shifts for the phosphorus atoms of diphenylphosphino groups bonded to an α-carbon atom of thienyl and pyridyl rings. The values measured in $CDCl_3$ are δ −18.34 and −3.60 respectively, confirming the trend of a downfield shift when the diphenylphosphino group bonds to a pyridyl rather than to a thienyl moiety. This trend is probably a consequence of the deshielding of the phosphorus nucleus brought about because the pyridyl ring exerts a stronger electron withdrawing effect than the thienyl ring.[18]

Single crystals suitable for the determination of the crystal and molecular structure of **7** by X-ray diffraction methods were grown by slow evaporation of a solution of the compound in mixture of petroleum ether (60–80 °C) and diethyl ether (6 : 1, v/v). A perspective view of the molecule is given in Fig. 3 together with the atomic labeling scheme. Selected interatomic distances and angles are listed in Table 1. The pyridine and thiophene rings are essentially co-planar with the dihedral angle between the mean planes through each of the two rings being only 3.6°. An s-*cis* arrangement of the sulfur and nitrogen atoms about the interannular bond is adopted, in contrast to the s-*trans* arrangement observed for the 2,2′-bithienyl moiety in **1**. A feature also observed for the structure of **1** is that the lone pair on P(1) points away from the sulfur atom [S(1)] of the

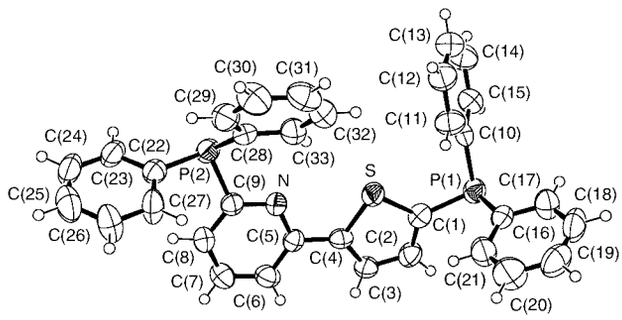
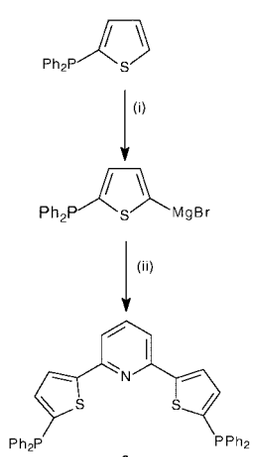


Fig. 3 ORTEP drawing of **7** with 50% thermal probability ellipsoids for the non-hydrogen atoms.

adjacent ring. However, the lone pair is not fully rotated away as this would require the S(1)–C(1)–P(1)–C(10) and S(1)–C(1)–P(1)–C(16) torsion angles to be not only less than 90° but also opposite in sign and equal in magnitude; the angles are 13.9 and −91.7° respectively. The torsion angles that define the orientation of the second phosphorus lone pair with respect to that of the adjacent nitrogen atom are −158.1 and 51.6° for N(1)–C(9)–P(2)–C(22) and N(1)–C(9)–P(2)–C(28) respectively. These values show that the vectors representing the lone pairs on the phosphorus and nitrogen atoms do *not* point in opposite directions, but rather lie on the same side of an imaginary plane drawn through P(2) and C(9) and perpendicular to the pyridine ring. The different orientations of the lone pairs on P(1) and P(2) with respect to the heteroatom in the adjacent ring can be attributed to the different steric requirements of the sulfur and nitrogen lone pairs, and to the different ring sizes and geometries of the respective heterocycles.

2,6-Bis[5′-(diphenylphosphino)-2′-thienyl]pyridine (8)

The method used to synthesise **8** involves the coupling of 2,6-dibromopyridine with the Grignard reagent of diphenyl-(2-thienyl)phosphine [prepared *in situ* by reaction of diphenyl-(2-thienyl)phosphine with *n*-BuLi and $MgBr_2{\cdot}Et_2O$ in diethyl ether] in the presence of the catalyst [$NiCl_2$(dppp)] [dppp = 1,3-bis(diphenylphosphino)propane]. This is illustrated in Scheme 8. Pure **8** is obtained in 52% yield after work-up and column



Scheme 8 *Reagents*: (i) *n*-BuLi, $MgBr_2{\cdot}Et_2O$; (ii) 0.5 equiv. 2,6-dibromopyridine, [$NiCl_2$(dppp)], THF.

chromatography on silica. It is a pale green microcrystalline solid that is stable in air. It is poorly soluble in most solvents, both polar and non-polar. The $^{31}P\{^1H\}$ NMR spectrum of **8** recorded in $CDCl_3$ exhibits a singlet at δ −18.28 that is only slightly downfield of that observed at δ −18.71 for **3**; clearly substitution of a thienyl unit in polythiophenes by a pyridyl moiety has little effect on the magnetic field at the phosphorus atom bonded to a thienyl ring.

Single crystals of **8** suitable for an X-ray diffraction study were obtained by slow evaporation of a solution of the compound in a mixture of hexane and diethyl ether (2 : 1, v/v). Fig. 4

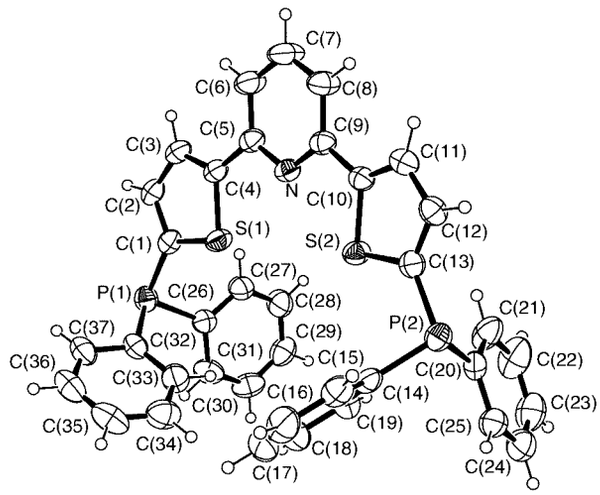


Fig. 4 ORTEP drawing of **8** with 40% thermal probability ellipsoids for the non-hydrogen atoms.

gives a perspective view of the molecule together with the atomic labeling scheme. Selected interatomic distances and angles are listed in Table 1. The 2,6-di-2′-thienylpyridyl moiety is essentially planar with dihedral angles between the two thiophene rings and the central pyridyl ring of only 1.3 [S(1)] and 4.3° [S(2)] respectively. The heteroatoms from adjacent rings adopt an s-*cis* arrangement with respect to rotation around the interannular bonds. This contrasts with the geometries observed in the solid state for the planar terpyridyl moieties of the 4′-phenyl-2,2′:6′,2″-terpyridyl and 6,6″-dibromo-4′-phenyl-2,2′:6′,2″-terpyridyl ligands, where the nitrogen lone pair of the central pyridine ring points in the opposite direction to those of the two outer pyridine rings.[19] As observed for the molecular structures of **1** and **7** the lone pairs on the phosphorus atoms are directed away from the adjacent sulfur atoms, as reflected by S(1)–C(1)–P(1)–C(26) and S(1)–C(1)–P(1)–C(32) torsion angles of −61.6 and 45.6° respectively, and S(2)–C(13)–P(2)–C(14) and S(2)–C(13)–P(2)–C(20) torsion angles of 33.6 and −71.2° respectively. Given that the phosphorus lone pair adopts this orientation in all three compounds, this appears to be an intrinsic structural feature of the diphenyl(2-thienyl)phosphine moiety.

Conclusions

The synthesis and characterisation of eight diphenylphosphine derivatives of α-linked polythiophenes and thienylpyridines are described. The structural features of these compounds have been exemplified by the crystal and molecular structure determinations of **1**, **7** and **8**. The eight compounds represent a new series of potentially useful ligands. All of the compounds are capable of bonding *via* the diphenylphosphino group(s) to a transition metal and, in the case of the derivatives with pyridine moieties as part of the compound structure, through the pyridine nitrogen atom(s) as well. However, coordination through a sulfur atom is unlikely as a thiophene sulfur is a very poor donor towards transition metals.[4] The synthesis and characterisation of their complexes with gold(I) will be reported in due course, as well as the results of a preliminary investigation into the ability of the gold complexes to exhibit cytotoxic activity with respect to cancer cells.

Experimental

General procedures

All manipulations were carried out either using standard Schlenk or vacuum techniques or in a nitrogen-filled drybox. Organic solvents employed for the reactions were first purified according to standard procedures,[20] and then distilled under nitrogen or degassed using freeze–pump–thaw techniques. ^{1}H NMR (200 MHz) and ^{13}C{^{1}H} NMR (50 MHz) spectra were recorded on a Varian Gemini 200 spectrometer at 25 °C with chemical shifts referenced to $SiMe_4$. ^{31}P{^{1}H} NMR (32.1 MHz) spectra were recorded at 33 °C on a Varian FT80A broad band spectrometer with chemical shifts referenced to 85% phosphoric acid (external). Mass spectra were obtained on a Hewlett Packard GCMS using electron impact (EI) ionisation. UV–vis absorption spectra were recorded at 22 °C using a Shimadzu UV-2101PC scanning spectrophotometer. Spectroscopic grade dichloromethane was used for these measurements. Microanalyses for %C, H and N were performed by the microanalytical laboratory at the University of Natal, Pietermaritzburg and by Galbraith Laboratories Inc., Knoxville, Tennessee, USA. Melting points were recorded on a Kofler hot stage apparatus and are uncorrected.

Materials

The following chemicals were obtained from the indicated suppliers and were used as received: 2-bromothiophene (ACROS); 2,5-dibromothiophene (Aldrich); 2,6-dibromopyridine (Fluka AG); $MgBr_2{\cdot}Et_2O$ (ACROS); *n*-BuLi, 1.6 M in hexane (Merck); PPh_2H and PPh_2Cl (Strem). The following compounds were prepared according to literature procedures: diphenyl(2-thienyl)-phosphine,[21] [$NiCl_2$(dppp)],[22] 2,2′-bithiophene,[23] 2,2′:5′,2″-terthiophene,[24] 5-bromo-2,2′:5′,2″-terthiophene,[13] 2-(2′-thienyl)-pyridine,[25] 2-bromo-5-(2′-pyridyl)thiophene,[14] 2,6-di-2′-thienyl-pyridine,[26] and [$PdCl_2$(dppb)].[27]

Synthesis of 5,5′-bis(diphenylphosphino)-2,2′-bithiophene 1

A solution of 2,2′-bithiophene (2.36 g, 14.2 mmol) in dry diethyl ether (30 mL) was added dropwise to a solution containing *n*-BuLi (31.2 mmol, 1.6 M, hexane) at 0 °C. The addition was completed in *ca.* 40 min during which time a yellow precipitate formed. The mixture was allowed to stir for 2 h at room temperature, after which a solution of PPh_2Cl (5.2 mL, 28.8 mmol) in dry diethyl ether (20 mL) was added dropwise with cooling (0 °C). The mixture was gradually brought to room temperature, stirred for 14 h, and 0.1 M HCl solution (30 mL) added followed by crushed ice. The product was extracted with CH_2Cl_2 (3 × 100 mL), the extracts washed with $NaHCO_3$ and NaCl solutions and dried over Na_2SO_4. The volume of CH_2Cl_2 was reduced *in vacuo* and a mixture of methanol–acetone (25 mL, 4 : 1, v/v) added. A yellow precipitate separated after cooling the mixture to −25 °C for 24 h. This was purified by means of centrifugal thin layer chromatography on a Chromatotron® (silica; hexane–diethyl ether, 8 : 1, v/v). Yield: 4.65 g, 61%, mp 191–192 °C. Found: C 71.8; H 4.8%. Calc. for $C_{32}H_{24}P_2S_2$: C 71.9; H 4.5%. ^{31}P{^{1}H} NMR ($CDCl_3$): δ −18.75 (s). ^{1}H NMR ($CDCl_3$): δ 7.10–7.22 (4H, ABX spin system, $^4J_{HP}$ 1.46, $^3J_{HP}$ 6.14, J_{AB} 3.57 Hz, $H_{Th\text{-}3}$ + $H_{Th\text{-}4}$), 7.30–7.44 (20 H, m, H_{Ph}). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 124.8 (d, $^3J_{CP}$ 8.0 Hz, $C_{Th\text{-}3}$), 128.5 (d, $^3J_{CP}$ 7.1 Hz, $C_{Ph\text{-}3}$), 129.0 (s, $C_{Ph\text{-}4}$), 133.0 (d, $^2J_{CP}$ 19.7 Hz, $C_{Ph\text{-}2}$), 137.3 (d, $^2J_{CP}$ 18.3 Hz, $C_{Th\text{-}4}$), 137.6 (d, $^1J_{CP}$ 6.8 Hz, $C_{Ph\text{-}1}$), 137.8 (d, $^1J_{CP}$ 30.1 Hz, $C_{Th\text{-}5}$), 143.4 (s, $C_{Th\text{-}2}$). MS (EI) *m*/*z*: 534.4 (M^+). UV–vis (CH_2Cl_2), λ_{max}/nm (ε/M^{-1} cm^{-1}): 230 (1.9 × 10^4), 350 (1.95 × 10^4).

Synthesis of 5-iodo-2,2′-bithiophene

2,2′-Bithiophene (3.30 g, 20 mmol) was dissolved in a mixture of CCl_4 (8 mL) and glacial acetic acid (10 mL). To this solution HIO_3 (0.7 g, 4 mmol) was added, followed by water (7 mL), iodine (2.3 g, 9 mmol) and finally a catalytic amount of concentrated H_2SO_4 (0.1 mL). The mixture was stirred at 40 °C until the purple colour of the iodine had disappeared. Water (20 mL) was added, the organic layer collected and the remaining mixture extracted with chloroform (2 × 20 mL). The combined extracts were washed with saturated solutions of $NaHCO_3$ and Na_2SO_3, dried over $CaCl_2$ and filtered. The solvent was evaporated until a brown solid mass was obtained. This was distilled under vacuum to give a yellow oil. On standing, the oil solidified. Washing the solid with cold hexane afforded a colourless product. GC analysis showed the material to be >95% pure. Yield: 3.36 g, 56%, mp 30–32 °C (lit.[11] 32 °C), bp 165–170 °C/1.5 mmHg (lit.[11] 108–109 °C/0.03 mmHg). MS (EI) *m*/*z*: 291.9 (M^+).

Synthesis of diphenyl(5-bromo-2-thienyl)phosphine

A mixture of 2,5-dibromothiophene (6.08 g, 25 mmol) and magnesium turnings (0.6 g, 25 mmol) in dry diethyl ether (25 mL) was refluxed for 1 h or until all the metal had dissolved. The solution was cooled to *ca.* 15 °C (cooling below this temperature causes precipitation of the Grignard reagent) and a solution of PPh_2Cl (4.5 mL, 25 mmol) in THF (20 mL) added dropwise over a 30 min period. When the addition was complete, the mixture was refluxed for 1 h and then stirred overnight at room temperature. The solution was evaporated to a quarter of its original volume and diethyl ether (100 mL) added, followed by a concentrated NH_4Cl solution (50 mL). The ether layer was separated and the aqueous layer extracted with diethyl ether (2 × 50 mL). The combined ether extracts were washed with brine and dried over $MgSO_4$. Three-quarters of the solvent were evaporated *in vacuo* and cold methanol added to the mixture. After standing for 1 day at −25 °C, an off-white precipitate formed. This was filtered off, and subsequently purified by means of centrifugal chromatography on a Chromatotron® (silica; hexane–diethyl ether, 8 : 1, v/v) to afford a colourless crystalline solid. Yield: 3.4 g, 40%, mp 69–70 °C. Found: C 55.7; H 3.8%. Calc. for $C_{16}H_{12}BrPS$: C 55.4; H 3.5%. ^{31}P{^{1}H} NMR ($CDCl_3$): δ −17.88 (s). ^{1}H NMR ($CDCl_3$): δ 7.03–7.18 (2H, ABX spin system, $^4J_{HP}$ 1.30, $^3J_{HP}$ 6.14, J_{AB} 3.66 Hz, $H_{Th\text{-}3}$ + $H_{Th\text{-}4}$), 7.32–7.44 (10H, m, H_{Ph}). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 118.2 (d, $^4J_{CP}$ 1.4 Hz, $C_{Th\text{-}5}$), 128.6 (d, $^3J_{CP}$ 7.1 Hz, $C_{Ph\text{-}3}$), 129.1 (s, $C_{Ph\text{-}4}$), 131.0 (d, $^3J_{CP}$ 8.5 Hz, $C_{Th\text{-}4}$), 131.8 (d, $^1J_{CP}$ 10.5 Hz, $C_{Th\text{-}2}$), 133.0 (d, $^2J_{CP}$ 19.6 Hz, $C_{Ph\text{-}2}$), 136.9 (d, $^2J_{CP}$ 30.1 Hz, $C_{Th\text{-}3}$), 137.2 (d, $^1J_{CP}$ 8.3 Hz, $C_{Ph\text{-}1}$). MS (EI) *m*/*z*: 345.8 (^{79}Br–M^+), 347.8 (^{81}Br–M^+). UV–vis (CH_2Cl_2), λ_{max}/nm (ε/M^{-1} cm^{-1}): 232 (1.25 × 10^4), 252 (sh, 1.17 × 10^4).

Synthesis of diphenyl(2,2′-bithienyl-5-yl)phosphine 2

(i) From 5-iodo-2,2′-bithiophene. 5-Iodo-2,2′-bithiophene (3.0 g, *ca.* 10 mmol) was dissolved in dry THF (25 mL). To this solution magnesium turnings (0.26 g, 11 mmol) were added. Two crystals of iodine were added as a catalyst, and the mixture was left to reflux for 5 h or until all the metal had dissolved. The solution was cooled to 0 °C and PPh_2Cl (2.0 mL, 11 mmol) added slowly. The solution was allowed to gradually warm up to room temperature and stirred for 14 h. The mixture was hydrolysed by addition of an ice-cold concentrated NH_4Cl solution (100 mL). The target compound was extracted with diethyl ether, the extracts combined, washed with brine and dried over $MgSO_4$. After drying and evaporation of the solvent, the residue was purified on a silica column: 2,2′-bithiophene was first removed with hexane–diethyl ether (20 : 1, v/v) as eluent, following which the target compound was eluted from the column using hexane–diethyl ether (5 : 1, v/v) as eluent. Evaporation of the solvent *in vacuo* afforded a yellow oil, which was left to solidify under a layer of methanol at −20 °C. Crystallisation occurred after *ca.* 10 weeks to afford an off-white powder that was washed with very cold methanol (*ca.* −15 °C) and dried *in*

vacuo. Yield: 0.84 g, 24%, mp 58–59 °C. Found: C 68.3; H 4.3%. Calc. for $C_{20}H_{15}PS_2$: C 68.6; H 4.3%. $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ −18.83 (s). ^1H NMR ($CDCl_3$): δ 6.97 (1H, dd, $^3J_{HH}$ 5.07, $^3J_{HH}$ 3.60 Hz, $H_{Th\text{-}4'}$), 7.10–7.25 (4H, $H_{Th\text{-}3}$ + $H_{Th\text{-}4}$ + $H_{Th\text{-}3'}$ + $H_{Th\text{-}5'}$), 7.30–7.47 (10H, m, H_{Ph}). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 124.1 (s, $C_{Th\text{-}3'}$), 124.5 (d, $^3J_{CP}$ 8.1 Hz, $C_{Th\text{-}3}$), 124.9 (s, $C_{Th\text{-}5'}$), 127.8 (s, $C_{Th\text{-}4'}$), 128.5 (d, $^3J_{CP}$ 6.8 Hz, $C_{Ph\text{-}3}$), 129.0 (s, $C_{Ph\text{-}4}$), 133.0 (d, $^2J_{CP}$ 19.6 Hz, $C_{Ph\text{-}2}$), 136.8 (d, $^1J_{CP}$ 29.4 Hz, $C_{Th\text{-}5}$), 137.3 (d, $^2J_{CP}$ 28.1 Hz, $C_{Th\text{-}4}$), 137.4 (s, $C_{Th\text{-}2'}$), 137.6 (d, $^1J_{CP}$ 8.4 Hz, $C_{Ph\text{-}1}$), 143.9 (s, $C_{Th\text{-}2}$). MS (EI) *m*/*z*: 349.8 (M^+). UV–vis (CH_2Cl_2), λ_{max}/nm (ε/M^{-1} cm^{-1}): 230 (1.34 × 10^4), 330 (1.60 × 10^4).

(ii) From 2-bromothiophene and diphenyl(5-bromo-2-thienyl)-phosphine. 2-Bromothiophene (1.63 g, 10 mmol) was dissolved in dry diethyl ether (20 mL) and added to a slurry of magnesium turnings (0.26 g, 11 mmol) in dry diethyl ether (50 mL) at a rate that maintained a gentle reflux. After the addition was complete, the reflux was continued until all the metal had dissolved. The mixture was cooled to room temperature and added slowly to a solution of diphenyl(5-bromo-2-thienyl)phosphine (3.47 g, 10 mmol) in dry diethyl ether (35 mL) containing [$NiCl_2$(dppp)] (0.05 g) at 0 °C. When the addition was complete, the mixture was allowed to stir for 14 h at room temperature, after which it was hydrolysed with a concentrated NH_4Cl solution containing ice. The product was extracted with CH_2Cl_2 (3 × 50 mL), washed with brine and dried over $MgSO_4$. Evaporation of the CH_2Cl_2 left a brown oil. This was chromatographed on a short silica column with ether as eluent; the first band contained the product. The ether was removed and the residue dissolved in hot hexane (50 mL), followed by addition of ethanol (50 mL). Evaporation of three-quarters of the solvent, followed by cooling to −25 °C over a period of 20 h, afforded an oily residue of impure **2**. The residue was left to stand under methanol at −20 °C. After *ca.* 10 weeks it solidified to give an off-white powder that was washed with very cold methanol (*ca.* −15 °C) and dried *in vacuo*. Yield: 0.87 g, 25%, mp 58–60 °C.

Synthesis of 5,5″-bis(diphenylphosphino)-2,2′:5′,2″-terthiophene 3

A suspension of 2,2′:5′,2″-terthiophene (3.72 g, 15 mmol) in dry diethyl ether (50 mL) was added dropwise to a flask containing *n*-BuLi (33 mmol, 1.6 M, hexane). The temperature was kept at 0 °C during the addition. A yellow–green precipitate formed when approximately half the required amount of the terthiophene had been added. After the addition was complete, the mixture was allowed to stir for 2.5 h at room temperature, then cooled to 0 °C and a solution of PPh_2Cl (5.5 mL, 30.5 mmol) in dry ether (30 mL) was slowly added. Once this addition was complete the solution was allowed to warm up to room temperature and left to stir for a further 15 h. Dry CH_2Cl_2 (50 mL) was added, followed by addition of dilute HCl (100 mL) and ice. The product was extracted several times with CH_2Cl_2 (300 mL). The organic layer was washed with $NaHCO_3$ and NaCl solutions and dried over $MgSO_4$. The solvent was evaporated to afford a yellow oily residue. On standing for 24 h at −5 °C the residue crystallised to give a yellow solid. The solid was washed with a cold mixture of methanol and acetone (50 mL, 10 : 1, v/v), dissolved in a small amount of CH_2Cl_2 and passed through a short silica column with hexane–diethyl ether (1 : 1, v/v) as eluent. Further purification on a Chromatotron® (silica; hexane–diethyl ether, 10 : 1, v/v). afforded a bright-yellow crystalline compound. Yield: 6.1 g, 66%, mp 148–149 °C. Found: C 69.9; H 4.1%. Calc. for $C_{36}H_{26}P_2S_3$: C 70.1; H 4.3%. $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ −18.71 (s). ^1H NMR ($CDCl_3$): δ 7.00 (2H, s, $H_{Th\text{-}3'}$), 7.13–7.25 (4H, m, ABX spin system; $H_{Th\text{-}3}$ + $H_{Th\text{-}4}$), 7.32–7.48 (20H, m, H_{Ph}). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 124.4 (d, $^3J_{CP}$ 8.1 Hz, $C_{Th\text{-}3}$), 124.8 (s, $C_{Th\text{-}3'}$), 128.6 (d, $^3J_{CP}$ 7.0 Hz, $C_{Ph\text{-}3}$), 129.0 (s, $C_{Ph\text{-}4}$), 133.0 (d, $^2J_{CP}$ 19.7 Hz, $C_{Ph\text{-}2}$), 136.0 (s, $C_{Th\text{-}2'}$), 137.3 (d, $^2J_{CP}$ 28.1 Hz, $C_{Th\text{-}4}$), 137.4 (d, $^1J_{CP}$ 8.1 Hz, $C_{Ph\text{-}1}$), 138.0 (d, $^1J_{CP}$ 29.4 Hz, $C_{Th\text{-}5}$), 143.5 (s, $C_{Th\text{-}2}$). MS (EI) *m*/*z*: 616.1 (M^+). UV–vis (CH_2Cl_2), λ_{max}/nm (ε/M^{-1} cm^{-1}): 230 (1.90 × 10^4), 253 (sh, 1.7 × 10^4), 388 (2.45 × 10^4).

Synthesis of diphenyl(2,2′:5′,2″-terthienyl-5-yl)phosphine 4

Magnesium turnings (0.060 g, 2.5 mmol) were added to a solution of 5-bromo-2,2′:5′,2″-terthiophene (0.82 g, 2.5 mmol) in dry THF (10 mL). The reaction flask was placed in an ultrasonic bath and two drops of freshly distilled 1,2-dibromoethane added. On switching on the ultrasound the mixture quickly turned brown, but the reaction was complete only after 1 h of sonication at room temperature. The flask was cooled to 0 °C and dry THF (10 mL) added, followed by dropwise addition of a solution of PPh_2Cl (0.45 mL, 2.5 mmol) in dry THF (5 mL). The mixture was allowed to reach room temperature and stirred for 1 h. The solvent was removed *in vacuo* and cold methanol added, resulting in the formation of a yellow–orange precipitate. Elution of the precipitate through a silica column with petroleum ether (60–80 °C) removed 2,2′:5′,2″-terthiophene and the starting material. The next yellow band was collected using hexane–diethyl ether (20 : 1, v/v) as eluent, the solvent removed and methanol added. A bright-yellow precipitate formed after 1 day at −25 °C. This was washed with methanol and dried under vacuum. Yield: 0.42 g, 39%, mp 77–78 °C. Found: C 66.2, H 4.1%. Calc. for $C_{24}H_{17}PS_3$: C 66.6, H 4.0%. $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ −18.71 (s). ^1H NMR ($CDCl_3$): δ 6.99–7.06 (3H, m, $H_{Th\text{-}3'}$ + $H_{Th\text{-}4'}$ + $H_{Th\text{-}4''}$), 7.15–7.27 (4H, m, $H_{Th\text{-}3}$ + $H_{Th\text{-}4}$ + $H_{Th\text{-}3''}$ + $H_{Th\text{-}5''}$), 7.32–7.48 (10H, m, H_{Ph}). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 124.3–125.0 (m, $C_{Th\text{-}3'}$ + $C_{Th\text{-}4'}$ + $C_{Th\text{-}4''}$ + $C_{Th\text{-}5''}$), 125.2 (d, $^3J_{CP}$ 7.0 Hz, $C_{Th\text{-}3}$), 128.6 (s, $C_{Th\text{-}3''}$), 129.2 (d, $^3J_{CP}$ 8.8 Hz, $C_{Ph\text{-}3}$), 129.6 (s, $C_{Ph\text{-}4}$), 133.8 (d, $^2J_{CP}$ 19.7 Hz, $C_{Ph\text{-}2}$), 137.7 (d, $^2J_{CP}$ 28.3 Hz, $C_{Th\text{-}4}$), 137.0–139.0 (m, $C_{Th\text{-}5}$ + $C_{Th\text{-}2'}$ + $C_{Th\text{-}5'}$ + $C_{Th\text{-}2''}$ + $C_{Ph\text{-}1}$), 144.2 (s, $C_{Th\text{-}2}$). MS (EI) *m*/*z*: 432.0 (M^+). UV–vis (CH_2Cl_2), λ_{max}/nm (ε/M^{-1} cm^{-1}): 228 (1.34 × 10^4), 250 (sh, 1.12 × 10^4), 374 (2.0 × 10^4).

Synthesis of diphenyl[5-(2′-pyridyl)-2-thienyl]phosphine 5

A solution of PPh_2Cl (3.6 mL, 20 mmol) in dry THF (20 mL) was added carefully to a slurry of lithium pieces (0.7 g, 100 mmol) in dry THF (10 mL) under argon. The mixture was gently warmed to ±50 °C until the reaction started and the solution turned orange. The mixture was refluxed for further 3 h. After cooling to room temperature, the solution was decanted into a reaction flask under nitrogen leaving unreacted lithium pieces behind. A solution of 2-bromo-5-(2′-pyridyl)-thiophene (4.8 g, 20 mmol) in dry THF (20 mL) was added dropwise to the solution at −78 °C over a period of 1.5 h. When the addition was complete, the mixture was allowed to warm up to room temperature and stirred for 14 h. Two-thirds of the solvent was evaporated and degassed dry diethyl ether (30 mL) added. The solution was extracted with 5 M HCl (2 × 20 mL) and then carefully basified with concentrated ammonia solution at 0 °C. The basified solution was extracted with diethyl ether (2 × 30 mL), the ethereal layers were combined, dried, filtered and evaporated to dryness. The residue was purified by column chromatography (silica; hexane–diethyl ether, 6 : 1, v/v), yielding a white microcrystalline compound. Yield: 4.61 g, 66%, mp 69–70 °C. Found: C 72.6, H 4.4, N 4.0%. Calc. for $C_{21}H_{16}NPS$: C 73.0, H 4.7, N 4.1%. $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ −18.35 (s). ^1H NMR ($CDCl_3$): δ 7.15 (1H, ddd, $^4J_{HH}$ 1.96, $^3J_{HH}$ 5.43, $^3J_{HH}$ 7.08 Hz, $H_{Py\text{-}5}$), 7.29–7.50 (11H, m, H_{Ph} + $H_{Th\text{-}4}$), 7.57 (1H, dd, $^4J_{HP}$ 1.32, $^3J_{HH}$ 3.62 Hz, $H_{Th\text{-}3}$), 7.61–7.70 (2H, m, $H_{Py\text{-}3}$ + $H_{Py\text{-}4}$), 8.50–8.56 (1H, m, $H_{Py\text{-}6}$). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 118.8 (s, $C_{Py\text{-}3}$), 122.2 (s, $C_{Py\text{-}5}$), 125.2 (d, $^3J_{CP}$ 8.5 Hz, $C_{Th\text{-}3}$), 128.5 (d, $^3J_{CP}$ 7.2 Hz, $C_{Ph\text{-}3}$), 129.0 (s, $C_{Ph\text{-}4}$), 133.1 (d, $^2J_{CP}$ 19.8 Hz, $C_{Ph\text{-}2}$), 136.7 (s, $C_{Py\text{-}4}$), 137.3 (d, $^2J_{CP}$ 29.2 Hz, $C_{Th\text{-}4}$), 137.6 (d, $^1J_{CP}$ 8.1 Hz, $C_{Ph\text{-}1}$), 140.6 (d, $^1J_{CP}$ 22.5 Hz, $C_{Th\text{-}5}$), 149.5 (s, $C_{Py\text{-}6}$), 150.9 (s, $C_{Th\text{-}2}$), 152.1 (s, $C_{Py\text{-}2}$). MS (EI)

m/*z*: 344.6 ($M^+ - 1$). UV–vis (CH_2Cl_2), λ_{max}/nm (ε/M^{-1} cm^{-1}): 231 (1.3×10^4), 271 (1.3×10^4), 324 (1.8×10^4).

Synthesis of 2-bromo-6-(2′-thienyl)pyridine

A solution of 2-bromothiophene (8.1 g, 50 mmol) in dry diethyl ether (50 mL) was added dropwise to magnesium turnings (1.2 g, 50 mmol) in dry diethyl ether (10 mL) to afford a solution of the Grignard reagent 2-thienylmagnesium bromide. This solution was added slowly to a mixture of 2,6-dibromopyridine (11 g, 46 mmol) and [$PdCl_2$(dppb)] (0.8 g, 1 mmol) in dry diethyl ether (50 mL) at 0 °C. The mixture was stirred at room temperature for 14 h, following which a concentrated aqueous solution of NH_4Cl (*ca.* 30 mL) was added. The ether layer was collected and the aqueous layer was extracted twice with diethyl ether (2×50 mL). The combined ether layers were washed with brine and dried over $MgSO_4$. Evaporation of the solvent afforded a dark green oil that was left to stand at 10 °C for 3 days. During this time solid 2,6-dibromopyridine separated out and was removed by filtration. GC analysis of the residual oil showed that no 2,6-dibromopyridine was present and that the product was *ca.* 95% pure. Yield: 7.26 g, 55%. ^{1}H NMR ($CDCl_3$): δ 7.08 (1H, dd, $^3J_{HH}$ 5.50, $^3J_{HH}$ 3.81 Hz, $H_{Th\text{-}4}$), 7.28 (1H, dd, $^3J_{HH}$ 7.05, $^4J_{HH}$ 1.65 Hz, $H_{Py\text{-}5}$), 7.37–7.68 (4H, m, $H_{Py\text{-}3}$ + $H_{Py\text{-}4}$ + $H_{Th\text{-}3}$ + $H_{Th\text{-}5}$). MS (EI) *m*/*z*: 239.2 (M^+, ^{79}Br, 98%) and 241.2 (M^+, ^{81}Br, 100%).

Synthesis of diphenyl[6-(2′-thienyl)-2-pyridyl]phosphine 6

A solution of *n*-BuLi (30 mmol, 1.6 M, hexane) was added dropwise with cooling (0–5 °C) to a solution of PPh_2H (5.3 mL, 30 mmol) in dry THF (50 mL). The mixture turned orange immediately. It was stirred at room temperature for at least 4 h to ensure completion of the reaction. The crude 2-bromo-6-(2′-thienyl)pyridine (7.26 g, *ca.* 30 mmol) obtained from the previous step was dissolved in dry THF (50 mL) and the solution added slowly at 0 °C to the orange mixture. The reaction mixture was allowed to reach room temperature and stirred for 14 h. The subsequent work-up operations were performed under an atmosphere of nitrogen with deoxygenated solvents wherever possible. Dilute HCl solution (20 mL, pH = 2) was added with cooling to the reaction mixture followed by diethyl ether (30 mL). The organic layer was separated, washed with water (50 mL) and dried over $MgSO_4$. The solvent was evaporated, methanol added to the solid residue and the mixture left to stand at 4 °C for 2–3 days. The solid was filtered off, crushed finely under nitrogen and washed with cold methanol to give an off-white microcrystalline compound. Yield: 4.32 g, 42%, mp 94–95 °C. Found: C 72.6, H 4.6, N 3.9%. Calc. for $C_{21}H_{16}NPS$: C 73.0, H 4.7, N 4.1%. ^{31}P{^{1}H} NMR ($CDCl_3$): δ −3.64 (s). ^{1}H NMR ($CDCl_3$): δ 6.99 (1H, ddd, $^3J_{HP}$ 2.40, $^4J_{HH}$ 2.00, $^3J_{HH}$ 6.02 Hz, $H_{Py\text{-}5}$), 7.05 (1H, dd, $^3J_{HH}$ 3.73, $^3J_{HH}$ 5.05 Hz, $H_{Th\text{-}4}$), 7.30–7.40 (7H, m, $H_{Ph\text{-}3}$ + $H_{Ph\text{-}4}$ + $H_{Th\text{-}5}$), 7.42–7.58 (7H, m, $H_{Ph\text{-}2}$ + $H_{Py\text{-}3}$ + $H_{Py\text{-}4}$ + $H_{Th\text{-}3}$). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 117.2 (s, $C_{Py\text{-}3}$), 124.6 (s, $C_{Th\text{-}3}$), 126.3 (d, $^2J_{CP}$ 21.5 Hz, $C_{Py\text{-}5}$), 127.7–127.9 (m, $C_{Th\text{-}4}$ + $C_{Th\text{-}5}$), 128.4 (d, $^3J_{CP}$ 7.2 Hz, $C_{Ph\text{-}3}$), 129.0 (s, $C_{Ph\text{-}4}$), 134.3 (d, $^2J_{CP}$ 19.7 Hz, $C_{Ph\text{-}2}$), 136.1 (d, $^3J_{CP}$ 4.1 Hz, $C_{Py\text{-}4}$), 136.4 (d, $^1J_{CP}$ 10.0 Hz, $C_{Ph\text{-}1}$), 147.3 (d, $^1J_{CP}$ 12.7 Hz, $C_{Py\text{-}6}$), 150.9 (s, $C_{Th\text{-}2}$), 151.8 (s, $C_{Py\text{-}2}$). MS (EI) *m*/*z*: 344.6 ($M^+ - 1$). UV–vis (CH_2Cl_2), λ_{max}/nm (ε/M^{-1} cm^{-1}): 230 (1.3×10^4), 264 (1.4×10^4), 278 (1.4×10^4), 318 (1.1×10^4).

Synthesis of diphenyl{5-[6′-(diphenylphosphino)-2′-pyridyl]-2-thienyl}phosphine 7

A solution of *n*-BuLi (3.85 mmol, 1.6 M, hexane) was added slowly to a solution of diphenyl[6-(2′-thienyl)-2-pyridyl]phosphine (1.32 g, 3.82 mmol) in dry THF (25 mL) at −78 °C and the mixture stirred for 1 h at this temperature. A solution of PPh_2Cl (0.70 mL, 3.9 mmol) in dry THF (10 mL) was added to the mixture at −78 °C. The mixture was then warmed gradually to room temperature and stirred for a further 16 h. The mixture was hydrolysed with a concentrated aqueous NH_4Cl solution (10 mL), extracted with dichloromethane (3×20 mL) and then washed with brine. The organic solvent was evaporated, cold methanol (10 mL) added and the residual yellow oil left to stand at −25 °C. After *ca.* 20–25 days the oil crystallised out. The solid was dissolved in a minimal volume of dichloromethane and purified by means of centrifugal thin layer chromatography on a Chromatotron® (silica; hexane–diethyl ether, 6 : 1, v/v). An off-white crystalline material was obtained as the final product. Yield: 0.77 g, 38%, mp 159–160 °C. Found: C 74.9, 4.7, 2.6%. Calc. for $C_{33}H_{25}NP_2S$: 74.9, H 4.8, N 2.6%. ^{31}P{H} NMR ($CDCl_3$): δ −3.60 (s), −18.34 (s). ^{1}H NMR ($CDCl_3$): δ 7.01 (1H, ddd, $^3J_{HP}$ 1.74, $^4J_{HH}$ 1.65, $^3J_{HH}$ 7.05 Hz, $H_{Py\text{-}5}$), 7.28 (1H, dd, $^3J_{HH}$ 5.98, $^3J_{HH}$ 3.67 Hz, $H_{Th\text{-}4}$), 7.30–7.53 (22H, m, H_{Ph} + $H_{Py\text{-}3}$ + $H_{Py\text{-}4}$), 7.59 (1H, dd, $^4J_{HH}$ 1.35, $^3J_{HH}$ 3.66 Hz, $H_{Th\text{-}3}$). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 117.3 (s, $C_{Py\text{-}3}$), 125.6 (d, $^3J_{CP}$ 7.9 Hz, $C_{Th\text{-}3}$), 126.7 (d, $^2J_{CP}$ 21.8 Hz, $C_{Py\text{-}5}$), 128.4 (d, $^3J_{CP}$ 7.2 Hz, $C_{Ph\text{-}3}$), 128.9 (s, $C_{Ph\text{-}4}$), 134.3 (d, $^2J_{CP}$ 19.6 Hz, $C_{Ph\text{-}2}$), 136.1 (d, $^3J_{CP}$ 3.7 Hz, $C_{Py\text{-}4}$), 136.6 (d, $^1J_{CP}$ 8.9 Hz, $C_{Ph\text{-}1}$), 137.1 (d, $^2J_{CP}$ 22.5 Hz, $C_{Th\text{-}4}$), 137.8 (d, $^1J_{CP}$ 13.6 Hz, $C_{Th\text{-}5}$), 147.5 (d, $^1J_{CP}$ 15.2 Hz, $C_{Py\text{-}6}$), 150.7 (s, $C_{Th\text{-}2}$), 152.2 (s, $C_{Py\text{-}2}$). MS (EI) *m*/*z*: 529.3 (M^+). UV–vis (CH_2Cl_2), λ_{max}/nm (ε/M^{-1} cm^{-1}): 233 (2.5×10^4), 265 (2.0×10^4), 323 (2.0×10^4).

Synthesis of 2,6-bis[5′-(diphenylphosphino)-2′-thienyl]pyridine 8

A solution of *n*-BuLi (10 mmol, 1.6 M, hexane) was added dropwise to a solution of diphenyl(2-thienyl)phosphine (2.68 g, 10 mmol) in dry diethyl ether (20 mL) at 0 °C. The mixture was stirred for 2 h and solid $MgBr_2 \cdot Et_2O$ (2.58 g, 10 mmol) was added portionwise under a nitrogen blanket over a period of 10 min. The reaction was allowed to proceed for 1 h and the solution then transferred *via* a cannula to a dropping funnel. The mixture was added dropwise to a solution of 2,6-dibromopyridine (1.18 g, 5 mmol) in dry THF (20 mL) at 0 °C to which [$NiCl_2$(dppp)] (0.10 g) had been added. The resulting solution was allowed to warm up to room temperature and stirred for 16 h. The mixture was hydrolysed with a concentrated aqueous NH_4Cl solution, extracted with dichloromethane (3×25 mL), washed with brine, dried and the solvent evaporated. The residue was washed with cold methanol (*ca.* 15 mL) and then recrystallised from methanol or, alternatively, purified by column chromatography (silica; hexane–diethyl ether, 2 : 1, v/v). Greenish crystals were obtained of the pure product. Yield: 1.65 g, 54%, mp 175–176 °C. Found: C 72.8, H 4.3, N 2.3%. Calc. for $C_{37}H_{27}NP_2S_2$: C 72.7, H 4.5, N 2.3%. ^{31}P{^{1}H} (CD_2Cl_2): δ −18.28 (s). ^{1}H NMR (CD_2Cl_2): δ 7.25 (2H, dd, $^3J_{HP}$ 5.82, $^3J_{HH}$ 3.66 Hz, $H_{Th\text{-}4}$), 7.31–7.47 (22H, m, H_{Ph} + $H_{Py\text{-}3}$), 7.58–7.68 (3H, m, $H_{Th\text{-}3}$ + $H_{Py\text{-}4}$). ^{13}C{^{1}H} NMR (CD_2Cl_2): δ 117.8 (s, $C_{Py\text{-}3}$), 126.0 (d, $^3J_{CP}$ 7.7 Hz, $C_{Th\text{-}3}$), 128.8 (d, $^3J_{CP}$ 7.1 Hz, $C_{Ph\text{-}3}$), 129.3 (s, $C_{Ph\text{-}4}$), 133.4 (d, $^2J_{CP}$ 19.9 Hz, $C_{Ph\text{-}2}$), 137.4 (d, $^2J_{CP}$ 26.1 Hz, $C_{Th\text{-}4}$), 137.8 (s, $C_{Py\text{-}4}$), 138.0 (d, $^1J_{CP}$ 7.8 Hz, $C_{Ph\text{-}1}$), 141.2 (d, $^1J_{CP}$ 30.8 Hz, $C_{Th\text{-}5}$), 150.9 (s, $C_{Th\text{-}2}$), 152.0 (s, $C_{Py\text{-}2}$). MS (direct injection): *m*/*z*: 610.75 ($M^+ - 1$). UV–vis (CH_2Cl_2), λ_{max}/nm (ε/M^{-1} cm^{-1}): 230 (3.3×10^4), 265 (2.7×10^4), 323 (2.7×10^4), 345 (2.8×10^4).

Crystal structure determinations †

Crystals of **1** (pale yellow needles), **7** (colourless blocks) and **8** (greenish blocks) were grown as follows: for **1**, by slow evaporation of a solution of the compound in chloroform; for **7**, by slow evaporation of a solution of the compound in petroleum ether (60–80 °C)–diethyl ether (6 : 1, v/v); for **8**, by slow evaporation of a solution of the compound in hexane–diethyl ether (2 : 1, v/v). Crystal data and details of the crystallographic

† CCDC reference numbers 169046–169048. See http://www.rsc.org/suppdata/p1/b1/b107389n/ for crystallographic files in .cif or other electronic format.

Table 2 Crystal and refinement data

	1	**7**	**8**
Formula	$C_{32}H_{24}P_2S_2$	$C_{33}H_{25}NP_2S$	$C_{37}H_{27}NP_2S_2$
Formula weight	534.57	529.54	611.66
Crystal system	Monoclinic	Monoclinic	Triclinic
Space group	$P2_1/c$	$P2_1/n$	$P\bar{1}$
a/Å	8.954(2)	8.408(5)	9.032(2)
b/Å	19.678(3)	15.978(6)	13.312(3)
c/Å	8.877(2)	20.402(7)	13.577(2)
α/deg	90	90	85.85(2)
β/deg	117.93(2)	101.11(4)	82.69(2)
γ/deg	90	90	73.77(2)
V/Å^3	1382(1)	2690(2)	1554(1)
Z	2	4	2
D_c/g cm^{-3}	1.285	1.308	1.308
T/K	293(2)	293(2)	293(2)
μ/mm^{-1}	0.328	0.263	0.302
F(000)	556	1104	636
Total no. of reflections measured	2508	3925	4946
Independent reflections	1923 [R_{int} = 0.0165]	3616 [R_{int} = 0.0251]	4301 [R_{int} = 0.0167]
Reflections observed [$I > 2\sigma(I)$]	1652	2173	3311
Refinement type	F^2	F^2	F^2
$R_1[I > 2\sigma(I)]$; R_1[all data]	0.0421, 0.0525	0.0525, 0.1276	0.0374, 0.0599
No. of refined parameters	164	335	380
(Shift/esd)$_{max}$	0.001	0.001	0.001
Max, min $\Delta\rho$/e Å^{-3}	0.46, −0.27	0.28, −0.24	0.47, −0.16

study for **1**, **7** and **8** are reported in Table 2. Intensity data were obtained on an Enraf-Nonius CAD4 diffractometer, using graphite monochromated Mo-Kα radiation and the ω-2θ scan technique. Unit cell parameters were obtained by least-squares fitting of 25 reflections monitored in the range $3° < \theta < 12°$. There was a sharp fall-off in the percentage of observed data [$I > 2\sigma(I)$] above $2\theta = 46°$, and for this reason data beyond this limit were not collected. The diffraction data were corrected for Lorentz, polarisation, and absorption (χ scans of 9 reflections) effects; the intensities of three standard reflections showed no variations greater than those predicted by counting statistics. The structures were solved by direct and Fourier methods and refined by full-matrix least-squares using SHELXS-97,[28] with anisotropic displacement parameters for all non-hydrogen atoms, and isotropic displacement parameters for the hydrogen atoms. The diagrams of the molecular structures were produced by the ORTEP program.[29]

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24 See ref. 5. The UV–vis absorption spectrum was measured in dichloromethane to allow direct comparison with the data from this work: λ_{max}/nm (ε/M^{-1} cm^{-1}): 253 (0.88×10^4), 356 (2.2×10^4).
25 See ref. 5. The UV–vis absorption spectrum was measured in dichloromethane to allow direct comparison with the data from this work: λ_{max}/nm (ε/M^{-1} cm^{-1}): 270 (sh, 0.83×10^4), 303 (1.5×10^4).
26 See ref. 5. The UV–vis absorption spectrum was measured in dichloromethane to allow direct comparison with the data from this work: λ_{max}/nm (ε/M^{-1} cm^{-1}): 260 (1.1×10^4), 287 (1.3×10^4), 333 (1.0×10^4).
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