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LETTERS

Fulvene formation on attempted protection of a C_2 symmetric ferrocenyl bisphosphine as its sulfide

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Abstract

Attempted protection of the phosphines in the C_2 symmetric ferrocene, 1,1′-bis[(*S*)-4-isopropyloxazolin-2-yl]-2,2′-diphenylphosphinoferrocene, as their sulfides failed to give the desired product. Fragmentation of the, typically stable, ferrocene system occurred with the phosphine substituted fulvene, 5-[(4*S*)-4-isopropyl-1,3-oxazolan-2-yliden]-1,3-cyclopentadienyl (diphenyl)phosphine sulfide, being isolated. © 1999 Elsevier Science Ltd. All rights reserved.

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The use of transition metal based catalysts to conduct organic transformations is becoming increasingly common.[1] A number of approaches have been reported to allow the introduction of asymmetry into this process, the most elegant of which is the use of optically active ligands for the metal.[2,3]

We are interested in chiral C_2 symmetric ligands and in partricular those based upon 1,1′-bis-diphenylphosphinoferrocene.[4,5] We recently reported a short, but racemic, synthesis of the diphosphine [1,1′-bis-(diphenylphosphino)-2,2′-bis-(methoxymethyl)]ferrocene,[6] direct resolution of this material was achieved by HPLC (Chiracel® OD-H), however, methods employed for large scale resolution[7,8] proved unsuccessful and an asymmetric synthesis was therefore required. Ferrocenes exhibiting planar chirality have been prepared by a number of routes. The application of chiral bases[9] has met with limited success, however, the use of an optically active functional group for the directed metallation of the ferrocene ring system has been more successful. Groups employed in this role include sulfoxides,[10] acetals,[11] hydrazones[12] and amines.[13,14] The oxazoline group[15–18] has proved extremely efficient in this regard allowing highly diastereoselective lithiation of the ferrocene to be carried out. Thus, our efforts have concentrated on this approach.

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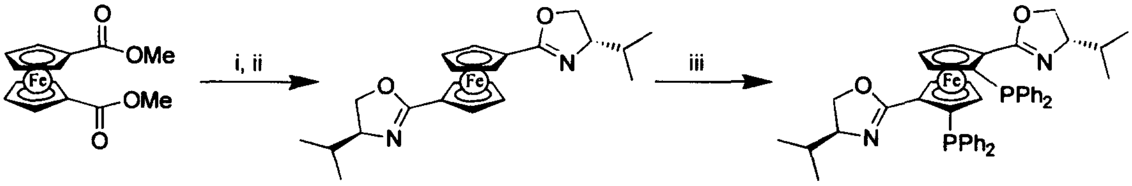
1,1′-Bis-(methoxycarbonyl)ferrocene, **1**, was prepared from ferrocene, via the stannane, as this procedure was more consistent regarding yields than other more direct alternatives (Scheme 1). Conversion to the amido alcohol and then ring closure by treatment with methanesulfonyl chloride and triethylamine proceeded to give the chiral oxazoline as expected. Lithiation with ^{s}BuLi in THF gave a 5:1 mixture of diastereoisomers of the bis-phosphine which were easily separated by chromatography [Al_2O_3, ethyl acetate:petroleum ether, bp 60–80°C (15:100)] resulting in optically pure material.[19] For our goals subsequent modification of the oxazoline group was required and a range of conditions were investigated. The phosphine moiety proved sensitive to a number of these and protection of this functionality was therefore deemed necessary.



1 **2** **3**

Scheme 1. Reagents and conditions: (i) (*S*)-valinol, Me_3Al, 94%; (ii) MsCl, Et_3N, 84%; (iii) ^{s}BuLi, Ph_2PCl, 66%

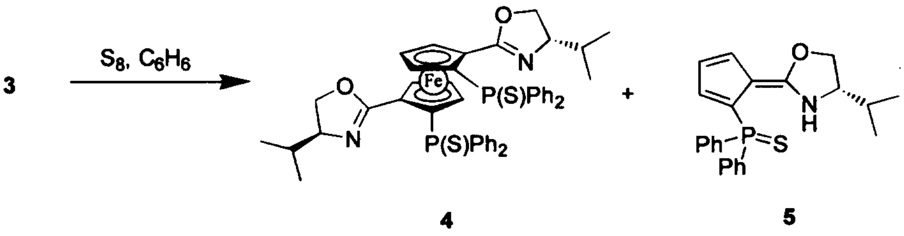
We have routinely converted ferrocenyl phosphines to their sulfides, as a means of protection and to aid in their isolation and purification. This is typically achieved in excellent yield by treatment with elemental sulfur, however initial attempts at the derivatization of **3** (Table 1: entries 1 and 2) proved unsuccessful with only starting material being recovered. A switch to benzene as the solvent resulted in complete consumption of **3**. However, variation in the reaction conditions (Table 1: entries 3–11) failed to give the desired bis-phosphine sulfide, **4** in greater than trace amounts (Scheme 2). The use of cyclohexene sulfide, a mild sulfurization reagent,[20,21] also proved unsuccessful (Table 1: entries 12–14).

As the desired bis-phosphine sulfide, **4** only accounted for some of the starting material the fate of the remainder needed to be established. An orange crystalline material was isolated and this was identified,

Table 1
Attempted formation of bis-phosphine sulfide, **4**

Entry	S_8/equiv.	Solvent	T/ °C	t/ h	Product
1	3.0	PhMe	110	3	**3**
2	3.0	PhMe	25	24	**3**
3	3.0	CH_2Cl_2	40	1	**5**[a]
4	3.0	C_6H_6	80	1	**5**[a]
5	2.2	C_6H_6	80	1.5	**5**[a]
6	2.2	C_6H_6	80	3	**5**[a]
7	2.2	C_6H_6	80	5	**5**
8	1.7	C_6H_6	25	18	**5**[a]
9	1.7	C_6H_6	25	96	**5**
10	1.7	C_6H_6	45	3	**5**[a]
11	1.0	C_6H_6	80	1	**5**[a]
12	2.0[b]	c	60 - 80	3	**5**[a]
13	3.0[b]	c	60 - 80	1.5	**5**[a]
14	3.0[b]	c	60 - 80	72	**5**

[a] Trace of **4** also detected by ^1H nmr and tlc
[b] Cyclohexene sufide
[c] Petroleum ether

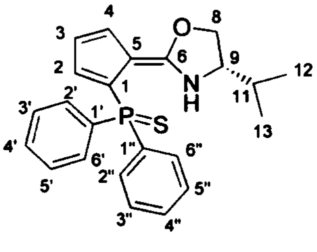


Scheme 2.

by 2D NMR studies, as the phosphine substituted fulvene, **5**.[†] This was later confirmed by single crystal X-ray analysis (Fig. 1).[‡]

Numerous attempts at regeneration of the ferrocene system, by treatment of **5** with $FeCl_2$, proved unsuccessful. In certain cases, the arylation of ferrocene has been shown to lead to fragmentation,[22] two recent reports have also described the generation of fulvenes from substituted ferrocenes; by the addition of acid to ferrocenyl methyl alcohols[23] and by the action of light on nitro-substituted ferrocenes.[24] The process described here is fundamentally different.

[†] 5-[(4*S*)-4-Isopropyl-1,3-oxazolan-2-yliden]-1,3-cyclopentadienyl(diphenyl)phosphine sulfide, **5**. A solution of 2,2′-bis-[(*S*)-4-isopropyloxazolin-2-yl]-(*S*)-(*S*)-1,1′-bis-(diphenylphosphino)ferrocene (85 mg, 0.11 mmol) and sulfur (8 mg, 0.25 mmol) in benzene (6 ml) was heated at reflux for 5 h. The solvent was removed under reduced pressure and the residue purified by flash column chromatography, eluting with ether:hexane (1:1) to give the title compound as a pale orange crystalline solid (63 mg, 0.16 mmol, 73%); mp 165–167°C (from dichloromethane-ether); silica gel tlc R_f 0.64 (hexane:ether, 1:4); $[\alpha]_D^{22}$ +185.3 (*c* 0.95, $CHCl_3$); (found C, 69.98; H, 6.13; N, 3.46. $C_{23}H_{24}NOPS$ requires C, 70.21; H, 6.15; N, 3.56.); ν_{max}/cm^{-1} (KBr) 2956, 1602, 1477, 1436, 1349, 1197, 1102, 1083, 1058, 1000; δ_H (270 MHz; $CDCl_3$) 10.67 (1H, s, NH), 7.65–7.75 (4H, m, H2′, H6′, H2″, H6″), 7.35–7.50 (6H, m, H3′, H4′, H5′, H3″, H4″, H5″), 7.06–7.10 (1H, m, H4), 6.13 (1H, m, H3), 5.92 (1H, m, H2), 4.50 (1H, t, H8β *J* 8.9 Hz), 4.22 (1H, dd, H8α *J* 5.9, 8.9 Hz), 3.85 (1H, m, H9), 1.51 (1H, octet, H11 *J* 6.7 Hz), 0.72 (3H, d, 3H12 or 3H13 *J* 6.7 Hz), 0.61 (3H, d, 3H13 or 3H12 *J* 6.7 Hz); δ_C (68 MHz; $CDCl_3$) 165.12 (C5), 134.6 (C1′ or C1″, d, $^1J_{C\text{-}P}$ 36 Hz), 133.38 (C1″ or C1′, d, $^1J_{C\text{-}P}$ 36 Hz), 132.62 (C2′/C6′ or C2″/C6″, d, $^2J_{C\text{-}P}$ 11 Hz), 132.39 (C2), 132.30 (C2″/C6″ or C2′/C6′, d, $^2J_{C\text{-}P}$ 11 Hz), 131.36 (C4′ or C4″, d, $^4J_{C\text{-}P}$ 3 Hz), 131.26 (C4″ or C4′, d, $^4J_{C\text{-}P}$ 3 Hz), 128.30 (C3′/C5′ or C3″/C5″, d, $^3J_{C\text{-}P}$ 4 Hz), 128.10 (C3″/C5″ or C3′/C5′, d, $^3J_{C\text{-}P}$ 4 Hz), 125.57 (C4, d, $^3J_{C\text{-}P}$ 10 Hz), 115.75 (C3, d, $^3J_{C\text{-}P}$ 16 Hz), 111.35 (C1, d, $^1J_{C\text{-}P}$ 98 Hz), 102.05 (C5 $^2J_{C\text{-}P}$ 13 Hz), 71.85 (C8), 62.37 (C9), 32.27 (C11), 18.24 (C12 or C13), 17.21 (C13 or C12); δ_p (162 MHz; $CDCl_3$) 35.56; *m/z* (CI^+) 395(20%), 394 ($M+H^+$, 72), 393 (M^+, 100), 217(18), 208(90), 51(16), 49(67); [found: $M+H^+$, 394.1396; $C_{23}H_{25}NOPS$ requires 394.1394].



Compound numbering for NMR assignment only

[‡] Crystal data for **5**: $C_{23}H_{24}NOPS$ M=393.5, orthorhombic, $P2_12_12_1$ (no. 19), a=8.892(1), b=10.589(2), c=22.296(2) Å, V=2099.4(5) Å^3, Z=4, D_c=1.245 g cm^{-3}, μ (Mo–Kα)=2.43 cm^{-1}, $F(000)$=832, T=293 K; orange/red prisms, 0.73×0.23×0.23 mm, Siemens P4/PC diffractometer, ω-scans, 2139 independent reflections. The structure was solved by direct methods and all of the non-hydrogen atoms were refined anistropically using full matrix least-squared based on F^2 to give R_1=0.0444, wR_2=0.103 for 1808 independent observed reflections [$|F_o|>4s(|F_o|)$, $2\theta\leq 50°$] and 225 parameters. The absolute stereochemistry of the structure was confirmed by a combination of R-factor tests [R_1^+=0.0444, R_1^-=0.0450] and by use of the Flack parameter [x^+=–0.05(18), x^-=+1.05(18)]. Deposited at the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ.

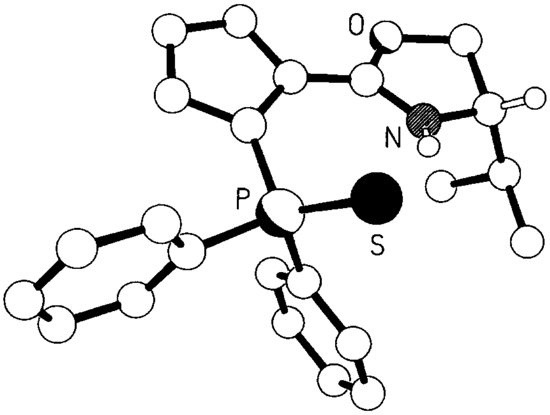


Figure 1. X-Ray structure of **5**

In summary, we have highlighted a novel example of the fragmentation of the, typically stable, ferrocene system by the action of sulfur. This may be due to the high affinity that iron has for this element and/or the steric crowding associated with these structures.

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