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A novel synthesis of 1,1′-unsymmetrical disubstituted heteroarylferrocene

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Abstract

Stepwise Stille coupling reaction of 1,1′-bis(tributylstannyl)ferrocene with different heterocyclic bromides was achieved in the presence of Pd-complex catalyst via two steps to afford unsymmetrical 1,1′-disubstituted heteroarylferrocene compounds. © 2000 Elsevier Science B.V. All rights reserved.

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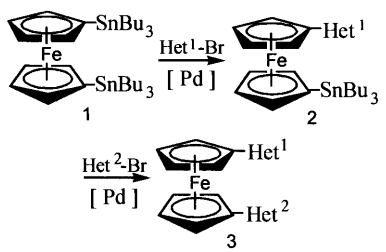
1. Introduction

Considerable attention was recently focused on the synthesis of 1,1′-heterodisubstituted ferrocene compounds [1–8] because of their potential applications in various fields such as electrochemistry [9–12], catalysis [13], organic synthesis [14,15] and materials sciences [16–19]. In a series of precursors synthesizing unsymmetrical 1,1′-disubstituted ferrocenes, the 1-lithio-1′-bromo, 1-lithio-1′-tributylstannyl and 1-lithio-1′-phosphinoferrocene are considered to be the most important ones, which can be generated through selective transmetalation of 1,1′-dibromoferrocene [2,4–6,20], 1,1′-bis(tributylstannyl)ferrocene [21,22], and 1,1′-ferrocenediylphenylphosphine [23] with *n*-butyllithium at low temperature. Many heteroannularly substituted ferrocene derivatives, such as bromo-, phosphino-, amino-, stannyl-compounds were prepared via this reaction. The bromo- and stannyl-compounds were usually used as intermediates to proceed further syntheses, while phosphino- and amino-compounds were used as ligands in some catalytic process.



Scheme 1.

Two popular methods are available for the synthesis of heteroarylferrocene compounds. The simpler one is direct introduction of heteroaryl groups into Cp-rings of ferrocene via the coupling reaction of the lithiated ferrocene moiety with heterocycles or lithiated heterocycles with bromoferrocene [8,23–29]. However, it was only suited to the synthesis of some special structural heterocyclic ferrocenes, such as α-ferrocenyl pyridine, polypyridine and fused pyridine derivatives. Another method was indirect formation of heteroarylferrocenes [30] through classical multistep cyclization approaches. Clearly, the lithiated ferrocene intermediates are only suitable for some special substrates, and classical methods are too tedious to synthesize complicated heteroarylferrocenes, especially unsymmetrical disubstituted heteroarylferrocene derivatives. The 1,1′-unsymmetrical disubstituted heteroarylferrocenes were scarcely reported so far, maybe due to the difficulties of their synthesis.

In our previous communications [28,29,31], we reported a simple way for the preparation of various

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monoheteroarylferrocene compounds via Stille coupling of tributylstannylferrocene with various heterocyclic bromides. Following our initial studies, we found that the 1,1′-bis(tributylstannyl)ferrocene ($Fc(SnBu_3)_2$) could proceed not only in selective transmetalation reaction but also do selective monosubstituted Stille across-coupling smoothly. In the present work we wish to report a new method of synthesizing unsymmetrical 1,1′-diheteroarylferrocenes.

2. Results and discussion

The different heteroaryls can be introduced stepwise into the Cp-rings of ferrocene as shown in Scheme 1.

To find the optimum conditions suitable for this reaction, two primary factors were examined: ratio of two substrates and reaction temperature. In the first step (entries 1–3), we used $PdCl_2(PPh_3)_2$ as the catalyst in dry DMF and illustrated that (i) if stoichiometrical 1,1′-bis(tributylstannyl)ferrocene($Fc(SnBu_3)_2$) was used, large monosubstituted heteroferrocene [32], unreacted bromide and some tributylstannyl-losing products (i.e. ferrocene and tributylstannylferrocene) were found, which lead to the difficult isolation of desired product; (ii) excess $Fc(SnBu_3)_2$ can promote the consumption of bromide, otherwise, the first coupling rate was correspondingly increased, which results in the decreased loss of the tributylstannyl group; (iii) 150% excess of $Fc(SnBu_3)_2$ is essential in the first step. In contrast, 120% of heterocyclic bromides(Het^2–Br) must be used in the second step (entries 4–9) to insure the desired coupling could proceed as quick as possible. Concerning the reaction temperature, we found that 100–125°C is a suitable range in the first step. Higher temperatures will lead to more loss of tributylstannyl group. In contrast, lower temperatures would prolong the reaction time in order to make the reaction complete, which equally results in more loss of tributylstannyl group. The results are summarized in Table 1.

To further simplify the operation procedure, we attempted to synthesize the title compounds in one pot under different ratio of substrates. The results, however, were all unsatisfactory because of the difficulties of tedious separation of the products. Therefore further investigation was not continued.

In conclusion, the selective substitution of 1,1′-bis(tributylstannyl)ferrocene by the Stille cross-coupling opens a convenient new area of synthesizing various unsymmetrical 1,1′-disubstituted heteroarylferrocene derivatives.

3. Experimental

Melting points were determined on a Thomas Hoover capillary melting point apparatus and were uncorrected. ^{1}H-NMR spectra were measured on a FC-80A spectrometer in $CDCl_3$ with tetramethylsilane as an internal standard. IR spectra were performed as KBr pellets on a Nicolet 179SX FTIR spectrometer. Mass spectra (MS) were taken on Finnigan TQ70 or HP-5988 AG. CMS mass spectrometer.

*3.1. 1-Tributylstannyl-1′-heteroarylferrocene (**2**)*

3.1.1. General procedure

To the mixture of 1,1′-bis(tributylstannyl)ferrocene (**1**, 6.15 g, 8.05 mmol) and $PdCl_2(PPh_3)_2$ (0.18 g, 0.26 mmol) in dry DMF(15 ml), a corresponding bromide (5.36 mmol) was added with stirring. The mixture was heated on an oil bath at 100–125°C for the time given in the table. After cooling the reaction mixture to r.t., saturated ammonium chloride solution was added into the mixture. Then the mixture was extracted with petroleum ether (30–60°C) or diethyl ether, washed with saturated KF solution and water. The organic layer was dried ($MgSO_4$), filtered and concentrated in vacuo. The crude product was subjected to column chromatography on neutral or alkaline Al_2O_3 and afforded corresponding products **2**.

Table 1
The results of stepwise Stille cross-coupling

Entry	Catalysts	Time (h)	Products	Yields (%)	M.p.(°C) [a]
First step					
1	$PdCl_2(PPh_3)_2$	1.0	**2a**	70	
2	$PdCl_2(PPh_3)_2$	1.5	**2b**	85	
3	$PdCl_2(PPh_3)_2$	1.5	**2c**	83	
Second step					
4	$PdCl_2$(dppf)	3.0	**3a**	75	226–228
5	$PdCl_2$(dppf)	3.0	**3b**	81	184–186
6	$PdCl_2$(dppf)	2.5	**3c**	65	194–196
7	$PdCl_2$(dppf)	2.0	**3d**	78	95–98
8	$PdCl_2$(dppf)	2.0	**3e**	60	171–173
9	$PdCl_2$(dppf)	1.5	**3f**	80	160–162

[a] Uncorrected.

3.2. 1-Tributylstannyl-1′-(2-nitropyrid-5-yl)ferrocene (**2a**)

Deep red oil (70%): ^{1}H-NMR($CDCl_3$) 8.66(d, $J = 2.2$ Hz, 1H), 8.20(d, $J = 8.2$Hz, 1H), 7.99(dd, $J = 2.2$, 8.2 Hz, 1H), 4.75(m, 2H), 4.49(m, 2H), 4.21(m, 2H), 3.96(m, 2H), 1.78–0.90(m, 27H); IR (cm^{-1}): 3080, 2958, 2927, 2867, 1577, 1533, 1462, 1089, 1024; Anal. Found: C, 54.64; H, 6.67; N, 4.38. Calc. for $C_{27}H_{38}FeN_2O_2Sn$: C, 54.36; H, 6.37; N, 4.69%.

3.3. 1-Tributylstannyl-1′-(8-methyl-6-nitro-quino-5-yl)ferrocene (**2b**)

Deep red oil (85%): ^{1}H-NMR($CDCl_3$) 9.28(d, $J = 2.2$ Hz, 1H), 8.58(d, $J = 2.3$ Hz, 1H), 8.29(d, $J = 2.2$ Hz, 1H), 8.19(d, $J = 2.3$ Hz, 1H), 4.79(m, 2H), 4.45(m, 2H), 4.24(m, 2H), 3.96(m, 2H), 2.99(s, 3H), 1.86–0.82(m, 27H); IR(cm^{-1}): 3084, 2958, 2927, 2865, 1612, 1528, 1093, 1026, 435; Anal. Found: C, 60.89; H, 6.23; N, 3.96. Calc. for $C_{32}H_{42}FeN_2O_2Sn$: C, 60.57; H, 6.00; N, 4.00%.

3.4. 1-Tributylstannyl-1′-(6-methyl-8-nitro-quino-5-yl)ferrocene (**2c**)

Deep red oil (83%): ^{1}H-NMR($CDCl_3$) 9.18(d, $J = 2.1$ Hz, 1H), 8.86(d, $J = 1.9$ Hz, 1H), 8.03(d, $J = 2.1$ Hz, 1H), 7.89(d, $J = 1.9$ Hz, 1H), 4.73(m, 2H), 4.42(m, 2H), 4.21(m, 2H), 3.95(m, 2H), 2.60(s, 3H), 1.82–0.80(m, 27H); IR(cm^{-1}): 3043, 2958, 2927, 2865, 1532, 1461, 1085, 1027; Anal. Found: C, 60.83; H, 6.18; N, 3.98. Calc. for $C_{32}H_{42}FeN_2O_2Sn$: C, 60.57; H, 6.00; N, 4.00%.

3.5. Unsymmetrical 1,1′-disubstituted heteroarylferrocene (**3**)

3.5.1. General procedure

The mixture of **2** (0.2 mmol) and the corresponding bromides (0.24 mmol) in dry DMF (5 ml) was heated on oil bath to 120°C, catalyst, $PdCl_2$(dppf) (0.88 mg, 0.0012 mmol) was added in one portion, then the mixture was stirred at 120–130°C for the time given in the table. After cooling to r.t., saturated aminium chloride solution was added and then extracted with ether or dichloromethane, washed with saturated KF solution, water, dried over $MgSO_4$, and the solvent was removed under reduced pressure. Finally, The residue was separated by column chromatography on silica gel eluting with petroleum–acetone to afford corresponding product **3**.

3.6. 1-(2-Nitro-pyrid-5-yl)-1′-(5-acetalthien-2-yl)ferrocene (**3a**)

Deep red solid (mp 226–228°C): ^{1}H-NMR($CDCl_3$, δ, ppm) 2.48(s, 3H), 4.40(m, 2H), 4.54(m, 2H), 4.61(m, 2H), 4.78(m, 2H), 6.62(d, $J = 3.7$Hz, 1H), 7.25(d, $J = 3.7$ Hz, 1H), 7.70(dd, $J = 1.9$, 8.4 Hz, 1H), 7.97(d, $J = 8.4$, 1H), 8.39(d, $J = 1.9$ Hz, 1H); IR(cm^{-1}, KBr) 1738, 1645, 1540, 1465, 1101, 1015, 486; MS (m/z) 432(M, 58.43%), 56(21.61%), 43(68.95%).

3.7. 1-(2-Nitro-pyrid-5-yl)-1′-(5-benzoylthien-2-yl)ferrocene (**3b**)

Deep red solid (mp 184–186°C): ^{1}H-NMR(400 Hz, $CDCl_3$) 4.41(s, 2H), 4.54(s, 2H), 4.64(s, 2H), 4.79(s, 2H), 6.68(d, 1H, $J = 3.8$), 7.22(d, 1H, $J = 3.8$), 7.50–7.62(m, 5H), 7.69(d, 1H, $J = 8.3$), 7.98(d, 1H, $J = 8.3$); 8.40(s, 1H); IR(cm^{-1}, KBr) 1725, 1618, 1530, 1460, 1101, 1024; MS (m/z) 432(M, 58.43%), 56(21.61%), 43(68.95%).

3.8. 1-(8-Methyl-6-nitro-quino-3-yl)-1′-(5-acetalthien-2-yl)ferrocene (**3c**)

Deep red solid (mp 194–196°C): ^{1}H-NMR(400 Hz, $CDCl_3$) 2.20(s, 3H), 2.87(s, 3H), 4.42(m, 2H), 4.50(m, 2H), 4.58(m, 2H), 4.81(m, 2H), 6.53(d, 1H, $J = 3.8$), 6.92(d, 1H, $J = 3.8$), 7.83(d, 1H), 8.28(s, 1H), 8.40(s, 1H); 8.98(s, 1H); IR(cm^{-1}, KBr) 1740, 1650, 1529, 1463, 1086, 1032; MS (m/z) 496(M, 100%), 56(7.80%), 43(12.04%).

3.9. 1-(8-Methyl-6-nitro-quino-3-yl)-1′-(5-benzoylthien-2-yl)ferrocene (**3d**)

Deep red solid (mp 94–98°C): ^{1}H-NMR($CDCl_3$) 2.79(s, 3H), 4.45(m, 2H), 4.51(m, 2H), 4.64(m, 2H), 4.86(m, 2H), 6.63(d, 1H, $J = 4.0$), 6.98(d, 1H, $J = 4.0$), 7.40–7.78(m, 5H), 7.89(d, 1H), 8.16(s, 1H), 8.43(s, 1H); 9.03(s, 1H); IR(cm^{-1}, KBr) 1727, 1610, 1519, 1466 1071, 1026, 969, 504; MS (m/z) 558(M, 100%), 105(29.49%), 77(19.97%), 57(18.41%), 56(6.45%), 43(12.04%).

3.10. 1-(6-Methyl-8-nitro-quino-3-yl)-1′-(5-acetylthien-2-yl)ferrocene (**3e**)

Deep red solid (mp 171–173°C): ^{1}H-NMR($CDCl_3$) 2.16(s, 3H), 2.61(s, 3H), 4.45(m, 2H), 4.52(m, 2H), 4.84(m, 2H), 4.86(m, 2H), 6.45(d, 1H, J3.9), 6.82(d, 1H, $J = 3.9$), 7.75(d, 1H), 7.83(d, 1H), 8.07(d, 1H), 9.19(s, 1H); IR(cm^{-1}, KBr) 1721, 1651, 1596, 1531, 1117, 1032, 497; MS (m/z) 496(M, 8.56%), 57(13.17%), 43(22.54%).

3.11. 1-(6-Methyl-8-nitro-quino-3-yl)-1′-(5-benzoylthien-2-yl)ferrocene (**3f**)

Deep red solid (mp 160–162°C): ^{1}H-NMR($CDCl_3$) 2.44(s, 3H), 4.41(m, 2H), 4.48(m, 2H), 4.63(m, 2H), 4.81(m, 2H), 6.53(d, 1H, $J = 4.0$), 6.97(d, 1H, $J = 4.0$), 7.40–7.95(m, 8H), 8.96(d, 1H); IR(cm^{-1}, KBr) 1722, 1620, 1527, 1467 1088, 1026, 498; MS (m/z) 558(M, 28.11%), 105(26.28%), 77(33.92%).

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References

[1] G.G.A. Balavoin, J.-C. Daran, G. Iftime, E. Manoury, C. Moreau-Bossuet, J. Organomet. Chem. 567 (1998) 191.
[2] I.R. Butler, S.C. Ouayle, J. Organomet. Chem. 552 (1998) 63.
[3] C.-S. Li, J.C. Medina, G.E.M. Maguire, E. Abel, J.L. Atwood, G.W. Gokei, J. Am. Chem. Soc. 119 (1997) 1609.
[4] T.Y. Dong, C.K. Chang, S.H. Lee, L.L. Lai, M.Y.N. Chiang, K.J. Lin, Organometallics 16 (1997) 2773; 5816.
[5] T.Y. Dong, X.Q. Lai, Z.W. Lin, K.-J. Lin, Angew. Chem. Int. Ed. Engl. 36 (1997) 2002.
[6] X.-Q. Lai, T.-Y. Dong, J. Chem. Soc. Chem. Commun. (1994) 2347.
[7] C. Guillon, P. Vierling, J. Organomet. Chem. 464 (1994) C42.
[8] I.R. Butler, S.J. Mcdonald, Polyhedron 14 (1995) 529.
[9] K. Uosaki, T. Kondo, X.-Q. Zhang, M. Yanagida, J. Am. Chem. Soc. 119 (1997) 8367.
[10] C.-R. Zhang, K.-Z. Yang, W.-R. Jin, Thin Solid Films 284–285 (1996) 533.
[11] X.D. Cai, Y.S. Jiang, W.S. Yang, D. Zhang, Y.W. Cao, Z.J. Zhu, T.J. Li, Gaodeng Xuexiao Huaxue Xuebao 17 (1996) 1899.
[12] P. Stepnicka, R. Gyepes, Organometallics 16 (1997) 5089.
[13] (a) H. Brunner, M. Janura, Synthesis (1998) 45. (b) J.T. Yli-Kauhaluoma, J.A. Ashley, C.H. Lo, L. Tucker, M.M. Wolfe, K.D. Janda, J. Am. Chem. Soc. 117 (1995) 7041.
[14] P. Stepnicka, J. Podlaha, R. Gyepes, M. Polasek, J. Organomet. Chem. 552 (1998) 293.
[15] Y.J. Wu, X.L Cui, Y.H. Lin, H.Z. Yuan, X.A. Mao, J. Organomet. Chem. 543 (1997) 63.
[16] X.D. Cai, D. Zhang, Y.S. Jiang, Y.W. Cao, Huaxue Xuebao 55 (1997) 650.
[17] Y.W. Cao, X.D. Chai, W.S. Yang, R. Lu, Y.S. Jiang, T.J. Li, M. Blanchard-Desce, J.M. Lehn, Thin Solid Films 284–285 (1996) 859.
[18] N.J. Thompson, J.W. Goodby, K.J. Toyne, Liq. Cryst. 13 (1993) 381.
[19] K.J. Toyne, N.J. Thompson, Brit., 2,269,383 (1994); C.A. 121, 46783.
[20] L.L. Lai and T.-Y. Dong, Synthesis (1995) 1231.
[21] M.E. Wright, Organometallics 9 (1990) 853.
[22] T. Sammakia, H.A. Latham, J. Org. Chem. 61 (1996) 1629.
[23] I.R. Butler, Polyhedron 11 (1992) 3117.
[24] K. Schlogl, M. Fried, Monatsh Chem. 94 (1963) 537.
[25] I.R. Butler, N. Burke, L.J. Hobson, H. Findenegg, Polyhedron 11 (1992) 2435.
[26] A.N. Nesmeyanov, V.A. Sazonova, V.N. Drozd, Doklady Akad. Nauk. SSSR 154 (1964) 158(C.A. 60, 9309).
[27] J.G.P. Delis, P.W.N.M. van Leeuwen, K. Vrieze, N. Veldman, A.L. Spek, J. Fraanje, K. Goubitz, J. Organomet. Chem. 514 (1996) 125.
[28] C.-M. Liu, J.-J. Zhai, Y.-X. Ma, Y.-M. Liang, Synth. Commun. 28 (1998) 2371.
[29] C.-M. Liu, Q.-H. Xu, Y.-M. Liang, Y.-X. Ma, J. Chem. Res. (1999) 636.
[30] M.G.A. Shvekhgeimer, Uspekhi Khim. 65 (1996) 43.
[31] C.M. Liu, B.-H. Chen, W.-Y. Liu, X.-L. Wu, Y.-X. Ma, J. Organomet. Chem. 598 (2000) 348.
[32] C.M. Liu, W.Y. Liu, Y.M. Liang, Y.X. Ma, Synth. Commun. 30 (2000) 1755.