Journal of Fluorine Chemistry 131 (2010) 1237–1240

Contents lists available at ScienceDirect

Journal of Fluorine Chemistry

journal homepage: www.elsevier.com/locate/fluor

# Pt(II)$Cl_2(DMSO)_2$-catalyzed cross-coupling of polyfluoroaryl imines

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ARTICLE INFO

*Article history:*
Received 26 April 2010
Received in revised form 28 June 2010
Accepted 29 June 2010
Available online 6 July 2010

*Keywords:*
Platinum(II)
Polyfluoroarene
Cross-coupling

Dedicated to Professor Russell P. Hughes,
Recipient of the 2010 ACS Award for
Creative Work in Fluorine Chemistry.

ABSTRACT

$PtCl_2(DMSO)_2$ has been identified as a readily accessible and effective C–F activation precatalyst. We report herein the study of reaction optimization and substrate scope. A comparison is made with previously reported $[Pt_2Me_4(SMe_2)_2]$ and $PtCl_2(SMe_2)_2$ precatalysts.

## 1. Introduction

The activation of carbon–fluorine bonds has been an active research area for more than 20 years. The challenge of activating C–F bonds has been overcome by numerous metal complexes and the results have been summarized in several reviews [1]. Up until recently, the research focus has been dominated by metal-mediated and metal-catalyzed hydrodefluorination reactions [2], resulting in reduction of the strong C–F bond. Such strategies have potential for use in fluorocarbon remediation. Over the last decade, considerable attention has been devoted to the selective activation and cross-coupling of polyfluorinated compounds [3–5]. Given the emergence of fluorine in bioactive molecules [6], such strategies have the potential for generating fluoroaromatic building blocks for use in pharmaceutical and industrial applications.

In 2007, our group reported the first example of Pt-catalyzed cross-coupling of aryl fluorides. A range of polyfluoroaryl imines with different substitution patterns can be methylated in high yield and selectivity using $[Pt_2Me_4(SMe_2)_2]$ (**1**) and dimethylzinc, even in the presence of other potentially reactive functionalities [4a]. In a subsequent paper, we reported that the mechanism is consistent with the following steps (Scheme 1): (1) C–F oxidation addition of a low-valent, electron-rich Pt(II) complex to generate **B**; (2) transmetalation with dimethylzinc to generate **C** and (3) reductive elimination to furnish a $Csp^2$–$Csp^3$ bond, regenerating the active catalyst **A** [4b]. Each Pt(IV) intermediate in the catalytic cycle was postulated to be a 5-coordinate species, based on the observation that additional $SMe_2$ decelerated each stoichiometric step, as well catalysis. Moreover, a 6-coordinate trimethyl Pt(IV) species formed (**C-SMe$_2$**) was thought to be a resting state for the catalytic cycle; this species can re-enter the cycle by dissociation of $SMe_2$ [4b]. We have also shown that the same precatalyst can be used in catalytic C–O bond formation, by a different (and as yet, undefined) mechanism [4c].

Although (**1**) is a highly efficient precatalyst, its low stability even under inert atmosphere at −30 °C makes it less than ideal for synthetic applications. In an effort to discover a more user-friendly precatalyst, we recently reported that $PtCl_2(SMe_2)_2$ (**2**), a precursor of (**1**), is a viable as a air-, water- and thermal stable alternative to (**1**) [4d]. It is believed that (**2**) generates the active catalyst or some related species *in situ* by reacting with dimethylzinc. This precatalyst shares the same high selectivity and functional group tolerance as (**1**). However, although the practical advantage of using (**2**) is undoubtedly desirable, the major drawback it suffers is the lower reactivity compared to (**1**). With few exceptions, a significant decrease has been observed. Pre-treatment of (**2**) with dimethylzinc affords comparable activity to (**1**); however, this protocol is still less efficient than simply using (**1**).

In order to further extend the utility of Pt(II)-catalyzed C–F cross-coupling, we sought to test related platinum(II) complexes.

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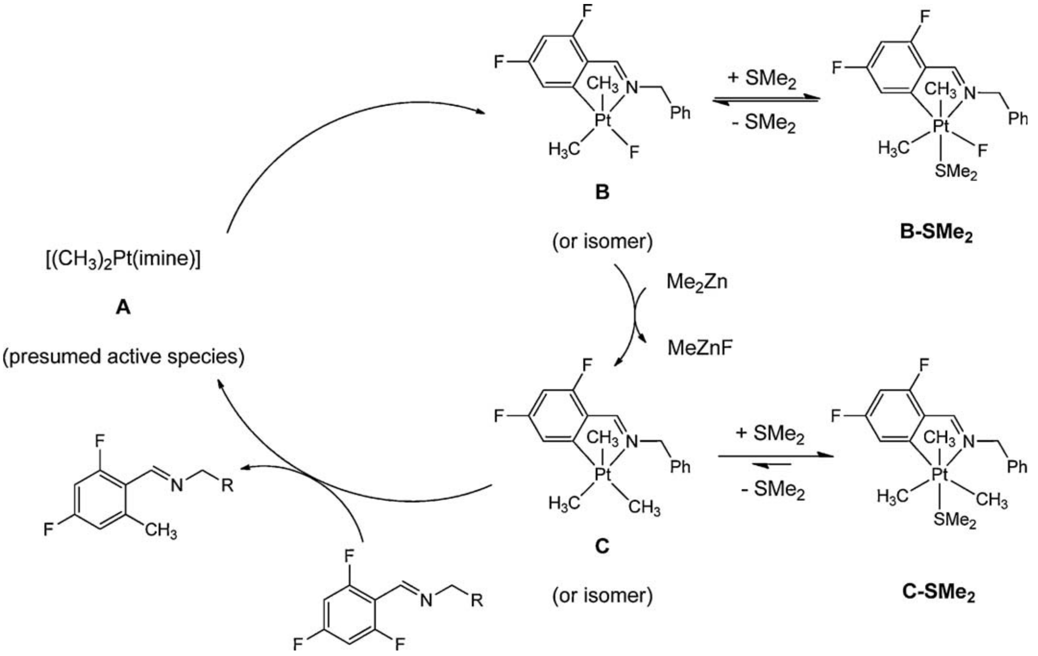
doi:10.1016/j.jfluchem.2010.06.018

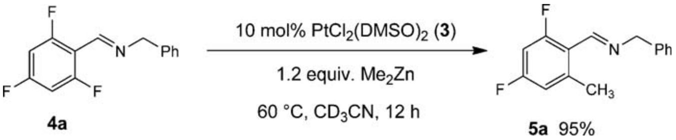


**Scheme 1.** Proposed mechanism of cross-coupling of aryl fluorides using precatalyst **1**.

We hypothesized that the use of a complex bearing a less-coordinating ligand than $SMe_2$ would facilitate the reaction. Presumably, such a species would generate the active catalyst faster than (**2**). Moreover, because 5-coordinate complexes are postulated to be involved in the catalytic cycle, a less-coordinating ligand should minimize the formation of off-cycle 6-coordinate species, such as **B-SMe$_2$** and **C-SMe$_2$** that could slow catalysis. We thus selected *cis*-$PtCl_2(DMSO)_2$ (**3**) for investigation.

## 2. Results and discussion

*Cis*-$PtCl_2(DMSO)_2$ (**3**) is an off-yellow microcrystalline that is indefinitely stable under air at ambient temperature [7]. This complex was readily synthesized from commercially available $K_2PtCl_4$ and DMSO in quantitative yield. Imine **4a** (0.034 mmol), *cis*-$PtCl_2(DMSO)_2$, (0.0034 mmol, 10 mol.%), dimethylzinc (0.041 mmol, 1.2 equiv.) were dissolved in $CD_3CN$ (1 mL) in a nitrogen-filled glovebox. The solution was transferred to an NMR tube, which was then removed from the glovebox. The solution was heated in an oil bath at 60 °C. Reaction progress was monitored periodically by $^1H$ and $^{19}F$ NMR spectroscopy. By comparison with 1,3,5-trimethoxybenzene as an internal standard, the reaction had proceeded cleanly to 95% yield in 12 h; no more imine starting material was observed (Scheme 2). In comparison, while complex (**1**) achieved the same result in approximately 8 h, complex (**2**) produced only 60% of the desired product even after 12 h. If (**2**) is pre-treated with $Me_2Zn$ for 6 h, higher yields can be obtained. Thus, complex (**3**) achieved comparable reactivity to (**1**), without requiring pre-activation.



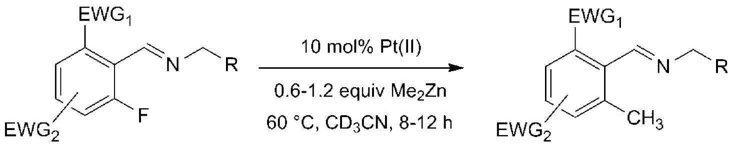
**Scheme 2.** $PtCl_2(DMSO)_2$-catalyzed cross-coupling.

The reaction of a series of imines was then explored. Table 1 shows a direct comparison of complexes **1**–**3**. The reaction conditions indicated in Scheme 2 were found to be the optimal conditions and were used for further studies. All spectroscopic data for known compounds matched the characterization data obtained in our earlier work [4a,d]. Overall, the complex (**3**) shows the same level of *ortho*-selectivity and functional group tolerance when compared to (**1**) and (**2**). Under the standard condition, the majority of the substrates reacted in comparable yield and reaction time to (**1**), which is a significant improvement over (**2**). These results indicate that *cis*-$PtCl_2(DMSO)_2$ (**3**) has the practical advantages afforded by $PtCl_2(SMe_2)_2$ (**2**) without compromising the efficiency and reactivity of $[Pt_2Me_4(SMe_2)_2]$ (**1**).

After successfully demonstrated the utility of complex (**3**) in C–F cross-coupling, we sought to investigate the nature of the catalytic species, anticipating that the outcome would be similar to that postulated for (**2**). In our previous work [4b], (**1**) was shown to be highly efficient in C–F activation, which is believed to be the rate determining step in the overall catalytic cycle. In comparison, heating the mixture of 0.8 equiv. of (**2**) [4d] or (**3**) with 1.0 equiv. of imine **4a** in $CD_3CN$ failed to achieve any observable C–F activation after 24 h at 60 °C. This result is consistent with a requirement for electron-rich late transition metal complexes to promote oxidative addition of the aryl C–F bond [8]. Likewise, this result is consistent with (**2**) and (**3**) generating the active catalyst *in situ*.

In the stoichiometric reaction between dimethylzinc and $PtCl_2(DMSO)_2$ (**3**), resonances in the $^1H$ NMR spectrum were observed, consistent with the formation of a Pt-$CH_3$ species. This species disappears over time and thus appears to be catalytically relevant. This result is also consistent with our earlier studies using (**2**) [4d]. Presumably, in both cases, it is such a Pt-$CH_3$ species that is the active catalyst, as addition of imine does result in cross-coupling. It is also noteworthy that despite the insolubility of (**2**)

**Table 1**
Comparison of precatalysts **1**–**3** in aryl fluoride cross-coupling.



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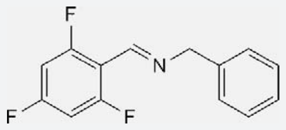
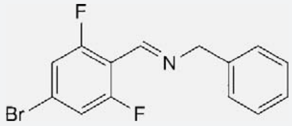
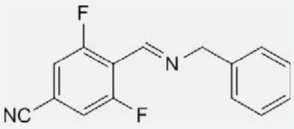
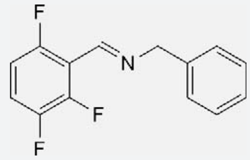
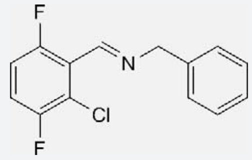
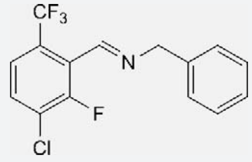
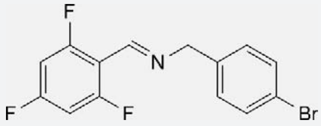
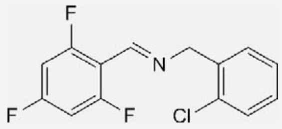
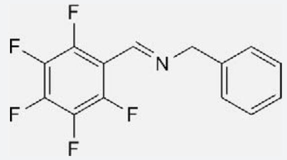
| | | $Pt_2Me_4(SMe_2)_2$ (**1**)[a,b] | $PtCl_2(SMe_2)_2$ (**2**)[a,c] | $PtCl_2(DMSO)_2$ (**3**)[a,d] |
|---|---|---|---|---|
|  | **4a** | 95% | 60% (95%)[e] | 95% |
|  | **4b** | 85% | 63% | 85% |
|  | **4c** | 85% | 95% | 95% |
|  | **4d** | 92% | 50% | 90% |
|  | **4e** | 95% | 30% | 95% |
|  | **4f** | 95% | 60% (95%)[e] | 95% |
|  | **4g** | 86% | 30% (95%)[e] | 85% |
|  | **4h** | 85% | 30% (85%)[e] | 85% |

**Table 1** (*Continued*)

| | | $Pt_2Me_4(SMe_2)_2$ **(1)**[a,b] | $PtCl_2(SMe_2)_2$ **(2)**[a,c] | $PtCl_2(DMSO)_2$ **(3)**[a,d] |
|---|---|---|---|---|
|  | **4i** | 74% | 20% | 70% |

[a] Yields based on $^1H$ NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard.

[b] Taken from Ref. [4a]; condition: 0.6 equiv. $Me_2Zn$, 8 h.

[c] Condition: 0.6 equiv. $Me_2Zn$, 8 h.

[d] Taken from Ref. [4d]; condition: 1.2 equiv. $Me_2Zn$, 12 h.

[e] Pre-treated with $Me_2Zn$ for 6 h.

and (**3**) in $CD_3CN$, both are readily solubilized by the addition of imine. This is consistent with imine coordination prior to C–F activation. Overall, this data is indicative of the same general mechanism being operative for complexes **1**–**3**.

## 3. Conclusion

In summary, we have established the general protocol for the $PtCl_2(DMSO)_2$-catalyzed methylation of polyfluorinated aryl imines. This precatalyst is an improvement over previous complexes, in that it is both highly active and is user-friendly. We believe this complex will prove to be very useful in Pt-catalyzed cross-coupling of aryl fluorides.

## 4. Experimental

Manipulation of organometallic compounds was performed using standard Schlenk techniques under an atmosphere of dry nitrogen or in a nitrogen-filled Vacuum Atmospheres drybox ($O_2 < 2$ ppm). NMR spectra were recorded on Bruker Avance 300 spectrometers. $^1H$ and $^{13}C$ chemical shifts are reported in parts per million and referenced to residual solvent. $^{19}F$ NMR spectra are reported in parts per million and referenced to $C_6F_6$ in acetone-$d_6$ ($-162.9$ ppm). Acetonitrile-$d_3$ and all other reagents were obtained from commercial sources and used as received. $Pt_2Me_4(SMe_2)_2$, $PtCl_2(SMe_2)_2$, $PtCl_2(DMSO)_2$ and all imines were prepared by the published procedures [4a,c,d, 7]. Dimethylzinc (2 M solution in toluene) was purchased from Aldrich and used without further purification.

### 4.1. General procedure

To an NMR tube in a nitrogen-filled glovebox was added 0.1 mL of $PtCl_2(DMSO)_2$ solution (0.034 mmol in 1.0 mL of $CD_3CN$, 0.10 equiv.), 0.1 mL of 1,3,5-trimethoxylbenzene solution (0.11 mmol in 1.0 mL of $CD_3CN$, 0.33 equiv.), 0.1 mL of imine solution (0.34 mmol in 1.0 mL of $CD_3CN$, 1.0 equiv.), 0.02 mL of dimethylzinc solution (2.0 M in toluene, 1.2 equiv.) and 0.18 mL of $CD_3CN$. The tube was fitted with a screw cap containing a PTFE septum. The tube was removed from the glovebox and the solution was heated in an oil bath at 60 °C for 12 h. Reactions were monitored by $^1H$ and $^{19}F$ NMR spectroscopy. Yields were determined using 1,3,5-trimethoxybenzene as internal standard. All reactions were conducted on the same scale. All products were then compared to the literature and confirmed to be identical [4a,c,d].

## Acknowledgements

We thank the following for support of this research: University of British Columbia, NSERC (Discovery Grant, Research Tools and Instrumentation Grants), AstraZeneca Canada (Award in Chemistry 2008), the Canada Foundation for Innovation (new Opportunities Grant) and the British Columbia Knowledge Development Fund.

## References

[1] (a) J.L. Kiplinger, T.G. Richmond, C.E. Osterberg, Chem. Rev. 94 (1994) 373–431;
(b) H. Amii, K. Uneyama, Chem. Rev. 109 (2009) 2119–2183;
(c) R.J. Kulawiec, R.H. Crabtree, Coord. Chem. Rev. 99 (1990) 89–115;
(d) H. Torrens, Coord. Chem. Rev. 249 (2005) 1957–1985.
[2] (a) M. Aizenberg, D. Milstein, Science 265 (1994) 359–361;
(b) M. Aizenberg, D. Milstein, J. Am. Chem. Soc. 117 (1995) 8674–8675;
(c) B.L. Edelbach, W.D. Jones, J. Am. Chem. Soc. 119 (1997) 7734–7742;
(d) J.L. Kiplinger, T.G. Richmond, J. Am. Chem. Soc. 118 (1996) 1805–1806;
(e) J. Vela, J.M. Smith, Y. Yu, N.A. Ketterer, C.J. Flaschenriem, R.J. Lachicotte, P.L. Holland, J. Am. Chem. Soc. 127 (2005) 7857–7870;
(f) T. Braun, D. Noveski, M. Ahijado, F. Wehmeier, Dalton Trans. (2007) 3820–3825;
(g) C. Douvris, O. Ozerov, Science 321 (2008) 1188–1190;
(h) G. Meier, T. Braun, Angew. Chem. Int. Ed. 48 (2009) 1546–1548;
(i) S.P. Reade, M.F. Mahon, M.K. Whittlesey, J. Am. Chem. Soc. 131 (2009) 1847–1861.
[3] M. Simizu, T. Hiyama, Angew. Chem. Int. Ed. 44 (2005) 214–231.
[4] (a) T. Wang, B. Alfonso, J.A. Love, Org. Lett. 9 (2007) 5629–5631;
(b) T. Wang, J.A. Love, Organometallics 27 (2008) 3290–3296;
(c) H.L. Buckley, T. Wang, O. Tran, J.A. Love, Organometallics 28 (2009) 2356–2359;
(d) H.L. Buckley, A.D. Sun, J.A. Love, Organometallics 28 (2009) 6622–6624.
[5] (a) B.L. Edelbach, B.M. Kraft, W.D. Jones, J. Am. Chem. Soc. 121 (1999) 10327–10331;
(b) T. Braun, R.N. Perutz, M.I. Sladek, Chem. Commun. (2001) 2254–2255;
(c) N. Yoshikai, H. Mashima, E. Nakamura, J. Am. Chem. Soc. 127 (2005) 17978–17979;
(d) A. Steffen, M.I. Sladek, T. Braun, B. Neumann, H.-G. Stammler, Organometallics 24 (2005) 4057–4064;
(e) T. Saeki, Y. Takashima, K. Tamao, Synlett 7 (2005) 1771–1774;
(f) T. Schaub, M. Backes, U. Radius, J. Am. Chem. Soc. 128 (2006) 15964–15965;
(g) T.J. Korn, M.A. Schade, S. Wirth, P. Knochel, Org. Lett. 8 (2006) 725–728;
(h) H. Guo, F. Kong, K.-I. Kanno, J. He, K. Nakajima, T. Takahashi, Organometallics 25 (2006) 2045–2048;
(i) T. Braun, J. Izundu, A. Steffen, B. Neumann, H.-G. Stammler, Dalton Trans. (2006) 5118–5123;
(j) T.J. Korn, M.A. Schade, M.N. Cheemala, S. Wirth, S.A. Guevara, G. Cahiez, P. Knochel, Synthesis 21 (2006) 3547–3574;
(k) K. Manabe, S. Ishikawa, Synthesis 23 (2008) 2645–2649;
(l) M. Arisawa, T. Suzuki, T. Ishikawa, M. Yamaguchi, J. Am. Chem. Soc. 130 (2008) 12214–12215;
(m) T. Hatakeyama, S. Hashimoto, K. Ishizuka, M. Nakamura, J. Am. Chem. Soc. 131 (2009) 11949–11963.
[6] (a) K. Muller, C. Faeh, F. Diederich, Science 317 (2007) 1881–1886;
(b) S. Purser, P. Moore, S. Swallow, V. Gouverneur, Chem. Soc. Rev. 37 (2008) 320–330;
(c) W.K. Hagmann, J. Med. Chem. 51 (2008) 4359–4369.
[7] (a) J.H. Price, A.N. Williamson, R.F. Schramm, B.B. Wayland, Inorg. Chem. 11 (1972) 1280–1284;
(b) P.-C. Kong, D. Iyamuremye, F.D. Rochon, Can. J. Chem. 54 (1976) 3224–3226.
[8] (a) M. Crespo, M. Martinez, J. Sales, Organometallics 12 (1993) 4297–4304;
(b) M. Martinez, J. Sales, Chem. Comm. (1992) 822–823.