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Selective intramolecular cleavage of the carbon–silicon bond by palladium salts

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Abstract

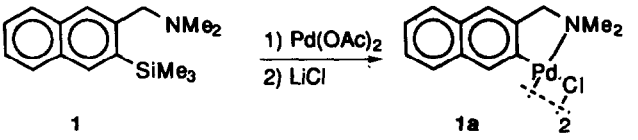
Several (aryl)trimethylsilane derivatives containing a potentially intramolecularly coordinating dimethylaminomethyl group were prepared and treated with Li_2PdCl_4 or $Pd(OAc)_2$. Highly selective cleavage of the aryl-C–Si bond took place to give the corresponding arylpalladium complexes. Similar reactions were observed for benzylic trimethylsilyl compounds. The yields of the reactions with Li_2PdCl_4 varied from 66 to 94%, but yields were > 90% when $Pd(OAc)_2$ was used.

Keywords: Palladium; Silicon

1. Introduction

Cleavage of the C–Si bond by electrophilic or nucleophilic reagents is well known, and both protic acids and Lewis acidic metal halides can be used as electrophiles [1]. One of the earliest examples of the latter was the reaction of tris[4-(dimethylamino)phenyl]silyl chloride with $HgCl_2$ to yield 4-(dimethylamino)phenylmercury(II) chloride [2]. Later, transition metals were found to attack the C–Si bond in the same way, providing a means of introducing metals into substrates in a regioselective manner [1,3]. Palladium for example is capable of cleaving the C–Si bond in alkyl-, vinyl- and allylsilicon compounds in moderate yields [4]. Also in some highly selective palladium-catalysed cross-coupling reactions of arylsilicon compounds, C–Si bond cleavage by palladium is an essential step [5]. A few cases are known in which palladium attacks the C–Si bond intramolecularly [6].

Recently, we observed an example of intramolecular displacement of a silyl moiety (see Eq. (1)) [7]. Although the reaction in itself is not new, its yield was remarkably high. We report below the applicability of this reaction in regioselective cyclopalladation.



(1)

2. Results

The aryl- and benzylic-trimethylsilyl compounds **1**, **2**, **4**, **5** and **6** (see Eq. (1) and Scheme 1) were prepared from the corresponding lithium derivatives by reaction with trimethylsilyl chloride. 3-Methyl-2-(dimethylamino)methyl-1-(trimethylsilyl)benzene (**3**) was prepared from 2,6-dichloro-1-[(dimethylamino)methyl]-benzene, by first introducing the trimethylsilyl group (mono-lithiation, followed by reaction with Me_3SiCl) and then the methyl group (lithiation, followed by reaction with methyl iodide). This order of introducing the substituents is necessary to prevent lithiation of the benzylic methyl substituent in the second step.

The palladation reactions of the trimethylsilylated substrates were initially carried out in MeOH with Li_2PdCl_4 as palladating agent. After 5 h of stirring of the mixture at room temperature, the precipitate was separated and washed with methanol. When $Pd(OAc)_2$ was used, after 1 h of stirring at room temperature, two

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Table 1
Reactions of Me_3Si substituted benzene and naphthalene derivatives with palladium salts

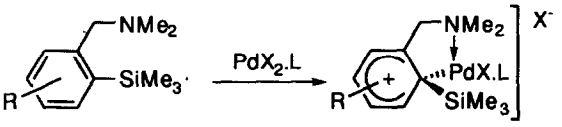
Substrate	Product	Yield (%) [a]	Yield (%) [b]
1 $C_{10}H_6CH_2NMe_2$-3-$SiMe_3$-2	**1a**	92	99
2 $C_6H_4CH_2NMe_2$-2-$SiMe_3$-1	**2a**	–	99
3 $C_6H_3CH_2NMe_2$-2-Me-3-$SiMe_3$-1	**3a**	94	99
4 $C_6H_2CH_2NMe_2$-2-CH_2SiMe_3-1-Me_2-3,5	**4a**	85	97
5 $C_{10}H_6CH_2NMe_2$-3-CH_2SiMe_3-2	**5a**	88	90
6 $C_{10}H_6CH_2NMe_2$-2-$SiMe_3$-1	**6a**	66	96

[1] Reaction with Li_2PdCl_4. [2] Reaction with $Pd(OAc)_2$ and LiCl, respectively.

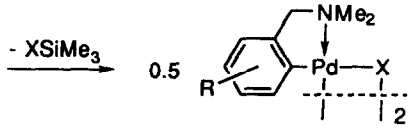
equivalents of LiCl were added to the red solution to precipitate the chlorine-bridged dimers. The yields obtained in both procedures are given in Table 1. (The reaction of the 3-naphthyl substrate **1** is included for the sake of completeness, although it was reported previously [7]).

3. Discussion

The cleavage of aryl–silicon bonds by palladium salts is normally carried out in polar solvents under fairly forcing conditions, *e.g.* trimethylsilylbenzene is cleaved only to the extent of 20% by Li_2PdCl_4 in THF after 6 h at 60°C [4b]. We may therefore conclude that intramolecular coordination plays an important role in the cyclopalladation under the mild conditions used here. It is probable that such coordination guides the initial electrophilic attack of the PdX cation on the C–H or C–Si bonds and also stabilizes the C–Pd bond in the final product by intramolecular coordination



$PdX_2.L = Li_2PdCl_4$, $PdCl_2(SMe_2)_2$ or $Pd(OAc)_2$



(2)

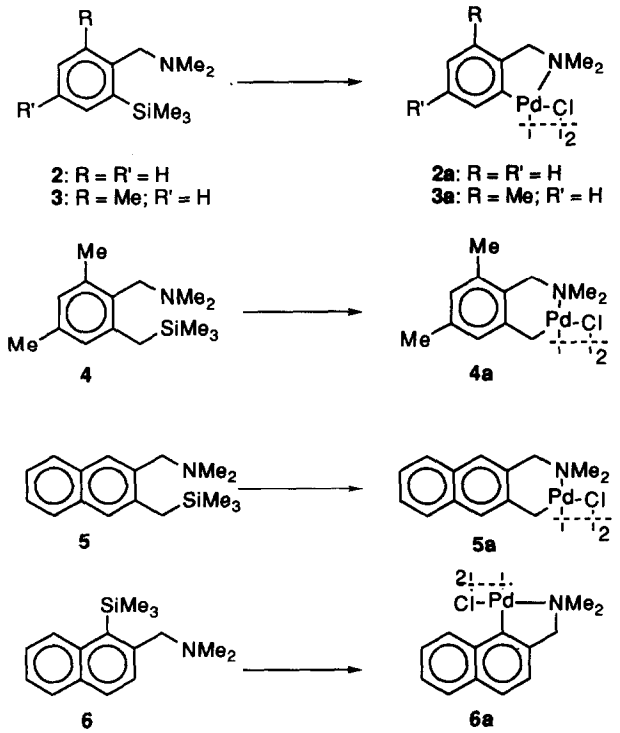
The cyclopalladations of the 3-naphthylsilyl substrate **1** and its parent compound 2-[(dimethylamino) methyl]-naphthalene have similar regioselectivities [8]. Substrate **1** had been prepared to block position 3 for palladation and induce palladation to take place at position 1. Both the high reactivity of the C–Si bond towards electrophilic palladation and the unfavourable steric interaction with proton H(8) may direct the palladation to position 3. However, the selective palladation of the regioisomer 2-(dimethylamino)methyl-1-(trimethylsilyl)naphthalene (**6**) in the 1-position to give 1-naphthylpalladium chloride (**6a**) shows that the reactivity of the C–Si bond is the factor determining selectivity. This reaction is also applicable to the corresponding benzene derivative 2-(dimethylamino)methyl-1-[(trimethylsilyl)methyl]benzene (**2**).

The chemoselectivity of the silicon-directed palladation may be different from that of direct palladation; 3-methyl-2-[(dimethylamino)methyl]naphthalene selectively reacts with palladium salts to give the 1-palladated product (i.e. aromatic palladation) [7], but its trimethylsilyl substituted derivate **5** undergoes benzylic palladation only.

When the trimethylsilyl substituent is present in the ring, as in **3**, the outcome of the palladation is the same as with the parent 3-methyl-2-[(dimethylamino)methyl]-naphthalene, i.e. in both cases aromatic palladation occurs to give **3a**, although both benzylic and aromatic protons are available [8]. In this case, the presence of the trimethylsilyl group merely increases the reactivity at the relevant site.

When two different benzylic sites for palladation are available in 3,5-dimethyl-2-(dimethylamino)methyl-1-(trimethylsilyl)benzene (**4**), it is found that only the carbon bearing the silyl moiety was palladated. Again, this points to a higher reactivity of the silicon-substituted benzylic site.

The method reported here provides a mild and very selective means of introducing a palladium center into



Scheme 1.

an aromatic system in high yield. Of course the same products can be obtained by direct reaction of the corresponding organolithium compound with, e.g. $PdCl_2(SMe_2)_2$. However, in our experience, the overall yield of the reaction of the organolithium species with Me_3SiCl, followed by reaction with a palladium salt is better, and the silicon-directed cyclopalladations are faster than the corresponding reactions involving C–H cleavage.

4. Experimental details

All reactions were carried out under dry deoxygenated nitrogen by use of standard Schlenk techniques. All solvents, except methanol were dried prior to use. Diethyl ether and THF were distilled from sodium-benzophenone ketyl. Acetonitrile was distilled from calcium hydride and stored over 4-Å molecular sieves. Dichloromethane was distilled from calcium hydride or anhydrous calcium chloride. {2-[(Dimethylamino)methyl]-3-naphthyl}lithium [9], 2-[(dimethylamino)methyl]phenyllithium [10], {2-[(dimethylamino) methyl]-1-naphthyl}-lithium [7], 1-bromo-2-[(dimethylamino)methyl]-naphthalene [7] and the complexes **1a**, **2a**, **5a** and **6a** [11] were prepared as described previously. ^{1}H- and ^{13}C-spectra were recorded on a Bruker AC-200 MHz or a AC-300 spectrometer. Elemental analyses were carried out by Dornis und Kolbe, Mikroanalytisches Laboratorium, Mülheim a. d. Ruhr, Germany.

4.1. Starting compounds

2-[(Dimethylamino)methyl]-3-(trimethylsilyl)phenyllithium. A solution of ^{t}BuLi (41.4 mmol) in pentane (24 ml) was added to a solution of 1-chloro-2-[(dimethylamino)methyl]-3-trimethylsilylbenzene (10 g, 41.4 mmol) in pentane at −78°C. The cooling bath was allowed to warm slowly to room temperature, and the mixture then stirred for 4 h at room temperature. The solution was decanted. The beige precipitate was washed with two portions of 30 ml of pentane and dried in vacuo. The yield was 8.1 g (38.1 mmol, 92%).

3,5-Dimethyl-2-[(dimethylamino)methyl]benzyllithium (97% yield), 3-chloro-2-[(dimethylamino)methyl] benzyllithium, (75% yield) and 1-chloro-2-[(dimethylamino)methyl]-3-phenyllithium (80% yield) were prepared similarly.

2,6-Dichloro-[(dimethylamino)methyl]benzene (starting material for 3). A solution of chloromethyl-2,6-dichlorobenzene (100 g, 0.51 mol) in THF (100 ml) was added dropwise to an ice cooled solution of dimethylamine (1.0 mol) in THF (200 ml). The mixture was stirred overnight at room temperature, the solvent then removed in vacuo and the residue was taken up in 300 ml of Et_2O. The solution was washed with two 150-ml portions of of 10% aqueous KOH. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. Vacuum distillation (b.p. 104°C, 0.4 mmHg) then gave 95.2 g of the product (0.47 mol, 92%).

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.25 (d, 2H, $J = 8.0$ Hz); 7.07 (t, 1H, $J = 8.2$ Hz); 3.63 (s, 2H, CH_2); 2.29 (s, 6H, NCH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 136.9 (CCl); 134.7 (CCH_2); 128.8 (C^4); 128.3 ($C^{2,5}$); 57.5 (CH_2); 45.5 (NCH_3).

2,4,6-Trimethyl-[(dimethylamino)methyl]benzene (starting material for 4). This was prepared by reaction of Me_2NH with 2,4,6-trimethylbenzyl chloride by a procedure analogous to that described above. The yield was 92%.

^{1}H NMR (300 MHz, $CDCl_3$): δ 6.88 (s, 2H, ArH); 3.42 (s, 2H, CH_2); 2.40 (s, 6H, NCH_3); 2.28 (s, 3H, *p*-CH_3); 2.27 (s, 6H, *o*-CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 137.9 (ArC); 136.3, 132.6 (ArC); 128.9 (C_4); 57.1 (CH_2); 45.2 (NCH_3); 20.9 (*p*-CH_3); 20.0 (*o*-CH_3). Anal. Found: C, 80.69; H, 10.57; N, 7.80. $C_{12}H_{19}N$ calcd.: C, 81.30; H, 10.80; N, 7.90%.

General procedure for the synthesis of trimethylsilylated substrates. A solution of trimethylsilyl chloride (1.52 ml, 12.0 mmol) in THF (10 ml) was added during 10 min to an ice-cooled solution of 12.0 mmol of the appropriate lithium compound (vide infra) in THF (40 ml). The mixture was stirred for 3 h at room temperature and the solvent then removed in vacuo. Purification by flash distillation yielded the pure compounds.

2-(Dimethylamino)methyl-3-(trimethylsilyl)naphthalene (1). 98% yield. ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.14 (s, 1 H, ArH); 7.90 (s, 1H, ArH); 7.90–7.86 (m, 2H, ArH); 7.52–7.48 (m, 2H, ArH); 3.73 (s, 2H, CH_2); 2.32 (s, 6H, NCH_3); 0.50 (s, 9H, $SiCH_3$). ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 141.9, 137.6, 136.0, 133.8, 132.2, 128.0, 127.5, 127.0, 126.5, 125.6, 65.1 (CH_2); 45.5 (NCH_3); 0.87 ($SiCH_3$). Anal. Found: C, 74.48; H, 8.98; N, 5.51. $C_{16}H_{23}NSi$ calcd.: C, 74.64; H, 9.01; N, 5.44%.

2-(Dimethylamino)methyl-1-(trimethylsilyl)naphthalene (6). 87% yield. ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.87–7.81 (m, 2H, ArH); 7.57 (d, 1H, $J = 8.5$ Hz); 7.52–7.46 (m, 3H, ArH); 3.73 (s, 2H, CH_2); 2.23 (s, 6H, NCH_3); 0.60 (s, 9H, $SiCH_3$). Anal. Found: C, 76.85; H, 8.92; N, 4.70. $C_{16}H_{23}NSi$ calcd. C, 74.64; H, 9.01; N, 5.44%.

2-(Dimethylamino)methyl-3-[(trimethylsilyl)methyl]-naphthalene (5). 92% yield, b.p. 155°C, 1.0 Torr. ^{1}H NMR (**3**, 300 MHz, $CDCl_3$): δ 7.90 (d, 1H, $J = 7.3$ Hz);

7.85 (m, 2H); 7.60 (s, 1H); 7.50 (m, 2H); 3.85 (s, 2H, CH_2N); 2.61 (s, 2H, CH_2Si); 2.42 (s, 6H, NCH_3); 0.21 (s, 9H, $SiCH_3$). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 138.6, 135.1, 133.2, 131.3, 128.9, 127.6, 126.7, 126.7, 125.6, 124.5, 63.2 (CH_2N); 45.7 (CH_2Si), 23.1 (NCH_3); −1.0 ($SiCH_3$). Anal. Found: C, 75.06; H, 9.22; N, 5.21. $C_{17}H_{25}NSi$ calcd.: C, 75.21; H, 9.28; N, 5.16%.

2-(Dimethylamino)methyl-(trimethylsilyl)benzene (2). 92% yield. ^1H NMR (200 MHz, $CDCl_3$); δ 7.60–7.18 (m, 4H, ArH); 3.52 (s, 2H, CH_2); 2.22 (s, 6H, NCH_3); 0.33 (s, 9H, $SiCH_3$).

2-(Dimethylamino)methyl-3,5-dimethyl-[(trimethylsilyl)-methyl]benzene (4). 96% yield, b.p. 77°C, 0.9 Torr. ^1H NMR (200 MHz, $CDCl_3$): δ 6.71 (s, 1H, ArH); 6.65 (s, 1H, ArH); 3.28 (s, 2H, CH_2N); 2.35 (s, 2H, CH_2Si); 2.24 (bs, 6H, 2 CH_3); −0.02 (s, 9H, $SiCH_3$).

4.2. Synthesis of palladium complexes

Compound **3a** was prepared by the method used for the synthesis of **2a** [11].

^1H NMR (**2a**, 300 MHz, $CDCl_3$) (mixture of isomers); δ 7.10–6.90 (m, 1H, ArH); 6.78–6.75 (m, 2H, ArH); 3.92 (s, 2H, CH_2); 2.88 and 2.86 (2s, 6H, NCH_3); 2.17 (s, 3H, $ArCH_3$). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 144.9, 131.5, 131.2, 130.7, 126.3, 125.4, 71.5 and 71.3 (CH_2); 53.2 and 52.9 (NCH_3); 20.7 ($ArCH_3$). Anal. Found: C, 41.33; H, 4.89; N, 4.77. $C_{20}H_{28}Cl_2N_2Pd_2$ calcd.: C, 41.40; H, 4.86; N, 4.83%.

Synthesis of [2-CH_2NMe_2-3,5-$Me_2C_6H_2CH_2PdCl]_2$ (4a). This compound was prepared by reaction of 3,5-dimethyl-2-[(dimethylamino)methyl]-benzyllithium, with $PdCl_2(SMe_2)$ in a procedure analogous to that described for the synthesis of **5a** [7] in 80% yield.

^1H NMR (300 MHz, $CDCl_3$): δ 7.07 (bs, 1H, ArH); 7.83 (s, 1H, ArH); 3.12 and 3.08 (CH_2N and CH_2Pd); 2.68 and 2.65 (NCH_3); 2.28 ($ArCH_3$); 2.67 ($ArCH_3$). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 145.2, 138.5, 136.2, 130.3 and 130.2, 126.3, 125.0 and 124.7, 59.9 (CH_2N); 50.4 and 49.9 (NCH_3); 23.4 (CH_2Pd); 20.9 ($ArCH_3$); 19.5 ($ArCH_3$).

4.3. General procedure for the reactions of trimethylsilyl derivatives with palladium salts

To a solution of the appropriate substrate (1 mmol) in MeOH (10 ml) was added Li_2PdCl_4 in MeOH (1 ml). The mixture was stirred at room temperature for 5 h and the precipitate then collected, washed with two portions of 10 ml of MeOH and 10 ml of Et_2O, and dried in vacuo. When $Pd(OAc)_2$ was used (1 mmol) after 1 h of stirring at room temperature, LiCl (2 mmol) in MeOH (10 ml) was added to the red solution. The resulting suspension was stirred for 30 min, after which the work-up was carried out as described for the reaction with Li_2PdCl_4. The results are summarized in Table 1.

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