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Short communication

Allyl versus aryl C–H activation mediated by palladium acetate

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Abstract

In the presence of a catalytic amount of palladium acetate and a 2:1 stoichiometry of 1,4-benzoquinone, *N,N*-dimethyl-2-propenylbenzenemethylamine afforded *N,N*-dimethyl-2-benzazepinium in up to 85% yield. Under similar conditions related *N,N*-dimethyl-2-propenylbenzenamine and *N,N*-dimethyl-2-butenylbenzene-methylamine afforded the quinolinium and the isoquinolinium derivatives with 85 and 21% yields, respectively. Running these reactions in the presence of stoichiometric amounts of palladium acetate led to the formation of cyclopalladated compounds formed by the orthopalladation of the aryl ring. Thus, under these latter conditions the aromatic C–H activation is in competition with the allylic one. © 1997 Elsevier Science S.A.

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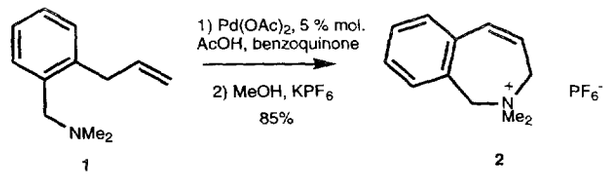
1. Introduction

We have shown recently that the intramolecular coupling reaction between a tertiary amine and an allylic carbon atom is indeed possible by means of allylic C–H bond activation [1], this reaction being achieved with stoichiometric amounts of palladium chloride. However, when using allylic acetate as starting material, catalytic amounts of $Pd(PPh_3)_4$ led to the expected heterocyclisation with reasonable yields [2]. As a procedure based on Palladium acetate/parabenzoquinone/acetic acid is known to efficiently promote the C–H activation at allylic positions [3], we wondered whether it could be an interesting alternative to the reactions studied by us so far. We now report some preliminary data concerning this study in which we show that, using this process, the ring closure occurs readily with allylic arylamines, but when varying the substrate using a wider range of alkenes, it appeared that the reaction is limited by an orthopalladation reaction at the aryl unit.

In a typical reaction, 2-(prop-2′-enyl)-*N,N* dimethylaminomethylbenzene was mixed with palladium acetate (5 mol%) and two equivalents of parabenzoquinone in acetic acid at 100°C during 4 h. The cyclised benzazepinium derivative was obtained with 85% yield.



1 2

When this procedure was applied to related substrates, i.e., 2-(prop-2′-enyl)-*N,N*-dimethylaminoaniline, **3**, and 2-(but-2′-enyl)-*N,N* dimethylaminomethylbenzene, **5**, the corresponding 6-membered heterocyclic ring compounds, **4**

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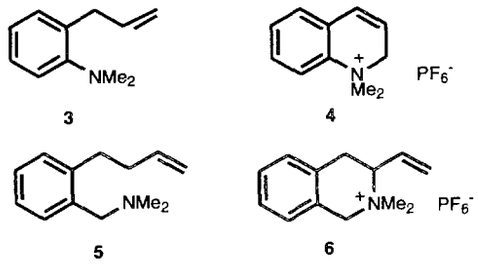
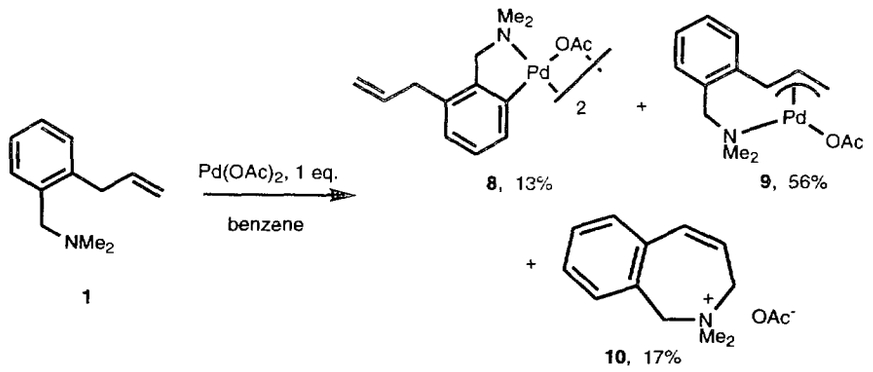
and **6** have been obtained in 85% and 12% yields, respectively, whereas with 2-(pent-2′-enyl)-*N*,*N* dimethylaminomethylbenzene, **7**, no cyclisation at all has been detected.



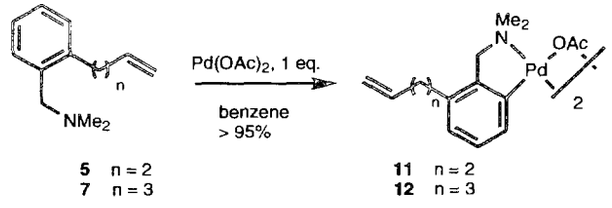
The mechanism of the reaction is obviously closely related to the one depicted recently when stoichiometric amounts of $PdCl_2$ were used [1]. It involves, at an early stage, the allylic C–H activation by palladium acetate leading to a palladium π-allyl compound from which the intramolecular N–C bond is formed via nucleophilic addition of the NMe_2 moiety at the Pd–allyl unit. The action of acetate nucleophile on alkenes in the presence of $Pd(OAc)_2$ has indeed been shown to proceed via allylic C–H abstraction followed by nucleophilic addition of the acetate rather than via Pd-mediated OAc addition across the alkene fragment [4].

In the case of the reaction studied here it appeared that the yield of the reaction seems to be dependent upon the nature of the alkene, as propenyl units were cyclised more readily than the alkene homologues having a longer chain.

We hoped to get some insight in how the reaction proceeds by performing it using stoichiometric amounts of palladium acetate. In the case of **1** the stoichiometric reaction with palladium acetate led to a mixture of products **8–10**.



In the case of the substrate **5** and **7**, i.e., having a butenyl and a pentenyl unit, respectively, in the position *ortho* to the CH_2NMe_2 unit, the reaction afforded high yields of the cyclopalladated compounds **11** and **12**.



These new organopalladium compounds **8**, **11** and **12** were difficult to obtain as dry solids as the work-up procedures usually afforded them as oily solids. It was therefore not possible to obtain good combustion analyses for them. Nevertheless, compounds **8**, **11** and **12** could be fully characterised by NMR methods. Thus, the structure of compound **12** was elucidated through both ^1H, ^{13}C and COSY 45 NMR. Particularly diagnostic of the structure is the disappearance of the *ortho* proton of the aryl ring and the diastereotopicity of the CH_2 and the NMe_2 units due to the acetate bridges that confer a nonplanar structure to the dimers [5]. In the presence of pyridine, the acetate bridge

splitting occurred and the NMR signal of the proton *ortho* to the Pd atom (which is in the vicinity of the pyridine ligand) is significantly high-field shifted, a feature that has often been observed in related compounds [6]. The intramolecular C–H activation by palladium that leads to these compounds has been extensively reviewed [7] and it is a very well-known process especially for nitrogen containing ligands such as those derived from benzylamine derivatives. Moreover, recently, additional evidence for the implication of Pd-mediated aromatic C–H activation has been brought about in various annulation reactions [8–10].

This result shows that in the presence of stoichiometric quantities of palladium acetate, the aryl C–H bond is also activated. An opposite trend was shown to occur in the presence of $PdCl_2(MeCN)_2$ as we observed preferentially the cleavage of the allylic C–H bond leading to π-allylic Pd complexes [1]. Although the reaction conditions were not identical in both cases, the results of the reactions observed with stoichiometric amounts of $Pd(OAc)_2$ shed some light on the reaction performed with catalytic amounts of $Pd(OAc)_2$, especially on those cases for which the heterocyclisation was not complete or did not occur at all. It seems thus that the orthopalladation reaction can indeed be in competition with the allylic C–H activation, this being particularly obvious in the case of the substrate **7** for which no cyclisation can take place. For **5** it seems that the allylic activation should be somewhat easier in the presence of catalytic amounts of Pd $(OAc)_2$ since 12% of heterocyclisation was observed. However, the occurrence of the orthopalladation should be responsible for the low yield of the desired 6-membered ring formation. Finally, for the substrate **1**, the kinetics of the orthopalladation seems to be less favourable so that the allylic activation is more readily achieved affording **9** and **10**.

In conclusion, this study has shown that palladium acetate can activate C–H bonds at allylic position towards intramolecular heterocyclisation with tertiary amine function, this reaction being mediated by catalytic amounts of $Pd(OAc)_2$. However, the efficiency of this reaction may be lowered since a cyclometallation reaction involving the *ortho* position of an aryl unit can compete with the allylic C–H activation reaction.

2. Experimental

General experimental conditions were the same as those used in previous papers from our laboratory [1].

2.1. 2,3-Dihydro-2-dimethyl-1H-2-benzazepinium hexafluorophosphate, 2

To a solution of 2-(prop-2′-enyl)-*N*,*N*-dimethylaminomethylbenzene (0.671 g, 3.83 mmol) in acetic acid (50 ml) were added *para*-benzoquinone (0.820 g, 7.66 mmol) and palladium acetate (0.043 g, 0.19 mmol, 5 mol%). The mixture was heated at 100°C during 4 h. The solvent was removed in vacuo and the resulting solids dissolved in MeOH (20 ml) to which KPF_6 (0.705 g, 3.80 mmol) was added and the solution was stirred for 1 h. The solvent was removed in vacuo and the solid was dissolved in acetone (10 ml). The solution was filtered through celite. This procedure was repeated 2 times after which THF was added to the concentrated solution (0.5 ml). Adding Et_2O afforded **2** as a white powder (1.04 g, 85%) which has been identified by comparison with an authentic sample [1].

2.2. 2-Dihydro-1-dimethylquinolinium hexafluorophosphate, 4

The procedure is identical to that described above starting from 2-(prop-2′-enyl)-*N*,*N*-dimethylaminobenzene, **3** (0.675 g, 4.19 mmol) affording **4** (0.970 g, 76%) as a grey powder that has been identified by comparison with an authentic sample [1].

2.3. N,N-dimethyl-1,2,3,4-tetrahydro-3-vinylisoquinolinium hexafluorophosphate, 6

The procedure is identical to that described above starting from 2-(but-2′-enyl)-*N*,*N*-dimethylaminobenzene, **5** (0.198 g, 1.06 mmol) affording **6** (0,042 g, 12%) as a brownish powder.

^{1}H NMR (CD_3COCD_3): 7.58–7.20 (m, 4H, Ar), 6.16 (ddd, 1H, –HC=, $^3J_{HH}$ = 6.4, $^3J_{HH\,cis}$ = 10.2, $^3J_{HH\,trans}$ = 16.9), 5.83 (dd, 1H, $=CH_{2\,trans}$, $^2J_{HH}$ = 1.0), 5.72 (dd, 1H, $=CH_{2\,cis}$), 4.86 and 4.74 (2d, 2H, $ArCH_2N$, $^2J_{HH}$ = 15.7), 4.54 (dt, 1H, CHN, $^3J_{HH}$ = 8.8), 3.36 and 3.17 (2s, 6H, NMe_2), 3.38–3.28 (m, 2H, $ArCH_2$).

2.4. Synthesis of compound 8

A solution of 2-(prop-2′-enyl)-*N*,*N*-dimethylaminomethylbenzene (0.671 g, 3.83 mmol) in benzene (5 ml) was added to a solution of palladium acetate (0.343 g, 1.53 mmol) in benzene (15 ml). A precipitate was formed after 15 min and the solvent was removed in vacuo after 1 h. The dry residue was dissolved in MeOH to which excesses of KPF_6 were added. The solvent was removed in vacuo and the remaining solid was dissolved in acetone. The solution

was filtrated and concentrated in vacuo. Addition of Et_2O afforded a yellow precipitate that was filtered. This solid was redissolved in Et_2O and after concentration of the solution thus obtained, the addition of *n*-pentane led to a yellow powder that is filtered and dried in vacuo. This led to a yellow oil which was shown by ^1H NMR to contain the cyclopalladated compound **8** exclusively (0.045 g, 9%).

The impossibility to isolate **8** in the form of a solid prevented us to perform combustion analyses.

^1H NMR ($CDCl_3$): 6.89–6.72 (m, 3H, Ar), 5.78 (ddt, –CH=, $^3J_{HH trans}$ = 15;2, $^3J_{HH cis}$ = 10.1, $^3J_{HH}$ = 6.2), 4.96 (dd, 1H, $=CH_{cis}$, $^2J_{HH}$ = 1.7), 4.83 (dd, 1H, $=CH_{trans}$), 3.35 and 3.18 (2 d, 2H, CH_2N, $^2J_{HH}$ = 13.9), 3.12 (d, 2H, $ArCH_2$) 2.73 and 2.02 (2 s, 6H, NMe_2), 2.02 (s, 3H, O_2CCH_3).

Compounds **9** and **10** have been identified in solution only by comparing their ^1H NMR spectra with those of authentic samples [1]. The ratio **8**:**9**:**10** (13:56:17%) has been determined by ^1H NMR, using 1,3,5 tri-*tert*-butylbenzene as an internal standard.

2.5. Synthesis of compound 11

A solution of 2-(but-3′-enyl)-*N*,*N*-dimethylaminomethylbenzene, **5** (0.190 g, 1.01 mmol) in benzene (5 ml) was added to a solution of palladium acetate (0.229 g, 1.02 mmol) in benzene (10 ml). The solution turned red after 30 min and the solution was stirred for an additional 30 min. The solvent was removed in vacuo and the residue was dissolved in CH_2Cl_2. After filtering through celite, this solution was stirred at RT, this leading to a yellow solution after 30 min. After 30 min stirring, the solvent was removed in vacuo. The residue was dissolved in Et_2O and filtered, then concentrated in vacuo. Addition of *n*-pentane afforded a yellow powder. It was filtered and dried in vacuo leading as for **8** to a yellow liquid (0.190 g, 54%). ^1H NMR indicated exclusively the presence of the cylometallated compound **11**.

^1H NMR ($CDCl_3$): 6.90–6.76 (m, 3H, Ar), 5.77 (ddt, –CH=, $^3J_{HH trans}$ = 17.0, $^3J_{HH cis}$ = 10.3, $^3J_{HH}$ = 6.3), 5.01–4.93 (m, 2H, $=CH_2$), 3.35 and 3.18 (2 d, 2H, CH_2N, $^2J_{HH}$ = 13.8), 3.12 (m, 2H, $ArCH_2$), 2.77 and 2.06 (2 s, 6H, NMe_2), 2.43 (m, 2H, $ArCH_2$), 2.17 (m, 2H, $CH_2CH=CH_2$), 2.03 (s, 3H, O_2CCH_3).

^{13}C NMR (C_6D_6): 180.5 (CO), 146.1, 145.1, 138.0, 135.3, 130.7, 125.4, 125.3 (7 C, $Ar_{(C)}$ + –CH = + $Ar_{(CH)}$), 115.3 (1C, $=CH_2$), 70.1 (1C, $ArCH_2N$), 52.3 et 51.2 (2C, NMe_2), 35.3, 34.5 (2C, $ArCH_2CH_2$) 24.9 (1C, O_2CCH_3).

2.6. Synthesis of compound 12

The procedure is the same as that used for the synthesis of **11**. Starting from 2-(pent-4′-enyl)-*N*,*N*-dimethylaminomethylbenzene, **7** (0.226 g, 1.11 mmol) and $Pd(OAc)_2$ (0.256 g, 1.14 mmol), afforded **12** as a yellow oil (0.267 g, 67%).

^1H NMR ($CDCl_3$): 6.82–6.72 (m, 3H, Ar), 5.76–5.67 (m, –CH=), 5.01–4.67 (m, 2H, $=CH_2$), 3.39 and 3.15 (2 d, 2H, CH_2N, $^2J_{HH}$ = 13.2), 3.12 (d, 2H, $ArCH_2$), 2.74 and 2.01 (2 s, 6H, NMe_2), 2.33 (t, 2H, $ArCH_2$, $^3J_{HH}$ = 5.5), 2.10–2.00 (m, 2H, $CH_2CH=CH_2$), 2.01 (s, 3H, O_2CCH_3), 1.20–1.12 (m, 2H, $ArCH_2CH_2$).

^1H NMR ($CDCl_3$ + PyD_5): 6.74 (d, 1H, $CH_{(Ar)}$, $^3J_{HH}$ = 7.4), 6.67 (t, 1H, $CH_{(Ar)}$, $^3J_{HH}$ = 7.4), 5.88 (d, 1H, $CH_{(Ar)}$, $^3J_{HH}$ = 7.4), 5.80 (ddt, 1H, –CH=, $^3J_{HH trans}$ = 17.0, $^3J_{HH cis}$ = 10.2, $^3J_{HH}$ = 6.6), 5.04–4.94 (m, 2H, $=CH_2$), 4.00 (s, 2H, CH_2N), 3.12 (d, 2H, $ArCH_2$), 2.81 (s, 6H, NMe_2), 2.47 (t, 2H, $ArCH_2$, $^3J_{HH}$ = 6.8), 2.11–2.04 (m, 2H, $CH_2CH=CH_2$), 1.89 (s, 3H, O_2CCH_3), 1.64–1.54 (m, 2H, $ArCH_2CH_2$).

^{13}C NMR ($CDCl_3$): 180.5 (CO), 145.1, 144.4, 135.8 (3C, $Ar_{(C)}$), 138.2 (1C, –CH=), 130.0, 125.0 (3C, $Ar_{(CH)}$), 115.0 (1C, $=CH_2$), 69.9 (1 C, $ArCH_2N$), 52.7 et 51.2 (2 C, NMe_2), 34.1 (1 C, $ArCH_2$), 33.5 (1 C, $CH_2CH=CH_2$), 29.9 (1C, $ArCH_2CH_2$), 24.5 (1C, O_2CCH_3).

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