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5,6-Membered CNN palladium pincer complexes of 3-benzyl-8-dimethylamino -3-azabicyclo[3.2.1]octane and 3-benzyl-9-dimethylamino-3-azabicyclo[3.3.1]nonane

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ABSTRACT

The unsymmetrical CNN pincer ligand precursors **4** and **7b** based on the structures of bicyclo[3.2.l]octane and bicyclo[3.3.l]nonane have been synthesized. The corresponding palladium pincer 5,6-membered complexes **5** and **9** were prepared by direct cyclopalladation of ligand precursors with Li_2PdCl_4 in MeOH. The molecular structure of the palladacycles was determined by ^1H and ^{13}C NMR and confirmed by X-ray diffraction analysis. The obtained complexes **5** and **9** exhibited good catalytic activity in the Suzuki reactions of aryl bromides with phenylboronic acid.

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1. Introduction

Palladium pincer complexes represent the class of palladacycles that is containing at least one σ-metal-carbon bond and two intramolecular coordinating linkages with heteroatoms. They are the point of active studies due to their high stability, possibility of structural modification and exhibited catalytic activity. For a long time only symmetric palladium pincer complexes based on aryl groups with equal side arms forming the combination of two identical typically 5-, less often 6-membered fused palladacycles were known. At the present time growing attention is focused on the development of new unsymmetrical pincer palladium complexes with two unequivalent side arms (YCY') or with one side arm, but containing two heteroatoms, in places suitable for metal complexation (CYY'). Structural modifications of the lateral coordination fragments affect the electronic properties of the palladium center and allow variation of chemical and catalytic features of the complex for the required use. Several reviews dedicated to the synthesis, properties and catalytic applications of symmetric and unsymmetrical palladium pincer complexes have been published for today [1–8]. Among them is a rather small group of CNN unsymmetrical pincer complexes in which the σ-bond Pd-C is stabilized by coordination with two nitrogen atoms [9–18]. Most of them have proven to be active catalysts and (pre)catalysts. It should be noted that in all these complexes at least one N atom is sp^2 hybridized. In our previous works we have described the synthesis of the novel and very stable CNN pincer cyclopalladates based on 3,7- diazabicyclo[3.3.1]nonane (bispidine) structure with asymmetrically substituted N atoms, which are both sp^3 hybridized [19,20].

The bicyclo[3.3.l]nonane derivatives can be described as the equilibrium between three main conformations - chair-chair, chair-boat and boat-boat, where in the most cases the twin-chair or boat-chair conformations are favored [21]. The bispidine derivatives with chair-chair preferential conformation look like the perfect ligand precursors to form metallocomplexes (Fig. 1, **1**). Prior to the beginning of our research work, only bispidines with symmetrically substituted nitrogen atoms were used to obtain complexes with Pd and they formed exclusively NN coordination complexes (Figs. 1, **2**) [22–25].

However, when we used the bispidines with unsymmetrically

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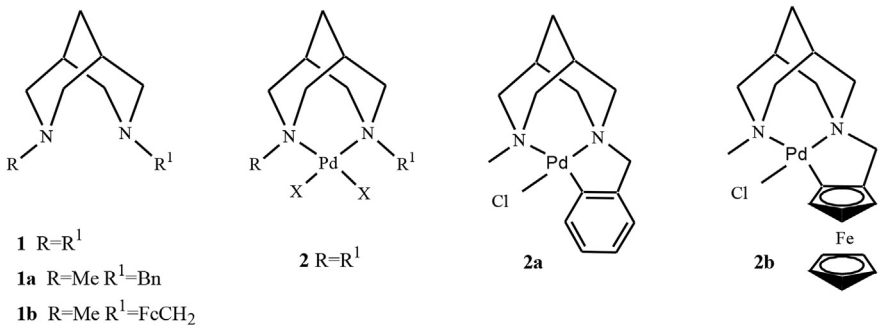


Fig. 1. The bispidine ligand precursors **1**, **1a**, and **1b**, NN coordination Pd complex **2** and unsymmetrical CNN pincer palladium complexes **2a** and **2b**.

substituted nitrogen atoms (Fig. 1, **a**, **1b**) for complexation with Pd only CNN pincer cyclopalladates were obtained in a good yield (Figs. 1, **2a**, **2b**) [19,20]. But when we took as a ligand precursor 3-benzyl-3-azabicyclo[3.3.1]nonane containing only one nitrogen atom rapid formation of palladium black was observed and we have failed to isolate any stable CN or NN palladium complexes. It can be assumed that for the compounds with the structure of 3-azabicyclo [3.3.l]nonane and 3-azabicyclo[3.2.l]octane the pincer complexes will be more stable. In order to form a pincer complex, it is necessary to insert a second heteroatom into the structure of bicyclic molecule. This requirement can be satisfied by introducing the amino group at a suitable place - at C9 and C8 of bicyclic framework respectively. In this case, the boat-chair conformation of the bicyclic ligand precursors will be convenient for the complexation with the metal and the formation of 5,6-membered CNN pincer palladacycles can be expected.

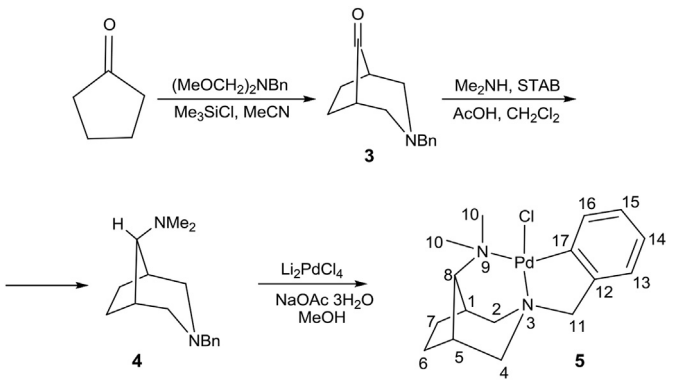
In this paper we report on the synthesis of two new unsymmetrical CNN pincer ligand precursors based on the bicyclic structures of bicyclo[3.3.l]nonane and bicyclo[3.2.l]octane and its corresponding palladium 5,6-membered complexes where both N are sp^3 hybridized. The obtained Pd complexes were examined as catalysts in the cross-coupling reactions of aryl halides with phenylboronic acid.

2. Result and discussion

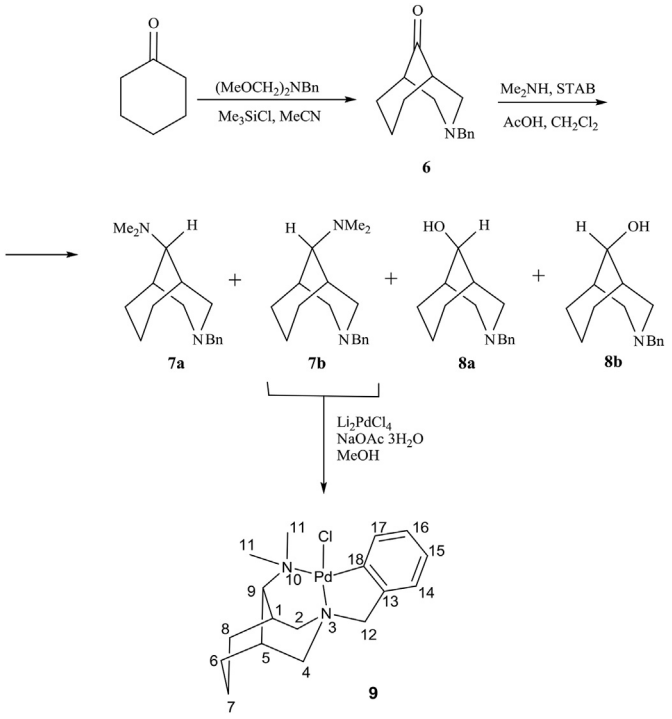
2.1. Synthesis and characterization

The unsymmetrical CNN pincer ligand precursors **4** and **7b** was prepared as shown in Schemes 1 and 2.

In the published syntheses of bicyclic ketones 3-benzyl-3-azabicyclo [3.2.1] octan-9-one (**3**) [26,27] and 3-benzyl-3-azabicyclo [3.3.1] nonan-9-one (**6**) [26–28] the best yields of the target products are obtained in a double Mannich reaction from cyclopentanone or cyclohexanone with N, N-bis(methoxymethyl) benzylamine in the presence of trimethylchlorosilane [27]. Using this technique afforded a 15% yield of ketone **3** and a 64% yield of ketone **6** (Schemes 1 and 2). At the next stage, the dimethylamino groups were introduced in the bicyclic molecules by the reaction of reductive amination of ketones **3** and **6** with dimethylamine and sodium triacetoxyborohydride. It is known that the addition or reduction reactions on the keto group in azabicyclic ketones take place with the possible formation of a mixture of diastereomers, the composition of which is controlled by steric effects and depends on the structure of the bicycle. Only the *syn* diastereomer is formed during the addition of MeMgBr to 3-methyl-3-azabicyclo [3.2.1] octan-8-one containing a saturated five-membered cycle [29,30]. When this compound is reduced by different methods, the *syn* isomer is also obtained mainly, and the *anti* compound is present only as a small admixture [31]. However, both the addition of organomagnesium and the reduction of the keto group for 3-methyl-3-azabicyclo [3.3.1] nonan-9-one lead to the formation of



Scheme 1. Synthesis of the ligand precursor **4** and unsymmetrical CNN pincer palladium complex **5**.



Scheme 2. Synthesis of the ligand precursor **7b** and unsymmetrical CNN pincer palladium complex **9**.

a mixture of the *syn* and the *anti* diastereomers, and the *anti*-compound is predominant [29–32]. As a result of the reductive amination of ketones **3** and **6**, we can also expect the formation of different diastereomers. However, the complexation with metals for ligand precursors with such a structure is possible only for their *syn* isomers.

The reductive amination of ketone **3** with dimethylamine and sodium triacetoxyborohydride in the presence of AcOH afforded a 69% yield of 3-benzyl-8-dimethylamino-3-azabicyclo[3.3.1]octane **4** (Scheme 1) as a single isomer. By analogy with the literature data, we have assumed that it is the *syn* isomer.

The reductive amination of ketone **6**, conducted under the same conditions, gave much more complicated results. In addition to the target 3-benzyl-9-dimethylamino-3-azabicyclo[3.3.1]nonane **7**, the product of the reduction of the ketone group 3-benzyl-9-hydroxy-3-azabicyclo[3.3.1]nonane **8** was obtained in an appreciable amount. These compounds were separated by SiO_2 chromatography. According to NMR data, both amine **7** and alcohol **8** turned out to be mixtures of isomers with a significant predominance of one of them (Scheme 2).

In the ^{1}H and ^{13}C NMR spectra of compounds **7** and **8**, two sets of well-separated signals corresponding to two diastereomers were presented.

For amine **7**, the ratio of diastereomers was determined by the comparing of the integral intensities of the methylene protons of the benzyl group of the two isomers in the ^{1}H NMR spectrum and was defined as 25: 100. In the ^{1}H NMR spectrum, a significant difference in the shielding of *exo* and *endo* protons adjacent to the cyclic amino group was observed. For the main isomer, this difference was 0.77 ppm, for the minor isomer, all four protons appeared as one broadened signal (Table 1, entry1), which indicated the proximity of the shielding of these protons. In the ^{13}C NMR spectrum, a distinction in the shielding of C at positions 2,4 and 6,8 for different isomers was observed. The signal of C(2,4) of the minor isomer is shifted to a strong field relative to the main isomer by 6.70 ppm. At the same time, the signal of C(6,8) of the minor isomer is shifted towards the lower field by 7.69 ppm regarding the main isomer. Thus, the difference in chemical shifts of the signals C(2,4) and C(6,8) for the main isomer is 35.34 ppm, and for the minor isomer this value is 20.95 ppm (Table 1, entry 4).

The ratio of diastereomers for compound **8** was determined by the comparing of the integral intensities of the H9 protons of the bicyclic skeleton and the methylene protons of the benzyl group of the two isomers in the ^{1}H NMR spectrum and turned up to be 30: 100. For this compound, the same differences in the chemical shifts of *exo* and *endo* protons adjacent to N3, as in the case of the amine **7** have been observed. For the main isomer, it is 0.68 ppm, which is significantly higher than the similar value (0.07 ppm) for the minor isomer (Table 1, entry 2).

In the ^{13}C NMR spectrum, the C(2,4) signal of the minor isomer is shifted upfield by 6.21 ppm and the signal C(6,8) of the minor isomer is shifted downfield by 7.10 relative to the main isomer. The difference in the chemical shifts of the C(2,4) and C(6,8) signals for the main isomer is 34.81 ppm, whereas for the minor isomer this value is 21.50 ppm. (Table 1 entry 5).

Similar patterns in changes in the chemical shifts of H and C signals of the two isomers were found for 3-methyl-9-hydroxy-3-azabicyclo [3.3.1] nonane (**A**), which was obtained by the reduction of ketone with sodium borohydride [33] (Table 1, entry 3 and 6). In this case, the main product have been defined as the *anti* isomer, and the *syn* isomer acts as a minor product. This allows us to assume that as a result of the reductive amination of ketone **6**, a mixture of diastereomers of alcohol **8** and amine **7** was obtained with a significant predominance of the *anti* isomer in both compounds.

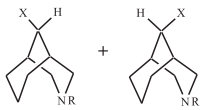
Direct cyclopalladiation of ligand precursor **4** was carried out by the reaction with Li_2PdCl_4 in the presence of stoichiometric amounts of sodium acetate monohydrate in methanol at room temperature. The interaction resulted in the isolation of unsymmetrical CNN pincer palladium complex **5** as the single product in a yield of 79%. When this reaction was carried out without sodium acetate, i.e., under conditions favorable for the formation of NN coordination complex, the only product was the same palladacycle **5** (59%).

Despite the fact that, according to our assumption, the main isomer in compound **7** is an *anti* isomer **7a** which is not able to form CNN complexes with metals, we hoped to obtain a cyclopalladation product from a mixture of isomers and isolate it due to the large difference in solubility of the ligand precursore and the complex. We managed to get the pincer complex **9** by direct cyclopalladation of the amine **7** with Li_2PdCl_4 in the presence of NaOAc x $3H_2O$ in methanol at room temperature in a yield of 16%. Such a low yield testifies in favor of our assumption that the *syn* isomer **7b** is a minor in the ligand precursor **7**. Considering content of **7b** in the mixture of isomers, the yield of complex **9** was 76%.

In the ^{1}H NMR spectra of CNN palladacycles, a decrease of the intensity of the signals of aromatic protons from 5H in the case of ligand precursors **4** and **7** to 4H for complexes **5** and **9** is observed, which confirms the occurrence of metalation of the phenyl ring. In the ^{13}C NMR spectra of palladium complexes the resonance of the new quaternary aromatic carbon C-Pd appeared at 144.55 ppm for **5** and 144.12 ppm for **9** and the resonance of another aromatic quaternary carbon C-C shifted downfield in comparison with that for starting ligand precursors. The chemical shift values of aromatic quaternary carbons of both complexes are in good agreement with each other, as well as with the previously obtained data for complex **2a** [18].

The NMR spectra data for the obtained CNN palladium complexes agree well with the microanalysis, IR and mass spectrometry data.

Table 1
The difference in the chemical shifts of the *syn* and the *anti* isomers of **7** and **8** in ^{1}H and ^{13}C NMR spectra.



anti *syn*

Entry	X	R		Minor isomer (*syn*), ppm			Major isomer (*anti*), ppm		
				H2,4(a)	H2,4(b)	Δ	H2,4(a)	H2,4(b)	Δ
1	NMe_2	Bn	**7**	2.60	2.60	0	2.99	2.22	0.77
2	OH	Bn	**8**	2.60	2.67	0.07	2.97	2.29	0.68
3[a]	OH	Me	**A**	2.47	2.60	0.13	2.87	2.20	0.67
				$C_{2,4}$	$C_{6,8}$	Δ	$C_{2,4}$	$C_{6,8}$	Δ
4	NMe_2	Bn	**7**	53.34	32.39	20.95	60.04	24.70	35.34
5	OH	Bn	**8**	52.86	31.36	21.5	59.07	24.26	34.81
6[a]	OH	Me	**A**	54.24	30.73	23.51	61.39	24.42	36.97

[a] From Ref. [33].

2.2. Crystal structure

The molecular structures of complexes **5** and **9** were confirmed by the X-ray analysis (Figs. 2 and 3). Single crystals of **5** and **9** were grown by slow evaporation of CH_2Cl_2 solution. In both complexes the five-membered Pd-cycle is characterized by the envelope conformation with the deviation of C(11) or C(12) atom by 0.370(2) and 0.477(2) Å in **5** and **9**, correspondingly. The principal geometric

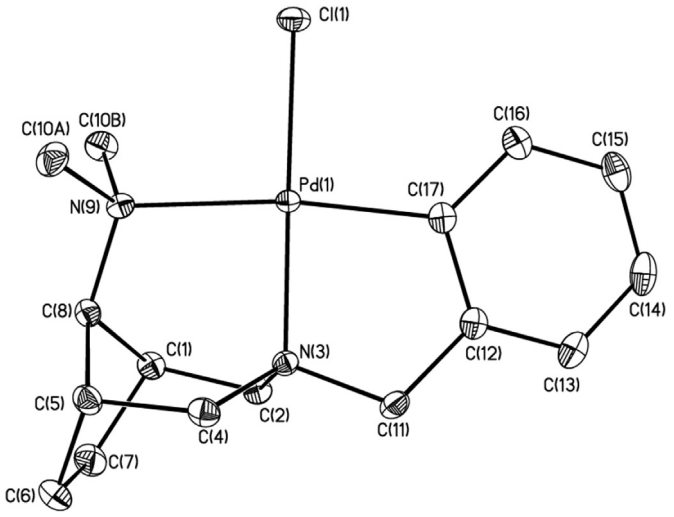


Fig. 2. The general view of **5** in representation of atoms by thermal ellipsoids (p = 50%). The selected bond lengths(Å): Pd(1)-Cl(1) 2.3197(3), Pd(1)-N(3) 2.064(1), Pd(1)-N(9) 2.176(1), Pd(1)-C(17) 1.986(1); bond angles (°): C(17)-Pd(1)-N(3) 84.82(5), C(17)-Pd(1)-N(9) 169.56(5), N(3)-Pd(1)-N(9) 87.74(4), C(17)-Pd(1)-Cl(1) 94.34(4), N(3)-Pd(1)-Cl(1) 178.83(3), N(9)-Pd(1)-Cl(1) 93.19(3).

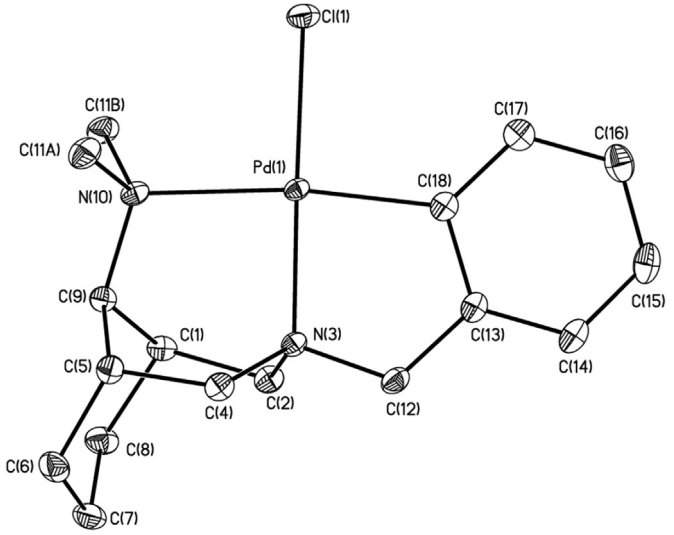


Fig. 3. The general view of **9** in representation of atoms by thermal ellipsoids (p = 50%). The selected bond lengths(Å): Pd(1)-Cl(1) 2.3220(4), Pd(1)-N(3) 2.070(1), Pd(1)-N(10) 2.179(1), Pd(1)-C(18) 1.985(2); bond angles (°): C(17)-Pd(1)-N(3) 84.40(6), C(17)-Pd(1)-N(9) 169.51(6), N(3)-Pd(1)-N(9) 87.99(5), C(17)-Pd(1)-Cl(1) 94.41(5), N(3)-Pd(1)-Cl(1) 178.80(4), N(9)-Pd(1)-Cl(1) 93.16(4).

parameters in complexes are almost identical. It should be noted that in both isomers the palladium atom is characterized by distortion of planar square coordination that can be illustrated by the values of dihedral angle between PdNN and PdCl(1)C planes that is 7.2°.

2.3. Catalytic studies

The palladium pincer complexes **5** and **9** were tested as pre-catalysts in several Suzuki cross-coupling reactions. All experiments were conducted under the conditions similar to those we used earlier in studies of the catalytic activity of other bicyclic cyclopalladates **2a** and **2b** (Fig. 1) [19,20]. This allowed us to compare the results obtained in this and previous works.

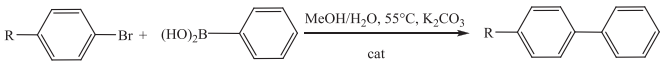
The Suzuki cross-coupling reactions were conducted with the phenylboronic acid and three aryl bromides in MeOH/H_2O for 5 h at 55 °C with K_2CO_3 as a base. In our previous studies, we used a catalyst loading of 0.5 mol%. In this work, we decided first of all to check the possibility of reducing the amount of catalyst. When using 0.5 mol% of catalysts **5** or **9** in the reaction of bromoanisole with phenylboronic acid, the yield of 4-methoxybiphenyl turned out to be close to quantitative (Table 2, entries 1 and 6). A decrease in catalyst loading in the same reaction to 0.1 mol% also leads to a high yield of the cross-coupling product (Table 2, entries 2 and 7). However, with a subsequent decrease in the loading of catalysts **5** or **9** to 0.05 mol%, the yield of the product drops sharply (Table 2, entries 3 and 8). Further experiments were carried out using 0.1 mol% of catalysts. When interacting with phenylboronic acid under the described conditions, both 4-bromotoluene (Table 2, entries 4 and 5) and 4-bromoacetophenone (Table 2, entries 9 and 10) form the corresponding biphenyls in high yields. Very similar results were obtained during the study of the interaction of 4-bromoanisole with phenylboronic acid under the same conditions using other CNN bicyclic pincer cyclopalladates **2a** and **2b** [19,20]. In this case, it seems that the structure of the bicyclic ligand does not have a noticeable effect on the catalytic activity of the complexes in cross-coupling reactions. However, CNN pincer Pd complexes **5** and **9** with two sp^3 N seem to be slightly more active catalysts for this reaction than the unsymmetric NCN pincer cyclopalladates with two sp^2 N presented in Ref. [34], considering the higher yield of the product in milder conditions in our case.

In some cross-coupling experiments the formation of small amounts of palladium black was observed. These inactive conglomerates are formed from active Pd^0 nanoparticles which are likely to be true catalists in the reaction. Such formation is typical for the processes involving phosphine-free cyclopalladated catalytic systems [35].

3. Conclusion

We have synthesized two new unsymmetrical pincer ligand precursors **4** and **7b** based on the structures of 3-azabicyclo[3.2.l] octane and 3-azabicyclo[3.3.l]nonane. In the molecules of ligand precursors, the bicyclic structure of which contains one N atom, the

Table 2
Catalytic cross-coupling Suzuki reaction[a].



10a-c **11a-c**

10a, 11a R=CH_3O
10b, 11b R=CH_3
10c, 11c R=CH_3CO

Entry	R	Cat	Mol%	Product	Yield[b] (%)
1	MeO	**5**	0.5	**11a**	99
2	MeO	**5**	0.1	**11a**	89
3	MeO	**5**	0.05	**11a**	13
4	Me	**5**	0.1	**11b**	91
5	MeC = O	**5**	0.1	**11c**	98
6	MeO	**9**	0.5	**11a**	99
7	MeO	**9**	0.1	**11a**	94
8	MeO	**9**	0.05	**11a**	9
9	Me	**9**	0.1	**11b**	95
10	MeC = O	**9**	0.1	**11c**	95

[a] *Reaction conditions:* aryl bromide (1 mmol), $PhB(OH)_2$ (1.5 mmol), K_2CO_3 (2.0 mmol), cat. **5** or **9**, MeOH (8 ml), H_2O (4 ml), 55 °C, 5 h.
[b] Isolated yields after column chromatography.

second heteroatom necessary for obtaining stable pincer cyclopalladates was introduced as NMe_2. The bicycle **4** was isolated as a single *syn* isomer. The only suitable for metal complexation syn isomer **7b** was obtained as a minor one in the mixture with its *anti* isomer. The corresponding CNN pincer complexes **5** and **9** where the palladium is coordinated with two sp^3 N atoms, was prepared by direct cyclopalladation of the ligand precursors. Both palladacycles **5** and **9** appeared to be the efficient catalyst in some cross-coupling reactions of aryl bromides with phenylboronic acid.

4. Experimental

4.1. General

The NMR experiments were carried out using a Bruker Avance™ 600 spectrometer operating at 600.22 MHz for ^1H and 150.93 MHz for ^{13}C and Bruker Avance™ 500 (500.13 and 125,77 MHz). ^1H chemical shift data are given in units δ relative TMS calibrated with $CHCl_3$ at 7.26 ppm. The multiplicity of a signal is indicated as follows: br, broad; s, singlet; d, doublet; m, multiplet; dd, doublet of doublets. ^{13}C chemical shifts are given relative TMS calibrated to the solvent, $CDCl_3$ at 77.26 ppm. The assignment of the signals in ^1H and ^{13}C NMR spectra has been performed by use of 2D COSY, HMQC and HMBC techniques on the basis of the Bruker program standard library. 2D inverse proton detected heteronuclear shift correlation spectra, gs-HMQC (^1H-^{13}C) and gs-HMBC (^1H-^{13}C) were obtained using standard pulse sequence from the Bruker library. The numbering of atoms used for NMR assignment is shown in Schemes 1 and 2. EI mass spectra were taken on a FINNIGAN POLARIS Q spectrometer at 70 eV and the temperature of the ion chamber 250 °C. IR spectra were recorded on a FT-IR Tensor 37 spectrometer (Bruker) in KBr pellets, thin film or nujol. The assignment of absorption bands in the IR spectra was made according to Ref. [36]. The TLC on Silufol UV-254 (Merck) was used to follow the course of reactions.

4.2. 3-Benzyl-3-azabicyclo[3.2.1]octan-9-one (**3**)

To a solution of *N,N*-Bis(methoxymethyl)benzylamine (50 g, 0.26 mol) in MeCN (200 ml) Me_3SiCl (56 ml, 0.44 mol) was added dropwise. After 15 min stirring cyclopentanone (23.2 ml, 0.26 mol) was added dropwise and the reaction mixture was stirred for 24 h. Then the mixture was concentrated, diluted with water (100 ml), treated with concentrated HCl (100 ml) and refluxed with stirring for 1 h. After cooling, the mixture was basified with solid sodium hydroxide to pH 10, extracted with AcOEt, washed with water and brine, dried over Na_2SO_4 and evaporated. The residue was purified by SiO_2 column chromatography with AcOEt/petroleum ether (0/100–3/97) to afford **3** (8.4 g, 15%) as a colorless oil, slowly crystallizing in the refrigerator. M.p. 37–38 °C. Anal.: C, 78.08; H, 7.89; N, 6.49%. Calc. for $C_{14}H_{17}NO$: C, 78.10; H, 7.96; N, 6.51%. IR (KBr, ν, cm $^{-1}$): 1751 (C=O), 734, 699 (C_6H_5). EI-MS, *m/z* (RI, %): 215 $[M]^+$ (51), 124 $[M - Bn]^+$ (42). ^1H NMR (600 MHz, $CDCl_3$) δ 7.42–7.30 (m, 4H, o- and m-Ph), 7.28 (t, $J = 7.0$ Hz, 1H, p-Ph), 3.62 (s, 2H, CH_2Ph), 3.00 (dd, $J = 11.1$, 3.2 Hz, 2H, CH_2N), 2.57 (d, $J = 10.8$ Hz, 2H, CH_2N), 2.18 (br s, 2H, H1, H5), 2.09 (q, $J = 4.9$ Hz, 2H, H6, H7), 1.91–1.85 (m, 2H, H6, H7). ^{13}C NMR (151 MHz, $CDCl_3$) δ 220.49 (C=O), 138.82 (*ipso*-Ph), 128.63 (o-Ph), 128.37 (m-Ph), 127.19 (p-Ph), 61.72 (CH_2N), 60.20 (CH_2Ph), 45.44 (C1, C5), 22.76 (C6, C7).

4.3. 3-Benzyl-3-azabicyclo[3.3.1]nonan-9-one (**6**)

To a solution of *N,N*-Bis(methoxymethyl)benzylamine (15 g, 0.077 mol) in MeCN (60 ml) Me_3SiCl (14.6 ml, 0.116 mol) was added dropwise. After 15 min stirring cyclohexanone (8.0 ml, 0.077 mol) was added dropwise and the reaction mixture was stirred for 24 h. Then the mixture was concentrated, diluted with water (30 ml), treated with concentrated HCl (30 ml) and refluxed with stirring for 1 h. After cooling, the mixture was basified with solid sodium hydroxide to pH 10, extracted with AcOEt, washed with water and brine, dried over Na_2SO_4 and evaporated. The residue was washed with hexane after SiO_2 column chromatography (AcOEt/petroleum ether: 0/100–5/95) to give **6** (11.1 g, 64%) as white crystals. M.p. 46–47 °C. Anal.: C, 78.63; H, 8.48; N, 6.27%. Calc. for $C_{15}H_{19}NO$: C, 78.56; H, 8.35; N, 6.11%. IR (KBr, ν, cm $^{-1}$): 1728 (C=O), 734, 700 (C_6H_5). EI-MS, *m/z* (RI, %): 229 $[M]^+$ (16), 138 $[M - Bn]^+$ (16). ^1H NMR (600 MHz, $CDCl_3$) δ 7.39–7.32 (m, 4H, o- and m-Ph), 7.33–7.27 (m, 1H, p-Ph), 3.49 (s, 2H, CH_2Ph), 3.18 (d, $J = 11.1$ Hz, 2H, CH_2N), 3.06–2.95 (m, 1H, H7), 2.58 (d, $J = 11.6$ Hz, 2H, CH_2N), 2.37 (br s, 2H, H1, H5), 2.19 (dd, $J = 14.1$, 5.6 Hz, 2H, H6, H8), 2.09–2.01 (m, 2H, H6, H8), 1.60–1.53 (m, 1H, H7). ^{13}C NMR (151 MHz, $CDCl_3$) δ 218.90 (C=O), 138.72 (*ipso*-Ph), 128.69 (o-Ph), 128.42 (m-Ph), 127.15 (p-Ph), 62.23 (CH_2Ph), 60.42 (CH_2N), 47.89 (C1, C5), 34.77 (C6, C8), 21.40 (C7).

4.4. 3-Benzyl-8-dimethylamino-3-azabicyclo[3.2.1]octane (**4**)

To a solution of **3** (5.2 g, 24 mmol) in CH_2Cl_2 (150 ml) were added dimethylamine (40% solution in water, 5.4 ml, 48 mmol), AcOH (1.4 ml, 24 mmol) and by portions sodium triacetoxyborohydride (STAB) (15.3 g, 72 mmol). The mixture was stirred for 8 h at room temperature, diluted with cold water, basified with sodium hydroxide solution to pH 10, extracted with CH_2Cl_2, washed with brine, dried over Na_2SO_4 and evaporated. The residue was purified by SiO_2 column chromatography with AcOEt/petroleum ether (10/90–20/80) to afford **4** (4.9 g, 69%) as a pale yellow oil. Anal.: C, 78.71; H, 9.83; N, 11.39%. Calc. for $C_{16}H_{24}N_2$: C, 78.64; H, 9.90; N, 11.46%. IR (thin film, ν, cm $^{-1}$): 732, 697 (C_6H_5). EI-MS, *m/z* (RI, %): 245 $[M+H]^+$ (53), 244 $[M]^+$ (40), 200 $[M\text{-}NMe_2]^+$ (30), 153 $[M\text{-}Bn]^+$ (100). ^1H NMR (500 MHz, $CDCl_3$) δ 7.37 (d, $J = 7.4$ Hz, 2H, o-Ph), 7.34–7.28 (m, 2H, m-Ph), 7.23 (t, $J = 7.2$ Hz, 1H, p-Ph), 3.56 (s, 2H, CH_2Ph), 2.64 (d, $J = 10.1$ Hz, 2H, CH_2N), 2.38 (dd, $J = 10.3$, 3.6 Hz, 2H, CH_2N), 2.25 (s, 6H, NMe_2), 2.10 (br s, 2H, H1, H5), 1.91 (t, $J = 4.2$ Hz, 1H, H 8), 1.86 (q, $J = 5.5$ Hz, 2H, H6, H7), 1.71–1.64 (m, 2H, H6, H7). ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.34 (*ipso*-Ph), 128.66 (o-Ph), 128.04 (m-Ph), 126.51 (p-Ph), 70.48 (C8), 62.27 (CH_2Ph), 52.86 (CH_2N), 44.53 (NMe_2), 36.66 (C1, C5), 27.31 (C6, C7).

4.5. 3-Benzyl-9-dimethylamino-3-azabicyclo[3.3.1]nonane (**7**) and 3-benzyl-9-hydroxy-3-azabicyclo[3.3.1]nonane (**8**)

To a solution of **6** (10 g, 44 mmol) in CH_2Cl_2 (300 ml) were added dimethylamine (40% solution in water, 11 ml, 87 mmol), AcOH (2.5 ml, 44 mmol) and by portions STAB (28 g, 132 mmol). After the stirring for 8 h at room temperature to the reaction mixture were added more STAB (13 g, 61 mmol) and AcOH (1.3 ml, 0.023 m) and the stirring was continued for 6 h else. Then the reaction mixture was diluted with cold water, basified with sodium hydroxide solution to pH 10, extracted with CH_2Cl_2, washed with brine, dried over Na_2SO_4 and evaporated. The residue was purified by SiO_2 column chromatography with AcOEt/petroleum ether (10/90–20/80) to afford **7** (4.1 g, 36%) as a pale yellow oil and **8** (3.8 g, 37%) as a white powder.

4.5.1. 3-Benzyl-9-dimethylamino-3-azabicyclo[3.3.1]nonane **7**

Anal.: C, 79.11; H, 10.18; N, 10.71%. Calc. for $C_{17}H_{26}N_2$: C, 79.02; H, 10.14; N, 10.84%. IR (KBr, ν, cm $^{-1}$): 747, 700 (C_6H_5). EI-MS, *m/z* (RI, %): 259 $[M+1]^+$ (24), 258 $[M]^+$ (11), 214 $[M\text{-}NMe_2]^+$ (26), 167 $[M - Bn]^+$ (100). *Major isomer*: ^1H NMR (600 MHz, $CDCl_3$) δ 7.37–7.30 (m, 4H, *o*- and *m*-C_6H_5), 7.28–7.22 (m, 1H, *p*-C_6H_5), 3.40 (s, 2H, CH_2Ph),

2.99 (d, $J = 10.8$ Hz, 2H, CH_2N), 2.68–2.64 (m, 1H, H7), 2.24 (s, 6H, $2NMe_2$), 2.24–2.21 (m, 2H, CH_2N), 1.93 (br s, 2H, H1, H5), 1.98–1.87 (m, 2H, H6, H8), 1.71 (br s, 1H, H9), 1.58–1.51 (m, 1H, H7), 1.49–1.46 (m, 2H, H6, H8). ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.65 (*ipso*-C_6H_5), 128.62 (*o*-C_6H_5), 128.19 (*m*-C_6H_5), 126.64 (*p*-C_6H_5), 68.29 (C9), 63.45 (CH_2Ph), 60.04 (CH_2N), 43.02 (NCH_3), 31.41 (C1, C5), 24.70 (C6, C8), 21.28 (C7). *Minor isomer*: ^1H NMR (600 MHz, $CDCl_3$) δ 7.37–7.30 (m, 4H, *o*- and *m*-C_6H_5), 7.28–7.22 (m, 1H, *p*-C_6H_5), 3.43 (s, 2H, CH_2Ph), 2.79–2.70 (m, 1H, H7), 2.60 (br s, 4H, CH_2N), 2.23 (s, 6H, 2 NCH_3), 2.02 (br s, 2H, H1, H5), 1.98–1.87 (m, 2H, H6, H8), 1.72 (s, 1H, H9), 1.65–1.58 (m, 2H, H6, H8), 1.49–1.46 (m, 1H, H7). ^{13}C NMR (151 MHz, $CDCl_3$) δ 140.11 (*ipso*-C_6H_5), 128.70 (*o*-C_6H_5), 128.11 (*m*-C_6H_5), 126.49 (*p*-C_6H_5), 67.92 (C9), 63.81 (CH_2Ph), 53.34 (CH_2N), 43.13 (NCH_3), 32.39 (C6, C8), 31.48 (C1, C5), 21.76 (C7).

4.5.2. 3-Benzyl-9-hydroxy-3-azabicyclo[3.3.1]nonane **8**

Anal.: C, 77.88; H, 9.07; N, 6.09%. Calc. for $C_{15}H_{21}NO$: C, 77.88; H, 9.15; N, 6.05%. IR (KBr, ν, cm^{-1}): 730, 697 (C_6H_5). EI-MS, *m/z* (RI, %): 231 $[M]^+$ (43), 140 $[M-Bn]^+$ (42). *Major isomer*: ^1H NMR (600 MHz, $CDCl_3$) δ 7.36–7.32 (m, 4H, *o*- and *m*-C_6H_5), 7.28–7.24 (m, 1H, *p*-C_6H_5), 3.78 (d, $J = 2.8$ Hz, 1H, H9), 3.40 (s, 2H, CH_2Ph), 2.97 (d, $J = 10.4$ Hz, 2H, CH_2N), 2.72–2.63 (m, 1H, H7), 2.29 (d, $J = 11.6$ Hz, 2H, CH_2N), 2.03–1.95 (m, 2H, H6, H8), 1.81 (br s, 2H, H1, H5), 1.51–1.59 (m, 3H, H6, H8, OH), 1.50 (dt, $J = 12.7$, 6.3 Hz, 1H, H7). ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.52 (*ipso*-C_6H_5), 128.62 (*o*-C_6H_5), 128.23 (*m*-C_6H_5), 126.74 (*p*-C_6H_5), 72.35 (C9), 63.24 (CH_2Ph), 59.07 (CH_2N), 35.54 (C1, C5), 24.26 (C6, C8), 21.29 (C7). *Minor isomer*: ^1H NMR (600 MHz, $CDCl_3$) δ 7.36–7.32 (m, 4H, *o*- and *m*-C_6H_5), 7.28–7.24 (m, 1H, *p*-C_6H_5), 3.69 (t, $J = 3.1$ Hz, 1H, H9), 3.41 (s, 2H, CH_2Ph), 2.67 (d, $J = 12.6$ Hz, 2H, CH_2N), 2.60 (d, $J = 11.4$ Hz, 2H, CH_2N), 2.57–2.49 (m, 1H, H7), 2.08 (br s, 1H, OH), 1.90 (br s, 2H, H1, H5),1.86–1.84 (m, 2H, H6, H8), 1.68–1.60 (m, 2H, H6, H8), 1.43 (dt, $J = 12.6$, 6.3 Hz, 1H, H7). ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.40 (*ipso*-C_6H_5), 128.70 (*o*-C_6H_5), 128.23 (*m*-C_6H_5), 126.74 (*p*-C_6H_5), 71.79 (C9), 63.64 (CH_2Ph), 52.86 (CH_2N), 36.20 (C1, C5), 31.36 (C6, C8), 20.35 (C7).

4.6. (8-Dimethylamino–3-azabicyclo[3.2.1]octane-3-ylmethyl) phenyl]-(C,N,N)-palladium chloride, **5**

Method A. A mixture of $PdCl_2$ (0.138 g, 0.78 mmol) and LiCl (0.066 g, 1.56 mmol) in MeOH (20 ml) was refluxed with stirring for 1 h and cooled. To the obtained solution was added a solution of **4** (0.191 g, 0.78 mmol) and sodium acetate monohydrate (0.107 g, 0.78 mmol) in MeOH (10 ml). The mixture was stirred for 24 h at room temperature and evaporated. The crude was diluted with water and extracted with CH_2Cl_2. The organic layers were washed with water and brine, dried over Na_2SO_4, filtered and evaporated. The solid residue was washed with ether and small amount of acetone and dried to afford **5** (0.237 g, 79%).

Method B. To a solution of Na_2PdCl_4 (0.125 g, 0.43 mmol) in MeOH (10 ml) was added a solution of **4** (0.104 g, 0.43 mmol) in MeOH (10 ml). The mixture was stirred for 24 h at room temperature and evaporated. The crude was diluted with water and extracted with CH_2Cl_2. The organic layers were washed with water and brine, dried over Na_2SO_4, filtered and evaporated. The solid residue was washed with ether and small amount of acetone and dried to afford **5** (0.097 g, 59%) as off-white crystals. Decomposes without melting at about 160 °C. Anal.: C, 49.54; H, 6.14; N, 7.15%. Calc. for $C_{16}H_{23}ClN_2Pd$: C, 49.88; H, 6.02; N, 7.27%. IR (KBr, ν, cm^{-1}): 738 (o-C_6H_4); IR (nujol, ν, cm^{-1}): 322 (Pd-Cl). EI-MS, *m/z* (RI, %): 384 $[M]^+$ (12), 243 $[M - PdCl]^+$ (98), 198 $[M\text{-}PdCl\text{-}NHMe_2]^+$ (44). ^1H NMR (500 MHz, $CDCl_3$) δ 7.70 (dd, $J = 7.1$, 1.8 Hz, 1H, H16), 6.99–6.90 (m, 2H, H14, H15), 6.82 (dd, $J = 7.0$, 1.4 Hz, 1H, H13), 4.23–4.12 (m, 2H, CH_2N), 3.99 (s, 2H, CH_2Ph), 2.76 (s, 6H, 2 NCH_3), 2.62 (br s, 2H, H1, H5), 2.42 (d, $J = 12.5$ Hz, 2H, CH_2N), 2.13 (t, $J = 3.7$ Hz, 1H, H8), 2.04–1.96 (m, 2H, H6, H7), 1.66 (q, $J = 5.8$ Hz, 2H, H6, H7). ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.56 (*ipso*-C_6H_4, C-C), 144.55 (*ipso*-C_6H_4, C-Pd), 136.10 (C16), 125.28 and 124.17 (C14 and C15), 120.01 (C13), 73.06 (CH_2Ph), 69.75 (C8), 64.43 (CH_2N), 48.75 (NCH_3), 33.91 (C1, C5), 30.85 (C6, C7).

4.7. (9-Dimethylamino-3-azabicyclo[3.3.1]nonane-3-ylmethyl) phenyl]-(C,N,N)-palladium chloride, **9**

A mixture of $PdCl_2$ (0.182 g, 1.0 mmol) and LiCl (0.087 g, 2 mmol) in MeOH (20 ml) was refluxed with stirring for 1 h and cooled. To the obtained solution was added a solution of **7** (0.266 g, 1.0 mmol) and sodium acetate monohydrate (0.140 g, 1.0 mmol) in MeOH (10 ml). The mixture was stirred for 24 h at room temperature and evaporated. The crude was diluted with water and extracted with CH_2Cl_2. The organic layers were washed with water and brine, dried over Na_2SO_4, filtered and evaporated. The residue was washed with ether and acetone and dried to afford **9** (0.064 g, 16%) as off-white crystals. Decomposes without melting at about 167 °C. Anal.: C, 50.89; H, 6.30; N, 6.82; Cl, 8.95%. Calc. for $C_{17}H_{25}ClN_2Pd$: C, 51.14; H, 6.31; N, 7.02; Cl, 8.88%. IR (KBr, ν, cm^{-1}): 743 (o-C_6H_4); IR (nujol, ν, cm^{-1}): 320 (Pd-Cl). EI-MS, *m/z* (RI, %): 399 $[M+H]^+$ (30), 398 $[M]^+$ (14), 257 $[M - PdCl]^+$ (100). ^1H NMR (600 MHz, $CDCl_3$) δ 7.71 (d, $J = 7.1$ Hz, 1H, H17), 6.99–6.88 (m, 2H, H15, H16), 6.81 (d, $J = 6.6$ Hz, 1H, H14), 4.01 (s, 2H, CH_2Ph), 3.94 (t, $J = 11.3$ Hz, 2H, CH_2N), 2.81 (br s, 2H, H1, H5), 2.70 (s, 6H, 2 NCH_3), 2.44 (d, $J = 12.2$ Hz, 2H, CH_2N), 1.87 (br s, 1H, H9), 1.82–1.65 (m, 2H, H6, H8), 1.63–1.50 (m, 4H, H6, H8, H7). ^{13}C NMR (151 MHz, $CDCl_3$) δ 147.94 (*ipso*-C_6H_4, C-C), 144.12 (*ipso*-C_6H_4, C-Pd), 136.16 (C17), 125.23 and 124.17 (C15 and C16), 120.02 (C14), 72.85 (CH_2Ph), 68.24 (C9), 59.28 (CH_2N), 46.59 (NCH_3), 31.15 (C6, C8), 29.14 (C1, C5), 14.18 (C7).

4.8. X-ray crystallography

Crystals of the complexes **5** and **9** suitable for X-ray analysis were obtained by recrystallization from CH_2Cl_2. The unit cells parameters and three-dimensional sets of intensities for complexes **5** and **9** were obtained on an APEX II CCD diffractometer using

Table 3
Crystal data and structure refinement parameters for **5** and **9.**

	5	9
CCDC	1826817	1826818
Empirical formula	$C_{16}H_{23}ClN_2Pd$	$C_{17}H_{25}ClN_2Pd$
Formula weight	385.21	399.24
Temperature (K)	120	120
Crystal system	Triclinic	Triclinic
Space group	P-1	P-1
Z(Z′)	2(1)	2(1)
a, Å	8.3929(3)	8.8441(5)
b, Å	9.2936(3)	9.3276(5)
c, Å	11.0549(4)	10.9346(6)
α, °	98.4989(6)	97.7403(10)
β, °	112.0717(6)	111.5282(10)
γ, °	95.1981(7)	97.7537(10)
V, $Å^3$	780.21(5)	814.67(8)
d_{calc}, $g \cdot cm^{-3}$	1.640	1.628
μ, cm^{-1}	13.52	12.98
F(000)	392	408
$2\theta_{max}$, ° (completeness)	58 (1.00)	58 (0.99)
Refl. collected	9657	9853
Refl. unique (R_{int})	4144 (0.0181)	4333 (0.0280)
Refl. with $I > 2\sigma(I)$	4037	4001
Variables	184	190
Final R_1 with $I > 2\sigma(I)$	0.0158	0.0207
wR_2 (all data)	0.0388	0.0483
GOF	0.973	1.055
Largest difference in peak/hole (e/$Å^3$)	0.458/-0.440	0.492/-0.420

molybdenum radiation [λ (Mo Kλ) = 0.71073 Å, ω-scans]. The substantial redundancy in data allowed empirical absorption corrections to be applied with SADABS by multiple measurements of equivalent reflections. The structures were solved by direct methods and refined by the full-matrix least-squares technique against F^2 in the anisotropic-isotropic approximation. C-H hydrogen atoms in all structures were placed in calculated positions and refined within the riding model. All calculations were performed with the SHELXTL software package [37]. Crystal data and structure refinement parameters are listed in Table 3.

4.9. General procedure for the Suzuki reaction

A mixture of aryl bromide (1 mmol), phenylboronic acid (1.5 mmol), K_2CO_3 (2 mmol), the palladium complex **5** or **9**, MeOH (8 ml) and H_2O (4 ml) was heated at 55 °C for 5 h. The reaction mixture was diluted with water and extracted with $CHCl_3$. The combined organic phase was dried over Na_2SO_4, evaporated and purified by chromatography on SiO_2 (petroleum ether/$CHCl_3$ = 8:1). The purified products were identified by ^1H NMR spectra.

5. Supplementary material

CCDC 1826817 (for **5**) and 1826818 (for **9**) contain the supplementary crystallographic data. These data can be obtained free of charge from the Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/data_request/cif.

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