– 30 °C. The resulting crystals were collected, washed with a minimum amount of cold hexane, and dried in vacuum. Yield of **4**: 2.9 g (44 % related to **1**). Mg turnings (302 mg, 12.4 mmol) were placed in a three-necked flask (100 mL) and treated with diethyl ether (10 mL). A solution of 3,5-bis(trifluoromethyl)-1-bromobenzene (3.6 g, 12.4 mmol) in diethyl ether (10 mL) was added dropwise to the magnetically stirred mixture. After 1 h the solution was transferred into a dropping funnel and slowly added to a solution of **4** (1.5 g, 3.1 mmol) in THF (25 mL). The mixture was then heated at reflux until the reaction was complete (~2 h). After removal of the solvents in vacuum the residue was dissolved in toluene. The solution was washed with degassed water and dried with anhydrous $Na_2SO_4$. The toluene was removed in vacuum, and the residue was recrystallized from acetone/methanol. Yield of **5a**: 3.3 g (89 %).

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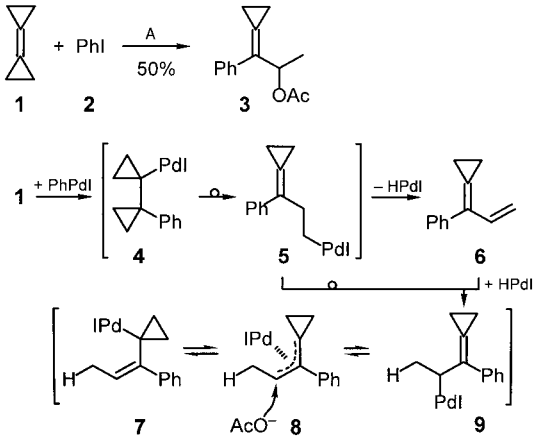
# Nucleophilic Trapping of π-Allylpalladium Intermediates Generated by Carbopalladation of Bicyclopropylidene: A Novel Three-Component Reaction**

Hanno Nüske, Mathias Noltemeyer, and Armin de Meijere*

*Dedicated to Professor Barry M. Trost on the occasion of his 60th birthday*

The construction of complex molecules from simple starting materials is a challenging task for chemists. One of the most elegant ways to achieve this is by utilizing so-called domino reactions.[1] Multicomponent reactions such as the Mannich and the Ugi reaction are examples of all-intermolecular domino reactions. Recently, our group has published a new all-carbon-coupling three-component reaction, the domino Heck – Diels – Alder reaction of bicyclopropylidene (**1**).[2] This sequence involves the Heck-type coupling of bicyclopropylidene (**1**)[3] with haloarenes and -alkenes to form 1-substituted allylidenecyclopropanes which then undergo [4+2] cycloadditions with dienophiles yielding 7-substituted spiro[2.5]oct-7-enes in a one-pot operation. In the course of a more extensive study of this methodology we became aware of a new reaction mode through the isolation of the side product **3**, the formation of which can only be rationalized by an intermolecular nucleophilic attack of an acetate anion stemming from the catalyst precursor on an intermediate π-allylpalladium species **8** (Scheme 1).[4]




Scheme 1. Mechanism of the nucleophilic trapping of π-allylintermediate **8**. A) 5 mol % $Pd(OAc)_2$, 10 mol % TFP, 5.0 equiv LiOAc, $K_2CO_3$, $Et_4NCl$, MeCN, 80 °C, 24 h.

The π-allylpalladium intermediate **8** must be formed after the initial carbopalladation and *β*-hydride elimination by readdition of the hydridopalladium species onto the newly formed double bond[5] via a σ-allylpalladium complex **9**. The ligand tris-(*α*-furyl)phosphane (TFP), which is known to retard *β*-hydride elimination[6] and thus favor the readdition of the hydridopalladium complex onto the double bond, proved to be best for this reaction, and the yield of the allyl acetate **3** could be raised up to 50 % by using LiOAc as an additional source of acetate.

In view of previous observations on the nucleophilic substitution reactions on 1,1-dimethyleneallylpalladium intermediates,[7] stabilized enolates and other carbon nucleophiles were tested. These were generated by separately deprotonating malononitriles and diethyl malonates with sodium hydride and then adding to the reaction mixture from **1**, the palladium precatalyst, and iodobenzene (**2**) to give the malonic acid derivatives **11a – c** in up to 77 % yield.[8] In accordance with earlier findings,[7] only products of the nucleophilic attack at the sterically less encumbered terminus of the allyl moiety were obtained (Scheme 2).

Especially interesting is the possible preparation of amino acid derivatives by this method. With O'Donnell's nucleophilic glycine equivalent **12**[9] the methylenecyclopropane derivative **13**, a substituted isomer of hypoglycin A in a protected form,[10] was obtained in 76 % yield (Scheme 3). Glycine methyl ester **14a**, in the presence of triethylamine in

[*] Prof. Dr. A. de Meijere, Dr. H. Nüske
Institut für Organische Chemie
Georg-August-Universität Göttingen
Tammannstrasse 2, 37077 Göttingen (Germany)
Fax: (+49) 551-399475
E-mail: Armin.deMeijere@chemie.uni-goettingen.de
Dr. M. Noltemeyer
Institut für Anorganische Chemie
Georg-August-Universität Göttingen
Röntgenstrukturabteilung
Tammannstrasse 4, 37077 Göttingen (Germany)

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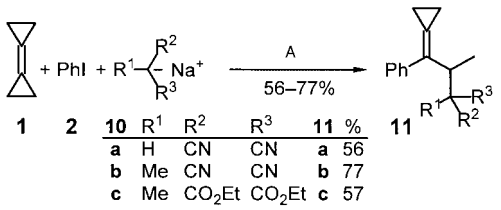
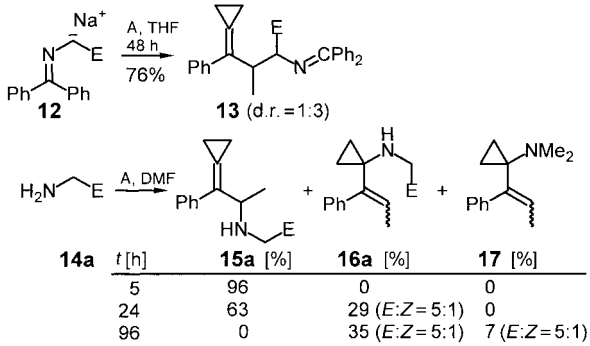



| 1 | 2 | 10 | $R^1$ | $R^2$ | $R^3$ | 11 | % | 11 |
|---|---|---|---|---|---|---|---|---|
| | | **a** | H | CN | CN | **a** | 56 | |
| | | **b** | Me | CN | CN | **b** | 77 | |
| | | **c** | Me | $CO_2Et$ | $CO_2Et$ | **c** | 57 | |

Scheme 2. Malonic ester derivatives as nucleophiles. A) 5 mol% $Pd(OAc)_2$, 10 mol% TFP, $Et_3N$, THF, 80 °C, 24–96 h.




| 14a | t [h] | 15a [%] | 16a [%] | 17 [%] |
|---|---|---|---|---|
| | 5 | 96 | 0 | 0 |
| | 24 | 63 | 29 (E:Z = 5:1) | 0 |
| | 96 | 0 | 35 (E:Z = 5:1) | 7 (E:Z = 5:1) |

Scheme 3. Preparation of C- and N-substituted amino acids. A) 1.0 equiv **1**, 0.5 equiv **2**, 5 mol% $Pd(OAc)_2$, 10 mol% TFP, $Et_3N$, 80 °C. E = $CO_2Me$.

this one-pot transformation, gave the substitution product **15a** after 5 h in nearly quantitative yield (96%). Interestingly, upon prolonged heating (24 h) of the reaction mixture, the yield of **15a** decreased to 63%, and in addition 29% of the regioisomer **16a** was isolated as a mixture of *E* and *Z* isomers (5:1). This indicates that the nucleophilic substitution of **8** with **14a** is reversible and that **16a** is the thermodynamically more stable product.

The successful application of the glycine ester as a nitrogen nucleophile led to the evaluation of a number of primary and secondary amines (Table 1). Very good results were achieved with primary amines, and the products were formed in good to excellent yields. No twofold substitution of the amine, which is a common side reaction of primary amines,[11] was detected.

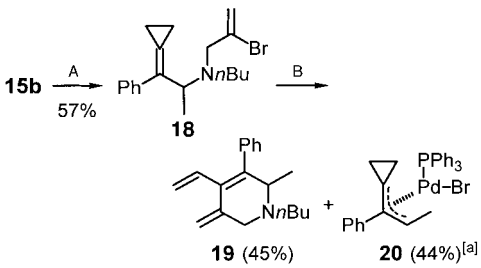
Table 1. The use of amines as nucleophiles in the new three-component reaction.[a]

| Entry | Amine | t [h] | Product (E/Z) | Yield [%] |
|---|---|---|---|---|
| 1 | $H_2NnBu$ (**14b**) | 48 | **15b** | 73[a] |
| 2 | $H_2NnBu$ (**14b**) | 24 | **16b** (6:1) | 15 |
| | | | **17** (5:1) | 19 |
| 3 | $H_2NiBu$ (**14c**) | 48 | **15c** | 73 |
| 4 | $H_2NtBu$ (**14d**) | 48 | **15d** | 95 |
| 5 | $H_2NBn$ (**14e**) | 1 | **15e** | 98 |
| 6 | $H_2NBn$ (**14e**) | 48 | **16e** (10:1) | 60 |
| | | | **17** (5:1) | 28 |
| 7 | (3-methylbut-1-yne-3-yl)amine (**14f**) | 24 | **15f** | 41 |
| 8 | $HNEt_2$ (**14g**) | 48 | **15g** | 75 |
| 9 | piperidine (**14h**) | 1 | **15h** | 79 |
| 10 | piperidine (**14h**) | 24 | **16h** (5:1) | 67 |
| 11 | morpholine (**14i**) | 1.5 | **15i** | 99 |
| 12 | morpholine (**14i**) | 20 | **15i** | 42 |
| | | | **16i** (>20:1) | 14 |
| 13 | morpholine (**14i**) | 48 | **15i** | 70[b] |

[a] Conditions: 2.00 equiv **1**, 1.00 equiv **4**, 3.00 equiv amine, 5 mol% $Pd(OAc)_2$, 10 mol% TFP, DMF, 80 °C. [b] 10 mol% P(*o*Tol)$_3$.

Secondary amines should not be too bulky, as diethylamine (**14g**) (Table 1, entry 6) gave **15f** in 75% yield, while dibenzylamine and diisobutylamine gave no coupling products. Piperidine (**14h**) and morpholine (**14i**) afforded compounds **15h** and **15i** in 79 and 99% yield, respectively, after only 1 h. In these cases prolonged heating also led to the formation of the thermodynamically favored products, for example after 48 h the products from **14h** and **14i** were completely converted to **16h** and **16i**. Interestingly, in the presence of tris(*o*-tolyl)phosphane, products of type **15** were formed exclusively, even after 48 h (Table 1, entry 13).

The allylamine **15b** from bicyclopropylidene (**1**), iodobenzene (**2**), and *n*-butylamine (**14b**) was further elaborated (Scheme 4). Alkylation of **15b** with 2,3-dibromopropene gave




Scheme 4. Intramolecular cross-coupling of the 4-aza-2-bromo-1,6-diene **18**. A) 1) $K_2CO_3$, $CH_2Cl_2$; 2) 2,3-dibromopropene, 0 → 25 °C, 20 h. B) 5 mol% $Pd(OAc)_2$, 10 mol% $PPh_3$, $Et_3N$, DMF, 80 °C, 24 h. [a] Yield based on amount of $Pd(OAc)_2$ used.

the 4-aza-2-bromo-1,6-diene **18**, which underwent an intramolecular Heck-type cross coupling with opening of the cyclopropane ring to yield the cross-conjugated 5-methylene-4-ethenyl-1,2,5,6-tetrahydropyridine **19** in 45% yield and, in addition, the 1,1-dimethyleneallylpalladium complex **20** (44% yield based on $Pd(OAc)_2$ used) could be isolated.[12]

The X-ray structure analysis of **20** (Figure 1) discloses that all three allyl carbon atoms are located at nearly the same distance[13] from the metal atom, with C(5) just barely closer to the palladium than C(3).[14] Thus, the preferred initial attack of any nucleophile at C(5) of a π-allylpalladium complex of type **20** must be attributed to the less pronounced

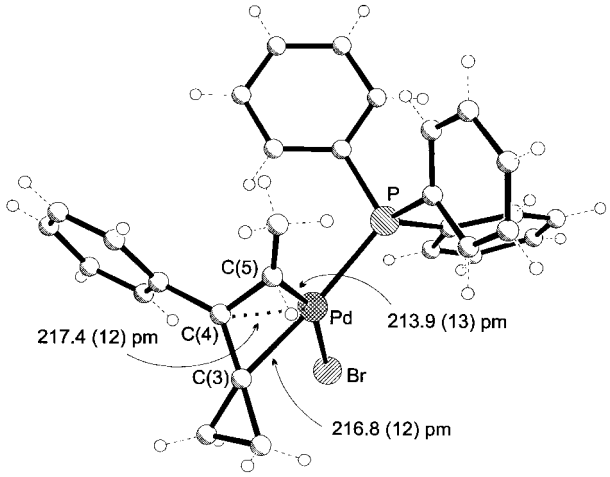



Figure 1. Structure of the π-allylpalladium complex **20** in the crystal.[12]

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steric encumbrance at this site and the fact that an $S_N2$-type attack on the cyclopropyl carbon C(3) has to pass through a highly strained transition structure.[15] The formation of complex **20** from **18** also shows that the attack at least of nitrogen nucleophiles on π-allylpalladium intermediates of type **8** must be reversible.

In conclusion, this new three-component reaction bears a significant combinatorial potential in that all three components may be varied just as in the previously described domino Heck–Diels–Alder sequence,[2] leading to a three-dimensional library of small molecules.

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[8] Representative procedure: 1-Cyclopropylidene-1-phenyl-2-morpholinopropane (**15i**): Morpholine (**14i**) (261 mg, 3.00 mmol) was added to a solution containing $Pd(OAc)_2$ (11.2 mg, 50.0 μmol; 5 mol%), TFP (23.2 mg, 100 μmol; 10 mol%), iodobenzene (**2**) (204 mg, 1.00 mmol), and bicyclopropylidene (**1**) (160 mg, 2.00 mmol) in DMF (0.5 mL), and the mixture was stirred for 1.5 h at 80 °C. After cooling to room temperature, the solution was added to water (10 mL), the mixture extracted with diethyl ether (5 × 20 mL), and the combined organic phases dried ($MgSO_4$). After removal of the solvent in a rotatory evaporator the residue was chromatographed on silica gel (25 g, column 2 × 20 cm, pentane/diethyl ether 5/1) to yield **15i** (240 mg, 99%) as a yellowish oil, $R_f = 0.55$. IR (film): $\tilde{\nu} = 3052, 2971, 2851, 2805$ (C–N), 1598, 1494, 1447, 1373, 1261, 1118, 1071, 926, 762, 698 cm$^{-1}$; $^1$H NMR (250 MHz, $CDCl_3$): $\delta = 1.21-1.43$ (m, 4H; *c*Pr-H), 1.28 (d, $^3J = 6.7$ Hz, 3H; 3-H), 2.42–2.63 (m, 4H; $CH_2NCH_2$), 3.58 (q, $^3J = 6.7$ Hz, 1H; 2-H), 3.69–3.78 (m, 4H; $CH_2OCH_2$), 7.23 (dd, $^3J = 7.0$, $^4J = 1.1$ Hz, 1H; 4′-H), 7.32 (dd, $^3J = 7.0$, $^3J = 7.2$ Hz, 2H; 3′-H, 5′-H), 7.82 (dd, $^3J = 7.2$, $^4J = 1.1$ Hz, 2H; 2′-H, 6′-H); $^{13}$C NMR (62.9 MHz, $CDCl_3$, DEPT): $\delta = 2.74$ (–, *c*Pr-C), 3.74 (–, *c*Pr-C), 15.77 (+, C-3), 50.73 (–, C-2″, C-6″), 64.99 (+, C-2), 67.36 (–, C-3″, C-5″), 123.76 ($C_{quat}$, *c*Pr-C), 126.35 (+, C-4′), 127.23 (+, Ar-C), 127.77 (+, Ar-C), 128.59 ($C_{quat}$, Ar-C), 139.99 ($C_{quat}$, C-1); MS (70 eV): *m*/*z* (%): 243 (12) [$M^+$], 228 (5) [$M^+ - CH_3$], 198 (1) [$M^+ - C_2H_4O$], 156 (1) [$M^+$ – morpholine – H], 128 (6) [$M^+$ – morpholine – $C_2H_4$], 114 (100) [$M^+ - C_6H_5 - C_4H_4$]; elemental analysis calcd for (%) $C_{16}H_{21}NO$ (243.4) calcd: C 78.97, H 8.70, N 5.76; found: C 79.20, H 8.69, N 5.92.

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## Insertion Reactions of Nitriles into the P–C Bond of $[(\eta^1\text{-}C_5Me_5)P\{W(CO)_5\}_2]$—A Novel Approach to Phosphorus-Containing Heterocycles**

Michael Schiffer and Manfred Scheer*

*Dedicated to Professor Dieter Sellmann in occasion of his 60th birthday*

In the thermal activation of $[Cp^*P\{W(CO)_5\}_2]$ (**1**; $Cp^* = \eta^1\text{-}C_5Me_5$), a Cp* migration from the P atom to the transition metal atom occurs to form the highly reactive intermediate $[Cp^*(CO)_2W{\equiv}P \rightarrow W(CO)_5]$ **A**.[1] The chemistry of this highly reactive intermediate **A** offers promising synthetic routes to a large variety of new phosphametallaheterocycles. Thus, the trapping reaction of **A** with phosphaalkynes[1] and alkynes[2] proceeds by formal [2+2] cycloaddition reactions to form novel main group element transition metal cage compounds. In continuation of these reactivity studies we attempted to employ nitriles for trapping reactions of intermediate **A**. Surprisingly, however, we observed insertion reactions into the P–C bond of the starting material.

Insertion reactions of organonitriles into metal–hydrogen and metal–carbon bonds are established processes.[3] Furthermore, it is known that nitriles insert into the Mo–Cl bond of $MoCl_5$,[4] into the Zr–O bond of $[Cp^*_2Zr{=}O]$,[5] and into E–N bonds (E = B,[6] Al,[7] P,[8] Pt[9]). Recently, Neumüller et al. reported on CsX-catalyzed trimerization reactions of acetonitrile with $EMe_3$ (E = element of Group 13) under elimination of $CH_4$ and formation of $[Me_2E\{HNC(Me)\}_2$-

[*] Prof. Dr. M. Scheer, Dr. M. Schiffer
Institut für Anorganische Chemie der Universität Karlsruhe
76128 Karlsruhe (Germany)
Fax: (+49) 721-608-7021
E-mail: mascheer@chemie.uni-karlsruhe.de

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