Haraguchi, H. Tanaka, K. Matsumoto, K. T. Nakamura, T. Miyasaka, *Tetrahedron Lett.* **1995**, *36*, 3867 – 3870.
[7] H. Zipse, *J. Am. Chem. Soc.* **1997**, *119*, 1087 – 1093.
[8] S. N. Müller, R. Batra, M. Senn, B. Giese, M. Kisel, O. Shadiro, *J. Am. Chem. Soc.* **1997**, *119*, 2795 – 2803.
[9] a) P. Renaud, P.-A. Carrupt, M. Gerster, K. Schenk, *Tetrahedron Lett.* **1994**, *35*, 1703 – 1706; b) P. Renaud, N. Moufid, L. H. Kuo, D. P. Curran, *J. Org. Chem.* **1994**, *59*, 3547 – 3552; c) P. Renaud, M. Gerster, *J. Am. Chem. Soc.* **1995**, *117*, 6607 – 6608; d) M. Gerster, P. Renaud, *Angew. Chem.* **1996**, *108*, 2523 – 2525; *Angew. Chem. Int. Ed.* **1996**, *35*, 2396 – 2399; e) M. Gerster, L. Audergon, M. Moufid, P. Renaud, *Tetrahedron Lett.* **1996**, *37*, 6335 – 6338; f) A.-R. Fhal, P. Renaud, *Tetrahedron Lett.* **1997**, *38*, 2661 – 2664.
[10] P. Renaud, M. Gerster, *Angew. Chem.* **1998**, *110*, in press; *Angew. Chem. Int. Ed.* **1998**, *37*, in press.
[11] Acceleration of radical cyclizations was recently reported: T. Ooi, Y. Hokke, K. Maruoka, *Angew. Chem.* **1997**, *109*, 1230 – 1231; *Angew. Chem. Int. Ed.* **1997**, *36*, 1181 – 1183. The rate of cyclization of aminyl radicals is also influenced by Lewis acids: C. Hau, O. M. Musa, F. N. Martinez, M. Newcomb, *J. Org. Chem.* **1997**, *62*, 2704 – 2710; for more examples, see reference [10].
[12] A. L. J. Beckwith, C. B. Thomas, *J. Chem. Soc. Perkin Trans. 2* **1973**, 861 – 872.
[13] The product of phenyl migration (neophyl rearrangement) is not observed under these conditions.
[14] Compound **4** was prepared according to the procedure of Beckwith et al.[12] For physical data and elemental analysis, see C. S. Marvel, N. S. Moon, *J. Am. Chem. Soc.* **1940**, *62*, 45 – 49.
[15] S. Kobayashi, *Synlett* **1994**, 689 – 701.
[16] a) M. P. Sibi, C. P. Jasperse, J. Ji, *J. Am. Chem. Soc.* **1995**, *117*, 10779 – 10780; b) M. P. Sibi, J. Ji, *Angew. Chem.* **1996**, *108*, 198 – 200; *Angew. Chem. Int. Ed.* **1996**, *35*, 190 – 192.
[17] In the absence of Lewis acids, the *ortho*-methoxybenzoate rearranged slightly slower (procedure B: the ratio of rearrangement to direct reduction products was 84:16) than the hydroxy-substituted compound **7** (procedure B: the ratio of rearrangement to direct reduction products was 75:25; Table 1, entry 2). This small difference may be attributed to intramolecular protonation.
[18] The hypothesis of an ionic rearrangement followed by a radical reaction was discarded since treatment of **7** with $MeAl(OPh)_2$ or $Sc(OTf)_3$ left the bromide unchanged.
[19] A low diastereoselectivity ($\leq 60\%$ *ds*) was observed.
[20] Most reported 1,2-acyloxy shifts have been conducted at temperatures higher than 60 °C.

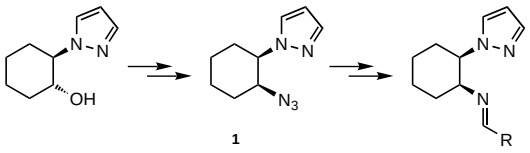
Transition Metal Complexes with Organoazide Ligands: Synthesis, Structural Chemistry, and Reactivity**

Michael Barz, Eberhardt Herdtweck, and Werner R. Thiel*

Organoazides are important starting materials for a multitude of organic reactions,[2] such as in the synthesis of alkylamines from alkyl alcohols or halides ($R{-}X \rightarrow RN_3 \rightarrow R{-}NH_2$) or heterocycles (e.g. [2+3] cycloaddition).[3] The most remarkable aspect in the reactivity of organoazides is the loss of dinitrogen, which can occur thermally, photochemically, or by acid or transition metal catalysis.[4] The highly reactive nitrenes ("R–N") that are generated from the RN_3 fragment, can rearrange to the corresponding imines, insert into C–C bonds, form amines by intra- or intermolecular hydrogen abstraction ("R–N" $\rightarrow R{-}NH_2$), or undergo cycloaddition in the presence of unsaturated substrates (e.g. "R–N" + $C_2H_4 \rightarrow R{-}N(C_2H_4)$).[5]

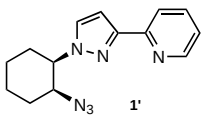
An illustrative example of the stabilization of a "nitrene fragment" at a transition metal center was described by Bergman and Proulx with the reaction of $[Cp_2TaCH_3(PMe_3)]$ with phenylazide, which led to the formation of the tantalum imido complex $[Cp_2TaCH_3(=N{-}C_6H_5)]$.[6] In the intermediate $[Cp_2TaCH_3(N_3{-}C_6H_5)]$, the transition metal center is coordinated by the terminal nitrogen atom (N3) of the azido functionality. This compound was, to our knowledge, the only structurally characterized transition metal complex bearing a RN_3 ligand.[7] This is surprising since many coordination complexes of the azide ion (N_3^-) are known.[8] Here we report the first structurally characterized organoazide complexes, which are coordinated by the alkylated nitrogen atom (N1) to the transition metal center.

For some time we have investigated new chiral chelating ligands for applications in enantioselective catalysis, where the donor centers are linked by 1,2-disubstituted cycloalkanes.[1, 9] The cyclohexaneazide **1** was obtained as a key



1

intermediate during the synthesis of new multidentate imine ligands following this strategy.[9c] Surprisingly, hydrogenation of **1** to the corresponding amine with palladium/charcoal in ethanol proceeds rather slowly, in contrast to the behavior of the analogous pyrazolyl pyridine derivative **1′**.[10] Therefore, investigation of the reactivity of **1** in solution in the presence of transition metal ions like Pd^{II} and Cu^{II}, which are known to be efficient catalysts for the decomposition of organoazides,[4] appeared promising.



1′

Reaction of **1** with $CuCl_2 \cdot 2H_2O$ in methanol leads quantitatively to the dinuclear Cu^{II} complex $[\{CuCl_2(\mathbf{1})\}_2]$ (**2**), which is thermally and photochemically (daylight) stable, and crystals suitable for X-ray structure analysis could be obtained by recrystallization from methanol. Reaction of **1** with $[PdCl_2(NCC_6H_5)_2]$ in CH_2Cl_2 gives the Pd^{II} complex $[PdCl_2(\mathbf{1})]$ (**3**) after dissociation of the benzonitrile ligands. In contrast to **2**, **3** is not stable in CH_2Cl_2 and decomposes slowly, even in the absence of light, to yield the amine complex **4**, which is also accessible from the corresponding amine[9c] and $[PdCl_2(NCC_6H_5)_2]$ (Scheme 1).

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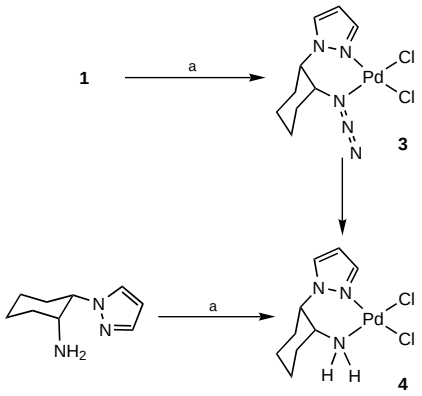


Scheme 1. Synthesis of **3** and **4**. a) $[PdCl_2(NCC_6H_5)_2]$, CH_2Cl_2, 15 min, room temperature. The conversion of **3** into **4** is slow.

Since **3** is stable in the solid state, crystals suitable for X-ray structure analysis could be obtained. The metal centers in complexes **2**[11] and **3**[12] are coordinated by the alkylated nitrogen atom of the azide fragment, which leads to the formation of stable six-membered metallacycles. Semiempirical calculations (AM1[13]) for the formation of adducts between the Lewis acids BMe_3, CH_3^+, and H^+ and the model bases methylazide and phenylazide showed greater stability for an electrophilic attack at the carbon-substituted nitrogen atom N1 (Table 1).

Table 1. Calculated (AM1[12]) differences of the enthalpies of formation ($\delta\Delta G = \Delta G_{N1} - \Delta G_{N3}$ [kcal mol^{-1}]) for the adducts of BMe_3, CH_3^+, and H^+ with N1 and N3 of methylazide and phenylazide.

	BMe_3	CH_3^+	H^+
CH_3–N_3	– 2.71	– 11.18	– 18.50
C_6H_5–N_3	– 0.10	– 9.66	– 16.81

Accordingly, the spectroscopic and structure chemical data of $[Cp_2TaCH_3(N_3C_6H_5)]$ prove that this compound cannot be considered an azide adduct of a Ta^{III} complex, but a Ta^{V} derivative bearing a phenyl diimine substituted imido ligand.[6] In contrast, complexes **2** and **3** are classical coordination compounds of the organoazide **1**, which is also confirmed by the bonding parameters (Figures 1 und 2).

A search in a structure database[7a] showed that the bonding parameters of organoazides vary relatively broadly. The N3–N4 distances in **2** and **3** (ca. 1.251 Å) are slightly longer than those of free aliphatic azides, whereas the N4–N5 distances (ca. 1.126 Å) are slightly shorter than the mean value for aliphatic azides. This observation can be explained by a decrease in double-bond character of the bond between N3 und N4 and a slightly increased triple-bond character of the bond between N4 and N5, as expected for an organoazide fragment coordinated with the alkylated nitrogen atom. The bending at the central nitrogen atom N4 (174.5(2)° in **2** and 177.1(4)°in **3**) is not as pronounced as in free aliphatic azides. The sterically demanding pyrazolyl substituent in both complexes is oriented equatorially at the cyclohexane ring, and the N_3 group occupies an axial position. An analogous conformation was found in the free chelating ligand **1**.[9c] In **2**, the Cu^{II}

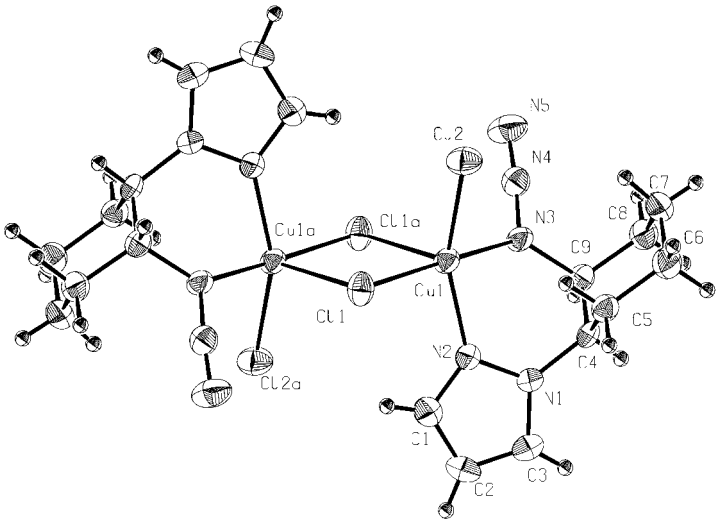


Figure 1. Structure of **2** in the crystal (PLATON plot[14]). Selected distances [Å] and bond and torsion angles [°]: Cu1–Cl1 2.2758(7), Cu1–Cl1a 2.7006(8), Cu1–Cl2 2.2130(7), Cu1–N2 1.985(2), Cu1–N3 2.079(2), N3–N4 1.251(3), N4–N5 1.123(3); Cu1-Cl1-Cu1a 89.27(2), Cl1-Cu1-Cl1a 90.73(2), Cl1-Cu1-Cl2 94.32(2), Cl1a-Cu1-Cl2 103.90(2), Cl1-Cu1-N2 92.73(5), Cl1-Cu1-N3 174.26(6), Cl1a-Cu1-N2 100.53(5), Cl1a-Cu1-N3 84.62(5), Cl2-Cu1-N2 154.45(6), Cl2-Cu1-N3 90.08(5), N2-Cu1-N3 84.83(7), Cu1-N3-N4 115.06(13), N4-N3-C9 114.93(17), N3-N4-N5 174.5(2); N1-C4-C9-N3 59.7(2).

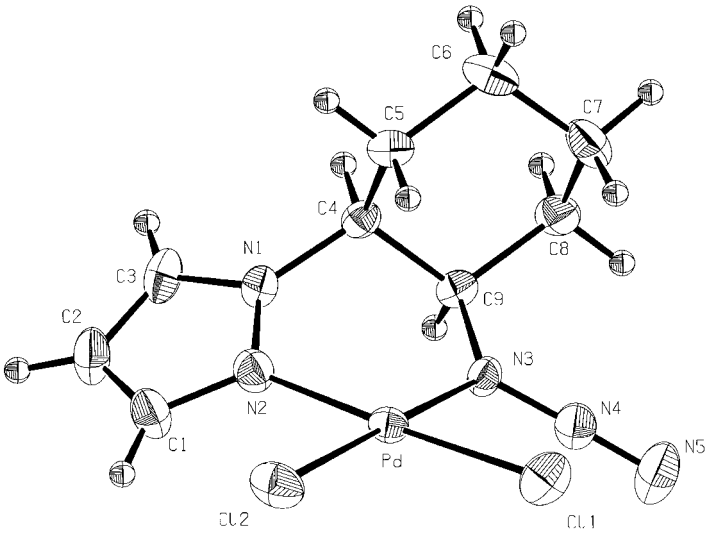
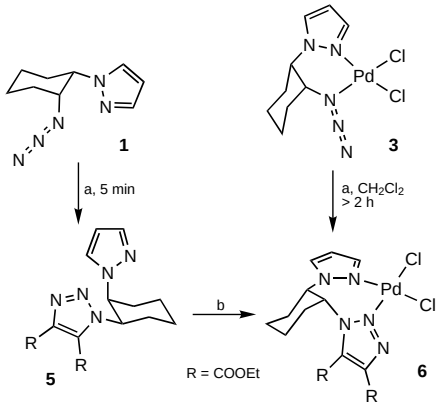


Figure 2. Structure of **3** in the crystal (PLATON plot[14]). Selected distances [Å] and bond and torsion angles [°]: Pd–Cl1 2.2735(12), Pd–Cl2 2.2805(11), Pd–N2 2.017(3), Pd–N3 2.056(3), N3–N4 1.251(5), N4–N5 1.129(5); Cl1-Pd-Cl2 91.81(4), Cl1-Pd-N2 176.91(10), Cl1-Pd-N3 89.55(9), Cl2-Pd-N2 90.89(10), Cl2-Pd-N3 177.12(11), N2-Pd-N3 87.82(13), Pd-N3-N4 118.2(2), N4-N3-C9 114.3(3), N3-N4-N5 177.1(4); N1-C4-C9-N3 – 62.9(4).

center is coordinated in a distorted trigonal-bipyramidal mode, with the donor sites Cl(1a), Cl(2), and N(2) in equatorial positions on the coordination polyhedron. There are three different Cu–Cl distances: two relatively short bonds between Cu^{II} and the terminal chloro and one bridging chloro ligand, and one relatively long bond between Cu^{II} and the second chloro ligand of the central planar Cu_2Cl_2 unit. In complex **3**, the Pd^{II} center is coordinated in a (distorted) square-planar geometry. All bond angles between *cis*-oriented

donor atoms and Pd^{II} are approximately 90°. The Pd–N2 (pyrazole) bond is significantly shorter than the Pd–N3 (azide) bond.

Initial investigations into the reactivity of coordinated organoazides showed that **3** undergoes [2+3] cycloaddition with diethyl acetylenedicarboxylate, which is a typical reaction for azides. *cis*-1-Pyrazolyl-2-triazolylcyclohexane (**5**) is generated from the azide **1** and EtOOC–C≡C–COOEt in a rapid and exothermal reaction (Scheme 2). The ^{1}H NMR spectroscopic data of **5** show that the bulky triazolyl substituent occupies an equatorial position on the cyclohexane ring.



Scheme 2. Synthesis of **5** and **6**. a) EtOOC–C≡C–COOEt, 40 °C. b) $[PdCl_2(NCC_6H_5)_2]$, CH_2Cl_2, 15 min, room temperature.

The Pd^{II} complex **6**, which can also be synthesized from **5** and $[PdCl_2(NCC_6H_5)_2]$, is obtained as a mixture of two conformers which are in equilibrium in solution: pyrazolyl equatorial, triazolyl axial and pyrazolyl axial, triazolyl equatorial, respectively (Scheme 2 only shows one of these conformers). The interconversion barrier of 67 ± 2 kJ/mol between these conformers was determined by ^{1}H NMR spectroscopy.

A triazaphospha tetracycle has been postulated as an intermediate in the decomposition of organoazides in the presence of tertiary phosphanes, a reaction which ultimately leads to phosphorane imines.[15] If the decomposition of organoazides in the presence of transition metals follows an analogous intramolecular mechanism, the inclusion of the organoazide fragment in a chelating ligand should decrease the rate of the decomposition for steric reasons. At present we are investigating the reactivity of **1** in the presence of Lewis acidic, d^2-configured transition metal centers. In these cases, **1** should yield, under evolution of N_2, d^0 imine complexes with a second chiral (hemilabile) donor, which will be of potential interest for catalysis.

Experimental Section

2: A solution of **1**[9c] (0.19 g, 1.00 mmol) and $CuCl_2 \cdot 2H_2O$ (0.17 g, 1.00 mmol) in MeOH (20 mL) was heated to 50 °C for several minutes. After removal of the solvent in vacuo, **2** was obtained as a green microcrystalline solid, which was washed twice with Et_2O (20 mL) and dried in vacuo. Yield: 0.32 g (97 %); correct elemental analysis; IR (KBr): $\tilde{\nu} = 2148$ cm^{-1} (ν_{N3}).

3: A solution of $[PdCl_2(NCC_6H_5)_2]$[16] (0.38 g, 1.00 mmol) in CH_2Cl_2 (20 mL) was treated with a solution of **1** (0.19 g, 1.00 mmol) in CH_2Cl_2 (10 mL). After 15 min of stirring at room temperature, the solution was filtered to remove traces of elemental palladium, the solvent was reduced to 15 mL, and the solution was layered with Et_2O (30 mL). **3** crystallized as orange prisms. In a side reaction, **4** was formed under evolution of gas as a tan-orange, microcrystalline solid. Yield: 0.45 g; correct elemental analysis when the amount of **4** determined by NMR spectroscopy is taken into account; ^{1}H NMR (400.13 MHz, 25 °C, $CDCl_3$): $\delta = 7.43$ (br, 1H), 7.38 (br, 1H), 6.14 (m), 5.21 (br d, 1H, $1 \times {}^3J_{H,H} = 11.5$, $2 \times {}^3J_{H,H} = 3.0 - 4.0$ Hz), 4.70 (ddd, 1H, $3 \times {}^3J_{4,H} = 3.0 - 4.0$ Hz), 2.20 – 1.40 (m, 8H); ^{13}C{^{1}H} NMR (100.25 MHz, 25 °C, $CDCl_3$): $\delta = 142.2$, 131.4, 107.0, 63.1, 60.3, 25.4, 24.3, 18.6, 18.7; IR (KBr): $\tilde{\nu} = 2147$ cm^{-1} (ν_{N3}).

5: **1** (2.41 g, 12.6 mmol) and diethyl acetylenedicarboxylate (2.14 g, 12.6 mmol) were heated in a 50-mL flask under vacuo for a short period until reaction ceased (quantitative yield by GC). After chromatography (neutral Al_2O_3, Et_2O) and removal of the solvent, the oily residue was crystallized from hexane/Et_2O. Yield: 3.09 g (68 %), colorless crystals. M.p. 71 °C; correct elemental analysis; ^{1}H NMR (400.13 MHz, 25 °C, $CDCl_3$): $\delta = 7.33$ (d, 1H, ${}^3J_{H,H} = 1.5$ Hz), 6.87 (d, 1H, ${}^3J_{H,H} = 1.50$ Hz), 5.99 (dd), 5.56 (ddd, 1H, $3 \times {}^3J_{H,H} = 4.0$ Hz), 4.70 (ddd, 1H, $2 \times {}^3J_{4,H} = 4.0$, $1 \times {}^3J_{H,H} = 12.0$ Hz), 4.31 (m, 4H), 2.71 (m, 1H), 2.30 – 2.01 (m, 5H), 1.68 – 1.56 (m, 2H), 1.33 (t, ${}^3J_{H,H} = 7.0$ Hz, 6H); ^{13}C{^{1}H} NMR (100.25 MHz, 25 °C, $CDCl_3$): $\delta = 160.1$, 158.6, 139.5, 138.5, 132.2, 126.8, 105.4, 62.8, 61.6, 61.6, 59.2, 29.6, 26.0, 24.5, 20.2, 14.1, 13.8.

6: A solution of $[PdCl_2(NCC_6H_5)_2]$ (0.38 g, 1.00 mmol) in CH_2Cl_2 (20 mL) was treated with a solution of **4** (0.36 g, 1.00 mmol) in CH_2Cl_2 (10 mL). After 15 min of stirring at room temperature, the solution was filtered to remove traces of elemental palladium. Then the solvent was removed in vacuo and the product precipitated by rapid addition of Et_2O (50 mL). Yield: 0.52 g (96 %), yellow-orange solid, correct elemental analysis; ^{1}H NMR (400.13 MHz, 60 °C, $CDCl_3$): $\delta = 7.60$ (br, 1H), 7.65 – 6.85 (br, 1H), 6.20 (br, 1H), 4.70 – 4.20 (br, 6H), 3.20 – 1.05 (br, 14H); ^{13}C{^{1}H} NMR (100.25 MHz, 60 °C, $CDCl_3$): $\delta = 159.6$, 158.0, 141.8, 137.7, 133.7, 132.8, 108.9, 64.2, 64.0, 62.8, 61.4, 29.8, 26.4, 25.1, 18.6, 13.7, 13.5.

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[1] M. Barz, H. Glas, W. R. Thiel, *Synthesis*, in press.
[2] *The Chemistry of the Azido Group*, (Ed.: S. Patai), Interscience, London, **1971**.
[3] R. A. Abramovitch, E. P. Kyba in ref. [2], p. 222.
[4] T. Sheradsky in ref. [2], p. 332.
[5] *Methoden der Organischen Chemie* (*Houben-Weyl*), *4th ed. 1952*, *vol.* X/3, **1965,** p. 813.
[6] G. Proulx, R. G. Bergman, *J. Am. Chem. Soc.* **1995**, *117*, 6382 – 6383.
[7] a) Cambridge Structural Database, Version 2.3.7, UNIX 97/2. In version 98/1 we found two other structures showing a terminally coordinating organoazide. b) G. Proulx, R. G. Bergman, *Organometallics* **1996**, *15*, 684. c) T. A. Hanna, H. M. Baranger, R. G. Bergman, *Angew. Chem.*, **1996**, *108*, 693; *Angew. Chem. Int. Ed. Engl.*, **1996**, *35*, 653.
[8] a) K. Vrieze, G. van Koten in *Comprehensive Coordination Chemistry, Vol. 2*, (Ed.: G. Wilkinson), Pergamon, **1987**, p. 225 – 242; b) U. Müller, *Struct. Bonding* **1973**, *14*, 141.
[9] a) M. Barz, E. Herdtweck, W. R. Thiel, *Tetrahedron: Asymmetry* **1996**, *7*, 1717 – 1722; b) C. L. Thurner, M. Barz, M. Spiegler, W. R. Thiel, *J. Organomet. Chem.* **1997**, *541*, 39 – 49; c) M. Barz, M. U. Rauch, W. R. Thiel, *J. Chem. Soc. Dalton Trans.* **1997**, 2155 – 2161; d) H. Glas, M. Spiegler, W. R. Thiel, *Eur. J. Inorg. Chem.* **1998**, 275 – 281.
[10] H. Glas, W. R. Thiel, unpublished results.
[11] X-ray structure analysis of **2**: green prisms from MeOH, $Mo_{K\alpha}$ radiation ($\lambda = 0.71073$ Å), STOE IPDS diffractometer, structure solution with Patterson methods (SHELXS-86), refinement with

SHELXL-93, all hydrogen-atom positions were found in the Fourier map and freely refined, $C_{18}H_{26}Cl_4Cu_2N_{10}$, $M = 651.4\ g\,mol^{-1}$, orthorhombic, space group *Pbca* (no. 61), $a = 8.396(1)$, $b = 18.756(1)$, $c = 15.781(1)$ Å, $V = 2485.1(4)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.741\ g\,cm^{-3}$, $\mu = 21.7\ cm^{-1}$, $T = 20\,^{\circ}C$, 30426 observed reflections, 1949 independent reflections used for refinement (1595 with $I > 4\sigma(I)$), 206 parameters refined, $R1 = 0.0255$, $\omega R2 = 0.0522$, GOF = 0.96, max./min. residual electron density 0.29/ − 0.25 e Å^{-3}.[12b]

[12] a) X-ray structure analysis of **3**: orange prisms from CH_2Cl_2/pentane, $Mo_{K\alpha}$ radiation ($\lambda = 0.71073$ Å), Enraf-Nonius MACH3 diffractometer, structure solution with Patterson methods (SHELXS-86), refinement with SHELXL-93, all hydrogen atoms were calculated in idealized positions, $C_9H_{13}Cl_2N_3Pd$, $M = 368.6\ g\,mol^{-1}$, monoclinic, space group $P2_1/n$ (no. 14), $a = 8.4828(6)$, $b = 9.4916(8)$, $c = 16.2852(15)$ Å, $\beta = 94.087(8)^{\circ}$, $V = 1307.9(2)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.872\ g\,cm^{-3}$, $\mu = 18.1\ cm^{-1}$, $T = -110\,^{\circ}C$, 2735 observed reflections, 2644 independent reflections used for refinement (2086 with $I > 4\sigma(I)$), empirical absorption correction $T_{min} = 0.939\ T_{max} = 1.000$, 154 parameters refined, $R1 = 0.0534$, $\omega R2 = 0.0667$, $GOF = 1.05$, max./min. residual electron density 0.62/ − 0.69 e Å^{-3}. b) Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-101 257. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

[13] The AM1 calculations were performed on a Silicon Graphics O2 Workstation with the MOPAC 6.0 package and the INSIGHT II Graphical User Interface (Biosym). a) M. J. S. Dewar, E. G. Zoebisch, E. F. Healy, J. J. P. Stewart, *J. Am. Chem. Soc.* **1985**, *107*, 3902 – 3909; b) M. J. S. Dewar, E. G. Zoebisch, *Theochem.* **1988**, *49*, 1 – 21; c) M. J. S. Dewar, C. Jie, E. G. Zoebisch, *Organometallics* **1988**, *7*, 513 – 521.

[14] A. L. Spek, *Acta Crystallogr. Sect. A* **1990**, *46*, C34 – C34.

[15] Y. G. Gololobov, L. F. Kasukhin, *Tetrahedron* **1992**, *48*, 1353 – 1406.

[16] J. R. Doyle, P. E. Slade, H. B. Jonassen, *Inorg. Synth.* **1960**, *6*, 216 – 219.

Covalent DNA – Streptavidin Conjugates as Building Blocks for Novel Biometallic Nanostructures**

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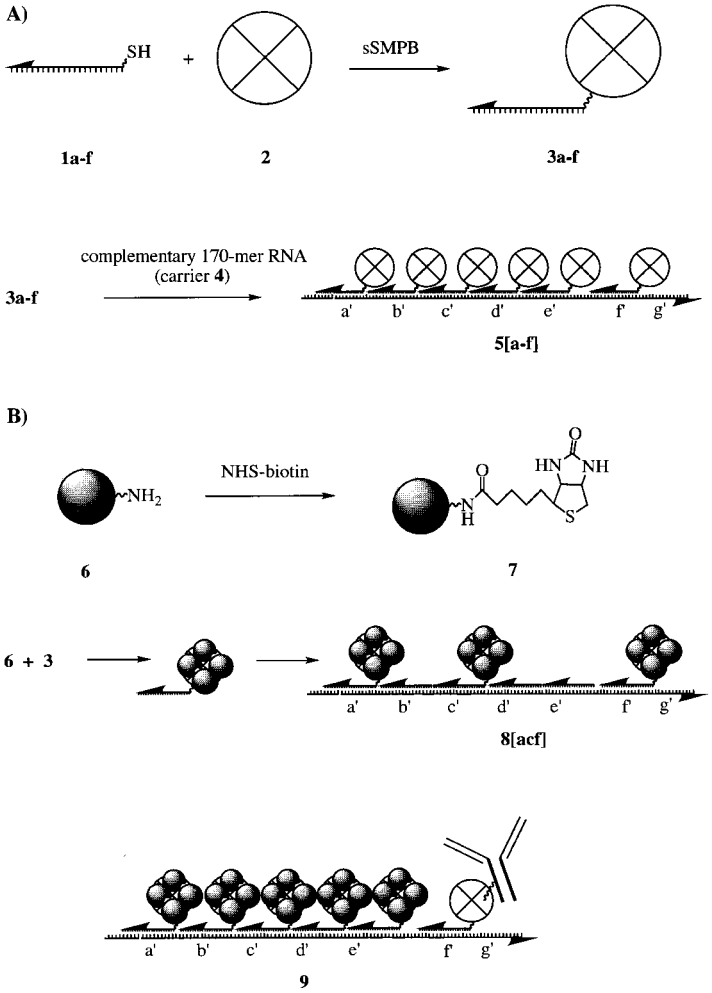
The generation of nanoscale structural and functional devices by self-assembly of small molecular building blocks is an important goal of nanotechnology.[1] Owing to its unique recognition capabilities, physicochemical stability, and mechanical rigidity, DNA is a promising construction material[2–4] for the fabrication of nanostructured scaffolds[3] and for the precise spatial positioning of conducting polymers,[5] proteins,[6] and nanocrystalline gold clusters.[7–9] Recently, we reported the synthesis of covalent conjugates of single-stranded DNA and streptavidin (STV).[6] In these adducts, the protein's native binding capacity for four biotin molecules is supplemented by a highly specific binding site for complementary nucleic acids, and the conjugates can thus be utilized as biomolecular adapters for positioning biotinylated components along a nucleic acid backbone. Here we report on the self-assembly of DNA – STV adducts **3** to form supramolecular aggregates **5** and the utilization of the adapters for the fabrication of nanostructured biometallic aggregates **8** and **9** from biotin-derivatized metal colloids (Scheme 1).



Scheme 1. Schematic representation of the DNA – protein hybrids. A) Generation of supramolecular aggregates from DNA – STV conjugates **3**, obtained by covalent coupling of 5′-thiol-modified oligonucleotides **1** and streptavidin **2**. The 3′-end of the oligonucleotide is indicated by an arrowhead, and the spacer chains between DNA and protein by wavy lines. The conjugates **3** with nucleotide sequences **a** – **f** self-assemble in the presence of RNA **4**, which contains complementary sequence sections, to form supramolecular aggregates **5**. B) Fabrication of biometallic aggregates by means of DNA – STV adapters **3**. Monoamino-modified 1.4-nm gold clusters **6** are converted into biotin derivatives, and the biotinylated clusters **7** are coupled with DNA – STV adducts **3.** The resulting hybrids are assembled in the presence of helper oligonucleotides **1** and RNA carrier **4** to form supramolecular aggregates **8**. (The letters in brackets indicate the protein components bound to the carrier.) Similarly, an antibody-containing aggregate **9** was constructed from gold-labeled **3a** – **e** and a conjugate from **3f** and biotinylated IgG, previously coupled in separate reactions.

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