Journal of Catalysis 350 (2017) 97-102

Contents lists available at ScienceDirect

Journal of Catalysis

journal homepage: www.elsevier.com/locate/jcat

Solid-supported nitrogen acyclic carbene (SNAC) complexes of gold: Preparation and catalytic activity



JOURNAL OF CATALYSIS

Svetlana Tšupova^a, Alban Cadu^{a,1}, Sónia A.C. Carabineiro^b, Matthias Rudolph^a, A. Stephen K. Hashmi^{a,c,*}

^a Organisch-Chemisches Institut, Ruprecht-Karls-Universität Heidelberg, Im Neuenheimer Feld 270, 69120 Heidelberg, Germany ^b Laboratório de Catálise e Materiais (LCM), Laboratório Associado LSRE-LCM, Faculdade de Engenharia, Universidade do Porto, 4200-465 Porto, Portugal

^c Chemistry Department, Faculty of Science, King Abdulaziz University (KAU), Jeddah 21589, Saudi Arabia

ARTICLE INFO

Article history: Received 4 January 2017 Revised 5 March 2017 Accepted 16 March 2017

Keywords: Gold Heterogenization Phenol synthesis Solid support Carbene Flow chemistry

ABSTRACT

A readily accessible route to obtain solid-supported nitrogen acyclic carbene (SNAC) complexes of gold was designed using flow chemistry, and an analogous homogeneous gold complex was synthesized for comparison. Both were screened for counter ions in order to perform the Hashmi phenol synthesis. A recyclability study was performed on the SNAC complex, which showed the high stability of this catalyst, with no observed leaching or gold nanoparticle formation. XPS analysis was employed to confirm the presence of gold and its oxidation state.

© 2017 Elsevier Inc. All rights reserved.

1. Introduction

Homogeneous gold catalysis has experienced a real "gold rush" in the past two decades, with early scattered reports of alkyne activation and simple nucleophilic additions emanating from Utimoto [1a] and Teles [1b] as well as entirely new reactivity patterns from the Hashmi group [2]. One key limitation of homogeneous catalysis, however, is the separation of the (metal) catalyst for purification of the product, or even its recovery for reuse. It is therefore of high interest to be able to conduct erstwhile homogeneously catalyzed reactions with a heterogeneous catalyst. One notable attempt was performed using nanogold particulates; however, the catalyst's recyclability remained limited [3]. One approach to maintain the advantages of a normally homogeneous, ligated metal catalyst is its immobilization onto a solid support. This was attempted for phosphine bound gold(I) [4] as well as with carbene ligated gold [5]. Gold C-scorpionate complexes were also successfully anchored on carbon materials [6]. One key limitation of these methods of immobilization is that the ligating groups must

E-mult dudress. hashini @nashini.de (A. Stephen K. Hashini)

be pre-synthesized at the start of the reaction sequence, before being mounted onto the solid support. It is our aim to provide a simple and modular route to access solid-supported nitrogen acyclic carbene (SNAC) gold complexes [7] as such, in this work, the use of (aminomethyl)polystyrene beads was employed as precursor to a SNAC-gold complex.

2. Experimental

2.1. Homogeneous catalyst synthesis

2.1.1. ((Benzylamino)((2,6-dimethylphenyl)amino)methylene)gold(1) chloride (**3**)

Dimethylphenylisonitrilegold(I) chloride

(70.6 mg, 0.2 mmol) was dissolved in CH_2Cl_2 (2 ml) and benzylamine (21.4 mg, 0.2 mmol) was added. The obtained mixture was stirred at room temperature (R.T.) for 2 days. Volatiles were removed and the residue was purified by column chromatography (petroleum ether/ CH_2Cl_2 1:1) giving the product as colourless solid (94 mg, quantitative yield). R_f (petroleum ether/ CH_2Cl_2 1:1) = 0.1. ¹H NMR (400 MHz, CD_2Cl_2) δ = 7.67 (s, 1H), 7.37–7.27 (m, 5H), 7.23 (dd, *J* = 8.6, 6.4 Hz, 1H), 7.16 (*d*, *J* = 7.5 Hz, 2H), 6.25 (s, 1H),



^{*} Corresponding author at: Organisch-Chemisches Institut, Ruprecht-Karls-Universität Heidelberg, Im Neuenheimer Feld 270, 69120 Heidelberg, Germany. *E-mail address:* hashmi@hashmi.de (A. Stephen K. Hashmi).

¹ Current address: Catalysis Research Laboratory (CaRLa), Im Neuenheimer Feld 584, 69120 Heidelberg, Germany.

4.89 (*d*, *J* = 6.2 Hz, 2H), 2.24 (s, 6H). ¹³C NMR (101 MHz, CD_2Cl_2) δ = 191.87 (s), 137.41 (s), 136.75 (s), 132.77 (s), 130.17 (d), 129.90 (d), 129.42 (d), 128.71 (d), 127.99 (d), 54.40 (t), 18.56 (q). FTIR (ATR) cm⁻¹: 3028, 2918, 1550, 1496, 1346, 1309, 1204, 1030, 775, 739, 704. HRMS (EI⁻) calcd. For C₁₆H₁₇AuClN₂: 469.0746; found: 469.0752.

2.2. Heterogeneous catalyst synthesis

2.1.2. Polystyrene supported ((benzylamino)((2,6-dimethylphenyl) amino)methylene)gold(1) chloride (**5**)



(430 mg, 1.19 mmol) was dissolved in CH_2Cl_2 (50 ml) in a twonecked flask protected from the light. The aminoresin (aminomethyl)polystyrene beads (790 mg, maximum 1.19 mmol NH₂, 70–90 mesh, 1–1.5 mmol NH₂ loading, purchased from Sigma– Aldrich, article number 515620) was loaded into a steel HPLC column (diameter 16 mm, length 30 mm, the dry resin occupied about half of the volume of the column) and then a small amount of CH_2Cl_2 was added to let the resin swell. The column was closed and connected to an HPLC pump. Then CH_2Cl_2 was pumped at a rate of 4 ml/min for 10 min. Then the solution of the isonitrile gold complex was pumped for 24 h at 4 ml/min flow rate in the looped system.

For the monitoring of the reaction, samples of the isonitrile gold complex solution were withdrawn every few hours and analyzed by ¹H NMR. From the consumption of the isonitrile gold complex, the degree of functionalization of NH_2 group on the resin could be estimated.

2.3. Catalysis experiments

2.3.1. Homogeneous catalyst screening

A stock solution of compound **3** (0.23 mg, 50 µmol in 0.25 ml) was placed in a 4 ml screw-cap vial, to which a stock solution of AgNTf₂ (0.21 mg, 50 µmol in 0.25 ml) was added. The obtained mixture was sonicated at R.T. for 5 min. Then, a stock solution of the substrate (0.5 ml, 0.1 mmol), containing hexamethylbenzene as internal standard was added and the obtained mixture was sonicated for 1 h and either worked up or left to stand for a further 23 h. The reaction was worked up by removing the solvent *in vacuo*, taking up the solid in CD_2Cl_2 and measuring ¹H NMR to determine the conversion, as compared to the internal standard.

2.3.2. Heterogeneous catalyst screening

SNAC-AuCl (16 mg for 5% gold loading, 25 mg for 8% gold loading) was dispersed in 0.5 ml of CH_2Cl_2 in a 4 ml screw-cap vial and silver salt (2 eq. with regard to gold) was added. The obtained mixture was sonicated at R.T. for 5 min. Then, a stock solution of the substrate (0.5 ml, 0.1 mmol), containing hexamethylbenzene as internal standard was added and the obtained mixture was sonicated for maximum of 1 h and left to stand for the remainder of the indicated reaction time (see Section 3.2.). The progress of the reaction was monitored by TLC. After reaction was complete, the resin was filtered of and the filtrate was analyzed by ¹H NMR to determine the conversion. The resin was washed with CH_2Cl_2 , transferred into a vial and used in the next run, exactly as described above. The repeated activation with silver salt was necessary after each run.

3. Results and discussion

3.1. Catalyst synthesis

In order to evaluate the possibility of carrying out the NAC synthesis with a solid-supported amine, the synthesis of the corresponding unsupported NAC **3** was first performed (Scheme 1). The isonitrile gold complex **1** was chosen based on recent experiences with the synthesis of HAAC complexes: [8] it possesses sufficient sterical bulk to allow it to be a stable catalyst, but not as bulky as to interfere with reaction rates. The benzylamine **2** was chosen to mimic the commercially available polystyrene-bound benzylic amines **4**. The reaction took 2 days; then, the starting isonitrile gold complex **1** was fully consumed. Purification by column chromatography gave the desired NAC gold complex **3** in quantitative yield.

Inspired by this success, the SNAC synthesis was attempted through different routes (Scheme 2). The aminopolystyrene resin **4** (1–1.5 mmol/g amine loading, 70–90 mesh) was dispersed in a 0.1 M solution of complex **1** in CH_2Cl_2 and stirred for 2 days at room temperature. After 2 days of stirring, the reaction mixture had been reduced to a fine slurry, which defied filtration. Therefore, an alternative to magnetic stirring was sought.

Inspired by our recent foray in flow chemistry [9], a looped flow system was used to circumvent the problem of product isolation (see Fig. 1): resin **4** was loaded into an empty HPLC column and washed extensively with CH_2Cl_2 , in order to swell it and to fill the column. Then, a solution of the isonitrile gold complex **1** in CH_2Cl_2 (1 eq. with regard to amino-groups on the resin) was pumped through at the flow rate of 4 ml/min for 24 h. The system



Scheme 1. Synthesis of NAC complex, analogous to planned supported NAC.



Scheme 2. SNAC complex synthesis.



Fig. 1. Experimental setup for SNAC synthesis.

was looped to optimize the use of the gold complex. The procedure was finished by pumping CH_2Cl_2 through to wash all the residues of unsupported gold from the HPLC system. The column was emptied and the resin was dried *in vacuo*. Unreacted **1** was collected and based on an internal standard, its consumption was used to estimate the degree of gold loading onto the resin [10]. From the disappearance of the starting isonitrile gold complex complex **1** in ¹H NMR spectrum, the degree of functionalization of the amino-groups on the resin was estimated. The progress of the reaction is shown in Fig. 2 and as can be seen, after 24 h: 26% of **1** was consumed.

In order to confirm the presence of gold in resin **5** as well as the oxidation state of the gold atoms, XPS measurements were performed. Fig. 3 shows the Au 4f peaks of SNAC **5**, and they consist of two peaks: Au $4f_{5/2}$ and Au $4f_{7/2}$, whose binding energies are characteristic of the Au⁺ oxidation state (the expected locations of peaks corresponding to Au⁰ and Au³⁺ are indicated for comparative purposes).

For an overall isonitrile gold complex consumption of 26%, the XPS showed 47% of surface nitrogen functionalization. This percentage decreased to 38% after ball-milling, indicating that proportionally more gold was bound to the polymer surface than within (see the Supporting Information for calculations). It is noteworthy that the presence of gold nanoparticles was not observed, even after five catalytic runs. As can be seen in Fig. 3, carbene N1s peaks correspond to those observed in a recently reported metal carbene complex (*circa* 400 eV) [12].

3.2. Catalytic activity

In order to evaluate the applicability of the obtained SNAC complex as catalysts, the gold catalyzed transformation of **6** into phenol **7** was chosen as test reaction [2,13]. Firstly, catalyst activation by different silver and sodium salts was attempted (Fig. 4). For comparison, catalytic experiments with homogenous complex **3** and the mixture of **3** with the starting aminopolystyrene resin **4** were performed. As can be seen, after 1 h the homogenous catalyst **3** performed comparably to the corresponding supported SNAC complex **5**, but an inferior performance of **5** after 25 h was observed. It is noteworthy, that when the untreated support is added to the **3**, the catalytic activity of the gold complex decreases significantly. Although the catalyst with PF_6 delivered the highest conversion, the yield was highest for NTf_2^- and other counter ions led to significantly less active catalysts.

Having found a suitable counter ion, the reusability of the SNAC catalyst **5** was studied. A catalyst loading of 8% was chosen in order to set a "full conversion" benchmark. As can be seen in Fig. 5, the first two runs were fast and comparable catalytic activity was observed. A drop in reaction rate was observed in runs 3 and 4. However, with an extended reaction time for run 4, a high yield of phenol could once again be achieved. In run 5 the reaction time was extended to 24 h and a quantitative yield was observed. The recovered catalyst was treated with another portion of $AgNTf_2$ after each run, and without that treatment no catalytic activity was observed, which we assign to chloride-poisoning of the cata-



Fig. 2. The monitoring of disappearance of 1 in SNAC synthesis.



Fig. 3. Au 4f XPS spectra of samples of heterogenized catalyst **5**, a. activated catalyst SNAC-Au-NTf₂, after 5 catalytic runs, b. unactivated catalyst SNAC-Au-Cl (top left) with the scale of sample b amplified (top right), and the remeasured samples after milling (bottom, left). Peak positions marked according to values of the literature [11]. Superimposed N 1s XPS spectra of the support, activated and unactivated catalyst 5 (bottom, right).



Fig. 4. Conversions and yields of phenol in the Hashmi phenol synthesis catalyzed by **5** and **3**. All the reactions performed at 5% loading of the catalyst. The loading of aminoresin **4** is calculated to match the ratio of amino-group/NAC complexes in catalyst **5**. Conversions and yields are determined from ¹H NMR using hexamethylbenzene as internal standard. a: **3**/AgNTf₂; b: **3**/4/AgNTf₂; c: **5**/AgNTf₂; d: **5**/AgPF₆; e:**5**/AgOF₆; f:**5**/AgOT₅; h:**5**/NaBAF₇.

lyst during the work-up (washing with standard-grade dichloromethane). Since the support showed negative impact on the activity of **3** (Fig. 4b), the addition of HPF₆ to the catalyst **5** was probed as means of enhancing its activity by lowering the nucleophilicity of the amine groups. However, it did not influence the outcome of the reaction. As part of the catalyst recycling, the reaction mixture was filtered to isolate the catalyst. The filtrate was neither catalytically active alone nor in the presence of AgNTf₂, and this indicates that negligible amounts of gold were leached from the support.

In order to probe the effect of a possible non-homogenous gold distribution over the resin during the catalyst synthesis, six samples from different parts of the column were taken (labelled a to f, from the front to the back of the column). As Fig. 6 shows, the conversions of five of the samples (a-c and e-f) were broadly com-



Fig. 5. Reusability study of SNAC complex 5 in the gold-catalyzed phenol synthesis. Averaged yields are reported. For the detailed breakdown and reaction conditions see Fig. 6.



Fig. 6. Catalytic activity and reusability of six samples of **5** in phenol synthesis. 8% of the SNACAuCl were dispersed in 0.5 ml of CH_2Cl_2 and 16% of AgNTf₂ were added. The mixture was sonicated for 5 min, then the stock solution of the substrate was added and the obtained mixture was sonicated for maximum 1 h. Yields are determined from integration of ¹H NMR using hexamethylbenzene as internal standard.

parable, with the exception of sample *d*, which gave lower conversion in all runs. Nonetheless, in the last run, with an extended reaction time, all the samples catalyzed a quantitative phenol formation. The similar results obtained for the six catalyst samples indicate a relatively similar distribution of the gold adsorption over the whole column.

4. Conclusion

In conclusion, a method for the synthesis of solid-supported nitrogen acyclic carbene gold complexes was developed and both NMR and XPS were employed to confirm the uptake of gold onto the resin. In order to preserve the structural integrity of the polymer beads, flow chemistry was employed during the catalyst formation step. Furthermore, the catalyst's activity was tested by applying it to the catalytic phenol synthesis. A recyclability study showed, that the solid-supported catalyst could be reused five times with little change in overall yield, provided that it was reactivated between iterations and that the reaction times were extended.

Acknowledgments

S.T. thanks the Fonds der Chemischen Industrie for her Kekule-Fellowship. A.C. is grateful to the Stenholm, Wilgott travel scholarship. SACC thanks Fundação para a Ciência e Tecnologia (FCT) for financial support through Investigador FCT program (IF/01381/2013/CP1160/CT0007), with financing from the European Social Fund and the Human Potential Operational Program. This work was financially supported by Project POCI-01-0145-FEDER-006984 – Associate Laboratory LSRE-LCM funded by FEDER through COMPETE2020 – Programa Operacional Competitividade e Internacionalização (POCI) – and by national funds through FCT. Authors thank Fundação das Universidades Portuguesas and DAAD for the bilateral project Ação Integrada Luso-Alemã Ref. A-13/16. Authors are also thankful to Dr. Carlos M. Sá (CEMUP) for assistance with XPS analyses. The gift of metal salts from Umicore is gratefully acknowledged.

Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jcat.2017.03.013.

References

- (a) Y. Fukuda, K. Utimoto, H. Nozaki, Heterocycles 25 (1987) 297–300;
 (b) J.H. Teles, S. Brode, M. Chabanas, Angew. Chem. Int. Ed. 37 (1998) 1415–
- 1417 (for a key review, see: A.S.K. Hashmi, Chem. Rev. 107 (2007) 3180–3211). [2] (a) A.S.K. Hashmi, T.M. Frost, J.W. Bats, J. Am. Chem. Soc. 122 (2000) 11553– 11554:
- (b) A.S.K. Hashmi, L. Schwarz, J.-H. Choi, T.M. Frost, Angew. Chem. Int. Ed. 39 (2000) 2285–2288.
- [3] S. Carrettin, M.C. Blanco, A. Corma, A.S.K. Hashmi, Adv. Synth. Catal. 348 (2006) 1283–1288.
- [4] (a) W. Cao, B. Yu, Adv. Synth. Catal. 353 (2011) 1903-1907;
 - (b) M. Raducan, C. Rodruguez-Escrich, X.C. Cambeiro, E.C. Escudero-Adan, M.A. Pericas, A.M. Echavarren, Chem. Commun. 47 (2011) 4893–4895;
 - (c) M. Egi, K. Azechi, S. Akai, Adv. Synth. Catal. 353 (2011) 287-290;
 - (d) C. Vriamont, M. Devillers, Ol. Riant, S. Hermans, Chem. Eur. J. 19 (2013) 12009–12017.
- [5] (a) A. Corma, E. Gutiérrez-Puebla, M. Iglesias, A. Monge, S. Pérez-Ferreras, F. Sánchez, Adv. Synth. Catal 348 (2006) 1899–1907;
 - (b) A. Corma, C. González-Arellano, M. Iglesias, S. Pérez-Ferreras, F. Sánchez, Synlett 11 (2007) 1771–1774;

(c) C. González-Arellano, A. Corma, M. Iglesias, F. Sánchez, Eur. J. Inorg. Chem. (2008) 1107–1115;

(d) M.A.N. Virboul, M. Lutz, M.A. Siegler, A.L. Spek, G. van Koten, R.J.M. Klein Gebbink, Chem. Eur. J. 15 (2009) 9981–9986;

(e) C. del Pozo, A. Corma, M. Iglesias, F. Sanchez, Organometallics 29 (2010) 4491-4498;

- (f) A.Kr. Ganai, R. Bhardwaj, S. Hotha, S.S. Gupta, B.L.V. Prasad, New J. Chem. 34 (2010) 2662–2670;
- (g) K.V. Kovtunov, V.V. Zhivonitko, A. Corma, I.V. Koptyug, J. Phys. Chem. Lett. 1 (2010) 1705–1708;
- (h) L. Lili, Z. Xin, G. Jinsena, X. Chunming, Green Chem. 14 (2012) 1710–1720; (i) S.M. Sadeghzadeh, RSC Adv. 4 (2014) 43315–43320;
- (j) S.M. Sadeghzadeh, RSC Adv. 4 (2014) 45515 45526 (j) S.M. Sadeghzadeh, RSC Adv. 5 (2015) 68947–68952
- (k) K.-I. Fujita, A. Fujita, J. Satob, H. Yasuda, Synlett (2016), http://dx.doi.org/ 10.1055/s-0035-1562134.
- [6] M. Peixoto de Almeida, L.M.D.R.S. Martins, S.A.C. Carabineiro, T. Lauterbach, F. Rominger, A.S.K. Hashmi, A.J.L. Pombeiro, J.L. Figueiredo, Catal. Sci. Technol. 3 (2013) 3056–3069.
- [7] During the late stage of this project the following was reported, using a similar strategy to obtain cross coupling Pd containing catalysts: V.N. Mikhaylov, V.N. Sorokoumov, K.A. Korvinson, A.S. Novikov, I.A. Balova Organometallics (2016) 1684–1697.
- [8] S. Tšupova, M. Rudolph, F. Rominger, A.S.K. Hashmi, Adv. Synth. Catal. 358 (2016) 3999–4005.

- [9] S. Tšupova, F. Rominger, M. Rudolph, A.S.K. Hashmi, Green Chem. 18 (2016) 5800–5805.
- [10] It should be mentioned that the best result is achieved when **4** was presoaked in CH_2Cl_2 for loading into the column. When a dry resin is used, there is a great risk of overpressure, due to swelling of the resin, and visual inspection revealed a gradient of gold distribution (see the catalytic activity section for the discussion of the distribution of gold along the column length).
- [11] J.F. Moulder, J. Chastain, Handbook of X-ray photoelectron spectroscopy: a reference book of standard spectra for identification and interpretation of XPS data, in: Physical Electronics Division, Perkin-Elmer Corporation, 1992.
- [12] J.B. Ernst, S. Muratsugu, F. Wang, M. Tada, F. Glorius, J. Am. Chem. Soc. 138 (2016) 10718–10721.
- [13] (a) A.S.K. Hashmi, T.M. Frost, J.W. Bats, Org. Lett. 3 (2001) 3769–3771;
 (b) A.S.K. Hashmi, T.M. Frost, J.W. Bats, Catal. Today 72 (2002) 19–27;

(c) A.S.K. Hashmi, J.P. Weyrauch, E. Kurpejovic, T.M. Frost, B. Miehlich, W. Frey, J.W. Bats, Chem. Eur. J. 12 (2006) 5806–5814;

(d) A.S.K. Hashmi, E. Kurpejović, M. Wölfle, W. Frey, J.W. Bats, Adv. Synth. Catal. (2007) 1743–1750;

(e) A.S.K. Hashmi, E. Kurpejović, W. Frey, J.W. Bats, Tetrahedron 63 (2007) 5879-5885;

(f) A.S.K. Hashmi, M.M. Rudolph, H.-U. Siehl, M.M. Tanaka, J.W. Bats, W.W. Frey, Chem. Eur. J. 14 (2008) 3703–3708;

(g) A.S.K. Hashmi, T. Hengst, C. Lothschütz, F. Rominger, Adv. Synth. Catal. 352 (2010) 1315–1337;

(h) M. Rudolph, M.Q. McCreery, W. Frey, A.S.K. Hashmi, Beilstein J. Org. Chem. 7 (2011) 794–801;

(i) S. Tšupovaa, F. Rominger, M. Rudolph, A.S.K. Hashmi, Green Chem. 18 (2016) 5800–5805.