SYNLETT
Spotlight

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Silver(I) Oxide

Compiled by Clémentine Gibard

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Introduction

Silver(I) oxide (Ag_2O) has been known for several centuries, and it is still widely used in synthetic chemistry, including in novel strategies. Ag_2O is a black powder that is prepared by the reaction of aqueous silver nitrate and hydroxide salts (eq. 1, Scheme 1).[1] However, thanks to its stability and low cost, organic chemists most frequently purchase it from commercial suppliers. This reagent has many applications: it can act as a base – due to the presence of oxide –, as an oxidant – due to its easy reduction to metallic silver –, as an halogen scavenger – due to the precipitation of silver halides –, or as a source of silver ion, particularly useful for organometallics preparation.

Ag_2O is poorly soluble in all common solvents including water. It is however readily soluble in ammonia, leading the Tollens' reagent[2] (eq. 2, Scheme 1) which possesses a historical importance in the development of organic chemistry. This also illustrates the fact that (as for other metal-based reagents), properties of Ag_2O may depend on the formation of complexes in the reaction medium.

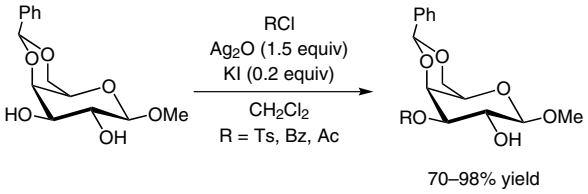
$$2\ AgNO_{3(aq)} + NaOH_{(aq)} \longrightarrow 2\ Ag_2O_{(s)} + 2\ NaNO_{3(aq)} \quad (1)$$

$$Ag_2O_{(s)} + 4\ NH_{3(aq)} + H_2O_{(l)} \longrightarrow 2\ [Ag(NH_3)_2]^{\oplus}_{(aq)} + 2\ OH^{\ominus}_{(aq)} \quad (2)$$

Scheme 1 Preparation of silver oxide and Tollens' reagent

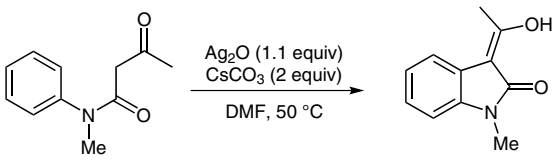
Abstracts

(A) *Selective Protection of Hydroxyl Groups*
Hydroxyl groups can be selectively protected in the presence of catalytic amounts of potassium iodide under neutral conditions. The high selectivity for the monofunctionalization is due to hydrogen-bonding interactions, resulting in an increased acidity for a specific hydroxyl group and selective deprotonation by Ag_2O.[3] The starting methyl 4,6-*O*-benzylidene-D-pyranoside is converted in good yield (70–98% yield), and the method can be applied to several protecting groups.[4]



70–98% yield

(B) *Free-Radical-Mediated Intramolecular C(sp^3)–C(sp^2) Coupling*
β-Ketoanilides are of synthetic interest as precursors for heterocyclic compounds which may display pharmaceutical activity. After numerous tests, the authors found that the product is obtained only in the presence of silver oxide. However, an external base is also required, the optimal one being cesium carbonate.[5]



63% yield

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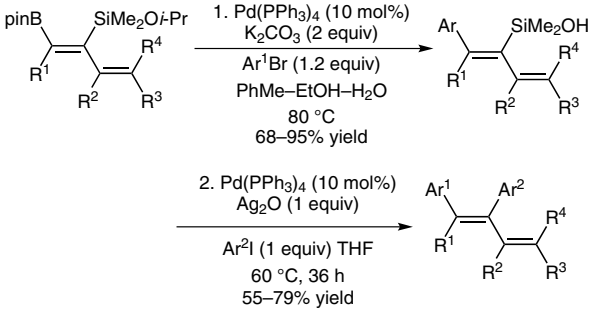
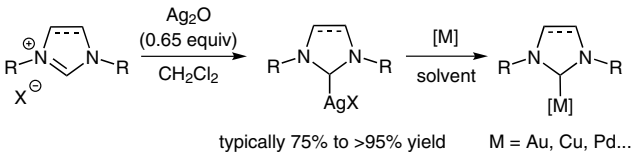
(C) *Sequential Suzuki–Miyaura/Hiyama–Denmark cross-coupling reactions*

Silver oxide was required in the second step of a sequence of Suzuki–Miyaura and Hiyama–Denmark cross-couplings to control the chemo- and stereoselectivity for a polysubstituted 1,3-diene product from a heavily substituted diene substrate. The proposed transition state involves a Si–O–Ag bond responsible for the formation of the α-coupled product. If a silver-free, non-coordinating, strong base is used, allylic rearrangement occurs instead, while the use of fluoride results in C–Si bond cleavage to yield a hydrogenated γ-product.[6]



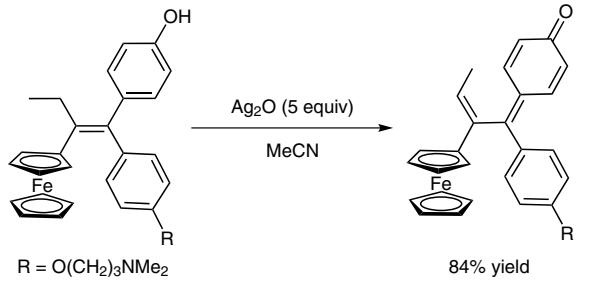
(D) S*ynthesis of Silver NHCs*

Silver oxide is a base and a source of Ag^+ in azolium salt metalation to yield silver *N*-heterocyclic carbenes. This double usefulness was first discovered by Lin in 1998.[7] Its mechanism was recently studied by DFT calculations.[8] Silver carbenes can serve as transmetalation reagents to access NHC complexes of several other metals. The Ag_2O strategy is currently of great synthetic relevance for the preparation of diversified metal–NHC complexes and can be performed with or without the isolation of the silver NHC.[9] Metal–NHC complexes display various applications, in particular in catalysis to replace analogous phosphine complexes.[10]



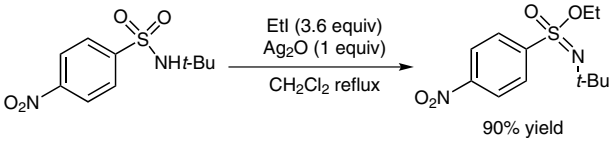
(E) *Oxidation of Ferrocene Phenols conjugated to Quinone Methides*

For a long time Ag^+ has been known to oxidize hydroquinone into benzoquinone.[11] The *in vivo* antiproliferative properties of ferrocenyl phenols (derivatives of ferrocifen)[12] are actually due to ferrocene-mediated oxidation to quinone methide metabolites. In order to prove this effect, the authors describe how to prepare these active quinone methides in the presence of silver oxide as the only reagent.[13]



(F) *O-Alkylation of Sulfonamides*

Ag_2O acts as a base and a halogen scavenger in a one-pot preparation of ethyl *N-tert*-butyl-4-nitrobenzensulfonimidate. Selective *O*-ethylation of *N-tert*-butyl-4-nitrobenzensulfonamide was accomplished using silver oxide in a non-coordinating solvent (CH_2Cl_2). This effect was suppressed in a coordinating medium (MeCN), yielding the thermodynamic *N*-ethylation product instead. The authors postulate a mechanism involving a six-membered metallacycle to explain such a reactivity which permits a straightforward access to the desired product. Ethyl *N-tert*-butyl-4-nitrobenzensulfonimidate allows simple ethylation of a large array of alcohols.[14]



References

(1) Janssen, D. E.; Wilson, C. V. *Org. Synth.* **1956**, *36*, 46.
(2) Tollens, B. *Ber. Dtsch. Chem. Ges.* **1882**, *15*, 1635.
(3) Bouzide, A.; Sauvé, G. *Org. Lett.* **2002**, *4*, 2329.
(4) Wang, H.; She, J.; Zhang, L. H.; Ye, X. S. *J. Org. Chem.* **2004**, *69*, 5774.
(5) Yu, Z.; Ma, L.; Yu, W. *Synlett* **2010**, 2607.
(6) Zhou, H.; Moberg, C. *J. Am. Chem.Soc.* **2012**, *134*, 15992.
(7) Wang, H. M. J.; Lin, I. J. B. *Organometallics* **1998**, *17*, 972.
(8) Hayes, J.; Viciano, M.; Peris, E.; Ujaque, G.; Lledos, A. *Organometallics* **2007**, *26*, 6170.
(9) Lin, I. J.B.; Vasam, C. S. Coord. *Chem. Rev.* **2007**, *251*, 642.
(10) *N-Heterocyclic Carbenes: From Laboratory Curiosities to Efficient Synthetic Tools*; Diez-Gonzales, S., Ed.; Royal Society of Chemistry: Cambridge, **2011**.
(11) Naruta, Y.; Maruyama, K. , In *Recent Advances in the Synthesis of Quinonoid Compounds, in: The Chemistry of the Quinonoid Compounds*; Vol. 2, Part 1; Patai, S.; Rappoport, Z., Eds.; Wiley: Chichester, UK, **1988**, 241.
(12) Hillard, E.; Vessières, A.; Thouin, L.; Jaouen, G.; Amatore, C. *Angew. Chem.* **2006**, *118*, 291.
(13) Hamels, D.; Dansette, P. M.; Hillard, E. A.; Top, S.; Vessières, A.; Herson, P.; Jaouen, G.; Mansuy, D. *Angew. Chem. Int. Ed.* **2009**, *48*, 9124.
(14) Maricich, T. J.; Allan, M. J.; Kislin, B. S.; Chen, A. I. T.; Meng, F. C.; Bradord, C.; Kuan, N. C.; Wood, J.; Aisagbonhi, O.; Poste, A.; Wride, D.; Kim, S.; Santos, T.; Fimbres, M.; Choi, D.; Elia, H.; Kaladjian, J.; Abou-Zahr, A.; Mejia, A. *Synthesis* **2013**, *45*, 3361.

