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Silver(I) oxide nanoparticles as a catalyst in the azide-alkyne cycloaddition

Anna M. Ferretti,^a Alessandro Ponti,^{a*} and Giorgio Molteni^{b+}

^aIstituto di Scienze e Tecnologie Molecolari (ISTM), Consiglio Nazionale delle Ricerche, via Golgi 19, 20133 Milano, Italy. ^bUniversità degli Studi di Milano, Dipartimento di Chimica, via Golgi 19, 20133 Milano, Italy

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ABSTRACT

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Silver oxide Nanoparticle Azide Alkyne 1,3-Dipolar cycloadditions The 1,3-dipolar cycloadditions between a number of azides and monosubstituted acetylenes have been carried out in the presence of catalytic amounts of silver(I) oxide nanoparticles. 4-Substituted 1,2,3-triazoles were usually the only products, while the presence of electron-withdrawing groups onto the azide moiety caused a loss of regioselectivity giving mixtures of 4-and 5-substituted 1,2,3-triazoles. A novel catalytic cycle has been proposed to rationalise this latter "non-click" behaviour.

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1. Introduction

Both metal^{1,2} and metal oxide³ inorganic nanoparticles (NPs) have recently emerged as effective catalysts in a number of synthetically useful transformations. For instance, the 1,3-dipolar cycloaddition between azides and monosubstituted alkynes have been successfully performed in the presence of Cu, Cu₂O, and CuO NPs.⁴⁻⁷ Within this framework, some of us described the use of colloidal copper/copper oxide NPs as a valuable catalyst for the azide-alkyne cycloaddition.⁸

Concerning the metal which follows copper in the 1B column of the Periodic Table, Ag₂O NPs have found application as sensors^{9,10} and antimicrobial materials¹¹ but most applications exploited Ag₂O NPs as catalysts. For instance, nanoscale Ag₂O was recognized as an active species in silver-titania photocatalysis¹²⁻¹⁴ and Ag₂O NPs have been used for the oxidation of CO to CO₂.^{15:17} Ag₂O NPs were less studied as a catalyst for synthetic organic chemistry. Just two reports are known which describes the use of $\approx 10 \text{ nm}^{18}$ and $\approx 1 \text{ µm}^{19} \text{ Ag}_2\text{O}$ NPs in the synthesis of propargylamines; a tentative reaction mechanism was there proposed involving the formation of a silver acetylide.¹⁸

Due to the known chemical and crystallographic similarity of Ag_2O and Cu_2O , we perceived that Ag_2O NPs could be used as a catalyst for the azide-alkyne cycloaddition, so we decided to investigate colloidal Ag_2O NPs under this respect. In the following sections, we will show that Ag_2O NPs coated with oleic acid behave as an effective catalyst in the reaction between azides and monosubstituted acetylenes

^tCorresponding author. Tel./fax: +39 025031 4141/4139.

2. Results and discussion

Uncoated silver(I)oxide nanoparticles (NPs) were synthesized by alkaline precipitation from aqueous silver nitrate solution.²⁰ A TEM image of the Ag₂O NPs is shown in Figure 1. The nanoparticles had approximately spherical shape and ranged in size from 2 to 14 nm. The diameter distribution had mean $\langle d \rangle = 5.3$ nm and standard deviation $\sigma_d = 1.3$ nm (dispersion $\sigma_d/\langle d \rangle = 25\%$).



Figure 1. TEM image of as-synthesized Ag_2O NPs (left) and the corresponding size distribution (right).

The powder X-ray diffractogram of the uncoated NPs is displayed in Figure 2 confirming the occurrence of genuine silver(I) oxide NPs.

E-mail address: giorgio.molteni@unimi.it (G. Molteni).

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Figure 2. Powder X-ray diffractogram of uncoated Ag_2O nanoparticles.

Since we planned to use Ag₂O NPs as a well-dispersed catalyst in toluene, we coated the as-synthesized NPs with oleic acid. These coated NPs showed good colloidal stability in toluene and were used for all of the azide-alkyne cycloadditions described below. We investigated the morphology of Ag₂O NPs after they were used as the catalyst (Figure 3).²² The nanoparticles maintained a spherical shape and their size resulted somewhat reduced, ranging from 1 to 12 nm. The diameter distribution had mean $\langle d \rangle = 3.4$ nm and standard deviation $\sigma d = 1.4$ nm (dispersion $\sigma_d / \langle d \rangle = 41\%$).



Figure 3. TEM image of Ag_2O NPs coated with oleic acid after use as a catalyst $(left)^{22}$ and the corresponding size distribution (right).

Catalysed azide-alkyne cycloadditions represent a fruitful field which had grown dramatically in the last decade.^{4,23,24} Hence, we decided to investigate scope and limitations of the reaction between arylazides **1** and alkynyl dipolarophiles **2** (Figure 4) in the presence of catalytic amounts of Ag₂O NPs (1.9-2.7% in weight with respect to **1**).



Figure 4. Reactants to be submitted to dipolar cycloaddition in the presence of Ag_2O NPs as the catalyst.

First of all, we performed such reactions by stirring an equimolecular mixture of the reactants at 30°C under nitrogen in anhydrous toluene as depicted in Scheme 1 and Table 1. Fully regioselective cycloadditions provided only the 1-aryl-4-

substituted 1,2,3-triazoles **3**. However, longer reaction times and lower product yields were experienced compared to the same reactions carried out in the presence of air-protected Cu/Cu-oxide nanoparticles as the catalyst.⁸



Scheme 1. Ag_2O NPs catalysed arylazide-alkyne cycloadditions in anhydrous toluene.

Table 1. Ag_2O NPscatalysedarylazide-alkynecycloadditions in anhydrous toluene.^a

Entry	\mathbf{R}^1 \mathbf{R}^2		t(h)	3 (%) ^b	
aa	H	COOMe	16	54 [°]	
ab	H	Ph	12	58	
ba	MeO	COOMe	12	50	
bb	MeO	Ph	9	44	

^aAt 30°C. ^bIsolated yields. ^cYield of **3aa** was 29% and 43% after 4 and 8 h, respectively.

Next, Ag₂O NPs-catalysed cycloadditions were performed in non-anhydrous toluene at 20°C (Scheme 2). Reaction times and product yields are given in Table 2, while structures of cycloadducts **3** and **4** were determined by analytical and spectroscopic methods which matches literature data.^{25,26} Easy filtration of the undissolved material allowed the recovering of the Ag₂O NPs which were reused without significant loss of catalytic activity.



Scheme 2. Ag₂O NPs catalysed arylazide–alkyne cycloadditions in toluene.

As can be inferred from comparison of the data in Table 1 and 2, the presence of small amounts of water²⁷ produced significant cycloaddition speed-up and product yield enhancement. It is also worth noting the loss of regioselectivity of the reactions between azides **1c,d** and methyl propiolate (Table 2, entry **ca** and **da**),

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which parallels previous results obtained by thermal cycloadditions.²⁵ A similar behaviour is not unprecedented, since it was reported in the cycloadditions between 4-chlorophenylazide and phenylacetylenes catalysed by silver(I)-N,N-diisopropyl(2-dicyclohexylphosphanyl)benzacomplexed mide.^{28,29} It is well-known that the classic Huisgen cycloaddition between arylazides and acetylenes^{30,31} can hardly occur at room temperature. Accordingly, we observed that in the absence of Ag₂O NPs azide 1a and methyl propiolate did not react appreciably after ten days at 20°C; the same fate occurred in the presence of sparingly soluble silver(I) bulk salts capable of Brønsted basic catalysis, namely Ag₂O, Ag₂CO₃, AcOAg and silver oleate. A further finding is related to the lack of reactivity of the internal dipolarophiles 4-heptyn-2-ol and dimethyl acetylenedicarboxy late (DMAD). The behaviour of propargyl bromide (Table 2, entry bd) may appear prima facie disappointing. However, this lack of reactivity is due to the sensitivity of Ag₂O NPs to the bromide ion present in the halide; the NPs are thus destroyed and replaced by bulk silver bromide which is unable to act as a catalyst.

Table 2. Ag₂O NPs catalysed arylazide–alkyne cycloadditions in toluene.^a

Entry	\mathbf{R}^1	\mathbf{R}^2	t (h)	$3(\%)^{b}$	$4(\%)^{b}$
aa	Н	COOMe	4	90	
ba	MeO	COOMe	4	95	
ca	Cl	COOMe	6	70	25
da	NO_2	COOMe	16	50	44
ab	Н	Ph	4	90	-
bb	MeO	Ph	3	92	-
bc	MeO	CH ₂ OH	7	90	—
bd	MeO	CH ₂ Br	7	< 2 ^{c,d}	< 2 ^{c,d}

^aAt 20°C. ^bIsolated yields. ^cNot fully characterised. ^d88% of unreacted **1b** was recovered.

All the above observations may find a rationale provided that the catalytic cycle depicted in Figure 5 does work.



Figure 5. Proposed catalytic cycle of the cycloaddition between arylazides 1 and monosubstituted acetylenes 2 in the presence of Ag_2O NPs.

The main catalytic cycle clearly resembles that of copper (I) catalyzed azide-alkyne "click" cycloadditions.⁴ Due to its d^{10}

electronic configuration, the silver (I) provided by the Ag₂O nanoparticle surface can coordinate two molecules of water and the terminal alkyne **2** giving the labile 18 electron complex **6**. Water displacement by azides **1a,b** can generate the reactive intermediate **7**, which leads to the corresponding 4-substituted 1,2,3-triazoles **3**. The ability of electron poor **1c,d** to act as a ligand may be by far less effective than that of **1a,b** on the basis of the corresponding σ + Hammett values.³³ In the former cases the upper part of the catalytic cycle would work providing mixtures of the corresponding regioisomers **3** and **4**.

This behaviour is different compared to that of the substituentinsensitive Cu(I) catalyzed cycloadditions and may be due to the weaker interaction between the azide N1 and Ag(I) of intermediate **7**. The latter argument is corroborated by the known fact that Cu(I) is more tenaciously bonded to N donors than Ag(I) is.³⁴ On the other hand, the formation of intermediate **6** is reasonable since σ -acetylide complexes of both Cu(I) and Ag(I) are known.³⁵

Since azide **8** (Scheme 3) displays roughly the same electronic features of 1d,³⁶ as a further stage of our work we submitted **8** to cycloaddition with methyl propiolate. The results summarised in Scheme 3 speak again in favour of the lack of regioselectivity as predicted by the above catalytic cycle.



Scheme 3. Ag₂O NPs catalysed cycloadditions between azide 8 and methyl propiolate in toluene.

2. Conclusions

The use of Ag_2O NPs in the azide-alkyne cycloaddition displayed several encouraging features, which can be summarised as follows: (i) the catalyst was effective, reusable after simple filtration and chemically robust, (ii) high product yields and cycloaddition regioselectivity were usually observed; (iii) the experimental procedure was simple, i.e. heating of the reaction mixture was avoided; (iv) a pronounced substituent effect was observed, whereas electron-withdrawing groups placed onto the azide moiety gave mixtures of regioisomeric cycloadducts. This latter feature resembles the behaviour of the thermal Huisgen reaction and could be regarded as a limitation, however the proposed catalytic cycle based onto the labile bis(aquo)-silver(I) acetilyde intermediate **6** should represent a novel and interesting insight in the growing field of metalcatalysed azide-alkyne cycloaddition.

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