EurJOC
European Journal of Organic Chemistry

A Journal of
ChemPubSoc Europe

Accepted Article

Title: Bimetallic Oriented (A□u□/C□u□2O) versus monometallic 1.1.1 A□u□ (0) or 2.0.0 C□u□2O Graphene supported Nanoplatelets as very efficient Catalysts for Michael and Henry Additions

Authors: Andrada Simion, Natalia Candu, Simona M. Coman, Ana Primo, Ivan Esteve-Adell, Véronique Michelet, Vasile I. Parvulescu, and Hermenegildo Garcia

To be cited as: *Eur. J. Org. Chem.* 10.1002/ejoc.201801443

Link to VoR: http://dx.doi.org/10.1002/ejoc.201801443

Supported by
ACES Asian Chemical Editorial Society

WILEY-VCH

Bimetallic Oriented ($\overline{Au}/\overline{Cu}_2O$) versus monometallic 1.1.1 $\overline{Au}$ (0) or 2.0.0 $\overline{Cu}_2O$ Graphene supported Nano-platelets as very efficient Catalysts for Michael and Henry Additions

Andrada Simion,[a] Natalia Candu,[a]Simona M. Coman,[a] Ana Primo,[b] Ivan Esteve-Adell,[b] Véronique Michelet,[c]* Vasile I. Parvulescu,[a]* Hermenegildo Garcia[b]*

Abstract: Michael and Henry addition reactions have been investigated using mono (*$\overline{Au}$ and $\overline{Cu}_2O$*) and bimetallic nanoplatelets (*$\overline{Au}/\overline{Cu}_2O$*) grafted onto few-layers graphene (*fl-G*) films as heterogeneous catalysts by comparison with homogeneous NaOH and K_2CO_3 ones. In the presence of the heterogeneous catalysts these reactions occurred in the absence of any extrinsic (NaOH and K_2CO_3) base with turnover numbers (TONs) at least four orders of magnitude higher. While the homogeneous catalysts provided TONs close to the unity for *$\overline{Au}/\overline{Cu}_2O$/fl*-G this was of the order of 10^7. These reactions also occurred with a very good selectivity to the targeted products. These performances are in line with the basicity of these catalysts demonstrated from CO_2 chemisorption measurements. The effect of the nano-size and the interaction of the nano-particles with the graphene are also important to achieve this high activity.

Introduction

Michael addition, as originally defined, [1] is the addition of an enolate of a ketoneor aldehyde or a doubly stabilized carbon nucleophile [2] to an α,β-unsaturated carbonyl compound at the β carbon. Thus, this reaction consists on the nucleophilic 1,4-addition of a carbanion or another nucleophile to an α,β-unsaturated carbonyl compound [3]. This reaction is catalyzed by both acid [4] and base [5] catalysts. More recently, the homogeneous catalysts utilized in this reaction were enlarged by using metal complexes [6] and organocatalysts [7]. Organic superbase, 1,1,3,3-tetramethylguanidine funcionalized graphene oxide has also reported to promote the Michael addition of malonates [8]. The use of metal complexes and organocatalysts has allowed expanding the scope of this reaction for the synthesis of complex molecules [9].

Besides these, heterogeneous catalysts exhibiting acid and base properties have also been investigated in this reaction [10]. In this context, among many other types of heterogeneous catalysts, the last two decades have seen an impressive number of examples showing the activity, and especially the selectivity of gold and copper in many catalytic reactions. For the particular case of the Michael addition the reported studies indicated that the selectivity can be controlled by tuning the oxidation state of Au from 0 to (I) and (III) [11]. Au support, consisting of an organic functionalized material or an oxide, should play the role controlling the charge density on the Au nanoparticles [12]**.** Au nanoparticles may exhibit an even more complex behavior. They can generate and stabilize electron–rich carbenes on their surface, after an electronic transfer to the anti–bonding valence orbitals of the C-O group of substrates [13]. Thus, beyond gold-catalyzed Michael additions, this constitutes an example of how gold nanoparticles modify the electronic density of unsaturated bonds [14]. The interaction of copper with organic functionalities of a support [15] or with the support itself [16] is producing quite similar effects in this reaction.

Besides Michael addition, the Henry reaction is other classic carbon–carbon bond formation reaction, consisting in the addition of a nucleophilic anion derived from nitroalkane to an electrophilic aldehyde or ketone [17]. Typically, it utilizes only a catalytic amount of a homogeneous catalyst that could be alkali metal hydroxides, alkoxides, carbonates, triflates, compounds of fluoride anion or nonionic organic amines [18]. Other homogeneous catalysts utilized in this reaction are metal complexes [19]. Base-heterogeneous catalysts as Mg-Al hydrotalcite have been used as well [20].

Beside catalytic activity, the use of Cu-complexes bearing various ligands has allowed also to gaindia- and stereoselectivity in the Henry reaction [21].

However, the literature referring to heterogeneous catalysts with Cu for the Michael reaction is scarce and refers either to immobilized Cu(II) complexes [22] or to MOF systems incorporating Cu [23]. For Au as catalyst, in our best knowledge there is no other precedent in this reaction.

Graphene, an allotrope of carbon, has been considered as an excellent suitable catalytic support due to its high carrier mobility, high electrical and thermal conductivity, high surface area (theoretical value of 2630 m^2/g), unique two-dimensional (2D) honeycomb lattice, high electron mobility, strong metal-

---

[a] A. Simion, Dr. N. Candu, Prof. S.M. Coman, Prof. V.I. Parvulescu
Department of Organic Chemistry, Biochemistry and Catalysis
University of Bucharest
4-12 Regina ElisabetaBlv., 030016, Bucharest, Romania
E-mail: vasile.parvulescu@chimie.unibuc.ro
[b] Dr. A.Primo, Dr. I. Esteve-Adell, Prof. H. Garcia
Instituto Universitario de TecnologiaQuimica Consejo Superior de Investigaciones Científicas
Universidad Politecnica de Valencia
Avda. de los Naranjos s/n, Valencia 46022, Spain
E-mail: hgarcia@qim.upv.es
[c] Prof. V. Michelet
Institut de Chimie de Nice, UMR 7272 CNRS, Parc Valrose, Faculté des Sciences
University Côte d'Azur
06100 Nice, France
E-mail: veronique.michelet@unice.fr

support interactions and easy surface functionalization [24-25]. In addition, doping graphene-nanosheets with heteroatoms became an attractive method of tuning its electronic and catalytic properties [26].

On the other side, graphene supported metal nanoparticles (MNPs) have already shown very active and selective properties for various organic transformations such as: oxidations [27], reductions [28-29] or coupling reactions [30-32]. In this context, we recently demonstrated that coupling reactions can be efficiently catalyzed by MNPs strongly grafted on few- and multilayer defective graphenes prepared by pyrolysis of natural polysaccharides containing metal salts (ie. $AuCl_4^-$ or Cu^{2+} as source of metal ions) [33]. Furthermore, the pyrolysis of thin films of alginate can provide *fl-G* (*fl* meaning few layers structures; G meaning defective graphene) of few nanometers thickness [34-35]. Under pyrolysis at 900ºC in inert atmosphere copper is orientated onto the graphene as (1.1.1) $\overline{Cu}$/*fl*-G which after exposure to air spontaneously render to oriented (2.0.0) copper (I) oxide nanoplatelets ($\overline{Cu_2}O$/*fl*-G). Under the same conditions, onto the few layers of graphene, Au^{3+} generates (1.1.1) oriented Au nanoplatelets ($\overline{Au}$/*fl-G*), where the lateral sides correspond to (0.0.1) oriented planes [9].

In order to prove the versatility of the graphene supported MNPs in coupling reactions in this study we extended the investigation of these materials from the monometallic to bimetallic $\overline{Au}$/$\overline{Cu_2}O$ /*fl*-G films looking for a synergistic effect in two important C-C coupling reactions, namely Michael and Henry additions [36]. Henry reaction is a *"nitroaldol condensation"* and one of the most atom-economical C-C coupling processes [37-38]. Under classical conditions, both reactions require basic or acidic catalysts in the presence of organic solvents, and long reaction times, which may lead to environmentally hazardous residues and undesirable by-products [39-43].

Results and Discussion

Monometallic $\overline{Cu_2}O$/*fl-G* and $\overline{Au}$/*fl-G* catalysts were exhaustively characterized as described in our previous works [31, 33]. Briefly, in accordance to TEM images combined with the analysis of the diffraction patterns of back scattered electrons, the oriented $\overline{Cu_2}O$/*fl-G* are constituted from Cu_2O nano-platelets which exhibit a preferential (2.0.0) facet orientation [33] while $\overline{Au}$/*fl-G* catalysts display a preferential (1.1.1) facet orientation irrespective the Au loading and the thickness of G [31]. To illustrate the materials used as catalysts in the present study that are also coincident with those previously reported [31], Figure 1 presents a transmission electron microscopy image of $\overline{Au}$/$\overline{Cu_2}O$/*fl*-G.

Catalytic performance of these oriented nanoplatelets on graphene were checked in two reactions controlled by completely different mechanisms, such as Michael (Scheme 1, Eq. 1) or Henry additions (Scheme1, Eq. 2). For the Michael addition, the experiments were carried out considering methyl acetoacetate (MeAcOAc) and ethyl acetoacetate (EtAcOAc) as activated methylene substrates and methyl vinyl ketone (MVK) as Michael acceptor.

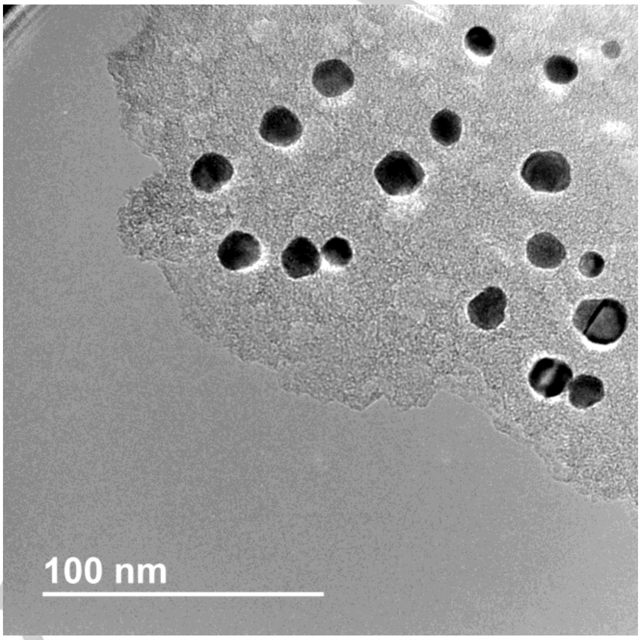
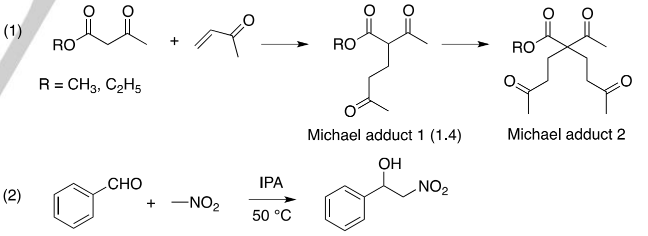


Figure 1. TEM image of the $\overline{Au}$/$\overline{Cu_2}O$/*fl*-G catalyst.

The considered Henry addition is the coupling of benzaldehyde with nitromethane to nitroaldol. Michael addition was investigated in water, while the Henry addition in both protic (isopropyl alcohol, IPA) and aprotic solvents (heptane).



Scheme 1. Michael addition of acetoacetates with MVK (1) and Henry reaction of benzaldehyde with nitromethane (2).

Comparative behavior of $\overline{Au}$/fl-G, $\overline{Cu_2}O$/fl-G and $\overline{Au}$/$\overline{Cu_2}O$/fl-G films as catalysts in Michael addition

Table 1 compiles results in the presence of $\overline{Cu_2}O$/fl-G, $\overline{Au}$/fl-G and $\overline{Au}$/$\overline{Cu_2}O$/*fl*-G catalysts. With acetoacetates as Michael donors the reaction may proceed in two steps (Scheme 1, Table 1), where the first step leads to the formation of mono adduct MA1 which can be subsequently deprotonated affording the addition of another MVK molecule with the formation, in the second step, of the MA2 product. The catalytic results show that the performances in this reaction are controlled by the nature of the catalyst and of the Michael donor. Prior controls using *fl*-G as catalyst showed the failure of this material to promote either the Michael or the Henry reaction. These preliminary blank controls clearly established that the presence of metal nanoparticlesis required to obtain catalytically active materials.

Working with MeAcOAc the homogeneous NaOH base catalyst (Table 1, entry 1) provides a very high conversion but with a relatively low selectivity to MA1 (~12.7%). In the absence of base, on *Au/fl-G* and *Cu_2O/fl-G* films (entries 2 and 3) the conversion is lower compared to the homogeneous catalyst, but the achieved selectivity in MA1 is very high. Under the same conditions, bimetallic *Au/Cu_2O/fl*-G films (entry 4) as catalyst, led to a high conversion comparable with that produced by the monometallic *Au/fl-G, Cu_2O/fl-G* but with a much higher selectivity in MA1 compared to all the individual catalysts.

Replacing the Michael donor with ethyl acetoacetate (EtAcOAc), led to an increase of the conversion for all the catalysts. Under these conditions the differences between the homogeneous catalyst (NaOH) and the heterogeneous graphenes are very small.

Table 1. Catalytic performances of *Au/fl-G, Cu_2O/fl-G and Au/Cu_2O/fl*-G films in the Michael addition of acetoacetates donors with MVK acceptor.

	Michael donor	Base	Graphene Catalyst	C[a] (%)	S[b] (%) MA1	S[b] (%) MA1
1	MeAcOAc	NaOH	no	100	12.7	87.3
2	MeAcOAc	no	*Au/fl-G*	32.4	75.7	24.3
3	MeAcOAc	no	*Cu_2O/fl-G*	31.1	77.4	22.6
4	MeAcOAc	no	*Au/Cu_2O/fl*-G	85.8	72.8	27.2
5	MeAcOAc	no	*Au(0.52wt%)/fl-G*	5.8	100	0
6	MeAcOAc	NaOH	no	100	10.2	89.8
7	EtAcOAc	no	*Au/fl-G*	97.0	45.7	54.3
8	EtAcOAc	no	*Cu_2O/fl-G*	92.3	63.1	36.9
9	EtAcOAc	no	*Au/Cu_2O/fl*-G	98.8	100	0
10	EtAcOAc	no	*Au/fl-G*	8.3	100	0
11	EtAcOAc	no	*fl-G*	0	0	0

Reaction conditions: Michael donor: 1 mmol: Michael acceptor: 1.5 mmoles, Catalyst: 0.12 mmoles NaOH or 1 piece of 1×1 cm^2 of Cu_2O /fl-G on quartz (0.20 mg of Cu total), or one piece of 1 × 1 cm^2 plate of Au/fl-G film (0.24 mg of Au total) or one piece of 1 × 1 cm^2 plate of Au/Cu_2O/fl-G (0.32 mg Au/Cu of 3/1), 5mg *Au(0.52 wt %)/fl-G,* 8 mL H_2O deionized, temperature: RT; time 18h. Note: [a]-Conversion refers to Michael donor transformation. [b]-selectivity to MA1 and MA2. Conversion and selectivities were determined by GC-MS.

However, for NaOH, and *Au/fl-G,* and *Cu_2O/fl-G* films this increase corresponded to a further decrease of the selectivity to MA1 (Table 1, entries 5, 6 and 7). Interestingly, the increase of the conversion for the bimetallic *Au/Cu_2O /fl*-G films catalyst did not affect the selectivity in MA1, which on the contrary becomes total. This behavior can be related to the different basic properties of *Au/Cu_2O /fl*-G in comparison to those of *Cu_2O /fl-G* or *Au/fl-G* films.

Indeed the CO_2 chemisorption on these catalysts results in different concentrations of basic sites and CO_2 desorption temperatures (Table 2). These results correspond to values resulted after the substraction of the CO_2 directly chemisorbed by the graphene support [44].

Table 2. CO_2 chemisorption results.

Sample	Temperature at Maximum (°C)	Adsorbed CO_2 (mmoles/g) x 10^{-3}
Au/fl-G	346	2.78
Cu_2O/fl-G	292	2.20
	350	0.94
Au/Cu_2O/fl-G	252	6.29
	347	3.99

The concentration of the basic sites decreased in the order *Au/Cu_2O/fl-G > Cu_2O/fl-G >Au/fl-G* while the strength of these sites, appreciated from the CO_2 desorbed at around 350^{o}C in the order *Au/Cu_2O/fl-G >Au/fl-G> Cu_2O/fl-G*. These results are in line with the catalytic data included in the Table 1 supporting the role of the basicity in this reaction.

Table 3. Time evolution of the conversion and selectivity to MA1 and MA2 for *Au/fl-G, NaOH* and *Au/Cu_2O/fl-G* in the Michael addition of MeAcOAc donor with MVK acceptor.

	Time (h)	Catalyst	C[a] (%)	S [b] (%) MA1	S [b] (%) MA 2	TON
1	5	*Au/fl-G*	14.3	92.6	7.4	$1.27x10^5$
2		*Cu_2O/fl-G*	12.8	93.5	6.5	$0.41x10^5$
3		*Au/Cu_2O/fl-G*	68.9	88.4	11.6	$1.43x10^7$
4		*Au/fl-G*	2.3	100.0	0	1.74
5		NaOH	84.9	28.8	71.2	7.07
6	9	*Au/fl-G*	21.7	85.2	14.8	-
7		*Cu_2O/fl-G*	19.4	86.6	13.4	-
8		*Au/Cu_2O/fl*-G	73.4	81.6	18.4	-
9		NaOH	100	22.4	77.6	-
10	18	*Au/fl-G*	32.4	75.7	24.3	-
11		*Cu_2O /fl-G*	31.1	77.4	23.6	-
12		*Au/Cu_2O/fl-G*	85.8	72.8	17.2	-
13		NaOH	100	12.7	87.3	-

14	30	*$\overline{Au}$/fl-G*	44.4	74.5	24.5	-
15		*$\overline{Cu_2}O$/fl-G*	42.5	75.7	24.3	-
16		*$\overline{Au}/\overline{Cu_2}O$/fl-G*	89.9	71.5	18.5	-
17		*NaOH*	100	7.0	93.0	-

Reaction conditions: Michael donor: 1 mmol: Methylacetoacetate (MeAcOAc), Michael acceptor: 1.5 mmoles, Catalyst: 0.12 mmoles NaOH or 1 piece of $\overline{Au}$/fl-G $\overline{Cu_2}O$/fl-G, $\overline{Au}/\overline{Cu_2}O$/fl-G or 5 mg Au/fl-G, solvent: 8 mL H_2O deionized, temperature: RT; Note: [a]-Conversion refers to Michael donor transformation. [b]-selectivity to MA1 and MA2. Conversion and selectivities were determined by GC-MS.

In order to better understand the kinetics of the Michael addition we measured the conversion and the selectivity in the Michael addition of MeAcOAc donor with MVK acceptor using NaOH, and the *$\overline{Au}$/fl-G, $\overline{Cu_2}O$/fl-G*, *$\overline{Au}/\overline{Cu_2}O$/fl*-G film catalysts at different reaction times. The results are listed in Table 3. With NaOH as catalyst the conversion becomes total after 5h. Further increase of the reaction time till 30h corresponded to a continuous deplete in the selectivity to MA1 in the favor to MA2 (93% selectivity), which is a typical behavior for a strong basic medium leading to a second addition. In terms of conversion, the monometallic *$\overline{Au}$/fl-G* and *$\overline{Cu_2}O$/fl-G* film catalysts provided much smaller conversions and better selectivities to MA1. Surprisingly was the behavior of the *$\overline{Au}/\overline{Cu_2}O$/fl*-G film which allowed indeed very good conversions but also selectivity to MA1 even after 30h. However, the calculation of the TONs after 5h showed a different order in activity than that presented in the Table 3. *$\overline{Au}/\overline{Cu_2}O$/fl-G* exhibits an almost seven times higher TON order than NaOH while *$\overline{Au}$/fl-G* and *$\overline{Cu_2}O$/fl-G* film catalysts almost five times. These values confirm, like in other coupling reactions the extremely high activity of the orientated metal nanoparticles [31, 33].Unoriented supported *Au/fl-G* nanoparticle catalysts were much less active compared to *$\overline{Au}$/fl-G* (five order difference in activity). However, in terms of TONs the activity of these nanoparticles is comparable to that of NaOH, namely, still high.

Comparative behavior of $\overline{Au}$/fl-G, $\overline{Cu_2}O$/fl-G and $\overline{Au}/\overline{Cu_2}O$/fl-G films in the Henry addition

The Henry addition (Scheme1, Eq. 2) has been investigated in the presence of the same *$\overline{Au}$/fl-G, $\overline{Cu_2}O$/fl-G* and *$\overline{Au}/\overline{Cu_2}O$/fl*-G film catalysts. This reaction is generally catalyzed by many organic bases, including carbonates, bicarbonates, alkali metal hydroxides, alkoxides, and organic nitrogen bases with the disadvantage of the difficulty in separation of various by-products [45]. Under basic conditions nitroalkanes are able to deprotonate the nitroaldol leading to a nitronate anion intermediate [46] which further reacts with aldehydes yielding β-nitroalcohols [47]. Table 4 summarizes the catalytic results on the investigated catalysts.

As Table 4 shows, using 2 mmoles of K_2CO_3 as a weak inorganic base, the reaction took place with a moderate conversion, but with a relatively high selectivity to the nitroaldol product. TON value calculated under these conditions was of 0.15. On the contrary, in the presence of *$\overline{Au}$/fl*-G and *$\overline{Cu_2}O$/fl*-G, although the conversions were smaller, in terms of activity, these catalysts presented much higher TONs. They increased till the order of 10^4. Importantly, an increase of the temperature from RT to 50ºC led to a further increase of the TON with one order of magnitude. The reaction by-product in these reactions was benzoic acid. For *$\overline{Cu_2}O$/fl*-G, in addition, benzaldehyde was further oxidized to benzoic acid which becomes the major by-product. Non-orientated Au/G and Cu_2O/G catalysts showed even higher TONs than the corresponding orientated catalysts that might be an evidence of an increased activity of the smaller particles.

Table 4. Catalytic efficiency of *$\overline{Cu_2}O$/fl*-G, *$\overline{Au}$/fl-G* and *$\overline{Au}$-$\overline{Cu2}O$/fl*-G films as catalysts in the Henry reaction.

	Solvent	Catalyst	C[a] (%)	S[b] (%)	TON
1[c]	no	*K_2CO_3*	59.8	91.8	0.15
2	no	*$\overline{Au}$/fl-G*	0	0	0
3[d]	IPA	*$\overline{Au}$/fl-G*	11.1	32.0	$4.6x10^4$
4	IPA	*$\overline{Au}$/fl-G*	64.7	46.2	$2.7x10^5$
5[d]	IPA	*Au(0.15wt %)/G[e]*	33.6	54.0	$4.4x10^6$
6	no	*$\overline{Cu_2}O$/fl-G*	0	0	0
7	Heptane	*$\overline{Cu_2}O$/fl*-G	0	0	0
8[d]	IPA	*$\overline{Cu_2}O$/fl*-G	7.9	30.2	$1.2x10^4$
9	IPA	*$\overline{Cu_2}O$/fl*-G	74.5	60.4	$1.2x10^5$
10	IPA	*Cu_2O(1 wt%)/G*[f]	89.3	0.3	$8.9\ x10^5$
11	no	*$\overline{Au}$-$\overline{Cu_2}O$/fl*-G	0	0	0
12	Heptane	*$\overline{Au}$-$\overline{Cu_2}O$/fl*-G	90.9	0.1	$9.4x10^6$
13	IPA	*$\overline{Au}$-$\overline{Cu_2}O$/fl*-G	97.4	96.7	$1.0x10^7$

Reaction conditions: 10 mmoles $MeNO_2$, 0.5 mmoles benzaldehyde, 24h, 50º C, 3mL solvent; catalyst: [a]conversion for benzaldehyde; [b]-selectivity to nitroaldol. [c] 2 mmoles of K_2CO_3; [d] RT; catalyst: 1 piece of 1×1 cm^2 of $\overline{Cu_2}O$ /fl-G on quartz (0.20 mg of Cu total), or one piece of 1 × 1 cm^2 plate of $\overline{Au}$/fl-G film (0.24 mg of Au total) or one piece of 1 × 1 cm^2 plate of $\overline{Au}/\overline{Cu_2}O$ /fl-G (0.32 mg Au/Cu of 3/1) or [e] 5 mg Au(0.15 wt%)/G; or [f] 5 mg Cu (1 wt%)/G; Conversion and selectivities were determined by GC-MS. Difference to 100% in selectivity is for benzoic acid.

However, like for the Michael addition the bicomponent *$\overline{Au}/\overline{Cu_2}O$/fl*-G films led to the best performances. Very high TONs and selectivities were achieved with this catalyst. Under the optimal reaction conditions of 50ºC for 24 h, they afforded an as high conversion of benzaldehyde as 97.4 % and a selectivity of 96.7 % in favor of nitroaldol.

Very important to notice, the catalysts were recycled five times with almost no changes in the catalytic behavior.

The role of the solvent in this reaction is very important. In an aprotic solvent such as heptane the conversions were either zero or the reaction was directed to benzaldehyde. It is assumed

10.1002/ejoc.201801443

that the measured basicity is the combined effect of the very small particle size of these films and the generated interaction between these and the graphene support.

The behavior of these catalysts in both Michael and Henry reactions should be associate to their properties as Lewis base. In Cu_2O oxide Cu (I) exhibits a d^{10} configuration [48] and basicity is associated to the presence of surface O^{2-} species. Au has also a d^{10} configuration and this property affords an increase of the basicity of the supported metal nanoparticles with direct catalytic effect [49]. On this basis the behaviour of the individual Cu_2O and Au/graphene catalysts as bases is well justified according to the literature.

The increase of the activity of bicomponent Cu_2O-Au/graphene catalyst should be the result of the direct interaction of Au with Cu_2O. Recent studies of Glorius et al.[49]. using gold deposited on CeO_2-ZrO_2-mixed oxides have shown that the density of acid sites was decreased, whereas the density of basic site was increased by modification with Au. A similar effect can results after the interaction with Cu_2O. This effect is more evident for the experiment described in entry 12.

Such a model is also supported by the results from Table 4 presenting the effect of the solvent. Heptane is not able to surpress the acidity induced by the two active species. On the contrary, IPA has two contributions in this reaction: i) to act as a solvent for the investigated substrates, and ii) to block any residual Lewis acidity. This effect is more evident for the catalysts containing Cu_2O which reached conversions of 97.4% and TONs of 10^7.

Conclusions

In summary, we have developed a simple and efficient procedure for Michael and Henry addition reactions using bimetallic nanoplatelets grafted onto few-layers graphene *$\overline{Au}$/$\overline{Cu_2O}$/fl*-G films as catalyst. These reactions occurred in the absence of any extrinsic base. Moreover, films of *$\overline{Au}$ and $\overline{Cu_2O}$ /fl*-G also exhibit a high catalytic activity to promote the Michael addition of acyclic active methylene and methine compounds to α, β-conjugated ketone or the Henry reaction of nitroalkane to β-nitroaldols. Noteworthy, by comparison to homogeneous NaOH or K_2CO_3, in the presence of the heterogeneous catalysts these reactions occurred with TONs at least four orders of magnitude higher. While the homogeneous catalysts provided TONs close to the unity for *$\overline{Au}$/$\overline{Cu_2O}$/fl*-G this was of the order of 10^7. Un-oriented supported nanoparticles *Au/fl-G* catalysts were much less active compared to *$\overline{Au}$/fl-G.* However, in terms of TONs the activity of these nanoparticles is comparable to that of NaOH, namely, still high. These performances are in line with the basicity of these catalysts demonstrated from CO_2 chemisorption measurements. The effect of the nano-size and the interaction of the nano-particles with the graphene is also important to achieve these properties.

Experimental Section

General procedure for the Michael addition.

To a solution of β-ketoesters as Michael donor (1 mmol of methyl acetoacetate or ethyl acetoacetate) in 8 mL of solvent (deionized H_2O) was added MVK as Michael acceptor (1.5 mmoles, 0.105 g), base (0.12 mmoles, NaOH) if required and one piece of 1 × 1 cm^2 plate of *$\overline{Cu_2O}$*/fl-G on quartz (0.24 mg of Cu total), one piece of 1 × 1 cm^2 plate of $\overline{Au}$/fl-G film or one piece of 1 × 1 cm^2 plate of *$\overline{Au}$/$\overline{Cu_2O}$ /fl*-G films as catalysts. The resulting mixture was left stirring at room temperature for 5-30 h. The reaction mixture was then filtered, extracted with ethyl acetate (3 x 10 mL) and the combined organic layer was dried over Na_2SO_4, filtered and concentrated.

Product analysis

Irrespective of reaction procedure, after reaction the catalyst was collected by filtration or was manually removed, and the reaction products were analyzed and identified by GC-MS (THERMO Electron Corporation instrument), Trace GC Ultra and DSQ, Trace GOLD with a TG-5SilMS column (30 m × 0.25 mm × 0.25 mm).

GS-MSanalysis of the reaction products using *Methyl acetoacetate* corresponded to: MA1: *Methyl 2-acetyl-5-oxohexanoate*: GC-MS, (m/z):186 (M^+, 2), 155 (12), 154 (12), 144 (100), 143 (18), 139 (25), 129 (15), 116 (40), 112 (56), 111 (57), 101 (21), 97 (17), 87 (64), 84 (64), 69 (17), 58 (20), 55 (29).MA2: GC-MS, (m/z): 256 (M^+, 1), 238 (20), 196 (24), 186 (87), 182 (15), 181 (66), 179 (87), 167 (48), 165 (22), 164 (42), 154 (88), 153 (63), 143 (43), 139 (82), 137 (33), 136 (40), 129 (90), 125 (33), 123 (73), 116 (47), 111 (100), 109 (56), 97 (63), 95 (32), 93 (65), 91 (23), 85 (18), 84 (12), 79 (14), 71 (32), 55 (25).

and for *Ethyl acetoacetate* to: MA1: Ethyl 2-acetyl-5-oxohexanoate: GC-MS, (m/z): 200 (M^+, 2), 158 (100), 139 (29), 130 (30), 112 (59), 111 (69), 101 (55), 84 (71), 73 (33), 55(17). MA2: GC-MS, (m/z): 270 (M^+, 1), 252(18), 209 (24), 200 (100), 181 (98), 179 (88), 167 (52), 165 (32), 164 (30), 157 (39), 154 (55), 153(25), 143(76), 139 (91), 137 (29), 136 (31), 125 (29), 123 (60), 121 (54), 115 (16), 111 (90), 109 (52), 97 (43), 95 (27), 93 (51), 71 (16), 55 (14).

General procedure for the Henry reaction.

All reagents were purchased from Sigma-Aldrich and used as received without further purification. To a glass sealed vial containing a magnetic stir bar with 3 mL of solvent (Isopropyl alcohol dried (IPA) or heptane) was added benzaldehyde (0.5 mmoles), nitromethane (10 mmoles) and catalyst. Resulting mixture was left stirring for 24h at room temperature or 50^0C.The reaction mixture was then filtered, concentrated and silylated. The products were analyzed and identified by using GC-MS (THERMO Electron Corporation instrument) and a Bruker Advance III UltraShield 500 MHz spectrometer, operating at 500,13 MHz for ^{1}H NMR, 125,77 MHz for ^{13}C NMR. For ^{1}H NMR were reported downfield from $CDCl_3$ (δ: 7.26ppm) and for ^{13}C NMR chemical shifts were reported in the scale relative to the solvent of $CDCl_3$ (δ: 77.0 ppm) used as an internal reference.

The recovered products were silylated (50 µL pyridine, 100 µL BSTFA (*N*,O-bis(trimethylsilyl) trifluoroacetamide) and TMCS (trimethylchlorosilane) silane agent), and analyzed by GC-MS. The identification of the products was made using a GC-MS (THERMO Electron Corporation instrument), Trace GC Ultra and DSQ, Trace GOLD: TG-5SilMS column with the following characteristic: 30m x0.25mm x 0.25um working with a temperature program (50 °C (2 min) to

250 °C at 10 °C/min (Hold 10.00 min) for a total run time of 32 min) at a pressure of 0.38 Torr with He as the carrier gas.

NMR analysis of 1-(4-methoxyphenyl)-2-nitroethanol corresponded to: ^{1}H NMR (CDCl$_3$) δ = 7.54-7.48 (m, 5H, H$_{Ph}$), 5.49-5.47 (dd, 1H, C*H*OH), 4.63-4.51 (m, 2H, C*HH*NO$_2$), 3.82 (s, 3H), 3.92 (br s, 1H, OH) ppm. ^{13}C NMR (CDCl$_3$) δ = 138.10 (C$_{Ph}$), 129.25 (2C, CH$_{Ph}$), 129.14 (CH$_{Ph}$), 125.93(2C, CHPh), 81.23 (2C, CH2NO$_2$), 71.04 (CHOH) ppm.

$\overline{\text{Au}}$/$\overline{\text{Cu}}_2$O/fl-G

Synthesis of catalysts

$\overline{\text{Au}}$/fl-G and $\overline{\text{Cu}}_2$O//fl-G catalysts were prepared according to previous reports [31, 33]. Preparation of $\overline{\text{Au}}$/$\overline{\text{Cu}}_2$O/fl-G was carried out following a close procedure. Alginate (0.5 g) from Aldrich (low molecular weight) was dissolved in a copper (II) nitrate aqueous solution (420 mg of Cu(NO$_3$)$_2$·2 H$_2$O in 25 ml of water). 0.23 g of acetic acid was added to dissolve alginate completely. The solution was filtered through a syringe having a 0.45 µm diameter pore size membrane filter to remove any impurity that could be present in commercial alginate. The films were supported on a quartz plate (2 × 2 cm^2) by casting 300 µl of filtered solution spinning at 4,000 rpm. for 1 min. Subsequently, films were immersed into a 1 mM aqueous solution of NaAuCl$_4$ (Aldrich) during 1 min to adsorb Au on Cu-containing alginate film, before proceeding to pyrolysis. The pyrolysis was performed under argon atmosphere (1 ml× min^{-1}) in a tubular oven at 5 ^{o}C·min^{-1} temperature increase rate up to 900 ^{o}C that was maintained for 2 h. The sample was, then, cooled at room temperature under argon. The resulting sample immediately after the pyrolysis consisted in an alloy of Au and Cu nanoplatelets grafted on G.

Preparation and analytic characterisation of un-oriented supported Au/fl-G nanoparticleswas carried out following the procedure described in [31]. The content of gold determined by ICP-OES was of 0.52 wt%.

Catalysts characterization

CO$_2$- and NH$_3$-TPD measurements were carried out using the same AutoChem II 2920 station. The samples (3–5mg), placed in a U-shaped quartz reactor with an inner diameter of 0.5cm, were pretreated under He (Purity 5.0, from Linde) at 120°C for 1h and then exposed to a flow of NH3 or CO$_2$ (from SIAD) for 1h. After that, the sample was purged with a flow of He (50ml min1) for 20 min at 25°C in order to remove the weakly adsorbed species. TPD was then started, with a heating rate of 10°C / min till 850°C. The desorbed products were analyzed with a TC detector. The desorbed NH$_3$ or CO$_2$, expressed as mmols per grams of catalyst, was determined using a calibration curve.

Acknowledgements

This work was supported by the Ministère de l'Education, de la Recherche et des Affaires Etrangères (Brancusi Program) of France (PN-III-CEI-BIM-PM, nr. 80BM/2017), UEFISCDI (PN-III-P4-ID-PCE-2016-0146, nr. 121/2017) and COST Action CA15106 (CHAOS)

Keywords: •graphene •coupling reactions •heterogeneous catalysts •mono and bimetallic nanoplatelets.

[1] (a) A. Michael, *J. Prakt. Chem.* **1887**, *35*, 349–356; (b) A. Michael, *J. Prakt. Chem.***1894**, *49*, 20–25.T. Tokoroyama, *Eur. J. Org. Chem.* **2010**, 2009–2016.

[2] E.P. Kohler, *J. Am. Chem. Soc*. **1907**, *37*, 385-386.

[3] R.D. Little, M.R. Masjedizadeh, O. Wallquist, J.I. McLoughlin, *Org. React.***1995**, *47*, 315–552.

[4] (a) C.F. Huebner, W.R. Sullivan, M.A. Stahmann, K. Paul, *J. Am. Chem. Soc*. **1943**, *65*, 2288–2291. (b) T. Mukaiyama, *Angew. Chem. Int. Ed. Engl.* **1977**, *16*, 817–826; *Angew. Chem*. **1977**, *89*, 858-866; (c) S.V. Pansare, K. Pandya, *J. Am. Chem. Soc*. **2006**, *128*, 9624–9625.

[5] (a) M.Ikawa, M.A.Stahmann,K. Paul, *J. Am. Chem. Soc.* **1944**, *66*, 902–906; (b) M. Iwamura, Y. Gotoh, T. Hashimoto, R. Sakurai, *Tetrahedron Lett*. **2005**, *46*, 6275-6277; (c) X. Xu, W.-H. Hu, M.P. Doyle, *Angew. Chem. Int. Ed*. **2011**, *50*, 6392-6395 **;** *Angew. Chem.* **2011**, *123*, 6516-6519.

[6] R. Martinez, M.-O. Simon, R. Chevalier, C. Pautigny, J.-P. Genet, S. Darses, *J. Am. Chem. Soc*. **2009**, *131*, 7887-7895.

[7] N. Halland, T. Hansen, K.A. Jørgensen, *Angew. Chem. Int. Ed*. **2003**, *42*, 4955–4957; *Angew. Chem.* **2003**, *115*, 5105-5107.

[8] J. Izquierdo, M.A. Pericàs, *ACS Catal.* **2016**, *6*, 348−356.

[9] K.C. Nicolaou, D. Rhoades, S.M. Kumar, *J. Am. Chem. Soc.* **2018**, *140*, 8303–8320.

[10] R. Ye, F.F. Faucher, G.A. Somorjai, *Mol. Catal*., **2018**, *447*, 65-71.

[11] (a) N. Morita, A. Yasuda, M. Shibata, S. Ban, Y. Hashimoto, I. Okamoto, O. Tamura, *Org. Lett.* **2015**, *17*, 2668–2671; (b) Z. Li, L. Song, L. Van Meervelt, G. Tian, E.V. Van der Eycken, *ACS Catal.* **2018**, *8*, 6388–6393.

[12] R. Pagadala, S. Maddila, V. Moodley, W.E. van Zyl, S.B. Jonnalagadda, *TetrahedronLett*. **2014**, *55,* 4006-4010.

[13] J. Oliver-Meseguer, M. Boronat, A. Vidal-Moya, P. Concepción, M.Á. Rivero-Crespo, A. Leyva-Perez, A. Corma, *J. Am. Chem. Soc.* **2018**, *140*, 3215–3218.

[14] A. Leyva-Pérez, J. Oliver-Meseguer, J.R. Cabrero-Antonino, P. Rubio-Marqués, P. Serna, S.I. Al-Resayes, A. Corma, *ACS Catal.* **2013**, *3*, 1865–1873.

[15] A. Megia-Fernandez, M. Ortega-Muñoz, J. Lopez-Jaramillo, F. Hernandez-Mateo, F. Santoyo-Gonzalez, *Adv. Synth. Catal*. **2010**, *352*, 3306-3320.

[16] T. Kawabata, M. Kato, T. Mizugaki, K. Ebitani, K. Kaneda, *Chem. Eur. J.***2005**, *11*, 288-297.

[17] L. Henry, *Comptes Rend*. **1895**, *120*, 1265–1268.

[18] (a) C. Palomo, M. Oiarbide, A. Laso, *Angew. Chem. Int. Ed.* **2005**, *44*, 3881-3884; *Angew. Chem.* **2005**,*117*, 3949-3952; (b) S.S. Ganesan, A. Ganesan, J. Kothandapani, *Synlett*, **2014**, *25*, 1847-1850; (c) H. Li, B. Wang. L. Deng, *J. Am. Chem. Soc.*, **2006**, *128*, 732-733.

[19] A. V. Gurbanov, S. Hazra, A.M. Maharramov, F.I. Zubkov, F.I. Guseinov, A. J. L. Pombeiro, *J. Organometal. Chem*. **2018**, *869*, 48-53.

[20] (a) B.F. Sels, D.E. De Vos, P.A. Jacobs, *Catal. Rev. Sci. Eng*. **2001**, *43*, 443-488 ; (b) B. M. Choudary, M.L. Kantam, B.J. Kavita, *J. Mol. Catal. A Chem*. **2001**, *169*, 193-197 ; (c) A. Cwik, A. Fuchs, Z. Hella, J. Clacens, *Tetrahedron,* **2005**, *61*, 4015-4021.

[21] (a) D. A. Evans, D. Seidel, M. Rueping, H. W. Lam, J. T. Shaw, C. W. Downey, *J. Am. Chem. Soc.*, **2003**, *125*, 12692-12693. (b) T. Risgaard, K.V. Gothelf, K.A. Jørgensen, *Org. Biomol. Chem.* **2003**, 1, 153-156. (c) T. Arai, M. Watanabe, A. Yanagisawa, *Org. Lett.* **2007**, *9*, 3595-3597; (d) W. Jin, X. Li, B. Wan, *J. Org. Chem.* **2011**, *76*, 484-491; [e] J. D. White, S. Shaw, *Org. Lett.* **2012**, *14*, 6270-6273.

[22] M.D. Jones, C.J. Cooper, M.F. Mahon, P.R. Raithby, D. Apperley, J. Wolowska, D. Collison, *J. Mol. Catal. A: Chem.* **2010,** *325*, 8–14.

[23] A.K. Gupta, D. De, P.K. Bharadwaj, *Dalton Trans.* **2017**, *47*, 7782-7790; M. Gupta, D. De, S.Pal, T.K. Pal, K.Tomar, *Dalton Trans.* **2017**, *46*, 7619-7627.

[24]S. Park, R. S. Ruoff, *Nat. Nanotechnol.* **2009**, *4*, 217–224.

[25] G. Bottari, M. Á. Herranz, L. Wibmer, M. Volland L. Rodríguez-Pérez, D. M. Guldi, A. Hirsch, N. Martín, F. D'Souza, T. Torres, *Chem. Soc. Rev.* **2017**, *46,* 4464-4500.

[26] A. Bostwick, F. Speck, T. Seyller, K. Horn, M. Polini, R. Asgari, *Science*, **2010**, *328*, 999-1002.

[27] M. D. Esrafili, P. Nematollahi, R. Nurazar, *Superlattices Microstr.* **2016**, *92*, 60–67.

[28] H. Woo, J. W. Kim, M. Kim, S. Park, K. H. Park, *RSC Adv*. **2015**, *5*, 7554-7558.

[29] A. Pourjavadi, M. Doroudian, A. Abedin-Moghanaki, *Appl. Organomet. Chem.* **2017**, *31*, e3881.

[30] M. Sarvestani, R. Azadi, *Appl. Organomet. Chem*. **2017**, *31*, e3667.

[31] A. Primo, I. Esteve-Adell, S. M. Coman, N. Candu, V. I. Parvulescu, H. Garcia, *Angew. Chem. Int. Ed,* **2016**, *55*, 607 – 612. *Angew. Chem.* **2016**, *128*, 617 – 622.

[32] H. Mahdavi, O. Rahmani, *Catal. Lett*. **2016**,*146*, 2292–305.

[33] A. Primo, I. Esteve, J. F. Blandez, A. Dhakshinamoorthy, M. Alvaro, N. Candu, S. M. Coman, V. I. Parvulescu, H. Garcia, *Nat. Commun*. **2015**, *6*, 8561.

[34] A. Primo, P. Atienzar, E. Sanchez, J.M. Delgado, H. Garcia, *Chem. Commun.***2012**, *48*, 9254–9256;

[35] A. Primo, E. Sánchez, J.M. Delgado, H. Garcia, *Carbon,* **2014**, *68*, 777–783.

[36] P. Perlmutter, *Conjugate Addition Reactions in Organic Synthesis*, Pergamon Press, Elmsford, New York, **1992.**

[37] J. Boruwa, N.Gogoi, P. Saikia, P. N. C. Barua, *Tetrahedron: Asymmetry*, **2006**, *17*, 3315–3326.

[38] C. Palomo, M. Oiarbide, A. Laso, *Eur. J. Org. Chem.* **2007**, 2561–2574.

[39] G. Bosica, K. Polidano, *J. Chem.* **2017**, Article ID 6267036.

[40] K. Akutu, H. Kabashima, T. Seki, H. Hattori, *Appl. Catal. A.* **2003**, *247*, 65–74.

[41] R. Ballini, G. Bosica, D. Fiorini, A. Palmieri, M. Petrini, *Chem. Rev*. **2005**, *105*, 933–971.

[42] B. M. Choudary , Ch. V. Rajasekhar , G. Gopi Krishna, K. Rajender Reddy, *Synth. Commun.* **2007**, *37*, 91-98.

[43] R. Ding, K. Katebzadeh, L. Roman, K.-E. Bergquist, U. M. Lindstrom *J. Org. Chem*. **2006**, *71*, 352-355.

[44] A. Primo,F. Neatu,M. Florea,V.I. Parvulescu, H. Garcia, *Nature Commun.* **2014**, *5*, 5291.

[45] S. E. Milner, T.S. Moody, A. R. Maguire, *Eur. J. Org. Chem*. **2012**, *16*, 3059-3067.

[46] R. Ballini, A. Palmieri, *Curr. Org. Chem.* **2006***, 10*, 2145–2169.

[47] F. A. Luzzio, *Tetrahedron*, **2001**, *57*, 915–945.

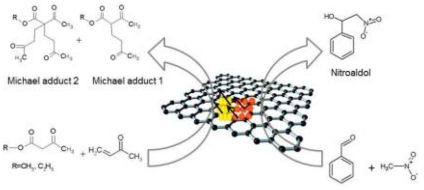
[48] P. A Korzhavyi, B Johansson, SKB Technical Report TR-11-08, October 2011, http://www.skb.se/upload/publications/pdf/TR-11-08.

[49] M. Glorius, M.A.C. Markovits, C. Breitkopf,*Catalysts*, **2018**, *8*, 358.

Entry for the Table of Contents

FULL PAPER

Michael and Henry addition reactions have been investigated using mono ($\overline{Au}$/*fl*-G *and* $\overline{Cu_2}$O/*fl*-G) and bimetallic nanoplatelets ($\overline{Au}$/$\overline{Cu_2}$O/*fl*-G) grafted onto few-layers graphene films as heterogeneous catalysts. These reactions occurred in the absence of any extrinsic base with TONs at least four orders of magnitude higher.



Bimetallic oriented $\overline{Au}$/$\overline{Cu_2}$O/*fl*-G nanoplatelets grafted on graphene

Graphene, Coupling reactions

Andrada Simion, Natalia Candu, Simona M. Coman, Ana Primo, Ivan Esteve-Adell, Véronique Michelet, Vasile I. Parvulescu,* Hermenegildo Garcia**

Page No. – Page No.

Bimetallic Oriented ($\overline{Au}$/$\overline{Cu_2}$O) versus monometallic 1.1.1 $\overline{Au}$ (0) or 2.0.0 $\overline{Cu_2}$O Graphene supported Nano-platelets as very efficient Catalysts for Michael and Henry Additions