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Deoxygenation of a variety of aromatic and aliphatic amine *N*-oxides has been carried out in excellent yield using dimethylphenylsilane as the reducing agent under the catalytic influence of a carbon nanotube–gold nanohybrid at room temperature. Low catalyst loading, good TON and TOF values, and recyclability of the catalyst are some of the salient features of our methodology.

Introduction

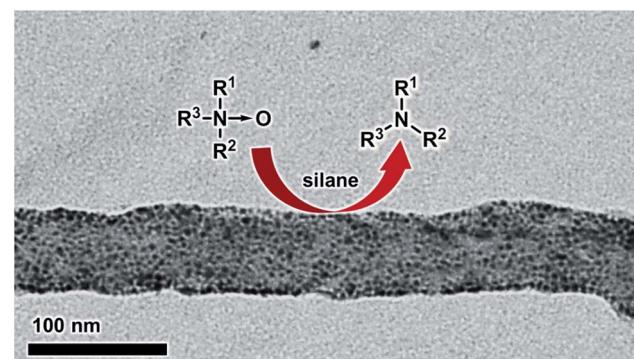
Deoxygenation of amine *N*-oxides to corresponding amines is a useful transformation in organic synthesis.¹ Execution of this transformation in a mild and highly selective fashion is of significance not only in synthetic chemistry but also in biology, for instance, for drug metabolism studies.² Although numerous stoichiometric and catalytic methods are reported in the literature for the reduction of amine *N*-oxides to amines,^{1,3–6} most of them require harsh reaction conditions and/or suffer from low activity or selectivity. Recently, Kaneda and co-workers have reported the deoxygenation of amine *N*-oxides using hydroxyapatite-supported gold nanoparticles (AuHAP)⁷ but the latter method is limited to pyridine *N*-oxides and requires rather high catalytic loadings.

In recent years, we have exploited the remarkable catalytic activity of nanoparticles of various metals such as Au, Ru, Rh and Pd supported on carbon nanotube (CNT)–organic bilayer assembly in diverse organic transformations.^{8,9} Carbon nanotubes were chosen as support due to their chemical inertness, high surface area, and ability to stabilize transient higher oxidation states of metals.¹⁰ The activity of our gold–carbon nanotube assembly (AuCNT) has already been demonstrated for the oxidation of silanes and alcohols, the reductive amination

and *N*-formylation of aldehydes, as well as in the one-pot alcohol oxidation–imine formation for the synthesis of quinoxalines.⁸ In a similar fashion, RuCNT was successfully employed for the selective reduction of nitroarenes to anilines and arylhydroxylamines, PdCNT for the room temperature Suzuki coupling of aryl halides and Tsuji–Wacker oxidation of terminal olefins, and RhCNT for the dehydrogenation of *N*-heterocycles.⁹ Herein we report for the first time the use of the AuCNT nanohybrid in the catalytic deoxygenation of amine *N*-oxides (Scheme 1).

Results and discussion

The AuCNT nanohybrid was assembled as reported elsewhere.^{8a} Briefly, carbon nanotubes were sonicated in the presence of a polymerizable anionic amphiphilic surfactant in water, resulting in the formation of nanoring-like structures at the surface of the CNTs. The rings were then polymerized by UV irradiation which permitted to reinforce the cohesion of the supramolecular assembly. In a second step, a polycationic polymer layer was deposited on the primary coating and gold nanoparticles were finally added to afford the final hybrid (AuCNT). The



Scheme 1 General scheme for the deoxygenation of amine *N*-oxides over AuCNT.

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† Electronic supplementary information (ESI) available: Copies of the ¹H, ²H, ¹³C spectra, a typical experimental procedure for amine *N*-oxide deoxygenation, and spectral data. See DOI: 10.1039/c5ra08845c



nanohybrid was obtained as an aqueous suspension ($[\text{Au}] = 3$ mM, as measured by ICP-MS). The deoxygenation of quinoline *N*-oxide **1a** to quinoline **2a** was chosen as the model reaction for our studies (Table 1). Two different silanes (*e.g.* iPr_3SiH and PhMe_2SiH) were screened as hydride source in dry THF, at room temperature, and under N_2 atmosphere (entries 1–2). Silanes were selected as hydride source because of their mildness and easy handling and the use of an anhydrous solvent in the above transformations was governed by the fact that water classically acts as oxygen atom source in the AuCNT-mediated oxidation of silanes into silanols.^{8a} While there was no reaction in the presence of iPr_3SiH (entry 1), which was attributed to the high steric demand of the reagent, quinoline **2a** was isolated in 84% yield in the presence PhMe_2SiH as the reducing agent (entry 2). Other solvents such as dichloromethane and toluene were less effective than THF affording quinoline **2a** in lower yields (76% and 78%, respectively, entries 3–4). As expected, there was no reaction in the absence of silane or catalyst confirming the requirement of both the reducing agent and the catalyst in this transformation (entries 5–6). The reaction also did not proceed when the multilayer CNT-assembly alone (without AuNP) or HAuCl_4 was used as the catalyst (entries 7–8).

Having confirmed the key role of AuCNT in catalyzing the silane-mediated deoxygenation of *N*-oxides **1**, we proceeded to investigate the scope of the reaction using various aromatic and aliphatic amine *N*-oxides **1a–l** (Table 2). Besides quinoline *N*-oxide **1a** which afforded quinoline **2a** in 84% yield (entry 1), isoquinoline *N*-oxide **1b** and several pyridine *N*-oxides **1c–h** were subjected to deoxygenation under our optimized conditions (entries 2–8). Thus, parent pyridine *N*-oxide **1c** and alkyl and aryl substituted pyridine *N*-oxides **1d** and **1e**, respectively, underwent smooth deoxygenation to provide corresponding pyridines **2c–e** in excellent yield (92–94%, entries 3–5). The remarkable functional group tolerance of our experimental conditions is evident from facile deoxygenation of pyridine *N*-oxides **1f–h**, bearing substituents such as bromine, thiol, and carboxylic acid, to pyridines **2f–h** in good to excellent yield (79–96%, entries 6–8).

entries 6–8). The deoxygenation of adenosine *N*-oxide **1i** to adenosine **2i** also took place in excellent yield (91%, entry 9), highlighting the wide applicability of our methodology to complex molecules including natural products. Representative examples for the deoxygenation of aliphatic, including alicyclic and benzylic, *N*-oxides **1j–l** to amines **2j–l** in high yield (88–91%, entries 10–12) further exemplified the scope of the AuCNT nanocatalyst, although two equivalents of silane were needed for the latter substrates.

Table 2 Scope of the deoxygenation of amine *N*-oxides^a

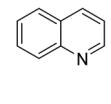
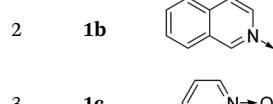
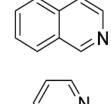
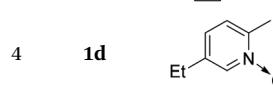
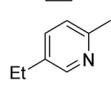
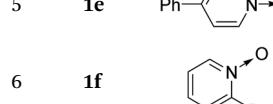
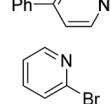
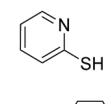
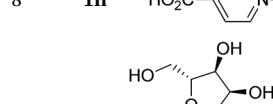
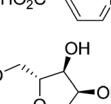
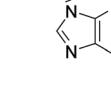
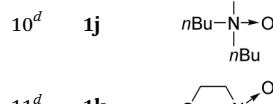
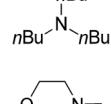
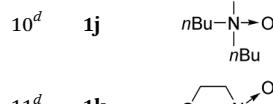
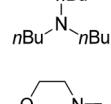
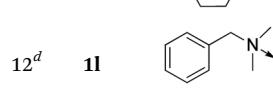
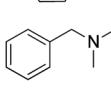
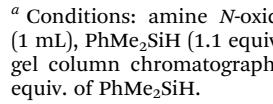
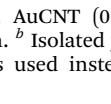
Entry	<i>N</i> -Oxide		Amine	Yield ^b (%)	
1	1a		2a		84
2	1b		2b		94
3	1c		2c		94
4	1d		2d		92
5	1e		2e		92
6	1f		2f		96
7	1g		2g		88
8	1h		2h		79
9 ^c	1i		2i		91
10 ^d	1j		2j		88
11 ^d	1k		2k		89
12 ^d	1l		2l		91

Table 1 Optimization of the reaction conditions^a

Entry	Silane	Catalyst	Solvent	Yield ^b (%)		
1	iPr_3SiH	AuCNT	THF	NR ^c		
2	PhMe_2SiH	AuCNT	THF	84		
3	PhMe_2SiH	AuCNT	CH_2Cl_2	76		
4	PhMe_2SiH	AuCNT	Toluene	78		
5	—	AuCNT	THF	NR ^c		
6	PhMe_2SiH	—	THF	NR ^c		
7	PhMe_2SiH	CNT	THF	NR ^c		
8	PhMe_2SiH	HAuCl_4	THF	NR ^c		

^a Conditions: amine *N*-oxide (0.1 mmol), catalyst (0.4 mol%), THF (1 mL), PhMe_2SiH (1.1 equiv.), N_2 , RT, 24 h. ^b Isolated yield after silica gel column chromatography. ^c No reaction.

^a Conditions: amine *N*-oxide (0.1 mmol), AuCNT (0.4 mol%), THF (1 mL), PhMe_2SiH (1.1 equiv.), N_2 , RT, 24 h. ^b Isolated yield after silica gel column chromatography. ^c DMSO was used instead of THF. ^d 2 equiv. of PhMe_2SiH .



In order to understand the nature of the catalysis, we carried out a partial deoxygenation of quinoline *N*-oxide **1a** under the optimized conditions (*vide supra*). After stirring for 7 h, the AuCNT catalyst was removed by centrifugation. At that point, only 22% conversion was reached, as determined by ¹H-NMR. The catalyst-free supernatant was then stirred for another 16 h, but no further conversion was detected, thus confirming the heterogeneous nature of the catalyst.

The efficacy of the AuCNT catalyst was further evaluated by performing the deoxygenation of quinoline *N*-oxide **1a** using only 0.03 mol % of the catalyst. After 24 h of reaction, quinoline **2a** was formed in 39% yield, which corresponded to a turn-over number (TON) of 1300 and a turn-over frequency (TOF) of 54 h⁻¹.

Recyclability of the AuCNT catalyst was assessed in the deoxygenation of quinoline *N*-oxide **1a** to quinoline **2a** as the model reaction (Table 3). At the end of the reaction, the mixture was centrifuged and the supernatant was subjected to usual work up to isolate quinoline **2a**. The recovered AuCNT catalyst was reused 4 times without any appreciable drop in the yield or the reaction rate.

The mechanism of the AuCNT/PhMe₂SiH-mediated deoxygenation of amine *N*-oxides was thereafter investigated using an isotopic labelling experiment. The classical silane source was replaced by deuterated PhMe₂SiD¹¹ and a reaction was set starting from quinoline *N*-oxide **1a** (Scheme 2). After the usual work-up, ²H-NMR showed the incorporation of deuterium at the

C2-position of quinoline. By analogy to what occurs with other noble metals, it is likely that phenyldimethyl silane undergoes oxidative Si-D insertion on the surface of the supported gold nanoparticles. This insertion produces an activated silane species that reacts with the *N*-oxide substrate with simultaneous transfer of a deuteride at C2. The transient intermediate then rearomatizes with concomitant elimination of silanol, affording deuterated **2a'** in 83% yield and with *ca.* 50% isotope incorporation.

Conclusions

Carbon nanotube–gold nanohybrid was found to be an efficient catalytic system to perform the silane-mediated reduction of a variety of aromatic and aliphatic amine *N*-oxides. Some attractive features of our methodology are: (i) the mildness of the reaction conditions as the deoxygenated amines were formed at room temperature, (ii) the very low catalytic loading (0.4 mol%), (iii) the possible recyclability of the catalyst, and (iv) the scope of the process that was also applied to aliphatic amines *N*-oxides. The results obtained in the context of this study thus compare favourably to previous reports in terms of overall efficiency.

Acknowledgements

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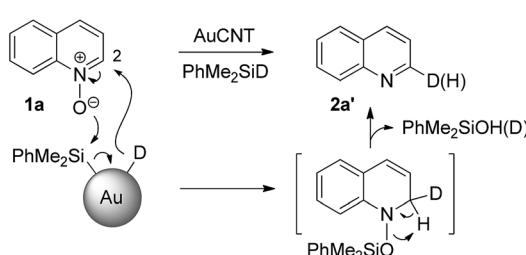
Notes and references

- (a) D. P. Sebesta, *Handbook of Reagents for Organic Synthesis: Reagents for Silicon-Mediated Organic Synthesis*, ed. P. L. Fuchs, 2011, p. 309; (b) S. Kano, *Ventron Alembic*, 1980, 19, 1; (c) T. Cohen, *U. S. C. F. S. T. I., AD Rep.*, 1965, **625414**, 14; (d) F. Devinsky, *Acta Fac. Pharm. Univ. Comenianae*, 1986, **40**, 63; (e) E. Ochiai, in *Aromatic Amine Oxides*, Elsevier, Amsterdam, 1967, pp. 184–209; (f) S. Oae, *Lect. Heterocycl. Chem.*, 1978, **4**, 69.
- P. Kulanthaivel, R. J. Barbuch, R. S. Davidson, P. Y. Gregory, A. Rener, E. L. Mattiuz, C. E. Hadden, L. A. Goodwin and W. J. Ehlhardt, *Drug Metab. Dispos.*, 2004, **32**, 966.
- CeCl₃·7H₂O-Zn: (a) B. W. Yoo, H. I. Jung, S. H. Kim, Y. S. Ahn and J. Y. Choi, *Bull. Korean Chem. Soc.*, 2013, **34**, 359, BiCl₃/In: (b) B. W. Yoo and J. W. Choi, *Synth. Commun.*, 2009, **39**, 3550, NbCl₅/Zn: (c) K. Oh and W. E. Knabe, *Tetrahedron*, 2009, **65**, 2966, RuCl₃·xH₂O: (d) S. Kumar, A. Saini and J. S. Sandhu, *Tetrahedron Lett.*, 2005, **46**, 8737, NaBr: (e)

Table 3 Recycling experiments^a

Entry	Cycle	Yield ^b (%)
1	Fresh	86
2	1 st reuse	84
3	2 nd reuse	85
4	3 rd reuse	84
5	4 th reuse	86

^a Conditions: amine *N*-oxide (0.1 mmol), AuCNT (0.4 mol%), THF (1 mL), PhMe₂SiH (1.1 equiv.), N₂, RT, 24 h. ^b Isolated yield after silica gel column chromatography.



Scheme 2 Proposed mechanism for the deoxygenation of amine *N*-oxides.



8 AuCNT: (a) J. John, E. Gravel, A. Hagège, H. Li, T. Gacoin and E. Doris, *Angew. Chem., Int. Ed.*, 2011, **50**, 7533; (b) R. Kumar, E. Gravel, A. Hagège, H. Li, D. V. Jawale, D. Verma, I. N. N. Namboothiri and E. Doris, *Nanoscale*, 2013, **5**, 6491; (c) D. V. Jawale, E. Gravel, V. Geertsen, H. Li, N. Shah, I. N. N. Namboothiri and E. Doris, *ChemCatChem*, 2014, **6**, 719; (d) R. Kumar, E. Gravel, A. Hagège, H. Li, D. Verma, I. N. N. Namboothiri and E. Doris, *ChemCatChem*, 2013, **5**, 3571; (e) N. Shah, E. Gravel, D. V. Jawale, E. Doris and I. N. N. Namboothiri, *ChemCatChem*, 2014, **6**, 2201; (f) N. Shah, E. Gravel, D. V. Jawale, E. Doris and I. N. N. Namboothiri, *ChemCatChem*, 2015, **7**, 57; (g) D. V. Jawale, E. Gravel, V. Geertsen, H. Li, N. Shah, R. Kumar, J. John, I. N. N. Namboothiri and E. Doris, *Tetrahedron*, 2014, **70**, 6140.

9 RuCNT: (a) D. V. Jawale, E. Gravel, C. Boudet, N. Shah, V. Geertsen, H. Li, I. N. N. Namboothiri and E. Doris, *Chem. Commun.*, 2015, **51**, 1739, PdCNT: (b) D. V. Jawale, E. Gravel, C. Boudet, N. Shah, V. Geertsen, H. Li, I. N. N. Namboothiri and E. Doris, *Catal. Sci. Technol.*, 2015, **5**, 2388; (c) S. Donck, E. Gravel, N. Shah, D. V. Jawale, E. Doris and I. N. N. Namboothiri, *ChemCatChem*, 2015, DOI: 10.1002/cctc.201500241, RhCNT: (d) D. V. Jawale, E. Gravel, N. Shah, V. Dauvois, H. Li, I. N. N. Namboothiri and E. Doris, *Chem.-Eur. J.*, 2015, **21**, 7039.

10 Reviews: (a) J. John, E. Gravel, I. N. N. Namboothiri and E. Doris, *Nanotechnol. Rev.*, 2012, **1**, 515; (b) E. Gravel, D. Bernard, I. N. N. Namboothiri and E. Doris, *Actual. Chim.*, 2015, **393–394**, 82.

11 S. B. Takale, S. M. Tao, X. Q. Yu, X. J. Feng, T. Jin, M. Bao and Y. Yamamoto, *Org. Lett.*, 2014, **16**, 2558.

