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Novel ruthenium–terpyridyl complex for direct oxidation of amines to nitriles†

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High catalytic activity and selectivity has been demonstrated for the oxidation of both aliphatic and aromatic amines to nitriles under benign conditions with dioxygen or air using the $Ru_2Cl_4(az\text{-}tpy)_2$ complex. The conversion was found to be strongly influenced by the alkyl chain length of the reactant with shorter chain amines found to have lower conversions than those with longer chains. Importantly, by using the ruthenium terpyridine complex functionalized with azulenyl moiety at the 4 position of central pyridine core provided a much higher reactivity catalyst compared with a series of ruthenium terpyridine-based ligand complexes reported. Mechanistic studies using deuterated benzylamine demonstrated the importance of RuOH in this reaction.

Introduction

Nitriles represent one of the most important class of organic compounds used as building blocks in pharmaceuticals, agrochemicals, herbicides, natural products, polymers and dyes.[1] They are also versatile intermediates in synthetic organic chemistry due to their easy conversion into amines, amides, carboxylic acids, aldehydes, esters, heterocycles, *etc.*[2] Commonly nitriles are synthesized *via* the dehydration of amides and aldoximes,[3] condensation of carboxylic acids with NH_3[4] and conversion of aldehydes,[5] alcohols[6] and esters.[7] The drawbacks of these methods include the use of harsh reaction conditions, toxic iodine derivatives as oxidants and polluting reagents as well as the formation of side-products.[8–14]

Increasingly, attention has been directed at finding catalysts which are able to oxidise organic substrates into nitriles with high conversion and selectivity both from economic and environmental perspective. In this regard, many metal based catalysts have been described in literature. For example, a range of amines can be oxidized to the corresponding nitriles using copper catalysts[15] or manganese catalysts,[16] whereas iron(II) and iron(III) were reported as being very efficient in the oxidative α-cyanation of tertiary amines with trimethylsilyl cyanide in the presence of *tert*-butylhydroperoxide.[17] An efficient aerobic oxidative cyanation of tertiary amines with sodium cyanide has been studied using vanadium based catalysts.[18] Hence, the carbon–carbon bond formation at the α position of the tertiary amines is an alternative route for the preparation of nitriles. Other reports recommended complex oxidation systems.[19]

Over the last few years, ruthenium compounds have been reported to be effective catalysts for the oxidation of amines to nitriles leading to remarkable results with iodosylbenzene[20] and persulfate ions[21] as oxidants especially in the presence of non benign oxidising agents such as hydrogen peroxide[22] and dioxygen.[23] Moreover, the ruthenium catalysts were also effective for the aerobic oxidation of several amines without the need of other toxic reagents both under homogenous[24,25] and heterogenous[26,27] catalytic conditions. Whilst ruthenium-based compounds have been shown to oxidise amines to nitriles under mild conditions, in particular using benzyl amine and activated aromatic amines, the reactions showed low selectivity. Better results were obtained for a ruthenium dioxo porphyrin complex which catalytically dehydrogenates benzyl amine and *n*-butylamine in the presence of air.[28] However, the direct oxidation of aliphatic amines to selectively produce alkyl nitriles remains a challenging target for this catalytic reaction.[29] The efficiency of the ruthenium-catalysts was improved

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in multicomponent coupled systems involving an electron-rich quinone and a co-catalyst of the Co(salen) type complex.[30] The disadvantage of these systems is the formation of significant amounts of by-products, the limited range of amines which can be transformed and the severe deactivation of the catalysts. Therefore, whilst it is true that much has been achieved in this field, significant improvements are needed to make this route commercially viable for nitrile production.

Terpyridine metal complexes have been extensively studied in view of their electronic and redox properties and in connection with applications in photocatalysis or energy conversion.[31,32] Recently, a ruthenium bearing terpyridine-ligand has also been reported as catalyst for aerobic oxidative dehydrogenation of benzylamines.[33] However, the reported catalytic reaction only involved aromatic amines as substrate and requires the presence of a base to form the corresponding nitriles.

We report, herein, a green and effective oxidation of both aliphatic and aromatic amines to nitriles, with molecular dioxygen using a ruthenium terpyridine complex, functionalized with azulenyl moiety at the 4 position of central pyridine core. In order to form the active conformation, Kanbara *et al.*[34] complexed the terpyridine ruthenium with a second ligand. Based on this state of the art, one of the objectives of this study was to achieve a ligand that can activate ruthenium for this reaction without the necessity to add a co-ligand. In this scope we prepared and investigated 4′ modified 2,2′:6′,2″-terpyridine with a donor electron group like azulenyl or substituted azulenyl fragments. The resulted complexes were compared with simple unsubstituted terpyridine complexes.

Experimental

Elemental analyses were performed on a Perkin Elmer CHN 240B. UV-Vis spectra were recorded on a Varian Cary 100 spectrophotometer. DRIFT spectra were collected using a NICOLET 4700 spectrometer from the accumulation of 200 scans in the range of 500–4000 cm^{-1} with a resolution of 4 cm^{-1}. NMR spectra were measured on a Bruker Avance DRX4 (^1H: 400 MHz, ^{13}C: 100 MHz) spectrometer. Mass spectra were recorded on a Varian 1200L QuadrupoleMS/MS spectrometer by direct injection in EI. Microwave irradiation was carried out using a Biotage Initiator 2.0 EXP – ED instrument. Electrochemical studies, consisting of cyclic voltammetry (CV) and differential pulse voltammetry (DPV) techniques, were performed using an electrochemical workstation (Autolab 12, Eco-Chemie, Utrecht, Netherlands) coupled to a PC running the GPES software to allow experimental control and data acquisition. A Pt (Metrohm, 3 mm in diameter) working electrode, Ag (wire)/AgCl as the reference electrode and a platinum disk as counter electrode (Metrohm, 3 mm in diameter) were used in a three-electrode configuration. The surface of both platinum electrodes was polished with an alumina (0.05 μm) slurry on a polishing pad, washed with distilled water and sonicated for 3 min in doubly distilled water then washed again with doubly distilled water. An electrolyte solution containing 0.1 M tetra(*n*-butyl)-ammonium tetrafluoroborate, $TBABF_4$ (Sigma, A. R. degree) was used as the supporting electrolyte, in dimethylformamide as the solvent (Sigma). Both the Ru(III) complexes as well as one of the two different organic ligands involved in the complex were examined using voltammetry. In each case, a 0.5 mM of the analyte solution was degassed for 5 min using extra-pure argon gas prior to each measurement and an inert atmosphere was maintained by purging argon at a low pressure above the solution during each measurement. All the peak potentials were measured relative to the Ag wire pseudo-reference electrode. The DPV-traces were baseline-corrected using the moving average application included in GPES version 4.9 software.

All reagents used were obtained from Sigma-Aldrich and used without further purification.

General procedure for the amine oxidation to nitriles

The oxidations were carried out in an autoclave, as follows: amine (25 mg, 0.14 mmol) was added to a suspension of $Ru_2Cl_4(az\text{-}tpy)_2$ (10 mg, 0.01 mmol) (Ru: 0.6 mol%) in methanol (5 mL) under dioxygen (Linde) (5 atm) or air (Linde) (25 atm) pressure. All amines (ethylamine, *n*-butylamine, iso-butylamine, *n*-hexylamine, *n*-octylamine, *n*-dodecylamine, *n*-stearylamine, benzylamine, 2-methoxy benzylamine, 4-methyl benzylamine, 4-chloro benzylamine) were purchased from Sigma-Aldrich and were of >99%, purity. The mixture was stirred (600 rpm) between room temperature–70 °C. It was observed that, after 20 min, the dioxygen pressure in the autoclave began to decrease, indicating the start of the reaction. Reactants and products were analysed by GC-MS, after filtration and centrifugation, using a Trace GC 2000 system with MS detector (Thermo Electron Scientific Corporation, USA) incorporating a TR-WAX capillary column. The injection chamber was set up at 200 °C and the temperature in the detector cell was 270 °C. Deuterated benzylamine was prepared by isotopic exchange using 0.5 moles (50 mL) benzylamine dissolved in 5 moles (100 mL) deuterated water. The solution was acidified using conc. HCl (37%, Sigma-Aldrich) and refluxed for 2 h. After cooling, the deuterated benzylamine was extracted from the aqueous solution using benzene before being removed by distillation. The same procedure was applied again to the isolated product to maximise the isotopic exchange. Infrared analysis of the product showed that the degree of exchange of the amino group was ~85%. No deuteration of C–H bonds was determined. The oxidations using isotopically-substituted benzylamine were carried out in dioxygen at 60 °C.

Dinuclear ruthenium(II) complex with 4′-azulenyl-2,2′:6′,2″-terpyridine

A mixture of $RuCl_3$ (Sigma-Aldrich) (103.5 mg, 0.5 mmol) and hydrazine hydrate (Sigma-Aldrich) (25 mg, 0.5 mmol) in methanol (5 mL) was stirred under inert atmosphere, at room temperature for 10 min. The methanolic solution was poured onto a suspension of 4′-azulenyl-2,2′:6′,2″-terpyridine ligand, L,[32] (179.5 mg, 0.5 mmol) in methanol (10 mL) and heated in a microwave system at 100 °C for 15 min to yield a deep red solution. The methanol was removed under vacuum and the obtained solid was washed with dichloromethane to remove traces of unreacted ligand

resulting in 504 mg of dark red crystalline powder (95% yield). UV-Vis (MeOH) [λ_{max}/nm (log ε)]: 273 (4.98), 288 (5.0), 307 (5.01), 380 (4.42), 513 (4.60); ^{1}H NMR (400 MHz, DMSO-d$_6$): δ_H7.34 (t, J = 6.8; 6.4 Hz, 2H, 5,5″-H), 7.53 (t, J = 9.6 Hz, 1H, 5‴-H), 7.63 (t, J = 9.6 Hz, 1H, 7‴-H), 7.65 (d, J = 6 Hz, 2H, 6,6″-H), 7.76 (d, J = 3.6 Hz, 1H, 3‴-H), 7.98 (t, J = 9.6 Hz, 1H, 6‴-H), 8.06 (t, J = 7.6 Hz, 2H, 4,4″-H), 8.7 (d, J = 3.2 Hz, 1H, 2‴-H), 8.71 (d, J = 9.6 Hz, 1H, 4‴-H), 9.10 (d, J = 8.4 Hz, 2H, 3,3″-H), 9.22 (d, J = 9.6 Hz, 1H, 8‴-H), 9.38 (s, 2H, 3′,5′-H) ppm. ^{13}C NMR (400 MHz, DMSO-d$_6$): δ_C 158.2 (Cq), 154.7 (Cq), 152.1 (Cq), 144.2 (Cq), 143.2 (C8‴), 139.8 (C4, C4″), 138.5 (C6‴), 138.1 (C2‴), 136.6 (Cq), 135.8 (C4‴), 127.6 (C5, C5″), 126.2 (C7‴), 126.05 (C5‴), 125.5 (C6, C6″), 124.8 (C3, C3″), 123.4 (C3′, C5′), 118.7 (C3‴) ppm. Anal. (%). Found (calc. for $C_{50}H_{34}Cl_4N_6Ru_2$): C 56.58 (56.51); H 3.27 (3.22); Cl 13.39 (13.34); N 7.98 (7.91). MS (ESI): 1062 (M) (m/z = 410, 860).

Dinuclear ruthenium(II) complex with 4′-(4‴,6‴,8‴′-trimethyl-azulenyl)-2,2′:6′,2″-terpyridine

A mixture of $RuCl_3$ (Sigma-Aldrich) (103.5 mg, 0.5 mmol) and hydrazine hydrate (Sigma-Aldrich) (25 mg, 0.5 mmol) in methanol (5 mL) was stirred under inert atmosphere, at room temperature for 10 min. The methanolic solution was poured onto a suspension of 4′-(4‴,6‴,8‴′-trimethyl-azulenyl)-2,2′:6′,2″-terpyridine (200 mg, 0.5 mmol) in methanol (10 mL) and heated in a microwave system at 100 °C for 15 min to yield a brown-red solution. The methanol was removed under vacuum and the obtained solid was washed with dichloromethane to remove traces of unreacted ligand resulting in 257 mg of dark red-brown crystalline powder (45% yield). UV-Vis (MeOH) [λ_{max}/nm (log ε)]: 271 (4.43), 308 (4.59), 477 (3.91). ^{1}H NMR (400 MHz, DMSO-d$_6$): δ_H 2.72 (s, 3H, Me(6‴)), 2.89 (s, 3H, Me(4‴)), 2.99 (s, 3H, Me(8‴)), 7.33 (t, J = 5.6 Hz, 2H, 5,5″-H), 7.39 (s, 1H, 5‴-H), 7.53 (d, J = 5.6 Hz, 2H, 6,6″-H), 7.62 (d, J = 4.0 Hz, 1H, 3‴-H), 8.02 (t, J = 7.8 Hz, 2H, 4,4″-H), 8.08 (s, 1H, 7‴-H), 8.12 (d, J = 4.0 Hz, 1H, 2‴-H), 9.01 (d, J = 8.0 Hz, 2H, 3,3″-H), 9.15 (s, 2H, 3′,5′-H) ppm. Anal. (%). Found (calc. for $C_{56}H_{46}Cl_4N_6Ru_2$): C 59.68 (60.10); H 3.61 (3.41); Cl 12.02 (12.10); N 6.59 (6.84). (ESI): 1104 (M) (m/z = 452, 902).

Dinuclear ruthenium(II) complex with 4′-(4-methylphenyl)-2,2′:6′,2″-terpyridine

A mixture of $RuCl_3$ (Sigma-Aldrich) (103.5 mg, 0.5 mmol) and hydrazine hydrate (Sigma-Aldrich) (25 mg, 0.5 mmol) in methanol (5 mL) was stirred under inert atmosphere, at room temperature for 10 min. The methanolic solution was poured onto a suspension of 4′-(4-methylphenyl)-2,2′:6′,2″-terpyridine (161.5 mg, 0.5 mmol) in methanol (10 mL) and heated in a microwave system at 100 °C for 15 min to yield a brown-red solution. The methanol was removed under vacuum and the obtained solid was washed with dichloromethane to remove traces of unreacted ligand resulting in 257 mg of dark red-brown crystalline powder (56% yield). ^{1}H NMR (400 MHz, DMSO-d$_6$): δ_H 2.51(s, 3H, 7-H), 7.49 (d, J = 6 Hz, 2H, 6,6″-H), 8.02 (t, J = 7.1 Hz, 2H, 5,5″-H), 8.12 (t, J = 7.6 Hz, 2H, 4,4″-H), 8.41 (d, J = 8.4 Hz, 2H, 2‴,6‴-H), 8.63 (d, J = 7.8 Hz, 2H, 3‴,5‴-H), 9.04 (d, J = 8.9 Hz, 2H, 3,3″-H), 9.35 (s, 2H, 3′,5′-H) ppm. ^{13}C NMR (400 MHz, DMSO-d$_6$): δ_C 157.2 (Cq), 153.7 (Cq), 148.1 (Cq), 140.35 (C4, C4″), 132.2 (Cq), 130.6 (Cq), 129.03 (C3‴,C5‴), 127.56 (C2‴, C6‴), 127.13 (C5, C5″), 126.02 (C6, C6″), 122.48 (C3, C3″), 118.07 (C3′, C5′), 21.01 (C7) ppm. Anal. (%). Found (calc. for $C_{44}H_{34}Cl_4N_6Ru_2$): C 53.64 (53.34); H 3.54 (3.44); Cl 14.49 (14.34); N 8.35 (8.46). (ESI): 990 (M) (m/z = 374, 788).

Dinuclear ruthenium(II) complex with 2,2′2″-terpyridine

The dinuclear ruthenium(II) complex with 2,2′2″-terpyridine was prepared following a procedure reported elsewhere.[35] Accordingly, $RuCl_3$ (Sigma-Aldrich) (103.5 mg, 0.5 mmol) was reacted with boiling 6 M hydrochloric acid (Sigma-Aldrich) for 24 h. The resulting pentachloromono-aquoruthenate(III) was separated as the potassium salt and recrystallized from 6 M hydrochloric acid. Thereafter, to an acidic solution of the soluble potassium salt was added a quantity of ligand only slightly greater than the stoichiometric equivalent for the formation of the 1 : 1 (metal–ligand) complex, and an excess of reducing agent such as or hydroxylammonium chloride (Sigma-Aldrich). The solution was then heated to 50–60 °C for several hours. Whilst at temperature, the pH of the solution was slowly and progressively raised with small additions of a dilute sodium hydroxide solution until neutralization was reached. In this way the ruthenium present was quantitatively transformed into $Ru_2Cl_4(tpy)_2$, which was isolated from thoroughly cooled solutions (92% yield). ^{1}H NMR (400 MHz, DMSO-d$_6$): δ_H 7.54 (d, J = 6 Hz, 2H, 6,6″-H), 7.6 (t, J = 6.8 Hz, 2H, 5,5″-H), 8.43 (t, J = 7.6 Hz, 2H, 4,4″-H), 8.84 (t, J = 8.4 Hz, 2H, 3,3″-H), 8.95 (t, J = 7.4 Hz, 1H, 4′-H), 9.23 (d, J = 8.0 Hz, 2H, 3′,5′-H). ^{13}C NMR (400 MHz, DMSO-d$_6$): δ_C 120.8 (C3, 3″), 121.0 (C5, 5″), 123.5 (C3′, 5′), 136.6 (C4, 4″), 137.6 (C4′), 148.9 (C6, 6″), 155.2 (Cq, Cq), 156.1 (Cq, Cq). Found (calc. for $C_{30}H_{22}Cl_4N_6Ru_2$): C 44.52 (44.41); H 2.75 (2.72); Cl 17.49 (17.51); N 10.35 (10.37). (ESI): 810 (M) (m/z = 284, 608).

Results and discussion

The σ-donor character of the cyclometalated ligand was previously reported to assist the ruthenium-promoted aerobic oxidation.[34a] On this basis, polypyridyl complexes containing the Ru(IV)═O group have been observed to act as stoichiometric or catalytic oxidants for a variety of organic and inorganic substrates.[36] However, to achieve an effective oxidation catalyst therein, another key feature was reported to be the presence of a Cl ligand that easily dissociate allowing the substrate to coordinate to the vacant position. Lowering the redox potential necessary to enable the aerobic oxidation of the ruthenium center was achieved by introducing a second ligand.[37]

Complexes with 2,2′2″-terpyridine presented no activity in oxygen or aerobic oxidation of benzylamine that demonstrates the structure of this complex is not proper for this reaction. In addition, the complex decomposed. This in line with previous reports showing that higher oxidation states of aquo or hydroxo polypyridyl complexes of ruthenium are relatively unstable

under certain reaction conditions.[36] Under the same experimental conditions ruthenium(II) complexes with 4′-(4-methylphenyl)-2,2′:6′,2″-terpyridine and substituted azulenyl fragment with electron donating groups like 4′-(4,6,8-trimethyl-azulenyl)-2,2′:6′,2″-terpyridine led to poor conversions of 34 and 30%, respectively. This observation persuaded us to explore the 4′ modification of 2,2′:6′,2″-terpyridine with a another donor electron group like azulenyl fragment.

The Ru_2Cl_4(az-tpy)$_2$ complex showed high catalytic activity for the oxidation of amines to nitrile with dioxygen (Scheme 1). The results are listed in Table 1. With low ruthenium catalyst loadings (Ru: 0.6 mol%), high reaction yields in short reaction times (2–5 h) were achieved for the oxidation of both aliphatic and aromatic amines with $-CH_2NH_2$ functional groups. The catalytic oxidation of primary amines is temperature dependent, for example, oxidation of benzylamines to benzonitriles in methanol at room temperature reached 25% yield after 5 h whilst at 60–70 °C quantitative conversion occurred within 2 h. It should be noted that no benzonitrile was formed under identical conditions in the absence of the ruthenium catalyst. Oxidation of aliphatic amines with long alkyl chains required shorter reaction times. For example, *n*-dodecylamine and *n*-stearylamine were converted into the corresponding nitriles within 5 h, while after 2.5 h the conversions were 62% and 58%, respectively. In contrast, after 5 h, only 8% conversion was found for ethylamine. For butylamines an effect of the steric environment has been shown. Thus, the conversion of *n*-butylamine after 5 h was 15%, while for the iso-isomer 24 h were necessary to reach 18%. The oxidation of *n*-hexylamine and *n*-octylamine occurred with a higher reaction rate than the oxidation of *n*-butylamine but with the same selectivity.

In all the cases the selectivity was 100% to the corresponding nitrile. Compared with previous reported results using ruthenium catalysts, this represents a significant progress concerning the selective oxidative conversion of amines to nitriles. For example, the best ruthenium-complex used for this catalytic reaction, a ruthenium–porphyrin catalyst, is able to convert both aliphatic and aromatic amines to the corresponding nitriles but only at high temperature (50 °C) with the best results reported for activated benzylamines.[27] In comparison, multicomponent coupled systems involving ruthenium and a range of co-catalysts with additional electron-rich components were less effective in nitrile formation with a maximum selectivity of 88% achieved for benzonitrile.[28] More recently, better results were reported for ruthenium-catalyzed amine oxidation using cobalt oxides as the support.[25] However, this cobalt-supported ruthenium catalyst only proved to be efficient for the oxidation of activated benzylamines again showing the importance of the Ru_2Cl_4(az-tpy)$_2$ complex described, herein, which efficiently catalyzes the oxidation of both aliphatic and aromatic amines with high selectivity in the corresponding nitriles. It is worth emphasising the fact that, the Ru_2Cl_4(az-tpy)$_2$ complex was also capable of selectively oxidizing ethylamine and bulky iso-butylamine. This is unusual for the ruthenium-catalyzed oxidation of amines to nitriles.

Repeating these experiments in air (10 atm, 75 °C) compared with pure O_2 led to lower conversions (Table 2). For example the total conversion of benzylamine to benzonitrile was achieved in 5 h in air compared with 2 h under O_2. Under, these conditions ethylamine and iso-butylamine gave no reaction. With both air and O_2 100% selectivity was observed in all cases.

In all these examples, after reaction, the catalyst was found to be recyclable at least three times. For benzylamine the oxidation occurred with no change in conversion in the first two cycles and decreased to 96% after the third cycle.

As it has been mentioned in the experimental part the catalyst showing the highest activity, *i.e.* the di-nuclear species of type Ru_2Cl_4(az-tpy)$_2$ resulted from the stoichiometric reaction of 4′-azulenyl-2,2′:6′,2″-terpyridine (az-tpy) with ruthenium chloride and hydrazine hydrate in methanol under microwave irradiation for 15 min (Scheme 2).

The diamagnetic nature of ruthenium(II) ions allowed the characterisation of the complex by NMR spectroscopy. The ^{1}H-NMR spectrum showed significant differences when compared with the spectrum of the free ligand (Fig. S1, ESI†). The shift in the signals are mainly due to the influence of the metal electrons on the magnetic field of the organic framework with the terpyridine moieties locked in the *cis* position. The nitrogen ligation of the ligand is also confirmed by upfield ^{13}C resonances of the adjacent groups comparing the free ligand and the metal complex (Fig. S2, ESI†). Furthermore, the UV-Vis

$$R\text{-}CH_2\text{-}NH_2 \xrightarrow[MeOH]{O_2/Ru_2Cl_4(az\text{-}tpy)_2} R\text{-}C{\equiv}N + H_2O$$

Scheme 1 Direct oxidation of amines with oxygen (R = alkyl, aryl).

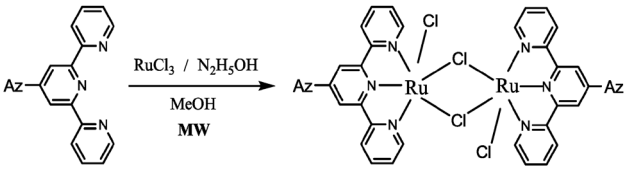
Table 1 Ruthenium(II) catalysed oxidation of amines with oxygen (60 °C)

Substrate	Time (h)	Conversion (%)	Product	Selectivity (%)
n-Dodecyl amine	5	100	*n*-Dodecane nitrile	100
n-Stearylamine	5	100	*n*-Stearylo nitrile	100
Benzylamine[a]	2	100	Benzonitrile	100
Ethylamine	5	8	Acetonitrile	100
n-Butylamine	5	15	*n*-Butanenitrile	100
iso-Butylamine	24	18	iso-Butyronitrile	100
n-Hexylamine	5	58	*n*-Hexanenitrile	100
n-Octylamine	5	67	*n*-Octanenitrile	100
2-Methoxy benzylamine	5	34	2-Methoxy benzonitrile	100
4-Methyl benzylamine	5	100	4-Methyl benzonitrile	100
4-Chloro benzylamine	5	66	4-Chloro benzonitrile	100

[a] Room temperature, after 5 h, 25% benzonitrile formation.

Table 2 Ruthenium(II) catalyzed oxidation of amines with air

Substrate	Time (h)	Conversion (%)	Product	Selectivity (%)
n-Dodecyl amine	5	50	*n*-Dodecane nitrile	100
n-Stearylamine	5	30	*n*-Stearylo nitrile	100
Benzylamine	5	100	Benzonitrile	100
Ethylamine	5	0	—	—
iso-Butylamine	5	0	—	—



Scheme 2 Schematic representation for formation of dinuclear ruthenium(II) complex with 4′-azulenyl-2,2′:6′,2″-terpyridine.

spectrum of the complex is characterized by the intense absorption bands attributed to the π–π* transitions associated with the aromatic rings of the ligands. The metal to ligand charge transfer (MLCT) transition of the ruthenium complex was observed at around 513 nm (Fig. S3, ESI†).

The dinuclear nature of the catalyst was assigned by mass-spectrometry and further confirmed by electrochemical investigations both by cyclic voltammetry (CV) and differential pulse voltammetry (DPV). The CV of the dinuclear complex exhibits two relatively well-defined coupled peaks, confirmed also by DPV measurements. The cyclic voltammograms of Ru_2Cl_4-(az-tpy)$_2$ solution (0.05 mM) at different scan rates, are presented in Fig. 1. As expected, these show two anodic peaks on the forward scan and two cathodic peaks on the reverse scan, thus confirming the proposed structure. The first anodic couple appears at a half-peak potential $E_{1/2,1}$ = 0.166 V while, the second at $E_{1/2,2}$ = 0.454 V, each showing a very small variation with the variation of scan rate between 50 mV s^{-1} to 500 mV s^{-1} of ~8 mV and 4 mV, respectively. The peak-to-peak separations are $\Delta E_{p,1}$ = 70 mV and $\Delta E_{p,2}$ = 65 mV demonstrating that they are almost reversible. These results are in good agreement with the anodic peak potentials determined from DPV ($E_{pa,1}$ = 0.141 V and $E_{pa,2}$ = 0.433 V). This behaviour is consistent with two single electron reactions according to the following equations:

$$Ru^{2+}Ru^{2+} \rightarrow Ru^{2+}Ru^{3+} + e^-$$

$$Ru^{2+}Ru^{3+} \rightarrow Ru^{3+}Ru^{3+} + e^-$$

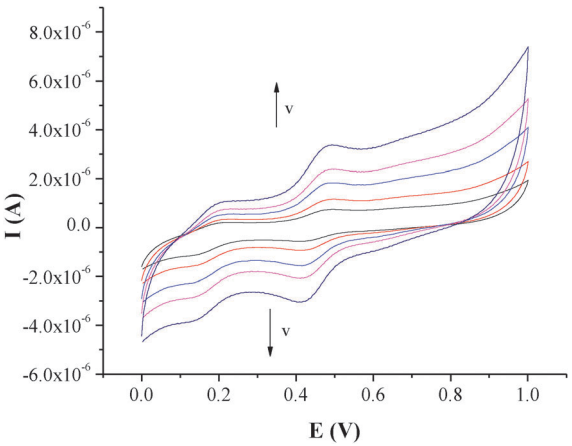


Fig. 1 Cyclic voltammograms of a solution of 0.5 mM Ru_2Cl_4(az-tpy)$_2$ at different scan rates (50 – black, 100 – red, 200 – blue, 300 – magenta, 500 – navy mV s^{-1}), over the potential range 0.0–1.0 V.

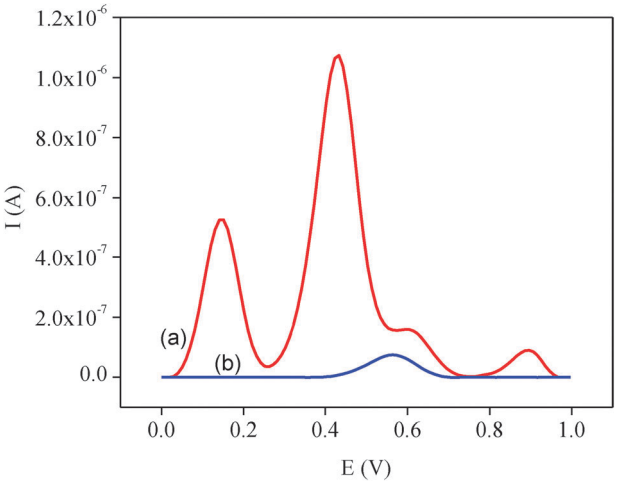


Fig. 2 DPV-traces, after baseline correction procedure, of 0.5 mM Ru-az-tpy (curve a) and 0.5 mM az-tpy (curve b), with SP = 10 mV and MA = 50 mV, in the potential range 0.0–1.0 V.

Small anodic anodic peaks, shoulder-like, were also observed in DPV experiments (Fig. 2). The DPV experiment (Fig. 2, curve a) exhibits two other small anodic peaks at more positive potentials. The first one, shifted in the anodic direction, at 0.624 V is assigned to the anodic potential of the ligand. The second, at 0.896 V, is attributed to a supplementary oxidation of the $Ru^{3+}Ru^{3+}$ to $Ru^{3+}Ru^{4+}$ and occurs at a very low anodic current. The ligand is, however, stabilized by the ruthenium coordination and is harder to be oxidized as compared with the free ligand in solution. The DPV-trace of the ligand indicates an anodic peak occurring at 0.564 V (Fig. 3, curve b).

A key feature of the ruthenium catalyst is the presence of labile bonds that makes the attack of the substrate at the metal centres possible. Therefore, the presence of halides (in our case chloride) as co-ligands in the coordination sphere of the

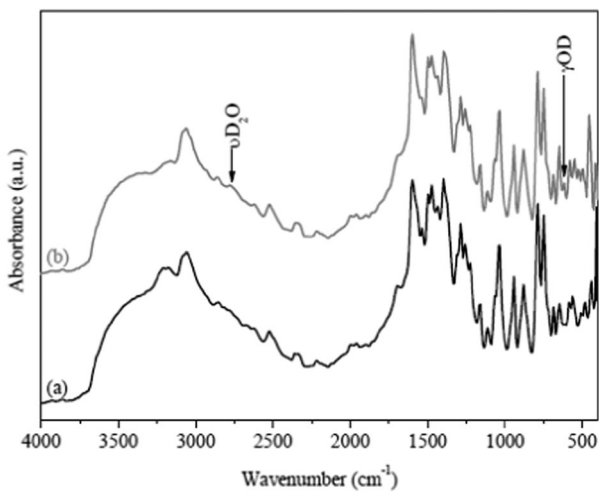


Fig. 3 DRIFT spectra of the fresh (a) and spent ruthenium–terpyridyl complexes following the reaction with D_2N–C_6H_5 (b).

ruthenium centers contributes to an increased catalytic activity of the dinuclear ruthenium(II) compound described, herein. Aiki *et al.* suggested that the redox behavior of the ruthenium(II) complex is the reason for its catalytic effectiveness with a low redox potential indicating a higher catalytic activity towards oxidation reactions.[33] Our data confirms this proposal. The insertion of the azulenyl fragment into the terpyridine scaffold led to an increased catalytic activity for the direct oxidation of amines with molecular oxygen. Unsubstituted terpyridine–ruthenium(II) complexes were reported to smoothly oxidize reactive benzylamines, depending on the used co-ligand, with no information for alkyl amines or benzylamine.[33] The data presented in this study demonstrates that, by using the azulenyl substitution of the terpyridine unit, very good conversions and selectivities can be achieved. Both aromatic and aliphatic substrates can be oxidized under benign, environmentally friendly conditions. Brandt and Wright[38] reported that terpyridine acts as a diacid base while Nakamoto[39] concluded that in basic solution and in organic solvents, the terpyridine molecule is *trans–trans*, in acidic solution the *cis–cis* form predominates, and at intermediate pH values the *cis–trans* form is present. The central ring in terpyridine acquires increased aromatic character because of the pyridine rings at the 2- and 6-positions.[40] Further modification of terpyridine with azulene may enhance the basicity of the central atom of pyridine.

The catalytic behaviour was confirmed by both the electrochemical measurements and by substituting azulenyl fragment with both donor and acceptor groups. Thus, after the substitution of the azulenyl fragment with electron donating groups like for example 4,6,8-trimethyl-azulene, the catalytic activity of the ruthenium(II) complex dramatically dropped and the oxidation of benzyl amine to benzonitrile took place with a maximum conversion of ~30%. An explanation of this behaviour is likely to be associated with the steric hindrance induced by the methyl groups which will limit the access of the substrate to the ruthenium centres. This assessment is also supported by the electrochemical investigations where the oxidation of the ruthenium centres occurs at a more positive potential (0.876 V). However, further work on substituted azulenyl moiety in the terpyridine–ruthenium(II) complexes is underway to elucidate these effects.

In order to investigate the possible reaction mechanism, experiments with deuterated benzylamine (D_2N–$CH_2C_6H_5$) were performed. Whilst the reaction was similar, the DRIFT spectra showed significant changes in the state of the catalyst. Fig. 3 shows spectra of fresh (a) and spent ruthenium–terpyridyl complexes (b) in the reaction with D_2N–$CH_2C_6H_5$. The new bands in the spectra of deuterated ruthenium–terpyridyl complex at 2780 cm^{-1} band[41] and 620 cm^{-1} (uncoupled γOD)[42] suggest (i) the formation of DHO (D_2O) in step (II), and then (ii) the further exchange of the catalyst OH group with deuterium in step (I) during recycle. These results are confirmed by a comparison of IR spectra of the pure D_2N–$CH_2C_6H_5$ and reaction mixture (Fig. 4). This comparison confirms the formation of benzonitrile and the disappearance of the specific N–D stretching vibration recorded at 2463 cm^{-1} in the IR spectrum of

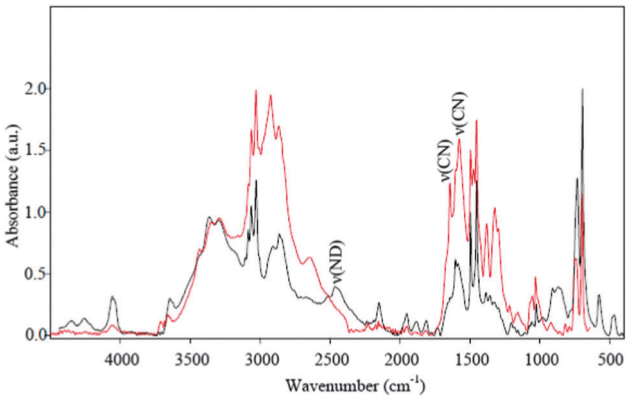


Fig. 4 IR spectrum of D_2N–C_6H_5 (black) and product oxidation – benzonitrile (red).

deuterated benzylamine. Moreover, two new bands at 1642 and 1576 cm^{-1} are observed in the spectrum of the mixture corresponding to the formation of benzonitrile. No other exchange was observed between C_6H_5–CH_2–ND_2 and C_6H_5–CH_2–NH_2 in the presence of water or generated D_2O. Oxidation appeared to be faster than additional isotopic exchange. 100% conversion was observed for C_6H_5–CH_2–NH_2 compared with 44% for C_6H_5–CH_2–ND_2 after 2 h was observed indicating that N–H cleavage is involved in the rate determining step.

Fig. 5 provides DRIFTs evidence of the evolution of the kinetics of the reaction. The decrease of the intensity of the NH band mapped the increase of the intensity of the CN band.

Based on the experimental evidence from this study, and in full agreement with previous reports,[24] a reaction mechanism has been proposed (Scheme 3). In the first step, Ru exchanges chlorine with a hydroxyl ligand[43] which further reacts with the amine. This ruthenium amine intermediate formed subsequently undergoes a β-hydrogen elimination to yield the corresponding imine and ruthenium hydride. A rapid dehydrogenation of the imine to form the nitrile occurs, while the catalyst is reactivated *via* the oxidation of the formed hydride by dioxygen. Thus, the water which initiates the catalytic reaction comes from the used solvent (methanol). To confirm that the effect of water in step (I) is

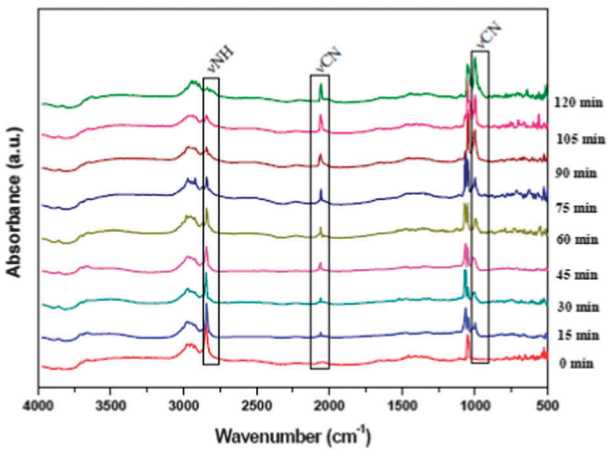
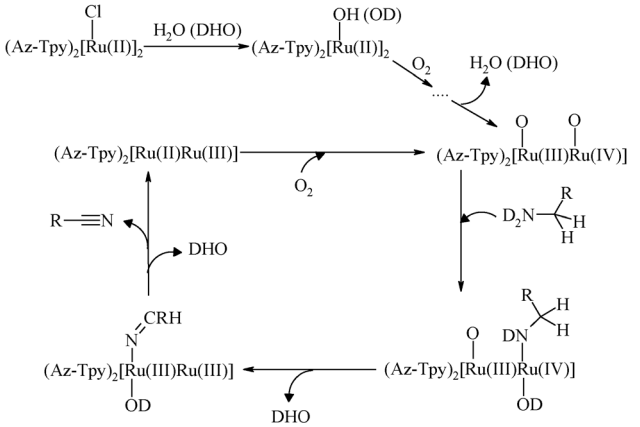


Fig. 5 DRIFTs evidence of the evolution of the kinetics of the reaction.



Scheme 3 Proposed mechanism of amines oxidation with oxygen by ruthenium(II) complex with 4′-azulenyl-2,2′:6′,2″-terpyridine.

essential for the reaction, experiments in dried methanol and *n*-heptane have also been carried out. Under these conditions the conversion of benzylamine was 10.3 and 5.4%, respectively. In these reactions, the selectivity towards benzonitrile also decreased to less than 40% due to the formation of (*E*)-benzyl(phenylmethylidene)amine. Furthermore, experiments in these solvents using dried air led to zero conversion. In addition, after introducing of one equivalent of water in the dried methanol the conversion increased to 93% with a 100% selectivity in benzonitrile. All these experiments confirm the important role of water.

Conclusions

Ru-complexes with 2,2′2″-terpyridine, 4′-(4-methylphenyl) 2,2′:6′,2″-terpyridine, 4′-(4,6,8-trimethyl-azulenyl)-2,2′:6′,2″-terpyridine and 4′-azulenyl-2,2′:6′,2″-terpyridine ligands were investigated in oxygen and aerobic oxidation of both aromatic and aliphatic amines to their corresponding nitriles. Among these complexes, the dinuclear Ru catalyst with 4′-azulenyl-2,2′:6′,2″-terpyridine has been shown to oxidize with high conversions and total selectivities amines to the corresponding nitriles. The conversion is influenced by the length of the alkyl chain. The investigation of these Ru–terpyridine complexes demonstrate that the primary coordination environment of Ru is very important in this reaction. Addition of an azulenyl fragment to the terpyridyl unit confers a higher reactivity to the ruthenium complex. The reactions occur under benign conditions with very high atom efficiency. In addition, this reaction can be carried out with air, instead of oxygen. The experiments carried out with deuterated benzylamine confirmed the role played by RuOH in this reaction, and helped in the elucidation of the reaction mechanism. A significant in rate was observed on deuterating the N–H bond thus indicating that the N–H bond breaking is part of the rate-determining step.

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Notes and references

1 (*a*) R. A. Sheldon, I. W. C. E. Arends and D. Dijisman, *Catal. Today*, 2000, **57**, 157–166; (*b*) A. Kleemann, J. Engel, B. Kutscher and D. Reichert, *Pharmaceutical Substance: Synthesis Patents, Applications*, Georg Thieme, Stuttgart, 4th edn, 2001; (*c*) J. S. Miller and J. L. Manson, *Acc. Chem. Res.*, 2001, **34**, 563–570; (*d*) F. F. Fleming and Q. Wang, *Chem. Rev.*, 2003, **103**, 2035–2077; (*e*) G. E. Dobereiner and R. H. Crabtree, *Chem. Rev.*, 2010, **110**, 681–703; (*f*) J. Kim, H. J. Kim and S. Chang, *Angew. Chem., Int. Ed.*, 2012, **51**, 11948–11959.

2 (*a*) S. J. Collier and P. Langer, *Sci. Synth.*, 2004, **19**, 403–425; (*b*) S.-I. Murahashi, *Sci. Synth.*, 2004, **19**, 345–402; (*c*) K. Yamaguchi, M. Matsushita and N. Mizuno, *Angew. Chem., Int. Ed.*, 2004, **43**, 1576–1580; (*d*) A. V. Gulevich, A. S. Dudnik, N. Chernyak and V. Gevorgyan, *Chem. Rev.*, 2013, **113**, 3084–3213; (*e*) R. E. Khidre and B. F. Abdel-Wahab, *Curr. Org. Chem.*, 2013, **17**, 430–445; (*f*) G. Abbiati, E. M. Beccalli and E. Rossi, *Top. Organomet. Chem.*, 2013, **43**, 231–290; (*g*) R. García-Álvarez, P. Crochet and V. Cadierno, *Green Chem.*, 2013, **15**, 46–66.

3 C. W. Kuo, J. L. Wu, C. M. Chu, C. F. Yao and K. S. Shia, *Chem. Commun.*, 2007, 301–303.

4 V. J. Huber and R. A. Bartsch, *Tetrahedron*, 1998, **54**, 9281–9288.

5 J. R. Hwu and F. F. Wong, *Eur. J. Org. Chem.*, 2006, 2513–2516.

6 (*a*) N. Iranpoor, H. Firouzabadi, B. Akhlaghinia and N. Nowrouzi, *J. Org. Chem.*, 2004, **69**, 2562–2564; (*b*) W. Yin, C. Wang and Y. Huang, *Org. Lett.*, 2013, **15**, 1850–1853.

7 R. C. Larock, *Comprehensive Organic Transformation*, VCH, 1989, pp. 976–993.

8 J. B. Lee, C. Parkin, M. J. Shaw, N. A. Hampson and K. I. McDonald, *Tetrahedron*, 1973, **29**, 751–752.

9 C. Zhu, C. Sun and Y. Wei, *Synthesis*, 2010, 4235–4241.

10 S. Chiampanichayakul, M. Pohmakotr, V. Reutrakul, T. Jaipetch and C. Kuhakarn, *Synthesis*, 2008, 2045–2048.

11 S. Iida and H. Togo, *Tetrahedron*, 2007, **63**, 8274–8281.

12 K. R. Reddy, C. Uma Maheswari, M. Venkateshwar, S. Prashanthi and M. Lakshmi Kantam, *Tetrahedron Lett.*, 2009, **50**, 2050–2053.

13 K. C. Nicolau and C. J. N. Mathison, *Angew. Chem., Int. Ed.*, 2005, **44**, 5992–5997.

14 H. Veisi, *Synthesis*, 2010, 2631–2635.

15 Y. Maeda, T. Nishimura and S. Uemura, *Bull. Chem. Soc. Jpn.*, 2003, **76**, 2399–2403.

16 K. Yamaguchi, K. Yajima and N. Mizuno, *Chem. Commun.*, 2012, **48**, 11247–11249.

17 W. Han and A. R. Ofial, *Chem. Commun.*, 2009, 5024–5026.

18 S. Singhal, S. L. Jain and B. Sain, *Chem. Commun.*, 2009, 2371–2372.

19 D. Biondini, L. Brinchi, R. Germani, L. Goracci and G. Savelli, *Eur. J. Org. Chem.*, 2005, 3060–3063.
20 F. Porta, C. Crotti and S. Cenini, *J. Mol. Catal.*, 1989, **50**, 333–341.
21 G. Green, W. P. Griffith, D. M. Hollinshead, S. V. Ley and M. Schröder, *J. Chem. Soc., Perkin Trans. 1*, 1984, 681–686.
22 S.-I. Murahashi, N. Komiya and H. Terai, *Angew. Chem., Int. Ed.*, 2005, **44**, 6931–6933.
23 K. Mori, K. Yamaguchi, T. Mizugaki, K. Ebitani and K. Kaneda, *Chem. Commun.*, 2001, 461–462.
24 K. Yamaguchi, J. W. Kim, J. He and N. Mizuno, *J. Catal.*, 2009, **268**, 343–349.
25 K. Yamaguchi and N. Mizuno, *Angew. Chem., Int. Ed.*, 2002, **41**, 4538–4542.
26 K. Yamaguchi and N. Mizuno, *Angew. Chem., Int. Ed.*, 2003, **42**, 1480–1483.
27 F. Li, J. Chen, Q. Zhang and Y. Wang, *Green Chem.*, 2008, **10**, 553–562.
28 M. T. Schümperli, C. Hammond and I. Hermans, *ACS Catal.*, 2012, **2**, 1108–1117 and references cited, therein.
29 A. J. Bailey and B. R. James, *Chem. Commun.*, 1996, 2343–2344.
30 Y. Blum, D. Czarkie, Y. Rahamim and Y. Shvo, *Organometallics*, 1985, **4**, 1459–1461.
31 A. Harriman and R. Ziessel, *Coord. Chem. Rev.*, 1998, **171**, 331–339.
32 (*a*) B. O'Regan and M. Grätzel, *Nature*, 1991, **353**, 737–740; (*b*) O. Kohle, S. Ruike and M. Grätzel, *Inorg. Chem.*, 1996, **35**, 4779–4787.
33 S. Aiki, A. Taketoshi, J. Kuwabara, T. Koizumi and T. Kanbara, *J. Organomet. Chem.*, 2011, **696**, 1301–1304.
34 (*a*) A. Taketoshi, A. Tsujimoto, S. Maeda, T. Koizumi and T. Kanbara, *ChemCatChem*, 2010, **2**, 58–60; (*b*) A. Taketoshi, T. Koizumi and T. Kanbara, *Tetrahedron Lett.*, 2010, **51**, 6457–6459.
35 G. Ciantelli, P. Legittimo and F. Pantani, *Anal. Chim. Acta*, 1971, **53**, 303–308.
36 L. Roecker, W. Kutner, J. A. Gilbert, M. Simmons, R. W. Murray and T. J. Meyer, *Inorg. Chem.*, 1985, **24**, 3784–3791.
37 (*a*) S. Aiki, A. Taketoshi, J. Kuwabara, T.-a. Koizumi and T. Kanbara, *J. Organomet. Chem.*, 2011, **696**, 1301–1304; (*b*) C. Di Giovanni, L. Vaquer, X. Sala, J. Benet-Buchholz and A. Llobet, *Inorg. Chem.*, 2013, **52**, 4335–4345; (*c*) M. Dakkach, A. Atlamsani, T. Parella, X. Fontrodona, I. Romero and M. Rodríguez, *Inorg. Chem.*, 2013, **52**, 5077–5087.
38 W. W. Brandt and J. P. Wright, *J. Am. Chem. Soc.*, 1954, **76**, 3082–3083.
39 K. Nakamoto, *J. Phys. Chem.*, 1960, **64**, 1420–1425.
40 L. C. Kamra and G. H. Ayres, *Anal. Chim. Acta*, 1976, **81**, 117–129.
41 L. E. Davies, N. A. Bonini, S. Locatelli and E. E. Gonzo, *Lat. Am. Appl. Res.*, 2005, **35**, 23–28.
42 P. Cambier, *Clay Miner.*, 1986, **21**, 191–200.
43 B. N. Chaudret, D. J. Cole-Hamilton, R. S. Nohr and G. Wilkinson, *J. Chem. Soc., Dalton Trans.*, 1977, 1546–1557.

