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Copper(II) and cobalt(II) tetrazole-saccharinate complexes as effective catalysts for oxidation of secondary alcohols

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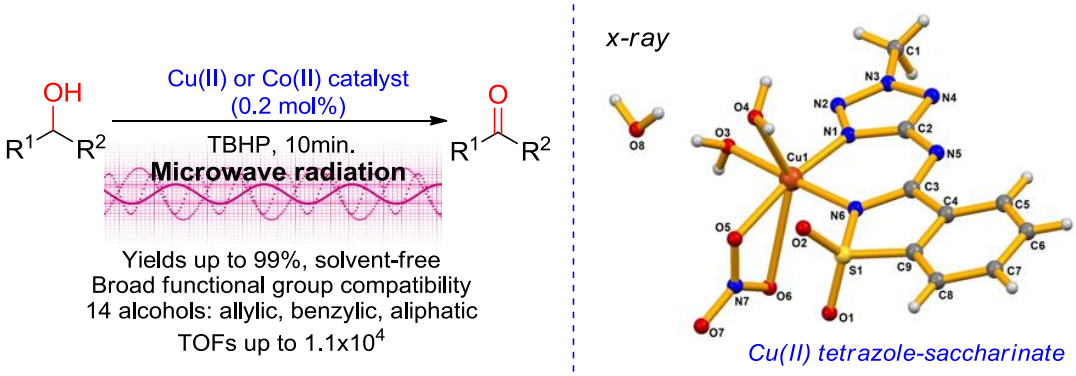
Graphical Abstract



HIGHLIGHTS

- Novel Copper(II) and cobalt(II) tetrazole-saccharinate complexes
- Catalysts for oxidation of secondary alcohols in a microwave assisted protocol
- Selective oxidation and broad functional group compatibility
- Excellent yields and high TON and TOF values for sec-alcohols oxidation

Abstract

Mononuclear Cu(II) and Co(II) complexes comprising 2-methyltetrazole-saccharinate bidentate *N*,*N*-chelating ligand have been synthesized for the first time and tested as homogeneous catalysts for oxidation of secondary alcohols in a solvent-free and microwave assisted protocol using aqueous *tert*-butyl hydroperoxide (TBHP) as oxidant. The developed catalytic system exhibits broad functional group compatibility, allowing efficient and selective conversion of a variety of secondary alcohols, including allylic ones, into the corresponding ketones. With typical 0.2 mol% content of the catalyst and under 20-50 W microwave irradiation, most reactions are complete within 10 min., presenting TONs up to 5.5×10^2 and TOFs up to 1.1×10^4 h^{-1}. No additives and co-oxidants have been used, while TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxyl) acts as inhibitor in most cases. A plausible reaction mechanism involving the new catalytic systems is outlined.

Keywords: Cu(II) and Co(II) catalysts; tetrazole-saccharinate ligands; secondary alcohols; alcohol oxidation; microwave irradiation

1. Introduction

Cumulative economic and environmental concerns force synthetic chemists to develop more effective, selective and atom-economical reactions, which can be performed under safe and mild conditions using renewable prime materials [1]. In this context, alcohols can be

considered as sustainable prospective substrates: [2] they can be generated from biomass [3], undergo various one-pot cascade transformations [4], and mix well with water as a suitable cheap and green solvent [5]. However, in spite all these attractive features, the limited reactivity of alcohols still hampers their wide application in green atom-, step-, redox- and pot-economic synthesis. One of the well-recognized ways to overcome this drawback is oxidative (dehydrogenative) activation of alcohols [2], since the derived aldehydes or ketones are generally more and differently reactive. This, allows to widen significantly the scope of alcohol transformations, including the cascade (tandem) one-pot ones [4].

Widespread interest has been directed toward the development of catalytic aerobic oxidation methods, but few of these reactions approach the synthetic utility and/or scope of traditional stoichiometric oxidants, such as chromium oxides, Dess-Martin periodinane, or activated DMSO methods. Copper/TEMPO catalyst systems have begun to address this limitation (TEMPO = 2,2,6,6-tetramethyl-1-piperidinyloxyl). Nevertheless, despite the formation of a large amount of undesirable products, stoichiometric alcohol oxidations with transition-metal compounds or sulfoxides are still in common use [2].

The use of molecular oxygen as a stoichiometric re-oxidant in combination with a catalytic metal has practical advantages due to the economic advantages related with O_2 and the formation of environmentally benign by-products (water and hydrogen peroxide). Recent protocols on green oxidation of alcohols usually involve active and selective recyclable catalysts that working with dioxygen, air, or other cheap oxidants. However, despite some remarkable advances, only few of the known methods are capable of offering an economic and practical oxidation toward a particular industrially important transformation. Many of the found catalytic systems suffer from high reagent cost, instability, employment of hazardous metals or oxidants, harsh reaction conditions, operational complexity, functional group incompatibility, or production of non-processable wastes [2].

In view of the above considerations, elaboration of new reaction schemes and catalytic systems for the selective oxidation of alcohols to carbonyl-containing compounds is an important task, and many efforts have been recently poured into this area [6]. Aqueous *tert*-butyl hydroperoxide (TBHP) is an essential component of many catalytic systems [6c,d], and solubility in water of the respective catalyst usually favours the high catalytic activity [6e].

Within our current interest on alcohol oxidation reactions [7], we developed a series of catalytic systems, where several homogeneous and heterogeneous catalysts were tested in combination with different oxidants and additives, for the oxidation of primary and secondary alcohols. Some of the elaborated systems were particularly effective, giving full conversion of

substrates under mild conditions. Nevertheless, the quest is continuing, and in this study we have established a new and even more efficient system based on novel copper and cobalt catalysts comprising a functional tetrazole-amino-saccharinate ligand. This catalytic system allows achieving quantitative yields and high TON (number of moles of product per mol of catalyst precursor) and TOF (TON per hour) values for the oxidation of a broad range of representative secondary alcohols. Very short reaction times, absence of a solvent and usage of low power microwave irradiation are factors that contribute to the effectiveness of the process. The presented simple but effective method may well compete with the best synthetic strategies described in the literature (Fig. 1) aiming the production of ketones from the corresponding secondary alcohols.

2. Experimental

2.1. Materials and methods

Unless otherwise noted, solvents and starting materials were obtained from Aldrich. All chemicals used were of reagent grade without further purification before use. ^{1}H and ^{13}C NMR spectra were recorded at room temperature on a Bruker Avance II 300 (UltraShield™ Magnet) spectrometer operating at 300 MHz (^{1}H) and 75 MHz (^{13}C). The chemical shifts are reported in ppm using TMS as internal standard. Carbon, hydrogen and nitrogen elemental and atomic absorption (Cu and Co) analyses were carried out by the Microanalytical Service of the Instituto Superior Técnico - University of Lisbon. FT-IR spectra (4000-400 cm^{-1}) were recorded on a VERTEX 70 (Bruker) spectrometer using KBr pellets.

Electrospray mass spectra (ESI-MS) were run with an ion-trap instrument (Varian 500-MS LC Ion Trap Mass Spectrometer) equipped with an electrospray ion source. For electrospray ionization, the drying gas and flow rate were optimized according to the particular sample with 35 p.s.i. nebulizer pressure. Scanning was performed from m/z 50 to 1200 in methanol solution. The compounds were observed in the negative or positive mode (capillary voltage ¼ 80–105 V).

Chromatographic analyses were performed in a Fisons Instruments GC 8000 series gas chromatograph with a DB-624 (J&W) capillary column (DB-WAX, column length: 30 m; internal diameter: 0.32 mm), FID detector and the Jasco-Borwin v.1.50 software; [GC conditions: $T_{injection}$ = 240 °C; $T_{initial}$ = 140 °C (1 min) raised 10 °C min^{-1} to 220 °C (1 min.); carrier gas: He]. The internal standard method was used for product quantification.

2.2. X-ray measurements

X-ray quality single crystals of complexes **6** and **7** were immersed in cryo-oil, mounted in Nylon loops and measured at a temperature of 296-297 K. Intensity data were collected using a Bruker AXS-KAPPA APEX II PHOTON 100 diffractometer with graphite monochromated Mo-Kα (λ = 0.71073) radiation. Data were collected using omega scans of 0.5° per frame and full sphere of data were obtained. Cell parameters were retrieved using Bruker SMART [9] software and refined using Bruker SAINT [10] on all the observed reflections. Absorption corrections were applied using SADABS [10]. Structures were solved by direct methods by using SIR-97 [11] and refined with SHELXL–2014 [12]. Calculations were performed using the WinGX-Version 2014.01 [13]. The hydrogen atoms attached to carbon atoms were inserted at geometrically calculated positions and included in the refinement using the riding-model approximation; Uiso(H) were defined as 1.2 Ueq of the parent carbon atoms for phenyl residues and 1.5 Ueq of the parent carbon atoms for the methyl groups. The hydrogen atoms of water molecules were located from the final difference Fourier map and the isotropic thermal parameters were set at 1.5 times the average thermal parameters of the belonging oxygen atoms. Least square refinements with anisotropic thermal motion parameters for all the non-hydrogen atoms and isotropic for the remaining atoms were employed.

2.3. Preparation of the saccharyl building block

The saccharyl building block, saccharyl chloride (**2**), was synthesized from commercially available saccharin, through halogenation. 3-Chloro-1,2-benzisothiazole-1,1-dioxide (**1**) was obtained from saccharin (10.2 g; 56 mmol) and phosphorus pentachloride (14.0 g; 66 mmol) heated at 180 °C, using a procedure reported previously [14]; colorless needles (7.00 g; 63% yield); m.p. 143–145 °C; IR_{vmax} (cm^{-1}): 1724, 1654, 1603 (C═C), 1346 (SO_2), 775 (Ar─H) and 692 (C─Cl); ^1H NMR ($CDCl_3$): d 7.85 (4H, m, Ar─H); elemental analysis: C, 41.5%, H, 2.0%, N, 6.9% (found); C, 41.7%, H, 2.0%, N, 7.0% (calculated for $C_7H_4NO_2SCl$); MS (EI): *m/z* 201 [M^+].

*2.4. Preparation of the tetrazolyl building block **4a***

The tetrazolyl derivative **4a** was prepared from commercially available 5-aminotetrazole monohydrate through methylation. This reaction produces a mixture of 1-

methyl-(1*H*)-tetrazole-5-amine and 2-methyl-(2*H*)-tetrazole-5-amine. The isomers have different solubility and are separated during work-up, as described.

A solution of sodium hydroxide (20% w/v) was added dropwise to a suspension of 5-aminotetrazole monohydrate (10.3 g; 0.1 mol) in water (30 mL), with a drop of phenolphthalein. The mixture was stirred until complete dissolution of the suspended material. Dimethyl sulfate (20 mL; 0.11 mol) was then added in small portions, keeping an alkaline medium through addition of aqueous sodium hydroxide. The final mixture was refluxed for 1 h, then cooled, and finally left in an ice bath, in the fridge, for 2 days. Colorless needles of 1-methyl-(1*H*)-tetrazole-5-amine (**4b**) were separated by filtration (6.1 g; 51% yield); m.p. 220–221 °C; ^{1}H NMR ($CDCl_3$): d 4.15 (3H, s); MS (EI): *m/z* 99 [M^+].

The filtrate collected was evaporated under reduced pressure to afford a solid residue. Water (50 mL) was added, and the mixture was then extracted with diethyl ether (3 × 50 mL). The organic extract was dried over anhydrous sodium sulfate, filtered and the filtrate evaporated to afford white crystals. Recrystallization from diethyl ether gave 2-methyl-(2*H*)-tetrazole-5-amine (**4a**) as colorless needles; (3.0 g, 25% yield); m.p. 104.5–105.5 °C; ^{1}H NMR ($CDCl_3$): d 3.32 (3H, s); MS (EI): *m/z* 99 [M^+].

*2.5. Preparation of the 2-methyltetrazole-saccharinate **5***

A mixture of 2-methyl-(2*H*)-tetrazole-5-amine (**4a**) (0.25 g; 2.56 mmol) and 3-chloro-1,2-benzisothiazole 1,1-dioxide (**2**) (0.53 g, 2.56 mmol) in dry THF (20 mL) was stirred at 60 °C during 24 h under a N_2 atmosphere. The solvent was then evaporated under reduced pressure and the remaining solid was washed with acetone, dried under vacuum at room temperature and recrystallised from a mixture of acetone/ethanol (1:1) to give the required product as colorless crystals; (0.48 g; 72% yield); m.p. 285–286°C; ^{1}H NMR (DMSO): d 8.49–8.50 (m, 1H), 8.10–8.13 (m, 1H), 7.90–7.92 (m, 2H), 4.42 (s, 3H); MS (EI): *m/z* 250 [M^+].

*2.6. Preparation of the copper(II) complex **6***

To a 10 mL methanol/$CHCl_3$ solution (1:1) of 2-methyltetrazole-saccharinate **5** (50 mg; 0.2 mmol) was added $Cu(NO_3)_2{\cdot}2.5H_2O$ (47 mg; 0.2 mmol) and the reaction mixture was stirred for 2h at room temperature until complete dissolution of the solids. The resulting blue solution was kept in open air at room temperature for crystallization. After 6 days, single blue crystals suitable for X-ray diffraction were isolated; (80.3 mg; 91% yield); elemental analysis (%): C, 24.32, H, 2,91, N, 22.12 (found); C, 24.41, H, 2.96, N, 22.14 (calculated for

$C_9H_{13}CuN_7O_8S$); IR (KBr; cm^{-1}): 3598 ν(OH), 3525, 3071, 1609, 1587, 1508, 1384 ν(NO_3^-), 1287 ν(C–N), 1160, 960, 807, 788, 660.

*2.7. Preparation of the cobalt(II) complex **7***

To a 10 mL methanol/DMSO solution (1:1) of 2-methyltetrazole-saccharinate **5** (50 mg; 0.2 mmol) was added $Co(OAc)_2 \cdot 4H_2O$ (50 mg; 0.2 mmol) and the reaction mixture was stirred for 3h at room temperature until complete dissolution of the solids. The resulting dark orange solution was kept in open air at room temperature for crystallization. After 10 days, single orange crystals suitable for X-ray diffraction were isolated; [70 mg; 51% yield; (93,3% yield based on ligand **5**)]; elemental analysis (%): C, 35.19, H, 3.24, N, 24.57 (found); C, 35.24; H, 3.25; N, 24.66 (calculated for $C_{20}H_{22}CoN_{12}O_6S_3$); IR (KBr; cm^{-1}): 3421 ν(OH), 1607, 1578, 1439, 1280 ν(C–N), 1251, 1150 ν(S═O), 1009, 956.

2.8. Catalytic assays under MW irradiation

Experiments with 2.5-5.0 mmol of substrates and 5.0-10.0 mmol of oxidant were conducted using a focused Anton Paar Monowave 300 microwave reactor in 10 mL glass vessels with 10 mm internal diameter, sealed with rubber membranes in a stirred mode with simultaneous cooling (IR temperature detector). A targeted temperature together with a maximum microwave power (10 or 50W) was set. The targeted temperature was reached within a few minutes. During the course of the reaction, the microwave power as well as the pressure (1 to 10 bar) varied. After the reaction, the reaction vessel was cooled down to room temperature and then the cap was carefully opened to slowly release the pressure. Following, 7 mL of acetonitrile together with benzaldehyde (1.25-2.50 mmol; internal standard for 1-phenylethanol reactions) or acetophenone (1.25-2.50 mmol; internal standard in all reactions excluding with 1-phenylethanol) were added to the reaction mixture. The final solution was analyzed by GC for quantification of oxidation products. Procedures for the isolation of selected products are included in Electronic Supplementary Information.

3. Results and discussion

Tetrazole and saccharin containing ligands are important motifs in coordination chemistry and catalysis [15,16]. The tetrazolyl moiety can coordinate through four nitrogen electron-donating atoms and may therefore act as a multidentate unit or as a bridging building block in supramolecular assemblies, thus being able to participate in at least seven distinct types of coordination modes with metal ions in the construction of metal–organic frameworks [15a].

Similarly, the saccharinate (1,2-benzisothiazole-3-one 1,1-dioxide) anion interacts with metal centers in different ways, generating relatively strong interactions in crystalline environments, mostly through hydrogen bonding [15b]. As a polyfunctional ligand, it can be engaged in N, O (C═O) or O (SO_2)-metal coordination, and act as a bidentate amidato-like bridging agent [15b,17].

In spite of their expectable potential as valuable ligands, mixed benzisothiazole-tetrazolyl systems have been scarcely investigated hitherto. Some time ago, we devised synthetic routes to a library of these compounds [18], with the aim of investigating their application as *N*,*N*-ligands for coordination with transition metals. Following this line, we chose the benzisothiazole-tetrazolyl derivative **5** (Scheme 1), to test its coordination capabilities with copper and cobalt metallic centers and to use the metal complexes in oxidation of secondary alcohols. Many copper and cobalt catalysts show high activity on alcohol oxidation protocols and tetrazolyl and benzisothiazolyl moieties should be resistant to oxidation conditions.

Accordingly, the 2-methyltetrazole-saccharinate pro-ligand **5** was prepared in three steps using a convergent synthetic strategy whereby the two tetrazole and saccharin building blocks **2** and **4a** (Scheme 1) were separately synthesised and then coupled to afford the target conjugate **5**. Following, the synthesis of Cu(II) and Co(II) metal complexes comprising ligand **5** proceeded at ambient conditions by reaction of **5** with $Cu(NO_3)_2{\cdot}2.5H_2O$ and $Co(OAc)_2{\cdot}4H_2O$ salts, respectively. Metal complexes **6** and **7** were isolated as mononuclear compounds where 2-methyltetrazole-saccharinate **5** acts as monoanionic bidentate *N*,*N*-chelating ligand (Scheme 1).

Complex **6** crystalizes with one water molecule as solvent of crystallization. In **6**, the Cu(II) ion exhibits a distorted octahedral N_2O_4 coordination environment with a monoanionic bidentate ligand, two coordinated water molecules and one bidentate nitrate ligand. Four basal positions are occupied by the four donor points N1 (imine nitrogen), O5 and O6 (nitrate oxygen) and O4 (water oxygen) whereas the axial positions are occupied by O3 (water oxygen) and N6 (imine nitrogen). The cobalt(II) complex **7** crystallizes in the monoclinic system with space group $P2_1/c$. The central cobalt(II) atom of **7** is hexacoordinated with a distorted octahedral N_4O_2 coordination. There are two monoanionic bidentate *N*,*N*-ligands, one water and one DMSO molecules coordinated to Co(II) ion. Detailed structural data for complexes **6** and **7** can be consulted in Tables S1-S3 in Supplementary Information.

The water-soluble Cu(II) and Co(II) complexes **6** and **7** catalyse the oxidation of 1-phenylethanol to acetophenone in a solvent-free and low power microwave (MW) assisted process, and the obtained results (for a catalytic amount of 0.1 to 0.5 mol%) are summarized in Table 1.

Within the studied conditions, the assays with copper catalyst **6** have shown consistently higher yields than those with cobalt complex **7**. For instance, with the Cu catalyst and using TBHP as oxidant at 120 °C, the almost quantitative and selective oxidation to acetophenone is achieved after a short time (10 min.) with a TON of 500 (TOF of 3.01×10^3) (entry 5), whereas for the Co catalyst, under the same conditions, the acetophenone yield is of 75% (entry 22). In addition, through the preliminary studies with 1-phenylethanol, five different oxidants were tested instead of TBHP (entries 12 to 16), leading to considerably lower yields in all cases. Importantly, the catalyst proved to be essential for the formation of acetophenone, as only trace amounts of the desired product were obtained under similar conditions if it was absent from the reaction mixture (entry 17). Tests performed with the free ligand **5** as the sole catalytic species, have shown low oxidation yields (entries 18-20). Additional assays using simple $Cu(NO_3)_2 \cdot 2.5H_2O$ and $Co(OAc)_2 \cdot 4H_2O$ salts, individually and blended with free ligand **5** (entries 26-29), proved the synergy between the metal species and the ligand towards the oxidation process, well expressed by the very good yields reached. Addition of TEMPO to different reaction systems leads to a perceptible yield decrease in all the studied cases (entries 6-8, 20, 23 and 24). From the outset of these studies with 1-phenylethanol, it became apparent that complexes **6** and **7** have a potential to function as effective catalysts in oxidative transformations of secondary alcohols. Thus, we further studied the scope of the catalytic reaction, fixing the amount of the catalysts at 0.2 mol% to substrate.

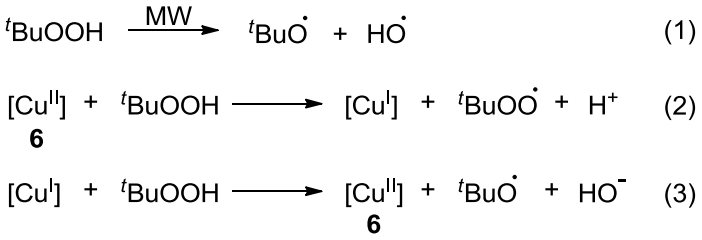
The scope was examined with a representative set of secondary benzylic, allylic and aliphatic alcohols using the optimized conditions for 1-phenylethanol (Table 2). Good to excellent yields were obtained in the oxidation of a wide range of substrates, including those with the functional groups susceptible to oxidation, such as primary and secondary amines or internal alkenes. In almost all the cases, the reactions are complete within 10-15 minutes at temperatures of 80-130°C, with high TONs and TOFs. No significant differences were observed between benzylic, allylic and aliphatic substrates.

As observed in the case of 1-phenylethanol oxidation, the copper catalyst **6** is more active than the cobalt one **7**, consistently leading to better results (Table 2). The only exception concerns ephedrine (2-(methylamino)-1-phenylpropan-1-ol), for which the cobalt catalyst led to a higher yield (entry 7). In the case of 1-phenylethane-1,2-diol (entry 3), 2-hydroxy-1-phenylethanone was isolated in moderate yield as the sole product, attesting the selectivity for oxidation of the secondary hydroxyl group with the catalyst **6**. Interestingly, the oxidation of cholesterol (entry 8) led to similar reaction yields with both catalysts generating 5-cholesten-3-one as the single product.

Likewise, for the allylic alcohols tested (entries 12 and 13), oxidation proceeds selectively at the secondary hydroxyl, preserving the double bonds to form the corresponding ketones in good yields. The yields presented in Table 2 for isolated products (entries 3, 6, 7, 8, 12 and 13) refer to selective oxidation of secondary hydroxyl groups. The unreacted substrates were measured, and the mass balance shows that there was no conversion into other products.

In fact, this protocol can compete with the best synthetic strategies described in the literature, being the observed selectivity an important feature. Classic oxidation methods generally use stoichiometric quantities of inorganic oxidants, notable chromium(VI) reagents [2a], or ruthenium or manganese salts [2a], and are, overall, highly toxic and environmentally polluting. Other classic non-green methods are based on the use of high valent iodine compounds (notably the Dess Martin reagent) or involve the stoichiometric use of DMSO (Swern oxidation) [2a]. These kinds of drawbacks do not arise with the presented method. Moreover, in comparison with recent selective methods used in the oxidation of representative series of secondary alcohols [8a-c], the low amount of catalyst used, reduced reaction times and the absence of solvent are common advantages of our system.

As suggested by previous literature on TBHP chemistry [19], a general mechanism for the microwave-assisted oxidation of secondary alcohols catalysed by the copper complex **6** can be envisaged (Scheme 2). TBHP decomposes to form *tert*-butylperoxyl, *tert*-butoxyl and hydroxyl radicals [19i-j]. The formation of these radicals should occur by two distinct pathways: *i)* via homolytic cleavage of O–O bond promoted by microwave radiation [19j-k] (eq. 1) without intervention of Cu(II) complex (**6**) or, *ii)* by a redox process mediated by **6** as depicted in equations (2) and (3) [19l].



The liberation of the hydroxyl proton from the alcohol will occur upon coordination to the metal since the acidity increases. The C-H hydrogen atom can be removed by *tert*-butoxyl radical (or hydroxyl radical) releasing *tert*-butanol (or water) and the corresponding ketone. Oxidation of the formed Cu(I) species by TBHP leads to the regeneration of the catalyst **6**, enabling turnover. In addition, chromatographic detection (GC-MS) of *tert*-butanol in the final mixture supports the stoichiometry of the reaction.

In view of the comparable reactivity displayed by the catalysts **6** and **7**, we believe that the mechanisms associated with their catalytic cycles should be similar. However, steric constrains associated with the presence of two benzisothiazole-tetrazolyl ligands in complex **7**, associated to the expected lower Lewis acidity of the Co(II) center compared with the Cu(II) one in complex **6**, contribute to the lower yields obtained with the cobalt catalyst. Another possible reason concerns the presence of more labile ligands in **6** than in **7**, what can favour the catalytic process.

The inhibitory effect of TEMPO on alcohol oxidation is illustrated in Scheme 3. As previously mentioned, the addition of this nitroxyl radical to the reaction system containing the Cu(II) or the Co(II) catalyst leads to a decrease in the yield. Acting as a radical trap, TEMPO reacts with radicals (*tert*-butoxyl and hydroxyl radicals) generated from TBHP, to form the peroxides **8** and **9**. The efficiency of hydroxyl radicals for the abstraction of hydrogen atoms from alcohols, as well as their ability to oxidize nitroxides to the oxoammonium cation **10** *via* formation of this kind of intermediates, is well documented [20].

Besides, assays performed using TBHP/TEMPO in the 1:2 mole ratio suggest that oxidation of TEMPO by *tert*-butoxyl and hydroxyl radicals can take place in parallel to H-atom abstraction from the alkoxide. Accordingly, for such a TBHP/TEMPO ratio, the reaction yield is reduced to nearly half of its value (Table 1: entries 8 and 24; Table 2: entry 5) suggesting that only half of the *tert*-butoxy and hydroxyl radicals stay free to abstract

hydrogen atoms. This type of reactivity with TEMPO is consistent with previous kinetic studies on hydroxyl radical reactions with nitroxides [20].

4. Conclusions

Two mononuclear Cu(II) and Co(II) complexes containing 2-methyltetrazole-saccharinate as a bidentate *N,N*-chelating ligand have been synthesized and successfully used as catalysts for the oxidation of secondary alcohols with aqueous TBHP, in a solvent-free and microwave assisted procedure. The catalytic oxidation of a representative series of benzylic, allylic and aliphatic secondary alcohols to the corresponding ketones proceeds selectively in a short time, exhibiting very good to excellent yields and a broad functional group compatibility. Selective oxidation of a substituted benzyl secondary alcohol in the presence of a primary alcohol was proved using a substrate containing both hydroxyl functional groups. In addition, it was confirmed that the addition of TEMPO into this system leads to a perceptible yield decrease. Within an assumed radical mechanism, the TEMPO additive acts as a radical trap quenching radical species generated from TBHP. The described protocol can be recorded as a practical method for the oxidation of diverse secondary alcohols bearing other functional or protective groups.

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Electronic supplementary information (ESI) available: Structural data for all the isolated compounds and selected structural data of X-ray structures of complexes **6** and **7.** CCDC numbers 1495047 and 1495046 for complexes **6** and **7** respectively (Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif).

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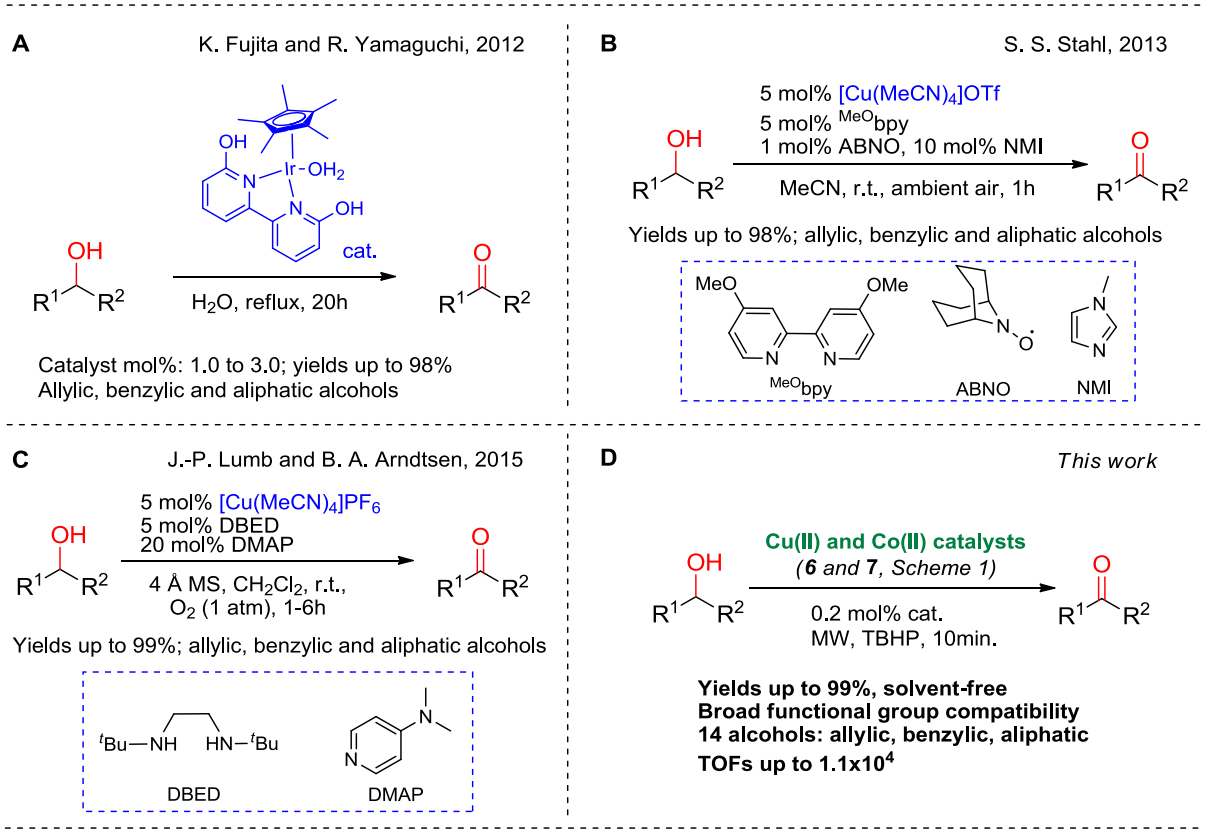
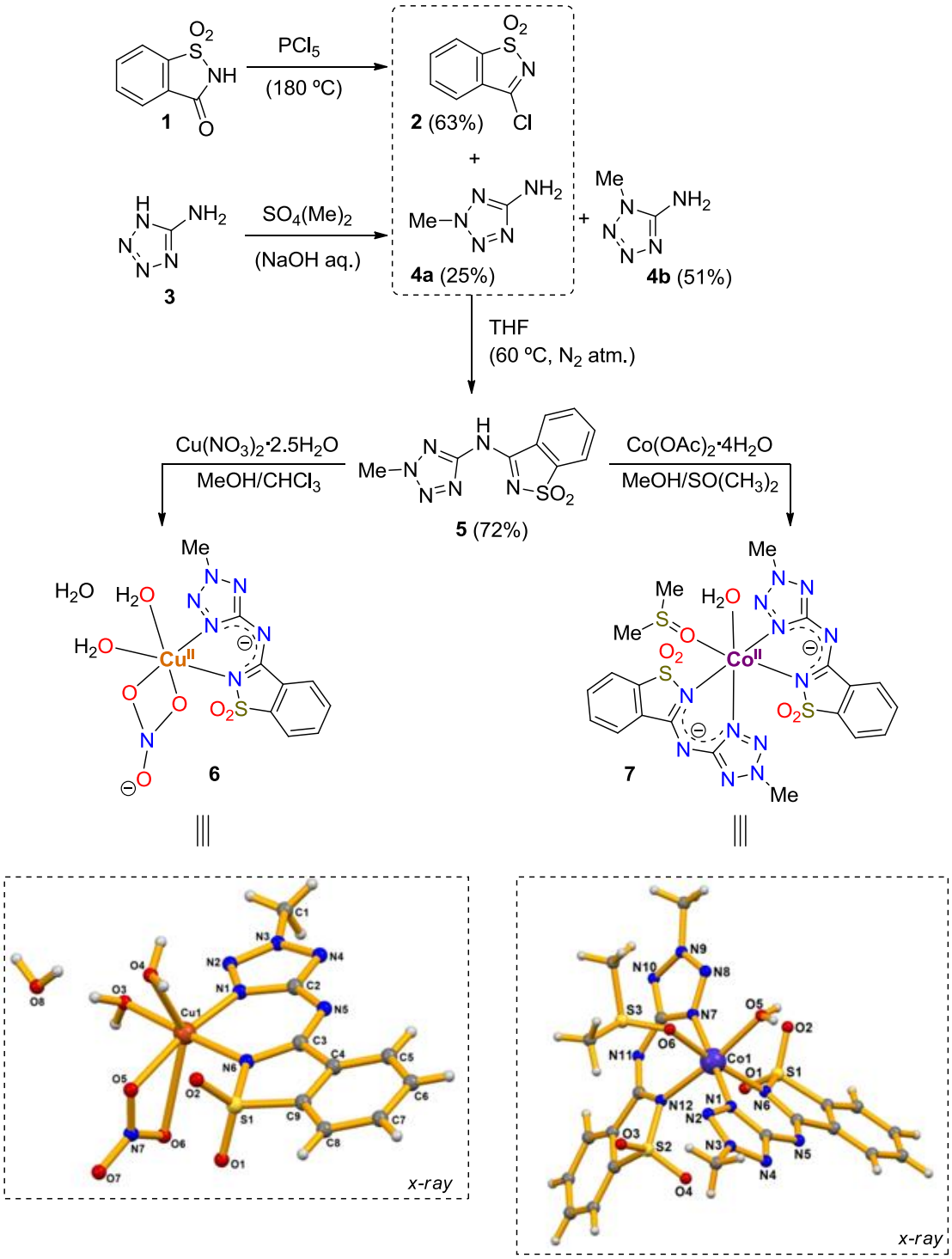
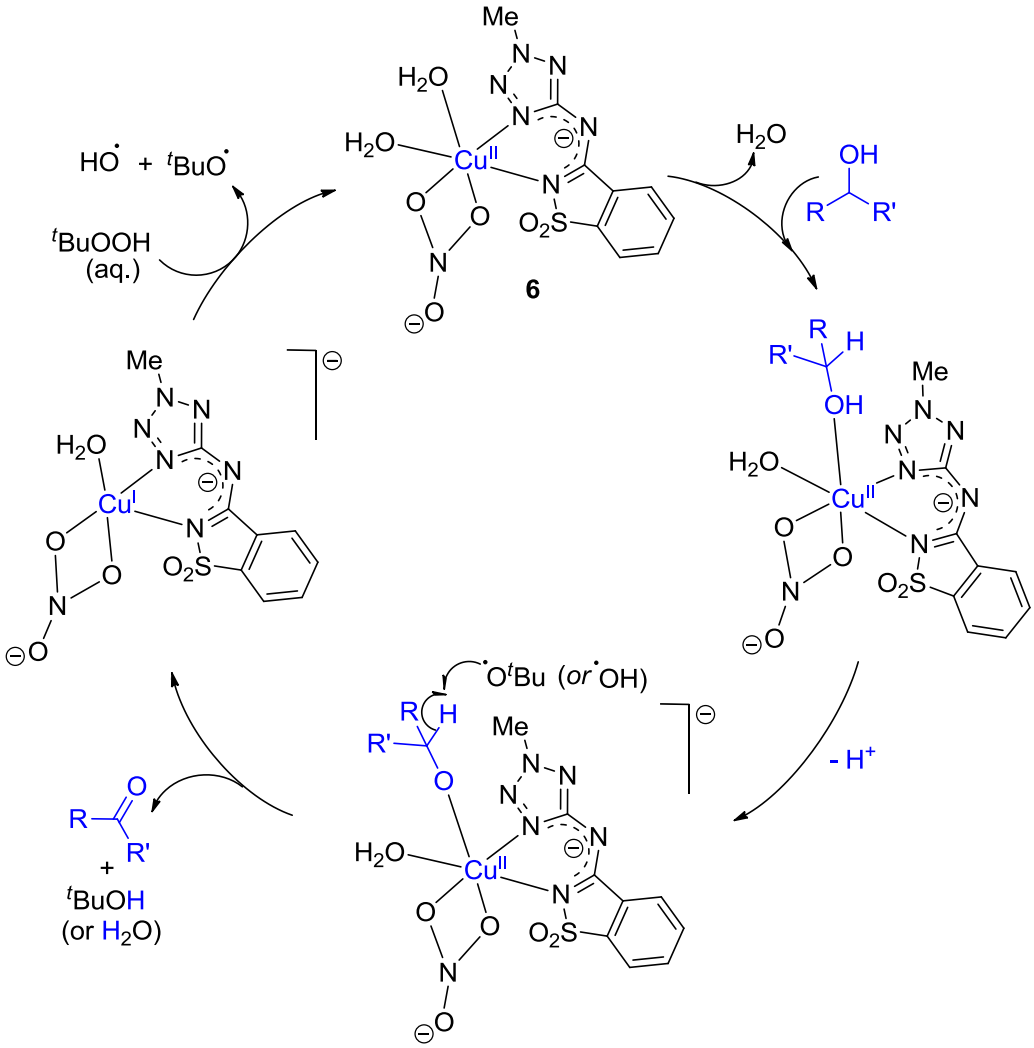


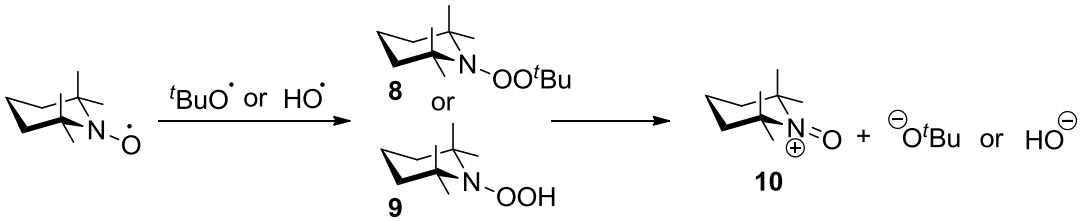
Fig. 1. Examples of recent synthetic methods for secondary alcohol oxidation: **A**) Dehydrogenative oxidation of secondary alcohols to ketones in water using Cp*Ir catalysts bearing a bipyridine ligand [8a]; **B**) Copper(I)/ABNO-catalyzed aerobic secondary alcohol oxidation [8b]; **C**) Oxidation of secondary alcohols using a Cu/DBED catalytic system [8c]; **D**) *This work*: copper(II) and cobalt(II) catalysts for solvent-free oxidation of secondary alcohols promoted by microwave radiation.



Scheme 1. Synthetic approach used to prepare complexes **6** and **7**.

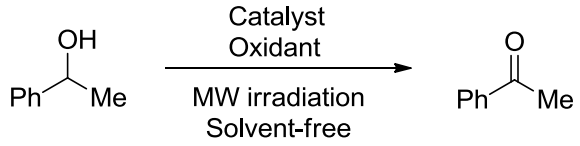


Scheme 2. Suggested catalytic cycle for the microwave assisted oxidation of secondary alcohols catalysed by copper complex **6**. [It is assumed that a water ligand and not the nitrato ligand is replaced by the alcohol]



Scheme 3. Oxidation of TEMPO by *tert*-butoxyl and hydroxyl radicals.

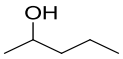
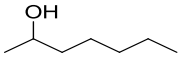
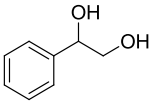
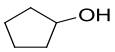
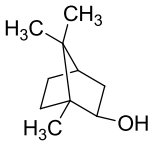
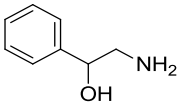
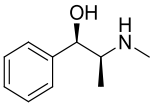
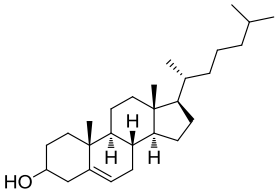
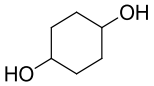
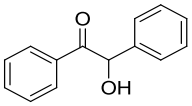
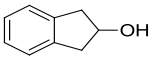
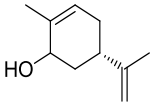
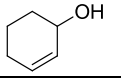
Table 1. Selected results for the MW-assisted oxidation of 1-phenylethanol.[a]



Entry	Catalyst (μmol)	Oxidant	Additive (μmol)	Reaction time (min.)	Yield (%)[b]	TON[c] (TOF)[d]
1[e]	**6**	TBHP	-	30	62.0	310 (620)
2[f]	**6**	TBHP	-	40	55.0	550 (833)
3[g]	**6**	TBHP	-	30	65.0	130 (260)
4	**6**	TBHP	-	5	89.7	448 (5.38×10^3)
5	**6**	TBHP	-	10	99.5	500 (3.01×10^3)
6	**6**	TBHP	TEMPO (5)	10	84.5	422 (2.53×10^3)
7	**6**	-	TEMPO (5)	10	2.1	11 (62.5)
8	**6**	TBHP	TEMPO[h]	10	52.3	261 (1.57×10^3)
9	**6**	-	-	10	1.8	9 (54)
10[i]	**6**	TBHP	-	2	71.7	359 (1.08×10^4)
11[i]	**6**	TBHP	-	6	94.6	473 (4.73×10^3)
12	**6**	UHP[j]	-	10	1.4	7 (42)
13	**6**	H_2O_2 (50%)	-	10	59.7	298 (595)
14	**6**	^{t}BuOK	-	10	1.0	5 (30)
15	**6**	SO_3HO_3K (4.5% active oxygen)	-	10	0.9	4.5 (27)
16	**6**	Oxone®	-	10	0.9	4.5 (29)
17	-	TBHP	-	10	6.6	33 (198)
18	**5**	TBHP	-	5	9.5	48 (285)
19	**5**	TBHP	-	10	26.2	131 (1.58×10^3)
20	**5**	TBHP	TEMPO (5)	10	3.8	19 (114)
21[e]	**7**	TBHP	-	30	12.6	63 (126)
22	**7**	TBHP	-	10	75.1	376 (2.25×10^3)
23	**7**	TBHP	TEMPO (5)	10	63.3	316 (1.90×10^3)
24	**7**	TBHP	TEMPO[h]	10	36.4	182 (1.09×10^3)
25	**7**	H_2O_2 (50 %)	-	30	29.9	150 (300)
26	**5** (5) + $Cu(NO_3)_2{\cdot}2.5H_2O$ (5)	TBHP	-	10	85.3	427 (2.56×10^3)
27	$Cu(NO_3)_2{\cdot}2.5H_2O$	TBHP	-	10	53.0	265 (1.59×10^3)
28	**5** (5) + $Co(OAc)_2{\cdot}4H_2O$ (5)	TBHP	-	10	41.5	207 (1.25×10^3)
29	$Co(OAc)_2{\cdot}4H_2O$	TBHP		10	16.4	82 (492)

[a]Reaction was carried out with 1-phenylethanol (2.5 mmol), catalyst (5.0 μmol, 0.2 mol%) and oxidant (5 mmol) in a MW reactor (power range: 20-50 W) at 120 °C without adding extra solvent. [b]Determined by GC. [c]Turnover number. [d]TOF = TON.h^{-1}. [e]80 °C, (MW power range: 5-10 W), 1-phenylethanol (5 mmol), TBHP (10 mmol). [f]80 °C, catalyst (0.1 mol%). [g]80 °C, catalyst (0.5 mol%). [h]TEMPO (10 mmol); [i]130 °C. [j]UHP: Urea Hydrogen Peroxide adduct (active oxygen 15-17%).

Table 2. Substrate scope for the MW-assisted oxidation of secondary alcohols catalysed by copper (**6**) and cobalt (**7**) complexes.[a]

Entry	Substrate	Catalyst	Reaction time (min.)	Temp. (°C)	Yield (%)[b]	TON[c] (TOF)[d]
1		**6**	10	100	78	390 (2.34 × 10^3)
		7	10	100	65	325 (1.95 × 10^3)
2		**6**	10	120	85	425 (2.55 × 10^3)
		7	10	120	81	405 (2.43 × 10^3)
3		**6**	10	120	59[e]	295 (1.77 × 10^3)
		7	10	120	43[e]	215 (1.29 × 10^3)
4		**6**	15	80	78	390 (1.56 × 10^3)
		7	15	80	65	325 (1.30 × 10^3)
5		**6**	20	120	90	450 (1.35 × 10^3)
			20	120	49[f]	245 (735)
		7	20	120	81	405 (1.22 × 10^3)
			20	120	37[f]	185 (555)
6		**6**	15	100	75[e]	375 (1.50 × 10^3)
		7	15	100	69[e]	345 (1.38 × 10^3)
7		**6**	10	100	62[e]	310 (1.86 × 10^3)
		7	10	100	72[e]	360 (2.16 × 10^3)
8		**6**	15	100	70[e]	350 (1.40 × 10^3)
		7	15	100	71[e]	355 (1.42 × 10^3)
9		**6**	10	120	62[g]	310 (1.86 × 10^3)
		7	10	120	55[g]	275 (1.65 × 10^3)
10		**6**	30	130	93	465 (930)
		7	30	130	85	425 (850)
11		**6**	15	130	91	455 (1.82 × 10^3)
		7	15	130	67	335 (1.34 × 10^3)
12		**6**	15	100	81[e]	405 (1.62 × 10^3)
		7	15	100	70[e]	350 (1.40 × 10^3)
13		**6**	10	100	85[e]	425 (2.55 × 10^3)
		7	10	100	81[e]	405 (2.43 × 10^3)

[a]Reaction was carried out with the substrate (2.5 mmol), catalyst (5.0 µmol, 0.2 mol %) and TBHP (5 mmol, 2 eq., 70 % in H_2O) in a MW reactor (power range: 20-50 W) without adding extra solvent. [b]Determined by GC; yields for selective oxidation of secondary alcohol function. [c]Turnover number. [d]TOF = TON.h^{-1}. [e]Isolated yield. [f] Addition of TEMPO (10 mmol). [g]Yield of diketone (sole product).